

# Theoretical study on two-photon absorption properties of a zinc ion probe based on ICT mechanism: effects of coordination mode

Received Oct. 20, 2017,  
Accepted Dec. 15, 2017,

DOI: 10.4208/jams.102017.121517a

<http://www.global-sci.org/jams/>

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**Abstract.** The one- and two-photon absorption, as well as the emission properties of a ratiometric zinc ion probe have been theoretically investigated employing the time-dependent density functional theory and response theory. Various coordination geometries have been considered. Special emphasis is placed on the effects of coordination mode on the optical properties. Our results demonstrate that upon combining with zinc ion, the one-photon absorption (OPA), emission and two-photon absorption (TPA) wavelengths show considerable red shift due to the enhanced internal charge transfer mechanism. Moreover, their intensities are enhanced to some extent. It is also shown that the red shifts are quite different for various coordination geometries. When the zinc ion is connected with the electron acceptor of the fluorophore, the OPA, emission and TPA wavelengths have larger red shifts induced by the lower energy gaps between the related molecular orbitals.

## 1. Introduction

In the past decade, two-photon microscopy (TPM) employing two near-infrared photons for excitation has become an important imaging tool for biomedical research due to its lots of advantages over one-photon microscopy, including increased penetration depth (>500 $\mu\text{m}$ ), lower tissue auto-fluorescence and self-absorption, as well as reduced photo-damage and photo-bleaching[1-3]. As such, to facilitate the use of TPM, a variety of two-photon (TP) probes for specific applications are greatly needed. Recently, the design and synthesis of TP fluorescent probes has become a rapidly emerging field, and then a large number of TP probes for diverse analytes, such as cation and anion ions, pH values, small molecules and proteins have been developed in experiments[1-5]. In parallel, the recognition mechanisms of the probes have also been discussed. It has been demonstrated that the internal charge transfer (ICT), photon-induced electron transfer (PET), resonance energy transfer (RET) and aggregation-induced emission (AIE) mechanisms usually support the fluorescence behaviors[2,3,6]. The combination of two or more mechanisms based sensors have also been reported in literatures[7,8].

Zinc ion is the second most abundant transition metal ion in living body and it plays an important role in many biological processes. Zinc ion dysbolism will result in many human diseases such as dysimmunity, Alzheimer's and Parkinson's diseases [2,3,9-11]. Therefore, it is necessary to detect the spatiotemporal distributions of the  $\text{Zn}^{2+}$  ions in living systems. In recent years, a number of  $\text{Zn}^{2+}$  ions turn-on or ratiometric TP probes have been synthesized and their bioimaging applications has been demonstrated [2,3]. However, the theoretical studies on  $\text{Zn}^{2+}$  ions probes are still in the primary stage [12-16].

In this paper, we choose a ratiometric  $\text{Zn}^{2+}$  ion TP probe as the model molecule. It has been reported that this probe undergoes significant increase of the two-photon absorption (TPA) cross sections by the  $\text{Zn}^{2+}$ -coordination induced ICT enhancement[17]. To explore the recognition mechanism of the probe and the structure-property relationships, we perform a theoretical study on the one-photon absorption (OPA), emission and TPA properties of the probe before and after combination with  $\text{Zn}^{2+}$  using density functional theory (DFT). It poses an interesting question as to whether the optical properties will be altered if the coordination geometries changes. This change may also affect the efficiency of molecular ICT of the probe. Therefore, we put an emphasis on the effects of coordination mode on TPA. To the best of our knowledge, this effect has not been investigated theoretically for TP sensors. Our research will provide useful guidelines for the design and synthesis of TP probes for metal ion.

## 2. Theoretical methods

The oscillator strength can be used to specify the intensity of OPA. It is expressed as

$$f_{op} = \frac{2\omega_i}{3} \sum_{\alpha} |\langle 0 | \mu_{\alpha} | i \rangle|^2, \quad (1)$$

where  $\alpha \in (x, y, z)$ ,  $\mu_{\alpha}$  is the dipole moment operator,  $\omega_i$  denotes the excitation energy from the ground state  $\langle 0 |$  to the excited state  $|i\rangle$ .

In the case of resonant degenerate TPA, the sum-over-state expression for the two-photon matrix element can be written as

$$S_{\alpha\beta} = \sum_s \left( \frac{\langle 0 | \mu_{\alpha} | s \rangle \langle s | \mu_{\beta} | f \rangle}{\omega_{si} - \omega} + \frac{\langle 0 | \mu_{\beta} | s \rangle \langle s | \mu_{\alpha} | f \rangle}{\omega_{si} - \omega} \right), \quad (2)$$

where  $\mu_{\alpha(\beta)}$  is the dipolar operator in the direction  $\alpha, \beta \in (x, y, z)$ ,  $\omega$  is

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the fundamental frequency of the laser beam which is assumed equal to half of the excitation energy  $\omega_f$  to the final state  $|f\rangle$ ,  $2\omega = \omega_f$ . The summation here includes all intermediate, initial and final states, where  $\omega_{si}$  represents the excitation energies for the intermediate state  $|s\rangle$ . In response theory, the two-photon matrix element  $S_{\alpha\beta}$  can be calculated through the single residues of the quadratic response function[18].

The total TPA cross section of molecules excited by a linear polarized single beam can be expressed as [19,20]

$$\delta_{ip} = \sum_{\alpha,\beta} (2S_{\alpha\alpha} S_{\beta\beta}^* + 4S_{\alpha\beta} S_{\alpha\beta}^*), \quad (3)$$

The macroscopic TPA cross section that can be directly compared with the experimental measurement, is defined as[20]

$$\sigma_{ip} = \frac{4\pi^2 a_0^5 \alpha \omega^2}{15c \Gamma_f} \delta_{ip}, \quad (4)$$

Here  $a_0$  is the Bohr radius,  $c$  is the speed of light,  $\alpha$  is the fine structure constant. The level broadening  $\Gamma_f$  of final state is assumed to have the commonly used value  $\Gamma_f = 0.1 \text{ eV}$ . The unit of TPA cross section is GM,  $1\text{GM} = 10^{-50} \text{ cm}^4/\text{s/photon}$ .

In this work, the geometrical structures of ground states are fully optimized by using DFT with the 6-31G(d,p) basis set and the B3LYP hybrid functional. On the basis of the optimized structures, the OPA properties are computed by the time-dependent DFT (TD-DFT) approach at B3LYP level with 6-31G(d) basis set. The first excited state geometry optimization and fluorescence properties are calculated using TD-DFT at the same level. All the calculations of optimization, OPA and emission properties are carried out in the Gaussian 09 program[21]. The TPA cross sections are obtained by response theory using the B3LYP functional with 6-31G(d) basis set in the Dalton 2013 package[22]. In addition, the effect of water solvent is taken into account with the self-consistent reaction field theory by means of the polarizable continuum model (PCM) in both Gaussian and Dalton calculations. Our previous works show that the B3LYP functional calculations can give reasonable TPA properties which are consistent with the trend of experimental observations[23-27].

### 3. Results and discussion

#### 3.1 Molecular structures

The chemical structures for the studied molecules are depicted in Figure 3.1.1. Probe AD uses 2-acetyl-6-dimethylamino naphthalene (acedan) as the fluorophore and di-2-picolyamine (DPA) as the  $\text{Zn}^{2+}$  receptor. It has been shown that acedan derivatives possess significant TPA cross section and has been widely used to design TP cation sensors[28]. The receptor DPA is connected with the acyl moiety which is the electron acceptor group of acedan. Hence, the acetyl group could get involved in coordination with  $\text{Zn}^{2+}$  and result in enhanced ICT transition. ADZn1, ADZn2 and ADZn3 are the possible coordination geometries which have the different coordination modes. Two  $\text{Cl}^-$  ions are added in order to facilitate calculations. In ADZn1, the oxygen atom does not participate in the coordination and all of the three nitrogen atoms of DPA group chelate to  $\text{Zn}^{2+}$  to complete the five-coordination geometry. But in both ADZn2 and ADZn3, the oxygen atom takes part in the coordination. In addition to the oxygen atom, one and three nitrogen atoms are connected with  $\text{Zn}^{2+}$  in ADZn2 and ADZn3

respectively. It is expected that the different coordination modes would give rise to the different geometries and electronic structures.

The corresponding optimized geometries are also illustrated in Figure 3.1.1. The frequency calculations for these geometries do not produce any imaginary frequencies. One can see that the DPA parts of these compounds have different structural characters. The oxygen or nitrogen atoms coordinate with  $\text{Zn}^{2+}$  with typical bond length of around  $2\text{\AA}$ , which is similar to the X-ray crystal structure[17]. The related bond lengths of the optimized molecules are displayed in Table 3-1. The permanent dipole moments and the energies of the zinc complexes are examined, and the results are also listed in Table 3-1. Table 3-1 reveals that ADZn3 has the largest dipole moment, and ADZn1 has the smallest one. It should be noticed that the permanent dipole moment of AD molecule is only 6.360 D which is much smaller than the values of the zinc complexes. It is also shown that ADZn1 has the lowest energy among the complexes and the energy differences between ADZn3 and ADZn1 are very small which are only 0.892 kcal/mol. Such small energy barriers indicate that they could be thermally populated.

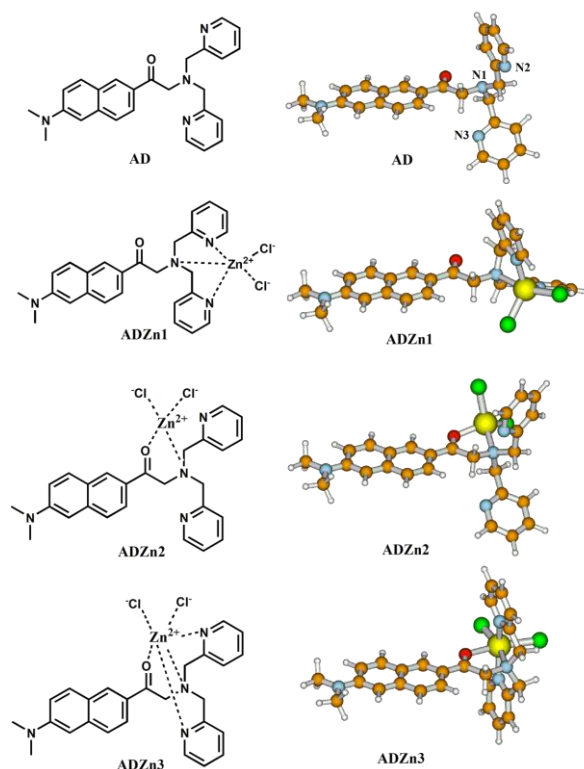


Figure 3.1.1: Chemical structures and corresponding optimized geometries for AD, ADZn1, ADZn2 and ADZn3.

Table 3-1. Selected bond lengths (in units of  $\text{\AA}$ ), permanent dipole moments  $\mu$  (in units of D) and energy differences  $\Delta E$  (in units of kcal/mol).

Mol.	Zn-O	Zn-N1	Zn-N2	Zn-N3	$\mu$	$\Delta E$
ADZn1		2.347	2.091	2.085	18.557	0
ADZn2	2.061	2.137			20.112	14.991
ADZn3	2.252	2.319	2.129	2.129	25.945	0.892