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# Evaluation of a simple and novel fluorescent anion sensor, 4-quinolone, and modification of the emission color by substitutions based on molecular orbital calculations

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**Abstract**—4-Quinolone (4-QO) was evaluated as a simple and novel fluorescent anion sensor, and the modification of its emission color was carried out. The series of 4-QO derivatives having molecular orbitals with different energy levels was designed by substitutions at the 6 and 7 positions based on the molecular orbital calculations. All derivatives showed drastic fluorescence enhancements in the presence of  $F^-$  via the intramolecular charge transfer mechanism, and the successful modification of the emission color was achieved. The anion-induced emission colors of these derivatives as well as their binding affinities for  $F^-$  could be predicted by ab initio quantum chemical calculations, indicating that the present calculations are useful in designing new anion sensors.

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## 1. Introduction

Anion sensing has been of great interest in biological and environmental sciences for several decades, and various fluorescent sensors have been developed for sensitive and simple detections.<sup>1–3</sup> As signaling mechanisms, photoinduced electron transfer,<sup>4–9</sup> intramolecular charge transfer (ICT),<sup>10–18</sup> excited-state proton transfer,<sup>19,20</sup> metal-to-ligand charge transfer,<sup>21</sup> excimer/exciplex formation,<sup>22–24</sup> and competitive binding<sup>25–28</sup> are reported. Particularly, ICT based on hydrogen bond formations between anions and NH or OH groups of the sensor molecules has been widely employed because of the simplicity and capability for multipoint interactions.

ICT fluorescent anion sensors can be classified into two types; one shows fluorescence quenching when binding to anions, and the other shows a fluorescence enhancement. For sensitive detection, the latter has the best advantages, nevertheless, only a few sensors of this type have so far been reported.<sup>11,13,15</sup> Therefore, the discovery and/or development of new ICT sensors of this type are strongly desired to establish a variety of methods for simple and sensitive anion sensing. In a previous study, we reported that some 4-quinolone (4-QO) derivatives are useful fluorophores with high fluorescence quantum efficiency and high stability

in aqueous media.<sup>29,30</sup> We have been focusing on the discovery of new photophysical properties of these compounds, and found that 4-QO shows a drastic fluorescence enhancement via the ICT mechanism in the presence of anions. Herein, we now report for the first time the anion-induced changes in the absorption and fluorescence of 4-QO.

In addition, we have modified the emission color of 4-QO by the substitution based on molecular orbital calculations. The emission color of a sensor is of great importance for simple and selective detection, because it is often needed to avoid potential interferences by fluorescence impurities present in environmental and biological samples. Until now, several reported studies have focused on modifying the emission color of a sensor molecule based on substituent effects.<sup>10,14,16,18</sup> However, the introduction of substituents was in most cases still empirical, and theoretical methods based on molecular orbital calculations have scarcely been exploited in spite of the fact that various fluorescent compounds have recently been designed using computational calculations.<sup>31–35</sup> To the best of our knowledge, there have been no reports demonstrating the theoretical modification of the emission color using a sensor molecule that shows a fluorescence enhancement upon binding to anions via the ICT mechanism.

In the present paper, we report a simple and novel fluorescent anion sensor, 4-QO, that shows a drastic fluorescence enhancement via the ICT mechanism. By substitutions based on molecular orbital calculations, 4-QO derivatives **1–6** (Fig. 1) were designed in order to produce different emission

**Keywords:** Anion sensor; 4-Quinolone; Intramolecular charge transfer; Fluorescence; Molecular orbital calculation.

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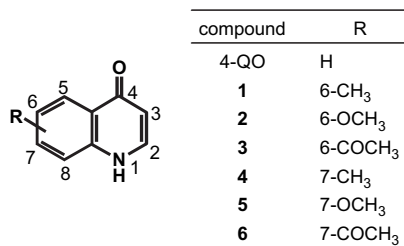


Figure 1. Structures of 4-QO derivatives.

colors from 4-QO. The binding affinities of these derivatives for anions were also considered using ab initio quantum chemical calculations.

## 2. Results and discussion

### 2.1. Anion response of 4-QO

The anion-induced changes in the absorption and fluorescence spectra of 4-QO were investigated using F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, HSO<sub>4</sub><sup>-</sup>, AcO<sup>-</sup>, and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> (as tetrabutylammonium salts). Figure 2 shows the absorption and fluorescence emission spectra in CH<sub>3</sub>CN when titrated with F<sup>-</sup>. The peak of the absorption spectrum was slightly red shifted from 330 to 338 nm and two isosbestic points at 332 and 299 nm were observed (Fig. 2a). In the fluorescence emission spectra, the intensity was drastically increased at 396 nm (Fig. 2b). With the titration of AcO<sup>-</sup> and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> similar changes were observed, while the titrations of other anions caused no change in both spectra. This suggests that 4-QO forms complexes only with F<sup>-</sup>, AcO<sup>-</sup>, and H<sub>2</sub>PO<sub>4</sub><sup>-</sup>. This anion-selectivity is thought to be dictated by the anion basicity; F<sup>-</sup>, AcO<sup>-</sup>, and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> are stronger hydrogen acceptors than other tested anions. The Job plots for the complexation of 4-QO with anions obtained from the absorption titration experiments showed a 1:1 stoichiometry for F<sup>-</sup> and 2:1 for AcO<sup>-</sup>, while, more than two complex species were suggested to be present for H<sub>2</sub>PO<sub>4</sub><sup>-</sup>. To confirm the recognition mechanism of 4-QO for anions, a <sup>1</sup>H NMR titration experiment was carried out. The <sup>1</sup>H NMR spectrum of 4-QO in DMSO-*d*<sub>6</sub> showed a singlet signal for the NH proton at 11.70 ppm (Fig. 3a). Upon addition of 1.0 equiv F<sup>-</sup>, the signal completely disappeared (Fig. 3b), which indicates hydrogen bond formation between the NH group of 4-QO and F<sup>-</sup>. Ab initio quantum chemical calculations were performed, and the structure of the complex of 4-QO with F<sup>-</sup> was optimized with B3LYP at the 6-31G(d) level. In the optimized structure, the distance between the NH proton and F<sup>-</sup> is 1.009 Å, also indicating the presence of a hydrogen bond between these atoms. The negative charge of F<sup>-</sup> calculated at the B3LYP/6-311+G(d,p) level using the optimized structure is -0.662; this means that a part of the negative charge is intramolecularly transferred from F<sup>-</sup> to 4-QO. For a further confirmation, we synthesized 1-methyl-4-QO that has the CH<sub>3</sub> group at the recognition point, and investigated its anion response that is observed in the absorption and fluorescence emission spectra. With the addition of all anions tested, no change in both spectra was observed. These results clearly indicate that 4-QO recognizes anions via the NH group.

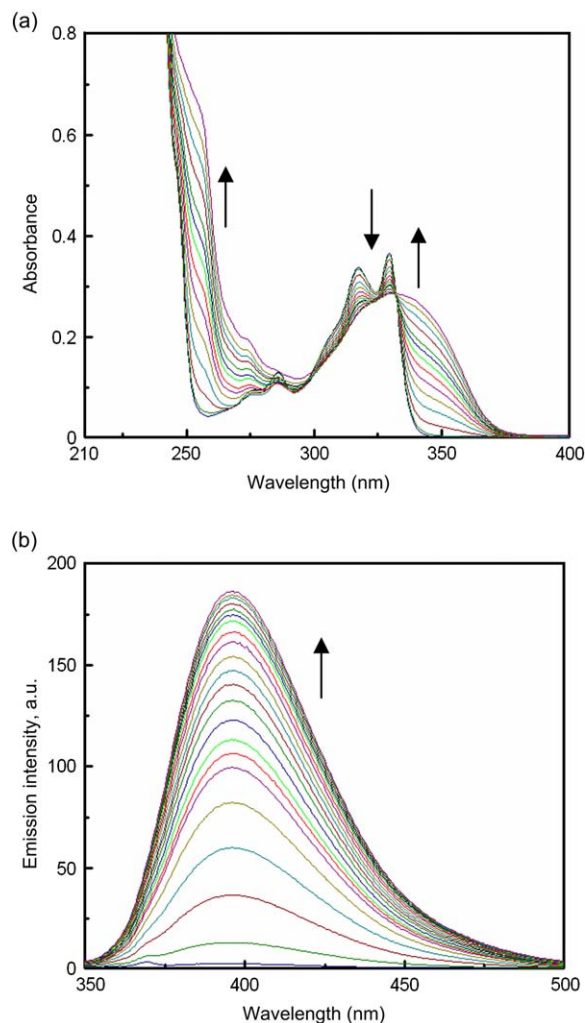


Figure 2. (a) Change in absorption spectra of 4-QO (30 μM in CH<sub>3</sub>CN) upon the addition of F<sup>-</sup> (0–0.3 mM); (b) change in fluorescence emission spectra of 4-QO (3 μM in CH<sub>3</sub>CN) upon the addition of F<sup>-</sup> (0–35 μM) with the excitation wavelength of 332 nm.

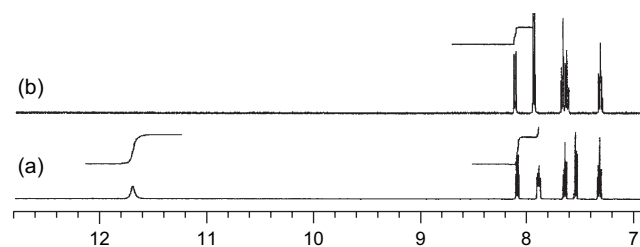


Figure 3. Partial <sup>1</sup>H NMR (500 MHz) spectra of 4-QO in DMSO-*d*<sub>6</sub> in (a) the absence, and (b) the presence of 1.0 equiv F<sup>-</sup>.

### 2.2. Design of 4-QO derivatives as novel anion sensors using molecular orbital calculations

Adding electron-donating and/or -withdrawing groups to fluorophores is generally known to cause changes in their HOMO–LUMO gaps, and it is expected that not only a shift in the absorption wavelength, but also a shift in the emission wavelength would be induced. The complexes of 4-QO with anions emit the fluorescence at 396 nm, representing a violet-blue color. Therefore, as novel anion sensors showing

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