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Optical Properties and Response Mechanism Analysis of Multi-branched Fluorescent Probes Based on Intramolecular Charge Transfer

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In this work, the optical properties of fluorescent probes used for detection of biothiol were studied by employing time-dependent density functional theory. By calculating the single photon absorption and emission properties of probe Mol.1, Mol.2 and Mol.3 before and after reaction with cysteine and homocysteine, we have investigated the effect of carbon-carbon triple bond and benzene ring on the properties of fluorescent probes. It is found that the oscillator strength of probe molecules increases gradually with the improvement of the structure of the electron donor triphenylamine and the addition of carbon-carbon triple bonds, and better properties of fluorescence probes have also been demonstrated. At the same time, the effect of different number of side branches on the molecular properties of the probe was also studied. The results showed that compared with single-branched molecule Z1 and tribranched probe Mol.3, two side probe molecules Z2 had higher oscillator strength and better detection effect. In addition, the new single-branched probe Mol.4 with the addition of carbon-carbon triple bonds and benzene rings has better probe properties and simpler structure than the tribranched probe Mol.3.

Key words: Fluorescent probe, Multi-branched molecule, Intramolecular charge transfer

I. INTRODUCTION

The detection of important biosulfates such as cysteine and homocysteine is highly correlated with the basic physiological processes of organisms [1, 2]. For example, levels of glutathione, cysteine and homocysteine in plasma are strongly associated with AIDS [3, 4], alzheimer's and Parkinson's disease [5]. Therefore, the search for highly selective and sensitive fluorescence probes for detection of polypeptide molecules such as cysteine and homocysteine has become a hot research field [6–14].

Recently, Zhang *et al.* used triphenylamine as the donor and an aldehyde group with high electron affinity as the receptor to design and synthesize the multi-branched D-π-A fluorescent probe molecule P1 [14] (named as Mol.3 in this work). The process of intramolecular charge transfer is conducive to the formation of high polar excited states [16, 17]. Tetrahydrothiazole was formed when the terminal aldehyde group of the probe molecule P1 reacted with the N terminal of the detection substance cysteine [18–21]. It may change the intramolecular charge transfer process and affect the intensity of fluorescence probe molecule. In the experiment, the probe molecule P1 was used to detect cysteine and homocysteine in the dimethylsulfoxide buffer solution. The results showed that the emission peak of molecule P1 was at 600 nm. After the reaction with cysteine and homocysteine, the emission peak of the product was at 435 nm. Compared with the probe, the emission peak underwent a blue shift of 165 nm. After the reaction of probe molecule P1 with biothiol, compared with the traditional detection of biothiol fluorescent probe molecules [22–27], the emission peak moved more [28, 29]. Moreover, the fluorescence intensity of cysteine and homocysteine can be detected more clearly before and after the reaction, and the imaging of cysteine and homocysteine can be better detected in biological cells. It can be seen from the above characteristics that molecule P1 is a good fluorescent probe for detecting cysteine and homocysteine in cells.

In this work, based on the experimental molecule P1, by calculating the single-photon absorption and emission characteristics of multiple probe molecules, the optical properties of the probe are studied and the molecular mechanism of the probe is characterized. Based on the same theory, the optical properties of multiple probes are compared, which provides guidance for further theoretical work.

II. MATERIALS AND METHODS

The optimization of molecular geometric structure was completed by using the Gaussian 09 program package at the DFT/B3LYP level. At the same time, in

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order to ensure the stability of the optimized structure, the frequency is calculated at the same level of calculation to ensure that no imaginary frequency occurs. Based on the optimized molecular geometry, the single-photon absorption property of the molecule was calculated by using the response theory method at the DFT/B3LYP level. On the basis of the first excited state structure optimized by the time dependent density functional theory (TD-DFT), the fluorescence emission properties were obtained at the same computational level. The 6-31G(d) group was selected for the above calculations. In addition, the polarization continuity model (PCM) was used to calculate the solvent effect of surrounding solvents.

The oscillator strength $\delta_{\rm op}$ that can be used to characterize the transition probability between each state is defined as

$$\delta_{\rm ope} = \frac{2\omega_{\rm f}}{3}\sum_{\alpha} |\langle 0|\mu_{\alpha}|f\rangle|^2 \tag{1}$$

where $\omega_{\rm f}$ donates the excitation energy required for a photon to jump to excited state f, μ_{α} is the molecular dipole moment operator.

The fluorescence lifetime is calculated according to the Einstein transition probability formula which is defined as

$$\tau = \frac{1.499}{(E_{\rm flu})^2\delta_{\rm ope}} \tag{2}$$

where $E_{\rm flu}$ is the transition energy with the unit of $\rm cm^{-1}$.

III. RESULTS AND DISCUSSION

A. Effect of carbon-carbon triple bond and triphenylamine structure on the optical properties of fluorescent probes in collateral structure

The experimental molecule Mol.3 synthesized by Zhang *et al.* in the experiment is centered on the triphenylamine with strong electron-donating ability and the aldehyde group with strong electron binding ability as the terminal group to form the D-π-A type molecule. The structure improves the efficiency of photon absorption, and experiments have shown that Mol.3 is a fluorescent probe with excellent probe properties. In order to further study the effect of carbon-carbon triple bonds and triphenylamine structure on the properties of fluorescent probes, we changed the number of carbon-carbon triple bonds and benzene rings in the side branches and designed the probe molecules Mol.1 and Mol.2. It can be seen from the figure that Mol.1 was designed on the basis of Mol.3 to remove the carbon-carbon triple bond and benzene rings, and the molecule had no independent and complete structure of triphenylamine. However, Mol.2 was designed with independent and complete structure of triphenylamine, only removing carbon-carbon triple bond. Through the design of two kinds of molecules and the calculation of optical properties, we will theoretically verify the effects of triphenylamine electron donor and carbon-carbon triple bonds on the properties of probe molecules. The product molecules of Mol.1, Mol.2, and Mol.3 reacted with cysteine and homocysteine were named as Mol.1+, Mol.2+, and Mol.3+, respectively. The planar structure and chemical reaction principle of the dendrimers Mol.1, Mol.2, and Mol.3 are shown in FIG. 1.

The probe molecules Mol.1−3 are a probe for the detection of cysteine and homocysteine *in vivo*, and the main component in the organism is water, so we calculated the relevant properties of the probe molecules Mol.1−3 in aqueous solution. According to the molecular frontier orbital theory, HOMO−LUMO is the key to determine the chemical reaction of the system and its various properties [30]. FIG. 2 is a frontier orbital energy diagram of the probe molecules Mol.1−Mol.3 and the products. As can be seen from the figure, the $\Delta E_{\rm H-L}$ values of the molecules Mol.2 and Mol.3 were reduced to 2.79 eV and 2.58 eV, respectively, compared to the $\Delta E_{\rm H-L}$=3.02 eV of the probe molecule Mol.1. "H" represents the highest occupied (HOMO) orbit, "L" represents the lowest unoccupied (LUMO) orbit and $\Delta E_{\rm H-L}$ represents the energy gap between HOMO and LUMO. Since the molecules Mol.2 and Mol.3 differ from the molecule Mol.1 in the number of carbon-carbon triple bonds and benzene rings, we can infer that as the carbon-carbon triple bond and the benzene ring increase, the $\Delta E_{\rm H-L}$ of the molecule decreases, which is more conducive to the transfer of electrons and the absorption process. After reaction with cysteine and homocysteine, the terminal aldehyde group of the system changes due to the binding of the probe molecule to the detector, and the energy gap of the product molecules Mol.1+, Mol.2+, Mol.3+ increase to 3.79 eV, 3.52 eV, 3.11 eV, respectively. Therefore, it is speculated that after the reaction with cysteine and homocysteine, the wavelength of the product shifts significantly with respect to the wavelength of the probe molecule.

By analyzing the absorption and emission processes of the probe molecules Mol.1, Mol.2 and Mol.3 before and after reaction with cysteine and homocysteine, we have studied its optical properties. Table I lists the maximum single photon absorption wavelengths of the three probe molecules in water and the corresponding oscillator strength and transition characteristics. The maximum one-photon absorption peak of the molecule Mol.3 is located at 479 nm. Compared with the experimental absorption peak 400 nm, it has a certain error. This error is caused by the solvent environment and experimental conditions. The maximum absorption peaks of Mol.1 and Mol.2 are located at 367 nm and 465 nm, respectively. After interaction with cysteine or homocysteine, the absorption peak of the product Mol.1+ red-shifted to 380nm, while the molecule Mol.2+ and Mol.3+ absorption peaks were blue-shifted to 407 nm and 466 nm, respectively. This is because the movement

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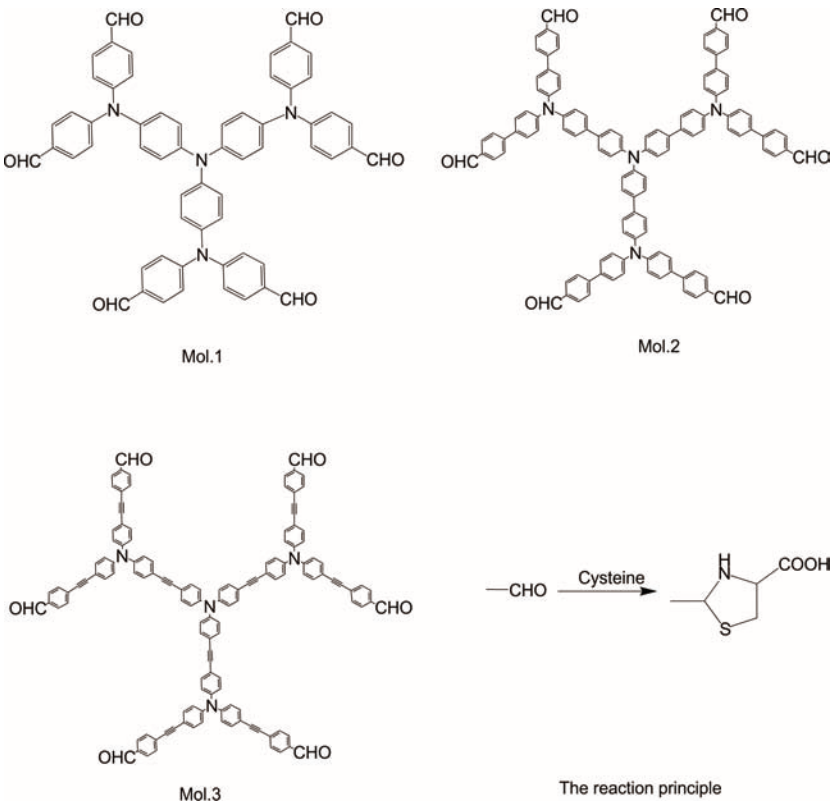

FIG. 1 The geometric structure of compounds Mol.1, Mol.2, Mol.3, and reaction principle.

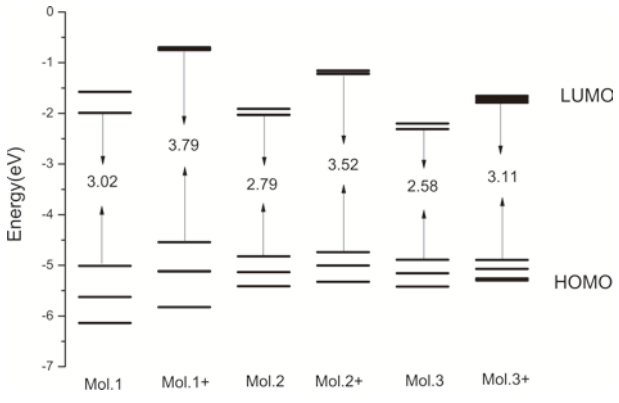

FIG. 2 Frontier orbital energies of the compounds Mol.1, Mol.2, Mol.3, and their products.

TABLE I One-photon absorption (OPA) properties in H_2O, including the excitation energy E_{opa} (in eV), the corresponding wavelength λ_{opa} (in nm), the oscillator strength δ_{opa} (in arb. unit) and transition feature. H and L denote the HOMO and LUMO, respectively.

Molecule	E_{opa}	λ_{opa}	δ_{opa}	Transition feature	
Mol.1	3.38	367	0.48	H−1→L+1	60.20%
Mol.1+	3.26	380	0.77	H→L+2	41.68%
				H→L	28.50%
				H→L+1	20.20%
Mol.2	2.67	465	0.54	H→L+3	85.32%
Mol.2+	3.04	407	1.76	H→L+1	84.80%
Mol.3	2.59	479/400*	1.26	H−1→L+1	55.22%
Mol.3+	2.66	466	2.49	H→L+1	83.20%

* Experimental results taken from Ref.[14].

of the absorption spectrum is caused by intramolecular charge transfer. The Mol.1 molecule and its product electron donor are no longer triphenylamine, so the change in optical properties is inconsistent with Mol.2 and Mol.3. Compared with the oscillator strengths of probe molecules Mol.1, Mol.2, and Mol.3 of 0.48, 0.54, 1.26, the oscillator strengths of the product molecules Mol.1+, Mol.2+, and Mol.3+ single photon absorption increased to 0.77, 1.76, and 2.49, respectively, and the oscillator strength Mol.3+>Mol.2+>Mol.1+. From these data, it can be seen that after the reaction with cysteine or homocysteine, the absorption intensity of the product is significantly enhanced, and the absorption intensity of Mol.3+ is the largest.

Table II shows the fluorescence emission properties of three groups of molecules in water, including the single photon emission wavelength of the molecule, the corre-

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TABLE II Fluorescent emission properties of the compounds in H_2O, including the emission energy $E_{\rm flu}$ (in eV) the corresponding emission wavelength $\lambda_{\rm ope}$ (in nm), and the oscillator strength $\delta_{\rm ope}$ (in arb. unit).

Molecule	$E_{\rm flu}$	$\lambda_{\rm ope}$	$\delta_{\rm ope}$	Transition feature	
Mol.1	1.77	699	0.05	H→L	97.8%
Mol.1+	0.51	2429	0.00	H→L	98.4%
Mol.2	2.01	615	0.28	H→L	95.1%
Mol.2+	2.60	477	1.84	H→L	93.3%
Mol.3	1.99	622/600*	0.50	H→L	91.7%
Mol.3+	2.39	519/435*	2.56	H→L	89.7%

* Experimental results taken from Ref.[14].

sponding oscillator strength, transition characteristics. As can be seen from Table II, the emission peaks of the molecules Mol.3 and Mol.3+ in the aqueous solution are 622 nm and 519 nm, and the emission peak of the product Mol.3+ produced a blue shift of 103 nm compared to the emission peak of the probe Mol.3, which is consistent with the experimental trend. According to FIG. 2, the energy gap of Mol.3+ is smaller than the energy gap of the molecular Mol.3, which is consistent with the conclusion that the inferred product has a blue shift of the emission peak. The intensity of the oscillator strength of the product Mol.1+ after the reaction of the probe Mol.1 is 0.00, so we can judge that the product molecule Mol.1+ does not emit light, and Mol.1 cannot be used as a fluorescent probe for detecting cysteine or homocysteine. The emission peak of Mol.2+ after Mol.2 reaction was shifted from 615 nm to 477 nm, and the oscillator strength increased from 0.28 to 1.84. There was obvious emission peak shift and oscillator strength enhancement before and after the reaction. Therefore, the molecule Mol.2 which removes the carbon-carbon triple bond is still an excellent probe in the performance of detecting cysteine and homocysteine. In summary, it can be inferred that the Mol.1, which simultaneously removes the carbon-carbon triple bond and the benzene ring, destroys the triphenylamine structure, making the intramolecular charge transfer process impossible, and thus cannot be used as a probe for detecting cysteine and homocysteine. On the basis of retaining the benzene ring, the probe Mol.2 only removes the carbon-carbon triple bond and does not destroy the structure of the triphenylamine, and can still be used as a detection probe. But due to the lack of carbon-carbon triple bond, the planarity of the molecules is reduced, which affects the detection effect. The oscillator strength of Mol.3+ is 2.56, which is much larger than the oscillator strength of the product Mol.2+ of 1.84, so the luminescence intensity of Mol.3+ is more obvious, and the probe Mol.3 exhibits better probe properties. Thus, it was verified that the triphenylamine structure and the carbon-carbon triple bond have an important influence on the properties of the probe molecule.

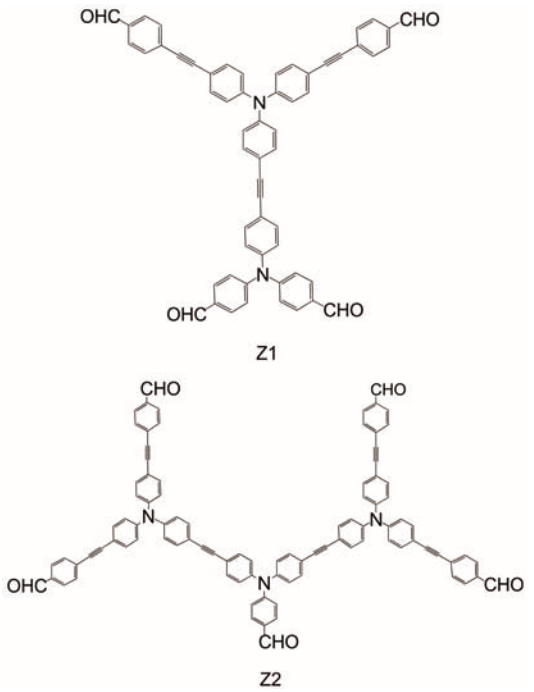

FIG. 3 The geometric structure of compounds Z1 and Z2.

B. Effect of number of molecular side branches on the properties of fluorescent probes

In order to further study the optical properties of the dendrimer probe molecule for the detection of biothiol, a better fluorescent probe was designed, combined with the experimental synthesis process [15], based on the experimental molecule Mol.3, without destroying the integrity of the central donor electron donor triphenylamine structure, while retaining the aldehyde-based acceptor structure and changing the number of side branches, a probe molecule Z1 for one side branch and a probe molecule Z2 for two branches were designed and carried out with theoretical calculations. We define that the products after reaction with cysteine and homocysteine correspond to the molecules Z1+ and Z2+, respectively. The molecular planar structure is shown in FIG. 3. FIG. 4 is frontier orbital energies of Z1, Z2, and its product. As can be seen from FIG. 4, the $\Delta E_{\rm H-L}$ of the product molecules Z1+, Z2+ and Mol.3+ relative to the probe molecules Z1, Z2, Mol.3 increased to 3.24 eV, 3.15 eV, 3.11 eV, respectively, which can speculate that the difference in energy difference before and after the molecular reaction is large, the product is blue-shifted, and has good probe properties.

In Table III, we list the energy of the probe molecules and corresponding products in water, the single-photon absorption wavelength, the oscillator strength, and transition characteristics. The single-photon absorption peaks of molecules Z1, Z2, and Mol.3 are at 523 nm, 487 nm, and 479 nm, respectively, and the correspond-

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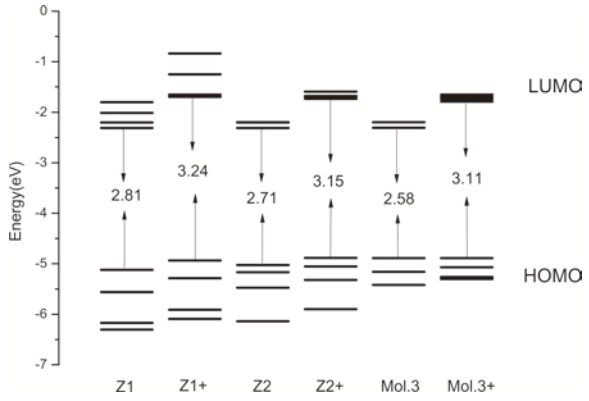

FIG. 4 Frontier orbital energies of the compounds Z1, Z2, Mol.3, and their products.

TABLE III OPA properties in H_2O, including E_{opa} (in eV), λ_{opa} (in nm), δ_{opa} (in arb. unit), and transition feature.

Molecule	E_{opa}	λ_{opa}	δ_{opa}	Transition feature	
Z1	2.37	523	1.38	H→L+1	92.35%
Z1+	2.82	439	2.03	H→L+1	92.74%
Z2	2.54	487	1.64	H→L+2	72.97%
Z2+	2.69	461	2.60	H→L	85.10%
Mol.3	2.59	479	1.26	H−1→L+1	55.22%
Mol.3+	2.66	466	2.49	H→L+1	83.20%

ing absorption intensities are 1.38, 1.64, and 1.26, respectively. After reaction with cysteine and homocysteine, the maximum single photon absorption peaks of Z1+, Z2+, and Mol.3+ were at 439 nm, 461 nm and 466 nm, respectively, and the corresponding absorption intensities were 2.03, 2.60, and 2.49, respectively. Compared with the single photon absorption peaks of the probe molecules Z1, Z2, and Mol.3, the product undergoes a certain blue shift and the absorption intensity is enhanced to some extent.

Table IV shows the fluorescent emission properties of the probe molecules Z1, Z2, Mol.3 and their corresponding products Z1+, Z2+, Mol.3+, including the energy and wavelength of single-photon emission in water, corresponding fluorescence oscillator intensity, transition characteristics. In water, the fluorescence emission peaks of molecules Z1, Z2, and Mol.3 are located at 582 nm, 600 nm, and 622 nm, and the corresponding oscillator strengths are 0.98, 0.74, and 0.50, respectively. After reaction with cysteine and homocysteine, the fluorescence emission peaks of the molecules Z1+, Z2+, and Mol.3+ are located at 502 nm, 511 nm, and 519 nm, and the corresponding oscillator strengths are 2.34, 2.94, and 2.56, respectively. The intensity of the emitted oscillator strengths has increased to varying degrees, and the oscillator strength of the product Z2+ is the largest. Blue shifts of 80 nm, 89 nm, and 103 nm occurred before and after the molecular reaction, respectively. Therefore, we can see that Z1, Z2, and Mol.3 all show excellent probe properties when detecting cysteine and homocysteine without destroying the donor structure of triphenylamine and the acceptor structure of aldehyde groups. The molecular structure of Z2 is relatively simple, and the intensity of the emission oscillator is large, which has relatively good research value.

TABLE IV Fluorescent emission properties of the compounds in H_2O, including E_{flu} (in eV), λ_{ope} (in nm), and δ_{ope} (in arb. unit).

Molecule	E_{flu}	λ_{ope}	δ_{ope}	Transition feature	
Z1	2.13	582	0.98	H→L	95.9%
Z1+	2.47	502	2.34	H→L	96.9%
Z2	2.07	600	0.74	H→L	91.2%
Z2+	2.43	511	2.94	H→L	90.8%
Mol.3	1.99	622	0.50	H→L	91.7%
Mol.3+	2.39	519	2.56	H→L	89.7%

Intramolecular charge transfer is an important factor in determining the optical properties of molecules. When a molecule is excited by a certain wavelength of light, the molecule transitions from the ground state to the excited state, and the charge distribution in the molecule changes during the process. Therefore, in order to more clearly and intuitively show the response process of the fluorescent probe molecules to the light field in the process of interaction with the light field, we use Multiwfn software to make the charge transfer difference diagram of the ground state and the excited state of the molecule, as shown in FIG. 5. The green and blue parts represent electrons and electron loss, respectively. As seen from FIG. 5, the green part mainly concentrates on the terminal aldehyde group of the probe molecules Z1, Z2 and Mol.3, and the blue part mainly concentrates on the central group triphenylamine structure. Therefore, it can be inferred that in the probes Z1, Z2, and Mol.3, the electrons are transferred from the triphenylamine group to the hydroxyl group at the end of the side branch, that is, there is a significant intramolecular charge transfer process. After reaction with cysteine and homocysteine, both the green and blue portions are relatively concentrated on the central structural portion of the molecule, and there are no obvious electron-accepting acceptors and donors, and the charge transfer of the product molecules Z1+, Z2+ and Mol.3+ changed significantly. The different structure between the probe and its product causes the existence of "intramolecular charge transfer" in the probe and the absence of the "intramolecular charge transfer" in the product, which affects the energy level structure of the molecule and thus affects the emission wavelength of the molecule. In addition, it can be seen from FIG. 5 that the green portions of the probes Z2 and Mol.3

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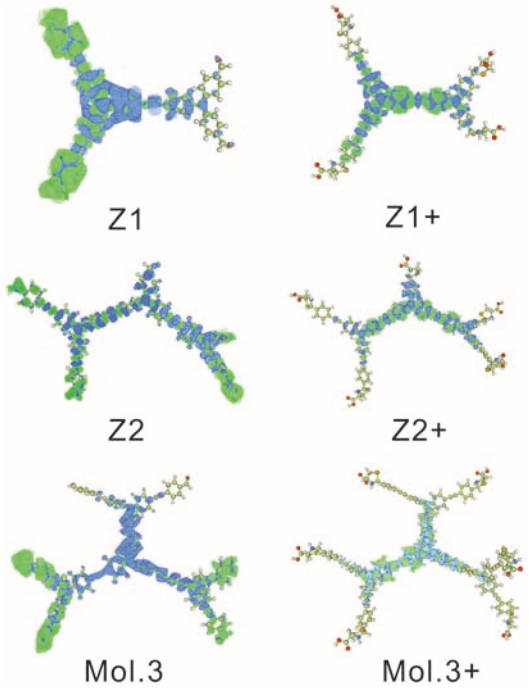

FIG. 5 The charge transfer between the excited state and the ground state. The blue and green areas represent electron loss and gain, respectively.

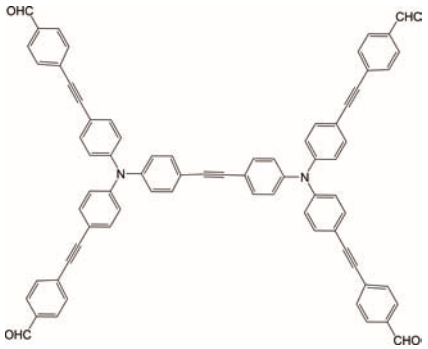

FIG. 6 The geometric structure of compound Mol.4.

TABLE V OPA properties in H_2O, including E_{opa} (in eV), λ_{opa} (in nm), δ_{opa} (in arb. unit), and transition feature.

Molecule	E_{opa}	λ_{opa}	δ_{opa}	Transition feature	
Mol.3	2.59	479	1.26	H−1→L+1	55.22%
Mol.3+	2.66	466	2.49	H→L+1	83.20%
Mol.4	2.44	507	1.75	H→L+1	47.34%
				H→L	43.78%
Mol.4+	2.73	454	2.27	H→L	93.51%

mainly accumulate on the terminal aldehyde groups of the two side branches, indicating that the receptor of the probe molecule is mainly the terminal group at the two side branches. However, due to the influence of the third side branch, the green part of the central molecule of the product molecule Z2+ is larger than that of Mol.3+, and the oscillator strength of emitted light is also greater than the intensity of the vibrator of Mol.3+, showing better probe properties.

C. Optical properties of the novel fluorescent probe Mol.4

Based on the above work, it can be known that the carbon-carbon triple bond and the benzene ring have a great influence on the optical properties of the probe. In order to find a fluorescent probe that can better detect cysteine and homocysteine, based on the single probe molecule Z1, we added a carbon-carbon triple bond and a benzene ring to the electron donor triphenylamine and the aldehyde group attached thereto, and designed a new molecule Mol.4, which had a high degree of symmetry. The molecular structure is shown in FIG. 6. As can be seen from the figure, the structure of the molecule Mol.4 increases The structure of the molecule Mol.4 increases the structure fo carbon-carbon triple bond and benzene compared to the molecule Z1. We performed a single photon absorption and emission calculation for the molecular Mol.4.

In Table V we list the energy of the probe Mol.3, Mol.4 and its product molecules Mol.3+, Mol.4+ in water, the OPA wavelength, the corresponding oscillator strength, transition contribution, and characteristics. The absorption wavelength of the probe Mol.4 is 507 nm, and the corresponding oscillator strength is 1.75. After reaction with cysteine and homocysteine, the absorption peak of the product was blue-shifted, the peak wavelength was 454 nm, and the oscillator strength increased from 1.75 to 2.27, which was consistent with the experimental probe Mol.3 before and after reaction.

Table VI shows the fluorescence emission properties of the probe molecules Mol.3, Mol.4 and their corresponding products Mol.3+, Mol.4+, including energy, wavelength, corresponding fluorescence oscillator intensity, transition characteristics for single photon emission in water. The emission peak of the probe Mol.4 was at 608 nm, and the oscillator strength was 0.69. After reacting with cysteine and homocysteine, the emission peak of the product molecule Mol.4+ was at 515 nm, and the oscillator strength was 2.53. We can see that the emission peak of the reaction product Mol.4+ has a blue shift of 93 nm compared with the emission peak of the probe Mol.4, and the oscillator strength has also increased from 0.69 to 2.53. Both the degree of blue shift and the oscillator strength are substantially identical to the probe molecule Mol.3. However, as can be seen from FIG. 1 and FIG. 6, the molecular structure of the probe Mol.4 is simpler than that of the probe Mol.3, which is more favorable for further theoretical research and it has played a guiding role in the experimental synthesis of fluorescent probes for the detection of biothiols.

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TABLE VI Fluorescent emission properties of the compounds in H_2O, including E_{flu} (in eV), λ_{ope} (in nm), δ_{ope} (in arb. unit).

Molecule	E_{flu}	λ_{ope}	δ_{ope}	Transition feature	
Mol.3	1.99	622	0.50	H→L	91.7%
Mol.3+	2.39	519	2.56	H→L	89.7%
Mol.4	2.04	608	0.69	H→L	94.7%
Mol.4+	2.41	515	2.53	H→L	96.4%

IV. CONCLUSION

In this work, the optical properties of various fluorescent probe molecules and their response mechanisms for detecting cysteine and homocysteine were studied at the level of density functional theory. The effects of carbon-carbon triple bond, benzene ring and side branch number on the properties of the probe were analyzed. On the same theoretical basis, the optical properties of multiple probes were compared. The calculation results showed that the number of the carbon-carbon triple bond, benzene rings and side branches had a certain influence on the properties of the fluorescent probe. With the addition of carbon-carbon triple bond and benzene ring, the structure of electron donor triphenylamine is gradually improved. Before and after the reaction, the relative molecular wavelength of the probe molecule becomes larger, and the oscillator strength is enhanced, showing better probe properties. By studying the number of lateral branches, it was found that single, double and triple branches have good probe properties. Since the nature of the probe is mainly determined by the transfer of electrons on the two side branches, the double-stranded probe molecule Z2 exhibits superior probe properties than the experimental molecule. In addition, the symmetric single-branched molecule Mol.4 designed according to the above results has the same excellent probe properties as the experimental molecules, but the structure is simple, which provides an important basis for further theoretical work and synthesis of probe molecules with better performance.

V. ACKNOWLEDGEMENTS

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[1] Z. A. Wood, E. Schröder, J. R. Harris, and L. B. Poole, Trends Biochem. Sci. **28**, 32 (2003).
[2] I. Graham, Ann. Intern. Med. **131**, 387 (1999).
[3] F. J. T. Staal, S. W. Ela, M. Roederer, M. T. Anderson, L. A. Herzenberg, and L. A. Herzenberg, Lancet **339**, 909 (1992).
[4] P. Aukrust and F. Mller, Nutrition **15**, 165 (1999).
[5] M. T. Heafield, S. Fearn, G. B. Steventon, R. H. Waring, A. C. Williams, and S. G. Sturman, Neurosci. Lett. **110**, 216 (1990).
[6] O. Nekrassova, N. S. Lawrence, and R. G. Compton, Talanta **60**, 1085 (2003).
[7] H. Refsum, A. D. Smith, P. M. Ueland, E. Nexo, R. Clarke, J. McPartlin, C. Johnston, F. Engbaek, J. Schneede, C. McPartlin, and J. M. Scott, Clin. Chem. **50**, 3 (2004).
[8] H. L. Chen, Q. Zhao, Y. B. Wu, F. Y. Li, H. Yang, T. Yi, and C. H. Huang, Inorg. Chem. **46**, 11075 (2007).
[9] O. Rusin, N. N. S. Luce, R. A. Agbaria, J. O. Escobedo, S. Jiang, I. M. Warner, F. B. Dawan, K. Lian, and R. M. Strongin, J. Am. Chem. Soc. **126**, 438 (2004).
[10] C. F. Chow, B. K. Chiu, M. H. W. Lam, and W. Y. Wong, J. Am. Chem. Soc. **125**, 7802 (2003).
[11] W. H. Wang, O. Rusin, X. Y. Xu, K. K. Kim, J. O. Escobedo, S. O. Fakayode, K. A. Fletcher, M. Lowry, C. M. Schowalter, C. M. Lawrence, F. R. Fronczek, I. M. Warner, and R. M. Strongin, J. Am. Chem. Soc. **127**, 15949 (2005).
[12] M. Zhang, M. X. Yu, F. Y. Li, M. W. Zhu, M. Y. Li, Y. H. Gao, L. Li, Z. Q. Liu, J. P. Zhang, D. Q. Zhang, T. Yi, and C. H. Huang, J. Am. Chem. Soc. **129**, 10322 (2007).
[13] F. Tanaka, N. Mase, and C. F. Barbas III, Chem. Commun. 1762 (2004).
[14] X. J. Zhang, X. S. Ren, Q. H. Xu, K. P. Loh, and Z. K. Chen, Org. Lett. **11**, 1257 (2009).
[15] C. Katan, F. Terenziani, O. Mongin, M. H. V. Werts, L. Porrs, T. Pons, J. Mertz, S. Tretiak, and M. Blanchard-Desce, J. Phys. Chem. A **109**, 3024 (2005).
[16] F. Terenziani, A. Painelli, C. Katan, M. Charlot, and M. Blanchard-Desce, J. Am. Chem. Soc. **128**, 15742 (2006).
[17] J. R. Falsey, M. Renil, S. Park, S. J. Li, and K. S. Lam, Bioconjug. Chem. **12**, 346 (2001).
[18] T. J. Tolbert and C. H. Wong, Angew. Chem. Int. Ed. **41**, 2171 (2002).
[19] M. Villain, J. Vizzavona, and K. Rose, Chem. Biol. **8**, 673 (2001).
[20] L. S. Zhang and J. P. Tam, Anal. Biochem. **233**, 87 (1996).
[21] Q. Q. Wu, Z. F. Xiao, X. J. Du, and Q. H. Song, Chem. Asian J. **8**, 2564 (2013).
[22] B. Tang, Y. L. Xing, P. Li, N. Zhang, F. B. Yu, and G. W. Yang, J. Am. Chem. Soc. **129**, 11666 (2007).
[23] J. Bouffard, Y. Kim, T. M. Swager, R. Weissleder, and S. A. Hilderbrand, Org. Lett. **10**, 37 (2008).
[24] J. H. Lee, C. S. Lim, Y. S. Tian, J. H. Han, and B. R. Cho, J. Am. Chem. Soc. **132**, 1216 (2010).
[25] L. L. Long, W. Y. Lin, B. B. Chen, W. S. Gao, and L. Yuan, Chem. Commun. **47**, 893 (2011).
[26] B. C. Zhu, X. L. Zhang, Y. M. Li, P. F. Wang, H. Y. Zhang, and X. Q. Zhuang, Chem. Commu. **46**, 5710 (2010).
[27] W. Y. Lin, L. L. Long, L. Yuan, Z. M. Cao, B. B. Chen, and W. Tan, Org. Lett. **10**, 5577 (2008).
[28] L. P. Duan, Y. F. Xu, X. H. Qian, F. Wang, J. W. Liu, and T. Y. Cheng, Tetrahedron Lett. **49**, 6624 (2008).
[29] C. K. Wang, Z. Zhao, M. C. Ding, X. J. Li, Y. H. Sun, and K. Zhao, Chin. Phys. B **19**, 230 (2010).
[30] K. Fukui, J. Phys. Chem. **74**, 4161 (1970).

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