1,3-Dipolar cycloaddition of alkynes to azides. Construction of operationally functional metal responsive fluorophores†

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The copper catalyzed 1,3-dipolar cycloaddition of 4-butoxyphenylazide with 2-, 3- or 4-ethynylpyridine furnishes 1,4-diaryltriazoles, which display turn-on fluorescence upon addition of metal cations.

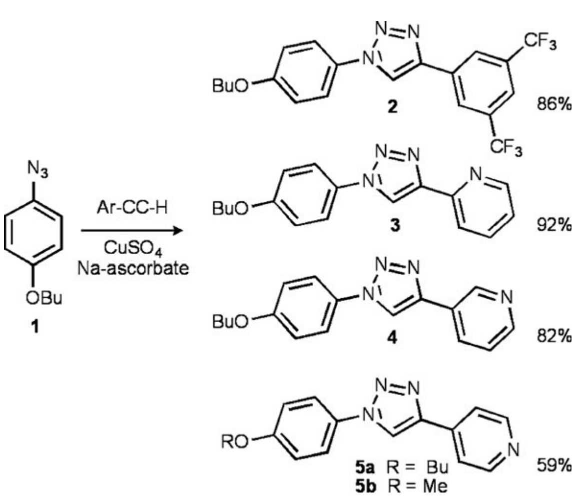
The uncatalyzed 1,3-dipolar cycloaddition reaction of azides and alkynes to form triazoles was described in 1965 by Szeimies *et al.*[1] It was retooled as "Click Reaction" by Sharpless and coworkers using copper catalysis to regioselectively generate 1,4-linked triazoles.[2] The copper catalyzed azide–alkyne reaction generated efficient[3] femtomolar enzyme inhibitors, adhesives for copper,[4] dendrimers and polymers to name just a few examples.[5–7] However, the 1,2,3-triazole unit, being aromatic, should be useful in connecting aromatic or unsaturated modules to give larger conjugated systems. We and others have exploited the 1,3-dipolar cycloaddition to make conjugated polymers,[8,9] while Zhou and Fahrni demonstrated that transformation of an alkyne into a triazole renders a coumarin dye fluorescent.[10] While these applications are interesting, simple 1,4-diaryltriazoles and their chromogenic properties are surprisingly under-examined.[11] We report herein the copper catalyzed ligation of different pyridylalkynes with 4-butoxyphenylazide and the metallochromic properties of the formed cycloadducts. A triazole can work as part of a chelating ligand in these simple dyes.

We have reacted **1** with 3,5-bistrifluoromethylphenylacetylene, 2-, 3- and 4-ethynylpyridine, utilizing copper sulfate in the presence of sodium ascorbate[12] in a water–THF–*tert*-butanol mixture to obtain the cycloadducts **2–5** (Scheme 1) in yields that range from 59 to 92% as beige to orange microcrystalline powders. According to NMR spectroscopy, only one regioisomer had formed, in each case the 1,4-triazole. To corroborate this assignment we obtained a crystalline specimen of **3** and performed an X-ray structure analysis. Fig. 1 shows the ORTEP of **3**. The bond lengths and bond angles are in excellent agreement with the expected values, the 1,4-connection of the triazole secured.

The cycloadducts **2–5a** are soluble in chloroform, dichloromethane and to a lesser extent in THF, ethyl ether and methanol or hexanes. Their solutions are colorless. While we were surprised that these materials were only weakly or non-fluorescent, the addition of either acid or metal salts led to a fluorescence increase in **2**, **3** and **5a** but not in **4**. Table 1 displays the pertinent photophysical properties of **2–5a**.

We exposed **5a** towards different metal triflates in dichloromethane and found that lithium, sodium and potassium ions led to a small decrease in emission intensity, while silver, magnesium, barium and calcium as their triflates led to a moderate increase in emission intensity. Zinc, manganese and copper triflates induced a large increase in the emissive intensity of **5a** (Fig. 2). Very similar results are obtained when the adduct **3** was exposed to different metal triflates (Fig. 3), however, the emission was somewhat blue-shifted and the enhancement factor was larger for manganese, zinc and barium triflates. Commensurate with the metal-induced increase of the fluorescence intensity, a significant red-shift (Fig. 3 bottom) was observed in absorption both for **3** and for **5a** (not shown).

To test if either the triazole or the pyridine or both units would coordinate to metal cations, we examined the adduct **2** which does not display pyridine but only the triazole motif. In this case, we observe an increase in the fluorescence but only for manganese, zinc, barium, copper and silver (Fig. 4). The emission wavelength is significantly blue shifted from that of **3** or **5a**. The lighter alkaline earth cations calcium and magnesium do not show any response, neither do the alkali metal



Scheme 1 Synthesis of the chromophoric triazoles **2–5**.

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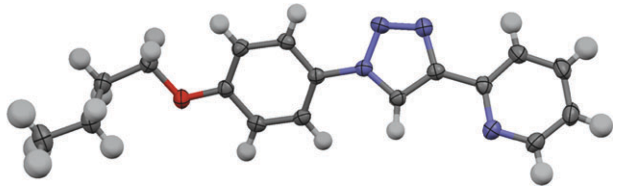


Fig. 1 ORTEP of **3**.

Table 1 Photophysical properties of **2–5**

	3	**4**	**5a**	**2**
Quantum yield	<0.01	—	<0.01	—
$\lambda_{\text{max abs}}$/nm	287	265	269	269
ε/l mol^{-1} cm^{-1}	18 600	21 700	27 700	25 300
$\lambda_{\text{max em}}$/nm	484	—	486	—
Stokes shift/cm^{-1}	14 200	—	16 600	—
	3 + Zn	**4** + Zn	**5** + Zn	**2** + Zn
Quantum yield	0.07	<0.01	0.14	0.05
$\lambda_{\text{max abs}}$/nm	326	269	269/317	254
$\lambda_{\text{max em}}$/nm	498	—	496	412
Stokes shift/cm^{-1}	10 600	—	17 000 11 400	15 100

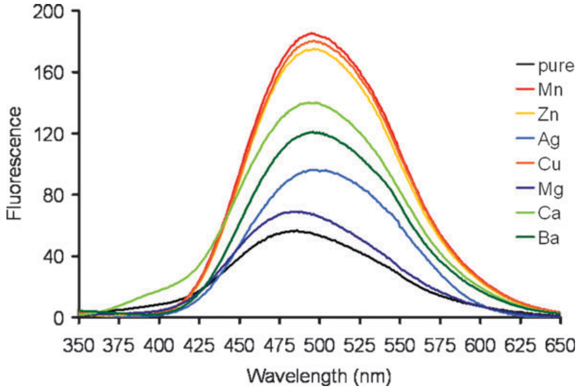


Fig. 2 Exposure of **5a** towards different metal triflates in dichloromethane solution.

cations. In absorption we only observe a small change (see ESI†). In the case of the *meta*-pyridine adduct **4**, the fluorescence is weak and does not appreciably increase upon the addition of metal salts.

Fig. 5 displays the titration of **3** with trifluoroacetic acid (TFA). The titration of **5** with TFA looks virtually identical to that of **3**, while the spectrophotometric titrations of **4** and **2** are similar to each other but display different features from those of **3** and **5a** (Fig. 6). One should note that the titration of **3** with TFA produces changes in the absorption spectrum that are very similar to those observed for the addition of metal cations. However, upon addition of a large excess of TFA we observed the appearance of a second, blue-shifted absorption band, which we attribute to a species in which both the pyridine and the triazole are protonated. What is the reason for these dramatic differences between **3** and **5a** and **2** and **4**, and why are none of the adducts **2–4**, **5a** strongly fluorescent in the absence of divalent cations? We note that the Stokes shifts for the non-metalated adducts are very large (**3**, **5a**) suggesting that there is a significant structural reorganization in the excited state.

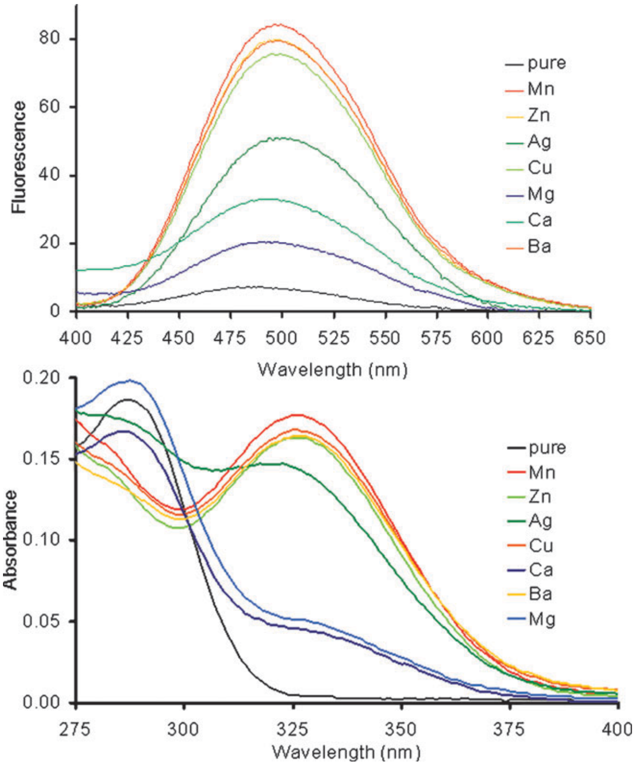


Fig. 3 Exposure of **3** towards different metal triflates in dichloromethane solution in emission (top) and absorption (bottom).

The lack of fluorescence in **2–5** is difficult to explain, as there is no easily visible mechanism for fluorescence quenching. The most probable reason would be charge transfer, leading to a charge separated excited state that would undergo radiationless deactivation. Alternatively, the excited state could be coupled to a vibrationally excited S_0 state, experiencing effective quenching. An interesting difference between **5a** and **5b**[11] is that **5a** does not show *any* appreciable fluorescence at short wavelengths before addition of a metal salt, in contrast to **5b**, which purportedly emits at 360 nm.[11] It is not clear what is the reason for the variation in behavior of **5a** and **5b**.

Resonance structures such as **I**, which are only accessible for **3** and **5a** but not for **2** or **4**, may be responsible for the

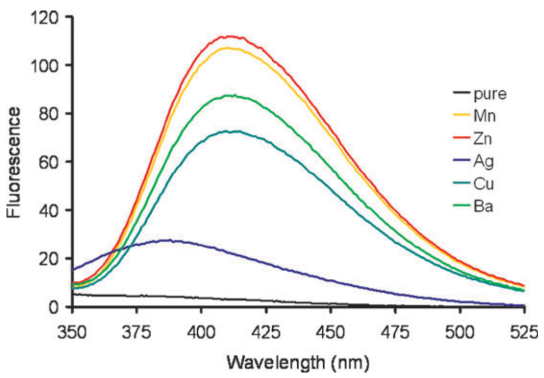


Fig. 4 Exposure of **2** towards different metal triflates in dichloromethane solution.

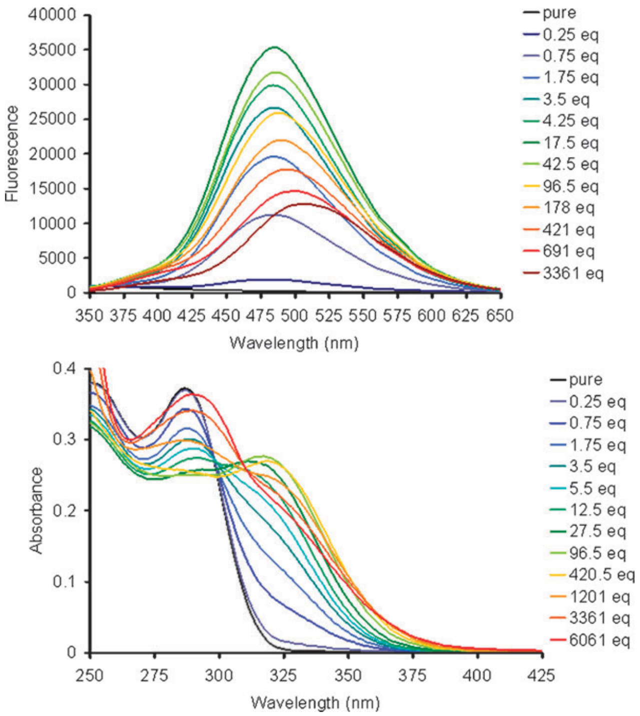


Fig. 5 Titration of **3** with TFA in emission (top) and absorption (bottom).

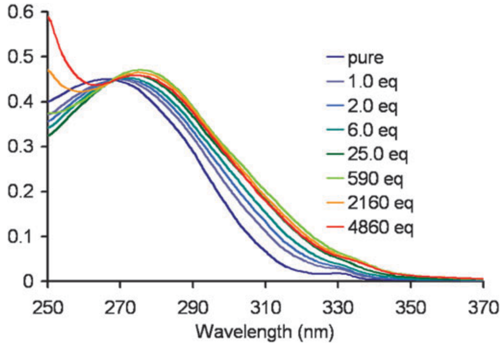
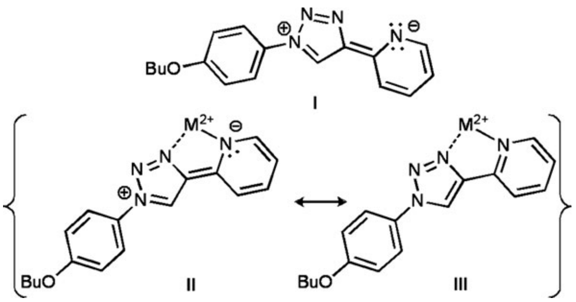


Fig. 6 Titration of **4** with TFA in absorption.

differentiation in metallochromic behavior. If the resonance structure **I** already contributes in the ground state, its contribution would be expected to be even higher in the excited state, leading to an enhanced excited state *basicity* of **3** and **5a**. Indeed, examining Fig. 5, one can qualitatively see that *changes in emission precede those in absorption* upon addition of TFA to a solution of **3** or **5a** (ESI†). The 2- or 4-pyridine group is important. There is a large bathochromic shift upon addition of metals, both in **3** and in **5a** but not in **2** or **4**, suggesting that the metal ions are primarily bound to the pyridine unit as shown in **II** and **III** for **3**.

However, in the *absence* of the pyridine groups the triazole in **2** can work as a metal ligating entity, but the metal cation induced changes in absorption are small.



In conclusion, we demonstrated that the 1,3-diploar cycloadducts **2**, **3** and **5** are metallochromic. While in the case of **2** the triazole nitrogen must be the coordinating site, we conclude from our studies of **3** and **5** that in these the pyridine units are the primary sites of complexation. We deem the structural motif of **3** particularly attractive, as it represents a modification of the bipyridine units often employed as metal coordinating sites. The surprising photophysics of **3** and **5a** can be best explained by assuming that their electron density is significantly influenced by the resonance structures **I** and **II**, not accessible for **2** or **4**.

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