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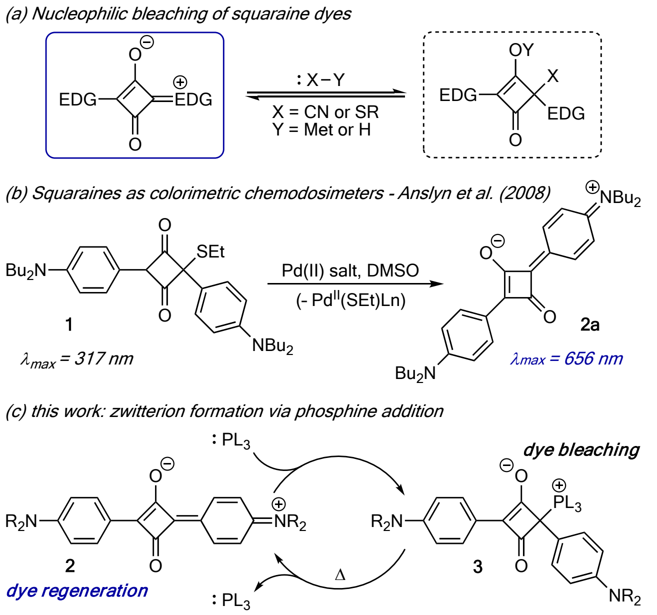
Nucleophilic addition of phosphorus(III) agents to the electrophilic core of intensely colored squaraine dyes gives a bleached zwitterionic adduct in good to excellent yields (up to 99%) at room temperature. The process can be reversed by adding specific transition metal complexes with high phosphorous(III) affinity.

While squaraine dyes are best well known for their chromophoric properties and use in non-invasive imaging of biological processes, nonlinear optics, photovoltaics, and ion sensing, the structural core represents a fascinating bonding motif of relatively unexplored synthetic potential.[1] Dianiline squaraines have two *para*-substituted anilines in a 1,3-orientation around the central, four-membered ring resulting in an electron deficient core with donor-acceptor-donor resonance stabilization. This orbital arrangement produces the narrow and intense absorption and fluorescence emission maxima bands in the near infrared region of light that are characteristic of this attractive class of dyes.[2,3] Because of its electrophilic nature, the central ring is susceptible to attack by sterically unencumbered nucleophiles (Figure 1a).[4,5] While this nucleophilic bleaching of squaraines is problematic in fluorescence imaging,[6] exploitation of this inherent electrophilicity is useful in the design and development of chemical sensing agents for trace analytes such as cyanide anion and thiols.

In 2008, Anslyn and coworkers demonstrated that bleached squaraine-thiol adducts are effective colorimetric dosimeters for Pd^{II} salts through the abstraction of thiolates from adduct **1** to regenerate the squaraine **2a** (Figure 1b).[7] During the course of their study, they discovered that unlike other Pd^{II} salts (i.e., $Pd(NO_3)_2$, $Pd(OAc)_2$), a decrease in the solution absorbance was observed when >0.75 equivalents of $Pd(PPh_3)_2Cl_2$ were added to **1**. Additionally, they noted that the presence of PPh_3 induced loss of the squaraine blue color, but the mechanism of this bleaching process was not pursued. In conceptually related work, Zhuang[8] and Rivera-Fuentes[9] independently reported the reversible addition of phosphines to cyanine dyes in high-resolution cell imaging by stochastic optical reconstruction microscopy (STORM) and photoactivatable probes for induction of intracellular reductive stress, respectively.[10] In contrast, addition of a phosphorus(III) reagent to squaraine **2** would result in a neutral, zwitterionic complex **3**, likely possessing distinctly different physiochemical properties (Figure 1c). Inspired by this prior art and our lab's previous explorations of phosphorus additions to electrophilic systems,[11] we initiated an investigation into the reactivity of dianiline squaraines with nucleophilic phosphorus(III) derivatives, and their potential as colorimetric sensing agents. Herein, we report our initial


(a) Nucleophilic bleaching of squaraine dyes

(b) Squaraines as colorimetric chemodosimeters - Anslyn et al. (2008)

(c) this work: zwitterion formation via phosphine addition

Figure 1. Additions to the central ring of squaraine dyes. (a) Established nucleophilic additions to squaraines. (b) Colorimetric sensors for trace metal impurities. (c) Reversible formation of bleached squaraine/phosphine adducts.

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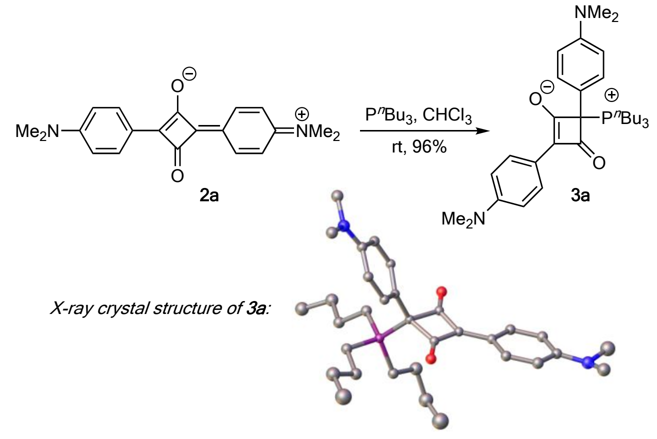
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x findings on the structure, stability, and reversible formation of zwitterionic squaraine-phosphine adducts.

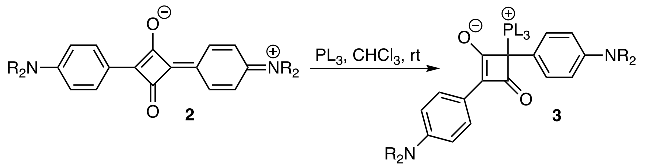
We began our study by investigating the addition of a nucleophilic trialkyl phosphine and an *N,N*-dialkylaniline squaraine dye. Initial exposure of dianiline squaraine **2a** to P^nBu_3 at room temperature resulted in a rapid bleaching of the dye's intense blue color (ca. 5 min) and isolation of the bench stable, pale yellow phosphine adduct **3a** in 96% yield (Scheme 1). Single crystal X-ray diffraction analysis of **3a** revealed a zwitterionic species which, to the best of our knowledge, is the first crystal structure of an adduct resulting from nucleophilic addition to a squaraine dye. The solid-state structure of **3a** has several notable features, including a distortion of the central ring geometry. As a result of the phosphine addition, the central four membered ring adopts a "kite quadrilateral" shape, rather than the square in **2a**, with two pairs of consecutive sides having unequal length. The shorter pair of bonds in the central ring are incorporated within a delocalized 3-oxopropenolate substructure that has two nearly identical C-O bond lengths of 1.230 and 1.237 Å. The associated O-C-C angles are 137° which is significantly larger than the expected angle of 120° for a linear version of this substructure.

To better understand the formation and stability of zwitterion adduct **3** as a function of the phosphorus(III) agent and dye structure, we conducted a series of experiments wherein **2a** and the more organic–soluble squaraine dyes **2b** and **2c** were exposed to either P^nBu_3 or $P(NMe_2)_3$ at room temperature (Table 1). In each experiment, one equivalent of PL_3 was added to a squaraine dye **2** in $CHCl_3$ at room temperature, and the resulting adduct obtained via recrystallization. The addition of P^nBu_3 to *N,N,N,N*-tetrabutyl and *N,N,N,N*-tetrabenzyl squaraines **2b** and **2c** provided the corresponding phosphine adducts **3b**-**c** in quantitative yield (entries 1 and 2). Similarly, the bulky, electron rich $P(NMe_2)_3$ gave zwitterionic adducts **3d**-**f** from squaraines **2a-c** respectively in excellent yields (entries 3-5). Separate samples of the zwitterionic adducts in $CDCl_3$ were monitored over time (>7 d) via ^1H NMR at room temperature and in each case there was <5% reversion to the parent squaraine. The adducts were also found to be permanently stable when stored as solid samples.



Scheme 1. Observed product **3a** for addition of P^nBu_3 to squaraine **2a**.

Table 1. Addition of phosphine derivatives to squaraine **2** to form adduct **3**.[a]



Entry	PL_3	R	Product	Yield (%)
1	P^nBu_3	Bu (**2b**)	**3b**	>99
2	P^nBu_3	Bn (**2c**)	**3c**	>99
3	$P(NMe_2)_3$	Me (**2a**)	**3d**	91
4	$P(NMe_2)_3$	Bu (**2b**)	**3e**	>99
5	$P(NMe_2)_3$	Bn (**2c**)	**3f**	86

[a] Conditions: **2** (0.1 mmol) and PL_3 (0.11 mmol) in room temperature $CHCl_3$ (0.1 M).

To evaluate the capacity of these stable dianiline squaraine-phosphorus(III) adducts to act as colorimetric metal sensors[12] we examined the chemodosimeric behavior of squaraine-phosphine complex **3b** by treating it with a series of transition metal catalysts commonly used in modern synthetic organic chemistry. Employing absorption spectroscopy to monitor the extent of dye regeneration, we observed rapid, partial reversion to the parent squaraine dye **2b** upon addition of both relatively electron rich and electron deficient Pd^{II}, Rh^{I}, Rh^{II}, Ir^{I}, Ag^{I}, Au^{III}, Cu^{I}, and Cu^{II} metal complexes. In contrast, addition of $NiCl_2$, $Ni(cod)_2$, $FeCl_3$, $TiCl_3$, or $TiCl_4$ did not lead to any noticeable amount of **2b**. The titration of $Au(PPh_3)Cl$ resulted in partial reversion back to **2b** after addition of 1.2 molar equivalents of Au^{I} (Figure 2a). Titration of complex **3b** with either $Pd(OAc)_2$ or $[Ir(cod)Cl]_2$ showed a weaker P^nBu_3 affinity as indicated by the greater stoichiometric amounts of transition metal complex needed to produce free **2b**. The reversion of **3b** with increasing concentration of $Pd(OAc)_2$ is further illustrated by the notable increase in absorbance depicted in Figure 2b. In contrast, $Rh(PPh_3)_3Cl$ was the least effective at promoting retroversion of **3b** to dye **2b**.

Interestingly, the extent of squaraine regeneration appears to correlate with the electronics and coordination capabilities of the complexes examined. For example, titration of the coordinatively unsaturated, square planar Wilkinson's catalyst proved less effective at phosphine abstraction. This observation is consistent if one considers the electron rich nature of Rh^{I} in combination with the unfavorable square pyramidal geometry the complex would have to adopt upon net loss of phosphine from adduct **3b**. In contrast, the electron deficient nature of $Pd(OAc)_2$ and the favorable square planar geometry upon phosphine coordination results in more efficient dye regeneration. The $[Ir(cod)Cl]_2$ complex bearing readily exchangeable neutral cyclooctadienyl ligands proved comparable to $Pd(OAc)_2$, while the relative electrophilicity of $Au(PPh_3)Cl$ results in the highest absorbance titration. It is important to note that even in the best case, full reversion back to **2b** was not observed, highlighting an important contrast with analogous squaraine-thiol adducts where the dye is more completely regenerated by Pd^{II} salts. However, an attractive feature of this squaraine-phosphine

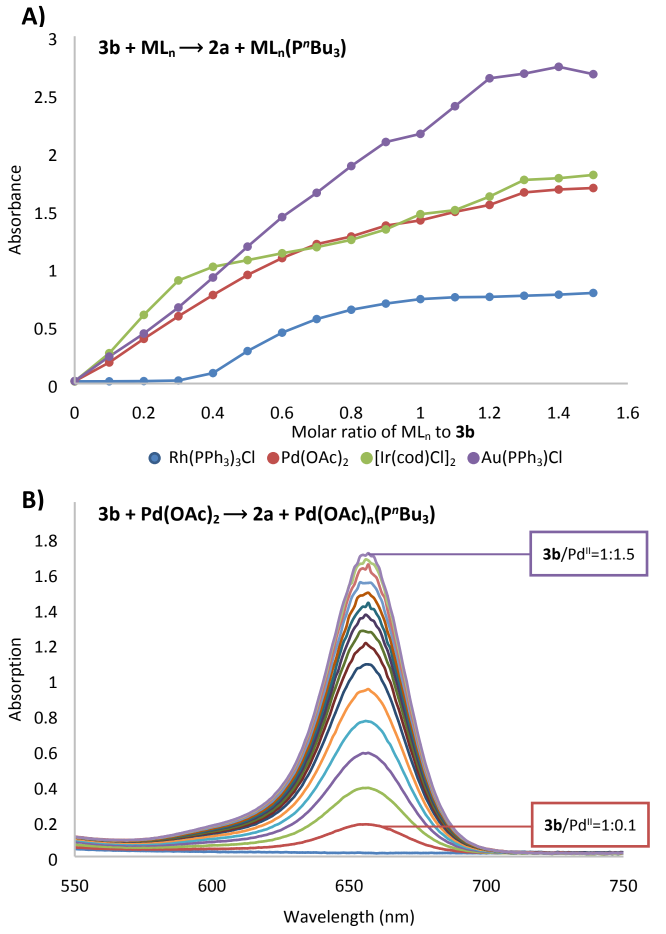


Figure 2. A) Titration plots showing partial regeneration of squaraine **2b** absorbance at 656 nm when separate solutions of **3b** (5×10^{-5} M in DMSO) were titrated with $Rh(PPh_3)_3Cl$, $Pd(OAc)_2$, $[Ir(cod)Cl]_2$, or $Au(PPh_3)Cl$. **B)** Appearance of squaraine **2b** absorption maxima band upon titration of adduct **3b** (3×10^{-5} M in DMSO) with increasing amounts of $Pd(OAc)_2$.

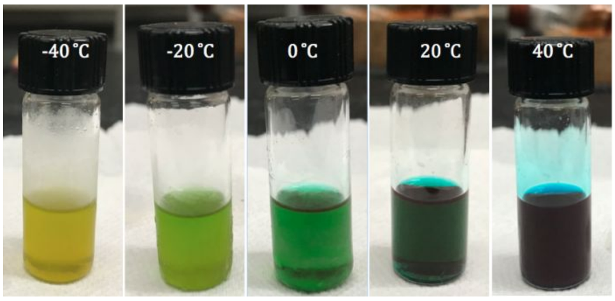


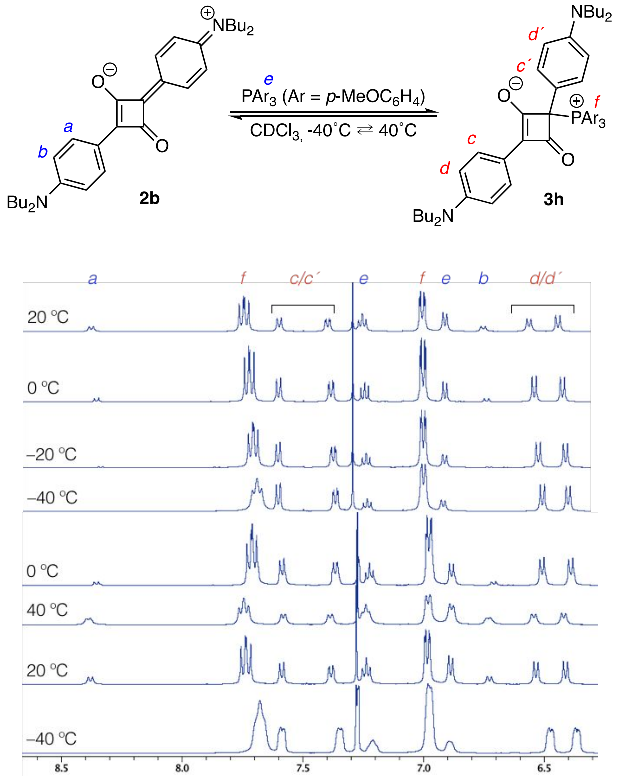
Figure 3. Photographs of a vial containing a binary mixture of $P(p\text{-}MeOC_6H_4)_3$ and **2a** in $CHCl_3$ at different temperatures. At 40 °C the solution exhibits a dark blue color indicating free squaraine, whereas cooling the mixture to –40 °C results in appearance of pale yellow adduct **3g**.

adduct is its potential to detect trace transition metal derivatives that are not sufficiently thiophilic for detection using a comparable squaraine-thiol adduct.

During our initial survey of squaraine reactivity with different phosphine agents, we observed that the addition of less nucleophilic $P(p\text{-}MeOC_6H_4)_3$ to squaraine **2a** at room temperature provided adduct **3g** in a comparatively low 51% yield. Intrigued by this comparatively low level of conversion to zwitterion **3g**, we examined the addition of $P(p\text{-}MeOC_6H_4)_3$ to squaraine **2a** in more detail. Speculating that the equilibrium between squaraine and phosphine adduct could be controlled thermally, we examined the relative ratio of **2a/3g** over a temperature range of –40 °C to 40 °C (Figure 3). As shown in Figure 2, the solution at 40 °C had the characteristic dark blue color of free **2a**, whereas cooling the solution incrementally to –40 °C indicated extensive conversion to the pale yellow-green adduct **3g**. Moreover, the thermochromic effect proved reversible as the dark blue color of the squaraine dye was restored upon warming the solution back to 40 °C.

In an effort to quantify this thermal cycling phenomenon, we used variable temperature ^1H NMR spectroscopy to monitor a single solution containing a binary mixture of $P(p\text{-}MeOC_6H_4)_3$ and the highly soluble squaraine **2b**. As illustrated in Figure 4, ^1H NMR spectra were acquired at different temperatures for the same sample, and revealed a dynamic ratio of **3h**:**2b** which depended strongly on the solution temperature. Upon introduction of $P(p\text{-}MeOC_6H_4)_3$ to **2b** at 20 °C, the ^1H NMR spectrum indicated a 2.3:1 ratio of **3h**:**2b**. As the temperature was *lowered*, the ratio of **3h**:**2b** *increased* to 7.7:1 at 0 °C, 97:3 at –20 °C, and at –40 °C there was no perceptible squaraine dye remaining. Warming the sample from –40 °C to 0 °C showed that the equilibrium was regenerated without observable degradation. Indeed, three further cycles of sample thermocycling between 40 °C to –40 °C showed no indication of sample decomposition. The increase in squaraine-phosphine adduct **3** formation at lower temperature is consistent with an entropy dominated Lewis acid-base equilibrium. It should be noted that the low temperature preference for **3** is opposite to that observed for squaraine-thiol adducts where dissociation is preferred as the temperature is decreased.[7a] As a molecular strategy, reversible squaraine thermochromism due to nucleophilic phosphorus(III) addition complements existing approaches that thermally control squaraine color by changing the degree of intermolecular packing within a squaraine-based polymer.[13]

In conclusion, the zwitterionic adducts resulting from rapid nucleophilic addition of phosphorus(III) reagents to dianiline squaraine dyes are a new class of molecular scaffolds that have the potential for further development into colorimetric sensors or thermochromic agents. While dependent on the overall nucleophilicity of the phosphorus reagent employed, the adducts from P^nBu_3 or $P(NMe_2)_3$ are characterized by a stable, highly crystalline structure with an intriguing "kite quadrilateral" core architecture. The resulting equilibrium between squaraine dye and phosphorus adduct serves as the basis for colorimetric chemodosimeter detection of transition metal complexes that have a high phosphorous (III) affinity. It is particularly noteworthy that the zwitterionic adducts formed using either P^nBu_3 or $P(NMe_2)_3$ are obtained in excellent yield and proved exceptionally stable at room temperature for prolonged time periods. The adduct **3b** acted as a colorimetric



Temperature (˚C)	3h:2b
20	2.3:1
0	7.7:1
–20	97:3
–40	>99:1
0	7.5:1
40	1.3:1
20	2.2:1
–40	>99:1

Figure 4. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$) for a single sample, showing how the equilibrium for reversible addition of P(*p*-$MeOC_6H_4)_3$ to squaraine dye **2b** to produce adduct **3h** changes with temperature. The sample temperature was cycled from 20 °C (top spectrum) through seven different temperatures to end up at –40 °C (bottom). The table provides the **3h**:**2b** ratio at each temperature, as determined by ^{1}H NMR peak integration.

chemodosimeter for detection of transition metal complexes that have high phosphorous (III) affinity. The ready availability of structurally diverse phosphorus(III) reagents provides ample opportunity for the fine tuning of desired sensing or thermochromic properties. Studies toward the development of this molecular framework in synthesis are also currently underway, and will be reported in due course.

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Conflicts of interest

There are no conflicts to declare.

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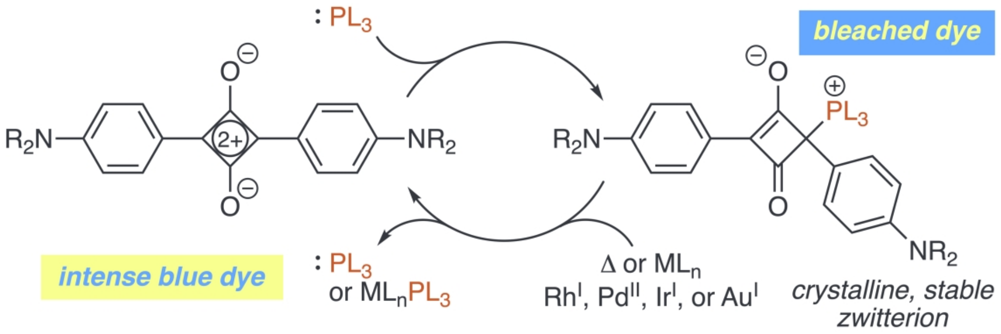

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