Palladium-Catalyzed Synthesis of *trans*-4-(*N,N*-Bis(2-pyridyl)amino)stilbene. A New Intrinsic Fluoroionophore for Transition Metal Ions
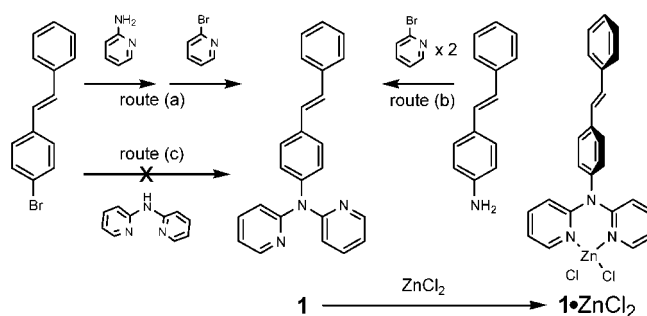
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ABSTRACT

The title compound (1) has been synthesized via sequential Pd-catalyzed amination reactions and investigated as an intrinsic fluoroionophore. The efficiency in the synthesis of 1 strongly depends on the order of couplings among the substrates. Compound 1 displays fluorescence quenching upon the binding of transition metal ions, where the binding-triggered conformational twisting and in turn the inhibition of internal charge transfer (ICT) play an important role.

Amine donor-π aromatic integrated systems generally exhibit characteristic electronic absorption and emission spectra associated with internal charge transfer (ICT).[1–3] Electronic or structural perturbations on the amine lone pair electrons influence the ICT properties and thus the electronic spectra, providing a useful signal transduction method for the design of chemosensors.[2,3] While manipulations on either the amine-based ionophores or the aromatic chromo-/fluorophores can independently lead to new intrinsic ion sensors, most efforts have been devoted to the latter with a prevailing usage of nitrogen-containing crown ethers as the ionophores over the past years.[2–4] We report herein the synthesis and character-
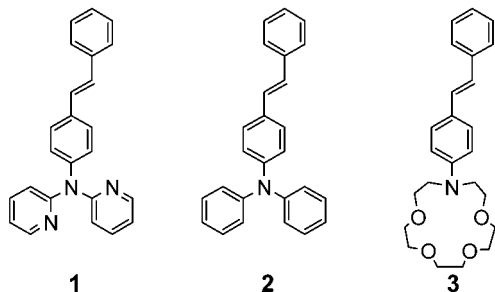
ization of a new and "uncrowned" intrinsic fluoroionophore **1**, which displays large fluorescence quenching in response to transition metal ions such as Ni^{2+}, Pb^{2+}, and Zn^{2+}. The cation binding ability of **1** is demonstrated by X-ray crystal structures and by comparison with that of reference compound **2**.

The design of the bis(2-pyridyl)amino group in **1** as an ionophore was based in part on the fact that 2,2′-bipyridine and bis(2-pyridylmethyl)amine (dipicolylamine) possess an excellent ability to coordinate transition metal ions and have

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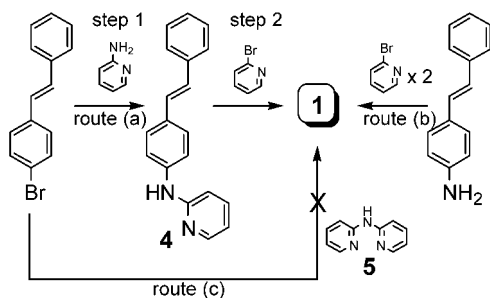
(4) For recent examples, see: (a) Lednev, I. K.; Hester, R. E.; Moore, J. N. *J. Am. Chem. Soc.* **1997**, *119*, 3456–3461. (b) Oguz, U.; Akkaya, E. U. *Tetrahedron Lett.* **1997**, *38*, 4509–4512. (c) Kollmannsberger, M.; Rurack, K.; Resch-Genger, U.; Daub, J. *J. Phys. Chem. A* **1998**, *102*, 10211–10220. (d) Collins, G. E.; Choi, L.-S.; Callahan, J. H. *J. Am. Chem. Soc.* **1998**, *120*, 1474–1478. (e) Crochet, P.; Malval, J.-P.; Lapouyade, R. *Chem. Commun.* **2000**, 289–290. (f) Rurack, K.; Rettig, W.; Resch-Genger, U. *Chem. Commun.* **2000**, 407–408. (g) Rurack, K.; Koval'chuck, A.; Bricks, J. L.; Slominskii, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 6205–6206.

demonstrated particular utility in the formation of chemo-sensors.[5,6] In addition, unlike the weakly fluorescent nature of the "crowned" counterpart **3**,[7] **1** is expected to display strong fluorescence even in polar solvents such as acetonitrile as a result of the "amino conjugation effect" in *N*-aryl substituted *trans*-4-aminostilbenes (e.g., **2**).[8] Highly fluorescent sensory molecules are favorable in performing the "on−off" type of fluorescence signaling.[3]

Although Pd-catalyzed aromatic amination reactions[9] have been widely employed in the synthesis of triarylamines,[10] examples are deficient in the synthesis of those bearing bis-(pyridyl)amino group(s). In this context, we have taken the synthesis of **1** as an example to search for efficient strategies for Pd-catalyzed preparation of *N,N*-bis(2-pyridyl)amino-arenes. As is outlined in Scheme 1, **1** could, in principle, be

Scheme 1. Synthetic Methodologies for **1**

prepared via three different synthetic routes (a, b, and c) of amination reactions starting with either *trans*-4-bromostilbene or *trans*-4-aminostilbene. In each route, the performance of five phosphine ligands, including three chelating phosphines,

BINAP, DPPF, and DPPP, and two nonchelating phosphines, P(t-Bu)$_3$ and P(o-tolyl)$_3$, along with Pd$_2$(dba)$_3$ as the catalysts were compared. The results are summarized in Table 1.

The relative efficiency of the phosphine ligands in preparing **1** via routes (a) and (b) is in the order of DPPF ≈ BINAP > DPPP ≫ P(t-Bu)$_3$ > P(o-tolyl)$_3$. This confirms the superior properties of chelating vs nonchelating phosphines in the Pd-catalyzed amination reactions of pyridine-containing substrates.[11,12] On the other hand, unlike routes (a) and (b), no reaction was observed for the method of route (c) under various conditions (Table 1).[13] Further mechanistic studies are required to gain a full understanding of this phenomenon.

The absorption and fluorescence spectra of **1** in acetonitrile are shown in Figure 1. Compound **1** is as expected strongly
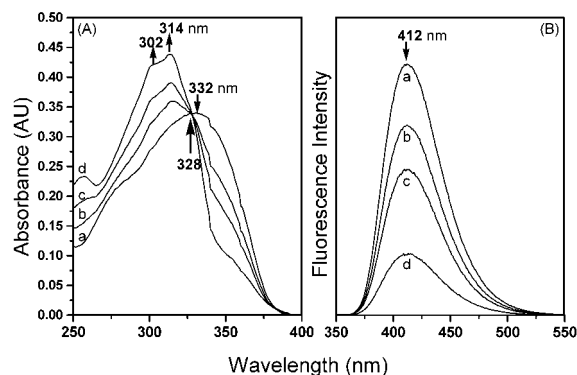

Figure 1. (A) Absorption and (B) fluorescence spectra of **1** in acetonitrile (10 μM, excitation at 330 nm) in the presence of (a) 0, (b) 0.3, (c) 0.5, and (d) 1.0 equiv of Ni(ClO$_4$)$_2$·6H$_2$O predissolved in MeCN (5 mM).

fluorescent in acetonitrile ($\phi_F = 0.57$).[14] Addition of Ni^{2+} to the solution of **1** results in fluorescence quenching and blue-shifted absorption spectra with enhanced vibrational structures. The isosbestic point (328 nm) found in a titration indicates the formation of 1:1 complexes. The binding constant, expressed as log K, determined by absorption spectroscopy[15] is estimated to be 5.1. Thus, the appearance of vibrational structures indicates the occurrence of binding-induced conformational restriction of **1**. Similar spectral

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(12) Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 7240−7241.

(13) Nonetheless, **1** can be formed, albeit in a low yield (<10%), when the reaction was carried out by premixing Pd$_2$(dba)$_3$ and (±)-BINAP before **5** and 4-bromostilbene were added.

(14) (a) Anthracene in hexane (($\phi_F = 0.27$)[12b] was used as the actinometer. (b) Birks, J. B. *Photophysics of Aromatic Molecules*; Wiley-InterScience: London, 1970.

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Table 1. Comparison of Yields of Different Routes for Palladium-Catalyzed Formation of **1**[a]

| | catalyst | | | | yield (%)[b] | | | |
| | | | | | route (a) | | | |
entry	Pd$_2$(dba)$_3$	phosphine[c]	time (h)	temp (°C)	step 1	step 2	route (b)[d]	route (c)[e]
1	2 mol %	4 mol % DPPF	22	80	86	90	41 (90)	nr (nr)
2	2 mol %	4 mol % BINAP	22	80	92	75 (91)	77 (89)	nr (nr)
3	2 mol %	4 mol % DPPP	22	80	52 (55)	34 (27)	(20)	nr (nr)
4	2 mol %	8 mol % P(t-Bu)$_3$	22	80	9	21	(3)	nr (nr)
5	2 mol %	8 mol % P(o-tolyl)$_3$	22	80	nr	5	(nr)	nr

[a] Solvent is anhydrous toluene, and base is sodium *tert*-butoxide. [b] Values in parentheses are under a double amount of catalyst. [c] For comparison, monodentate phosphines are double in amount to have the same concentration of the phosphine groups as bidentate phosphines. [d] Reaction time is 46 h. [e] No reaction (nr) was also observed under conditions with a different palladium source, (Pd(OAc)$_2$), a higher temperature (120 °C), and/or an extended reaction time (46 h).

responses also occurred for **1** in the presence of other transition metal ions tested in this work,[16] but the extent of fluorescence quenching (and log K) is relatively smaller, which is in the order of Ni^{2+} (5.1) > Pb^{2+} (4.9) > Zn^{2+} (4.8) > Y^{3+} (4.6) > Co^{2+} (4.4) > Cd^{2+} (3.2) (Figure 2). On
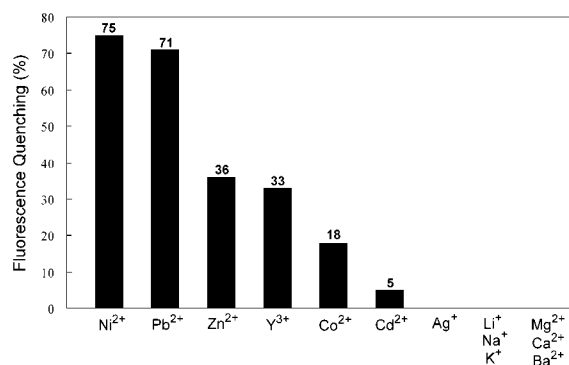

Figure 2. A comparison of the percent quenching of the fluorescence of **1** in acetonitrile (10 μM) in the presence of 1 equiv of metal ions (10 μM).

the other hand, Ag$^+$ and the alkali and alkaline earth metal ions Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, and Ba^{2+} result in negligible spectral variations.

Additional features in the fluorescence spectra of **1** in the titration of Zn^{2+} should be noted. As is shown in Figure 3A, a weak blue-shifted emission at 344 nm grows along with the decrease of emission at 412 nm, which parallels with the blue shifts of absorption spectra and can be attributed to the emission of the complex **1**·Zn^{2+}. Indeed, the 344-nm emission can be assigned to the locally excited (LE) state emission from the parent stilbene, which is weakly fluorescent in nature ($\phi_F \approx 0.05$).[17] Such an emission band was also found in the case of Y^{3+}, a diamagnetic metal ion.

Control experiments using the *N,N*-diphenyl analogue **2** ($\phi_F = 0.53$)[8] in place of **1** showed no spectral responses in

(16) Metal ions are from the corresponding perchlorate salts unless otherwise noted, including Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ba^{2+}, Pb^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Y^{3+}(nitrate), Ag$^+$, and Cd^{2+}(chloride).
(17) Görner, H.; Kuhn, H. J. *Adv. Photochem.* **1995**, *19*, 1−117.

both absorption and fluorescence spectra, confirming that the observed fluorescence quenching in **1** is a consequence of ion binding. The fluorescence of **2** in acetonitrile is also insensitive to strong acids such as trifluoroacetic acid and perchloric acid, consistent with the weak basicity (poor cation-coordination ability) of triarylamines. Nonetheless, a weak emission at 329 nm can be observed for **2** in the presence of an excess of strong acids, which can be attributed to the deconjugated stilbene LE emission (Figure 3B).
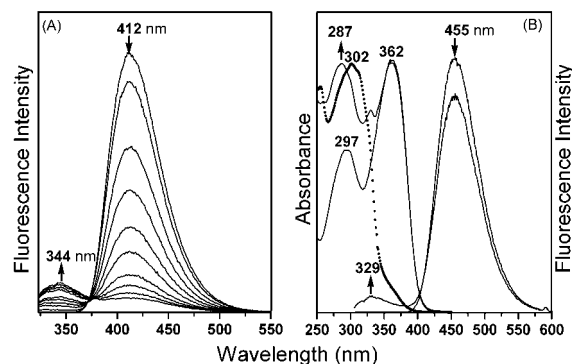

Figure 3. (A) Fluorescence titration spectra of **1** (10 μM) with Zn(ClO$_4$)$_2$·6H$_2$O (0−5 equiv) in acetonitrile (excitation at 313 nm) and (B) absorption and fluorescence spectra (excitation at 295 nm) of **2** (10 μM) in the absence and presence of 100 equiv of CF$_3$-COOH in acetonitrile (the dotted line is the absorption spectra of **1** in the presence of 5 equiv of Zn^{2+} for comparison).

Although a stilbene LE emission occurs in both **1**·Zn^{2+} and **2**·H$^+$, the spectral differences in both absorption and fluorescence (Figure 3) suggest a different nature of the LE states (vide infra). The requirement of bis(pyridine)s for effective ion binding can be further demonstrated by comparing the behavior of **1** with that of the monopyridine derivative **4** ($\phi_F = 0.24$) in acetonitrile. Among the six metal ions that induce spectral changes in **1** (Figure 2), only Pb^{2+} and Y^{3+} perturb the spectra of **4**; however, the extent of spectral perturbation is much smaller (e.g., less than 10% of fluorescence quenching under the same condition as **1** in Figure 2).

The results of X-ray crystal structures[18] of **1** and its Zn^{2+} complex **1·ZnCl₂** (Figure 4) not only further demonstrate
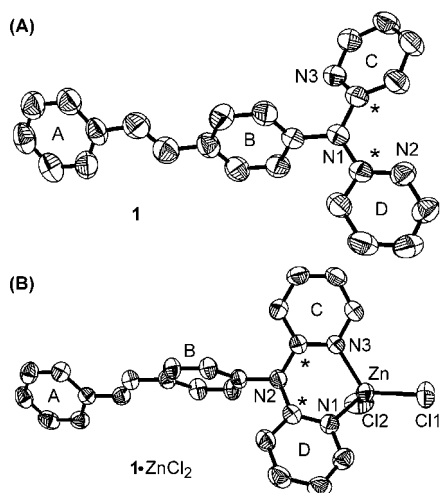

Figure 4. The single-crystal X-ray ORTEP (50% probability) structures of (A) **1** (represented by one of the two crystallographically independent but similar conformers) and (B) **1·ZnCl₂**.

the ion binding ability of **1** but also provide a clue to the origins of cation-induced fluorescence quenching. Cation coordination occurs as expected through both the pyridyl nitrogen atoms without the participation of the amino nitrogen. The sum of bond angles (θ) about the amino nitrogen atom are close to 360° in both **1** and **1·ZnCl₂** (359.2−359.9°), as is the case of **2**.[8] Compounds **1** and **1·ZnCl₂** also have similar dihedral angles (α) between the rings B and C and those between B and D (72.5−78.5°). On the other hand, the B ring of the stilbene group is almost perpendicular (87.6°) to the plane defined by the C*−N−C* fragment (Figure 4) of the bis(pyridyl)amino group in **1·ZnCl₂**, whereas the corresponding angle for **1** is much smaller (58.7−62.9°). Such a nearly orthogonal orbital alignment between the nitrogen lone pair and the stilbene π system in **1·ZnCl₂** is expected to largely reduce the ICT as well as the "amino conjugation"[8] properties and, in turn, to induce the spectral changes. Since Zn^{2+} itself is not a fluorescence quencher,[19,20] this might be the main source for

the fluorescence quenching of **1** upon the addition of Zn^{2+}. The different nature of the deconjugated stilbene LE states between **1·Zn²⁺** and **2·H⁺** based on the spectroscopic results (Figure 3) is consistent with this hypothesis, because the latter possesses a nontwisted origin of structural deconjuation. An inhibition of ICT resulting from a binding-triggered conformational twisting instead of the participation of the nitrogen lone pair in cation complexation[3] has also been proposed by Witulski et al. to account for the absorption and fluorescence behavior of N-9-anthrylaza-crown ethers upon the binding of alkali metal ions.[2] It is interesting to note that, despite the distinct structural differences in both the fluorophores and ionophores between **1** and 9-anthrylaza-crown ethers, their fluorescence sensing mechanisms are similar. The blue shifts of the absorption spectra of **1** in the presence of other transition metal ions shown in Figure 2 might also be a consequence of the binding-triggered twisting of the C−N bond, although the stilbene LE emission is absent in some cases. The paramagnetic nature (e.g., Ni^{2+} and Co^{2+}) and heavy-atom effect (e.g., Pb^{2+}) might contribute to the quenching of the CT as well as the stilbene LE fluorescence.[19]

In conclusion, our studies on **1** have shown that the N,N-bis(2-pyridyl)amino group in a triarylamine is a potential bidentate ionophore for transition metal ions. Such a property might be also related to the route-dependent formation of N,N-bis(2-pyridyl)aminoarenes via Pd-catalyzed amination reactions. In addition, the binding-triggered conformational twisting appears to play a key role in accounting for the metal ion-induced ICT inhibition and spectral changes in **1**. Further studies toward a better understanding of these aspects are in progress.

Supporting Information Available: Experimental procedures and characterization data for compounds **1**, **1·ZnCl₂**, and **4** and tables and figures of detailed crystallographic data of **1** and **1·ZnCl₂**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Data for the X-ray structure were recorded using a Siemens SMART/CCD diffractometer at 295 ± 2 K. There are two independent but similar conformations for **1** in the crystals, whereas the crystal of **1·ZnCl₂** consists of molecules with the same conformation. For detailed crystallographic data, see Supporting Information.

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(20) Indeed, the **1·ZnCl₂** crystals are fluorescent.