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Phosphate and Water Sensing with a Zinc-Dipicolylamine-Based Charge-Transfer Dye

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A D-π-A (donor-π bridge-acceptor) dye with a conjugated dipicolylamine group as the donor was synthesized and characterized. When zinc is bound to the dipicolylamine ligand, charge transfer strength from the donor is decreased resulting in a large blue-shift in the absorption spectrum with a quenching of dye emission. Upon addition of phosphate, changes in both the absorption and emission spectrum are observed with intermediate states between the starting zinc complex and free dye observed. The zinc-dye complex was found to react with two equivalents of phosphate or trace water to give the free dye. The water response is unexpected given the widespread use of the dipicolylamine group as an anion sensor in water. When the dipicolylamine group is part of conjugated D-π-A dye designs with zinc complexes, the dye is observed to act as a humidity sensor at low water amounts.

Introduction

The detection of phosphate in aqueous environments is of critical importance.[1] Optical phosphate detection commonly exploits the low solubility of metal phosphate salts by dissociating metals from chelating ligands to give a change in the optical properties of a chromophore.[1b,2] Zinc-bound dipicolylamines (DPAs) are a popular metal-ligand combination used in the literature for detections of anions.[1a,b, 3] Recently, the DPA ligand was used as a zinc chelate on the periphery of a squaraine dye with promising results reported (Figure 1). The zinc-squaraine dye (**Sq-Zn**) was found to have an optical response in the presence of CO_2, cyclic phosphates, and picric acid in aqueous environments through shifts in the absorption and emission spectra. The rational for this shift is presented as the electron density on the amine nitrogen of the DPA ligand being held by the zinc atom as a Lewis acid-Lewis base interaction. This removes electron density from the squaraine π-system resulting in a shift of the absorption spectrum to a higher energy absorption (584 nm relative to the non-zinc bound dye at 633 nm). Once an analyte coordinates to the zinc atom to displace the Zn–N bond, the electron density of the amine then is added to the squaraine π-system resulting a shift of the absorption spectrum to lower energy with an absorption maximum (λ_{max}) of 633 nm. This corresponds to a 0.16 eV shift in λ_{max} energy based on zinc coordination or dissociation.

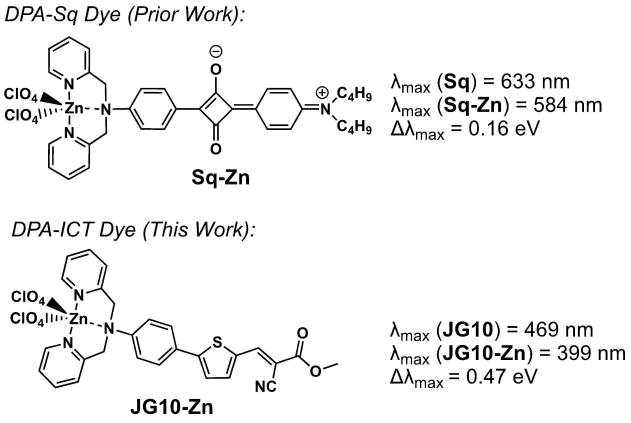

Figure 1. Comparison of the optical properties of a squaraine dye (**Sq-Zn**) to an ICT dye (**JG10-Zn**) with and without Zn bound.

Building on this hypothesis, an intramolecular charge transfer (ICT) dye could result in a large energy change upon coordination or dissociation of a zinc atom since the optical properties of these systems rely on the electron density being heavily localized on a donor group in the ground state, then shifting to an acceptor group upon photoexcitation. If the Zn atom is removing electron density from the amine group, photoexcitation would not generate a strong ICT event and a dramatic effect on the optical properties of an ICT system would be observed. To probe this theory, a D-π-A (donor-π bridge-acceptor) dye in conjugation with a DPA ligand as the donor was targeted for investigation. The π-bridge was selected as a thiophene which allows for strong ICT events, and the acceptor was selected as a cyanoacrylic ester which provides a convenient functional handle on the acceptor for further functionalization. A larger shift in the absorption energy

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upon metal atom association/dissociation is expected for this ICT dye which is more dependent on donor electron density for light absorption than non-charge transfer dyes.[4] Larger changes in absorption energy are desirable in providing a sensor system with a higher signal resolution by avoiding spectral overlap of the Zn-bound and unbound dye absorption spectrum.

Results and Discussion

Computational analysis of **JG10** and **JG10-Zn** via density functional theory (DFT) at the B3LYP/6-31G (d,p)[5] level of theory with an acetonitrile polarized continuum model (PCM) was conducted to probe if the target dye would absorb light via an ICT event.[6] The highest occupied molecular orbital (HOMO) of **JG10** was found to be mostly on the donor group benzene with a slightly smaller contribution from the thiophene π-bridge (Figure 2). The lowest unoccupied molecular orbital (LUMO) of **JG10** was found to be mostly on the cyanoacrylic acid acceptor with some contribution from the thiophene π-bridge. Time dependent (TD)-DFT was used to examine if the HOMO-LUMO transition was of significant enough oscillator strength to be observed readily experimentally and to evaluate the predicted change in the vertical transition upon coordination of Zn to **JG10**. TD-DFT at the B3LYP/6-31G (d,p) level shows a vertical transition of 510 nm (2.43 eV) with an oscillator strength of 1.18 and a contribution of 100% from the HOMO-LUMO transition for the first excited-state of **JG10**. This strong contribution from the HOMO and LUMO orbitals localized on separate regions of the **JG10** dye shows this is an ICT system as expected. Upon coordination of Zn, the relative contribution of thiophene to the HOMO orbital density of **JG10-Zn** (with 1 explicit MeCN molecule present) is slightly increased when compared to the benzene ring. This change in HOMO orbital position is subtle when **JG10** and **JG10-Zn** are compared. No notable change in the LUMO position is noted. However, TD-DFT reveals a substantial blue shift of the vertical transition to 430 nm (2.88 eV) with an oscillator strength of 1.27 and a contribution of 99% from the HOMO-LUMO transition to this first excited state. Encouragingly, the predicted 0.45 eV shift in vertical transition energies is significantly larger than the observed shift in absorption maxima energy for **Sq-Zn** at 0.16 eV.

With promising computational results for the target system, the synthesis of **JG10** and **JG10-Zn** was undertaken. **JG10** and **JG10-Zn** can be obtained synthetically beginning with the double alkylation of commercially available 4-bromoaniline (**1**) with 2 equivalents of 2-(chloromethyl)pyridine (**2**) to yield intermediate DPA–Br (**3**) in 77% yield (Scheme 1).[3g] A Miyuara borylation of **3** yields the DPA-pinacol boronic ester **4** in 50% yield. A Suzuki cross coupling of DPA-Bpin **4** with 5-bromo-2-thiophenecarboxaldehyde (**5**) gives the DPA-aldehyde **6** in 64% yield. The cyanoacrylic acid functionalized intermediate **7** could then be formed via a Knoevenagle reaction with **6** and cyanoacetic acid in 48% yield. The target methyl ester dye **JG10** was realized in 49% yield upon treatment of **7** with thionyl chloride then methanol in the presence of triethylamine. Chelation of zinc was achieved by dissolving **JG10** and zinc perchlorate ($Zn(ClO_4)_2$) in a 1:1 ratio in acetonitrile to quantitatively give **JG10-Zn**. The coordination was found to proceed on the order of minutes even at dilute concentrations of **JG10** (1×10^{-5} M) with only 2.5 equivalents of Zn (Figures S1 and S2). This rapid association of Zn to **JG10**, even under dilute conditions, suggests the dye-zinc interaction is significantly favorable in acetonitrile.

The optical properties of **JG10** and **JG10-Zn** were probed via absorption and emission spectroscopy (Figure 3). A λ_{max} of 469 nm is observed for **JG10** in acetonitrile. Upon coordination of zinc, a shift in λ_{max} to higher energy at 399 nm is observed. This change in absorption energy corresponds to a 0.47 eV shift which is a 3x larger shift in energy for this ICT system relative to the prior reported squaraine dye **Sq-Zn** that has a change in absorption energy corresponding to a 0.16 eV shift. Both of the experimental λ_{max} values and the energy change between **JG10** and **JG10-Zn** is closely correlated with the predicted values via TD-DFT analysis above. The large change in energy indicates that the charge transfer properties of **JG10** have been more dramatically affected upon coordination of zinc to the picoline donor group than observed for **Sq-Zn** as hypothesized.

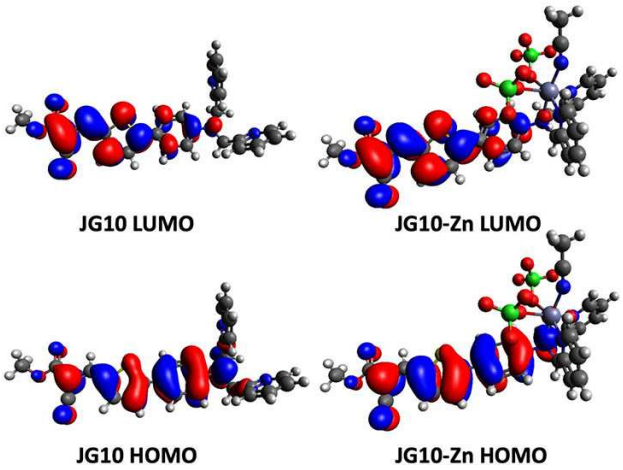
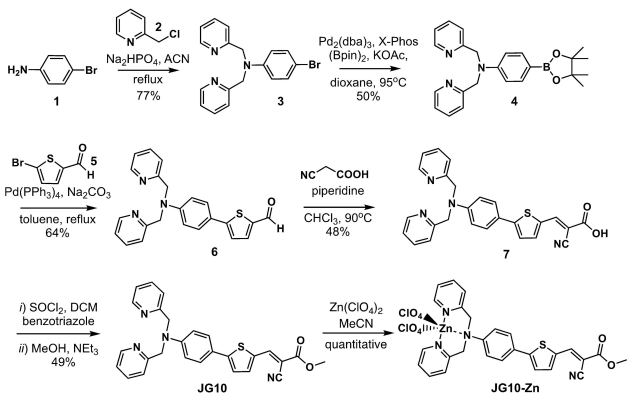


Figure 2. HOMO and LUMO orbitals of **JG10** and **JG10-Zn**.



Scheme 1. Synthetic route to the target dye **JG10-Zn**.

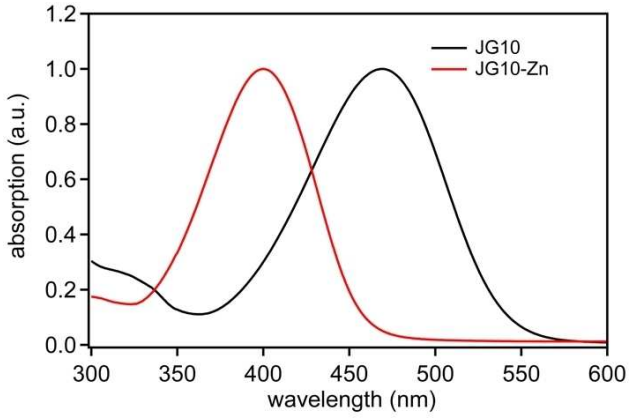


Figure 3. Absorption spectra of **JG10** and **JG10-Zn** in acetonitrile.

With the dye in hand, the detection of phosphate was examined by addition of tetrabutylammonium monobasic phosphate (TBAP) to dilute solutions of **JG10** in acetonitrile (Figure 4). At low equivalents of TBAP (0.001 to 0.5), no significant shift in the absorption spectrum was observed for the **JG10-Zn** complex on the minute timescale. This may indicate the zinc-phosphate complexation event is not instantaneous. A gradual shift in the absorption curve λ_{max} is observed from 0.75 equivalents of TBAP to 2.5 equivalents from 399 nm to 447 nm for measurements on the minute time scale. This gradual shift is attributed to a weakening of the Zn-amine bond without full dissociation of the Zn atom from the DPA. At larger equivalents than 2.5, the absorption curve returns to the initial non-zinc coordinated dye shape with a λ_{max} of 469 nm. This indicates that **JG10-Zn** is a sensor for phosphate with a <1 minute response time in dilute MeCN with ≥ 0.75 equivalents of TBAP. In addition, ^{1}HNMR studies showed a return of the non-zinc coordinated dye (**Figure S5**).

Fluorescence spectroscopy was used to further probe the effects of TBAP addition to solutions of **JG10-Zn**. An on/off observation is possible since Zn is known to quench the fluorescence of organic molecules when coordinated. As expected, **JG10-Zn** is non-emissive in MeCN (Figure 4). However, after addition of ~1 equivalent of TBAP to the solution, a significant fluorescence signal is observed in <1 minute. This is consistent with absorption spectrum data observed above in that even with dilute solutions the reaction resulting in the dissociation of Zn from the dye is rapid. Additionally, the emission is blue shifted relative to **JG10**. This suggests that initially a partially dissociated Zn complex is present in solution prior to full dissociation. This hypothesis is consistent with the absorption data showing a gradual change from high to low energy absorption as TBAP is added. Upon addition of additional equivalents of TBAP the emission spectrum returns to the identical shape and λ_{max}^{emis} value of **JG10**, which suggests complete dissociation of the Zn from the dye.

Upon extended exposure of **JG10-Zn** to the TBAP solution the absorption profile was found to change slowly with very low quantities of TBAP added at 1 x 10^{-12} equivalents relative to the dye at 1 x 10^{-5} M concentration (Figure 5). This result suggests a second, slower pathway is active for dissociation of Zn from **JG10-Zn**. Given the low solubility of zinc phosphate, it

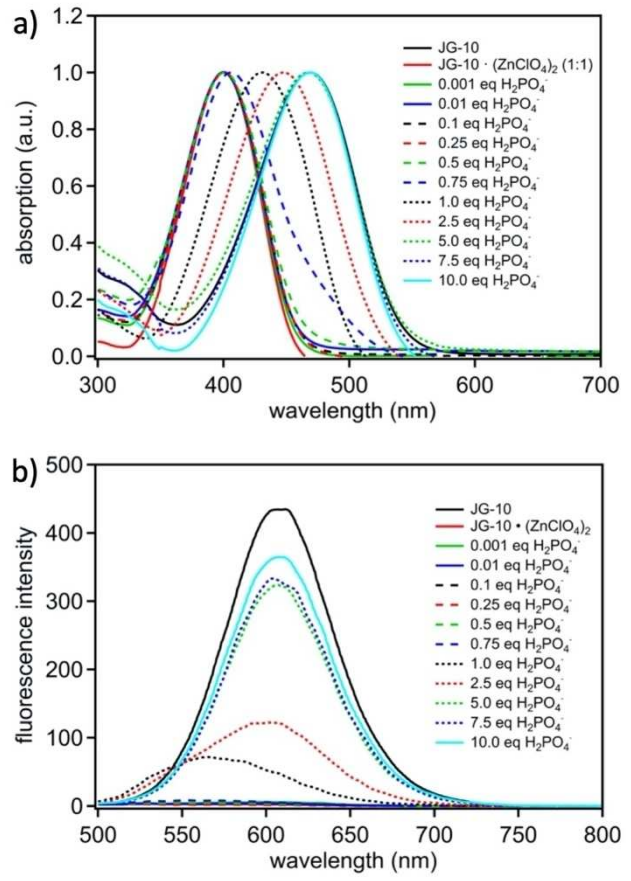


Figure 4. A) Absorption (top) and b) emission (bottom) spectra of **JG10** and **JG10-Zn** in acetonitrile with various equivalents of TBAP. The concentrations of the dyes were held constant at 1x10^{-5} M. All the absorption spectra with phosphate present were obtained immediately (<1 minute) after mixing with **JG10-Zn.**

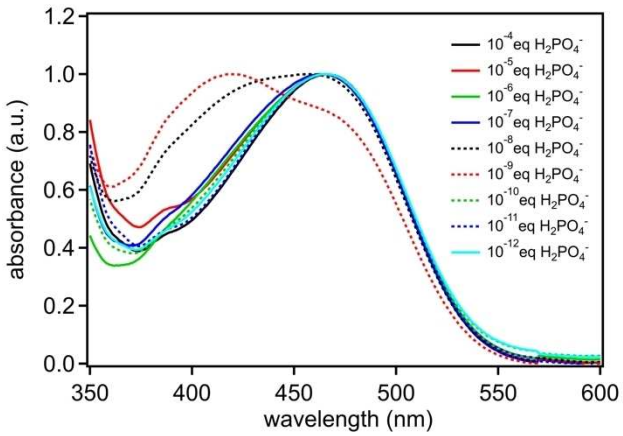


Figure 5. Absorption spectra of **JG10-Zn** in acetonitrile with various equivalents of TBAP. The concentration of **JG10-Zn** was held constant at 1x10^{-5} M, and the solutions were stirred overnight before spectrum were taken.

is unlikely a catalytic dissociation pathway is active. In fact, at very low concentrations of TBAP (1 x 10^{-4} equivalents to 1 x 10^{-12} equivalents) with extended time frames (overnight), the results often show anomalous behavior with respect to the amount of TBAP added. As an example, 1 x 10^{-9} equivalents of TBAP shows mostly **JG10-Zn** while 1 x 10^{-7} and 1 x 10^{-10} equivalents both show mostly **JG10** in solution (Figures 5 and **S3**).

Water concentration is often uncontrolled in many ambient condition experiments. Thus, the influence of water on the **JG10-Zn** complex was examined as a possible explanation for why the prior results were variable over longer timeframes. Under rigorously anhydrous conditions with more readily dried DCM and THF used as the solvents to avoid trace water in MeCN, at least 2 equivalents of TBAP is required to see a substantial change in the absorption spectrum indicating the conversion of **JG10-Zn** to **JG10** (**Figure S4**). This confirms **JG10-Zn** is a phosphate sensor under dry conditions which stoichiometrically reacts with phosphate as originally hypothesized even under anhydrous conditions. Further probing the effect of water, **JG10-Zn** was dissolved in dry DCM/THF and small quantities of H_2O were added in 10 μL increments to a 2 mL solution. Under these conditions, the emission rises from negligible with **JG10-Zn** linearly as more H_2O is added until the spectrometer detector response limit was reached (Figure 6 and **Figure S6**). A detection limit of water was noted at 0.1 M by loss of linearity in fluorescence intensity response versus water concentration (**Figure S7**). These spectra were taken after <1 minute of mixing time indicating that the dissociation of Zn from **JG10-Zn** occurs very rapidly with these quantities of water ($\sim$1 x 10^{-2} M or $\sim$1000 equivalents relative to **JG10-Zn**). These results highlight when an ICT dye such as **JG10** is used with a DPA donor the system is significantly sensitive to humidity. In general, these results highlight that careful controls must be performed when using the DPA donor group with Zn as a sensor, especially in aqueous environments since, at least in the case of ICT dyes, a significant background reaction with water can take place which is rapid if significant quantities of H_2O are present.

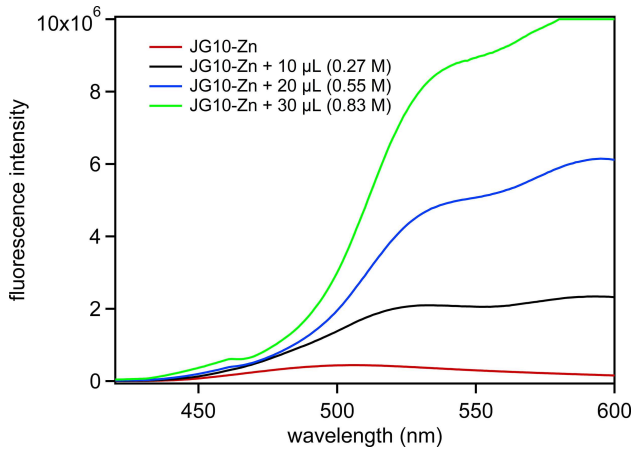


Figure 6. Fluorescence spectrum of a solution of **JG10-Zn** at 1 x 10^{-5} M in a 1:1 mixture of DCM:THF with varying amounts of water added.

Conclusions

An intramolecular charge transfer dye with a dipicolylamine donor/ligand group was designed and synthesized. The dye shows a substantial blue-shift in absorption curve maximum energy (0.47 eV) upon complexation to dicationic zinc. The emission of this dye-zinc complex was found to quench until the complex was exposed to monobasic phosphate which leads to an increase in emission and a shift of the absorption curve maximum to lower energy as the zinc is removed from the dipicolylamine ligand. Surprisingly, the dye-zinc complex was found to be moisture sensitive and could function as a water sensor with an obvious colorimetric change upon exposure to water. The water sensitivity seems to be unique to the use of dipicolylamine in conjugation with a charge transfer system since this group is used frequently in the literature in aqueous environments. These results highlight that care must be taken when assessing analyte sensing levels with dipicolylamine whereas in certain designs this group functions as a humidity sensor which can confound data analysis if water exposure is not carefully controlled.

Supporting Information Summary

Experimental procedures and compound characterization data can be found in the supplementary information for this article. ^{1}H and ^{13}C spectra are provided in the SI as well as supplementary UV-Vis characterizations.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: colorimetric · D-π-A dye · humidity sensor · phosphate sensor · sensor

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