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Cyanide Detection Using a Triazolopyridinium Salt

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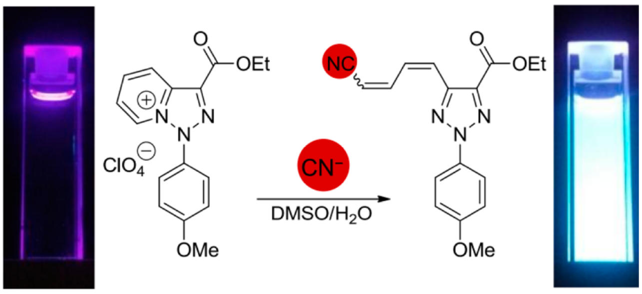
ABSTRACT



A triazolopyridinium salt chemodosimeter has been developed that displays a 60-fold enhancement in fluorescence upon reaction with cyanide. The novel, fast, selective and sensitive reaction-based indicator relies on the pseudopericyclic ring opening of the bridgehead nitrogen-containing detector.

Despite its toxicity,[1,2] cyanide (CN^-) is still widely used in mining, metallurgy, and various chemical industries, inevitably resulting in the pollution of water supplies.[3,4] As a result, considerable attention has been devoted in recent years to the development of CN^- sensors.[5] Traditionally, hydrogen bonding or supramolecular interactions have been used in the detection of low concentrations of cyanide in solution.[6−8] These approaches, however, usually result in poor selectivity over other common anions.[9] The burgeoning field of reaction-based indicators has made progress in this area because of the unique reactivity of CN^- toward a variety of organic functional groups[10,11] including C=O,[9,11b,11h,11j] C=N,[11f,g] and C=C.[11k,i] Other advantages of this approach include the irreversible formation of chemical bonds that can provide chemodosimetric information[10c] and lead to remediation as well as detection.[9b] There is an ever-present need to develop new reaction-based CN^- sensors, as these can help overcome lingering obstacles in its detection,[10] such as selectivity, sensitivity, response times, sensor stability, reaction conditions, etc.[11] Here we report a

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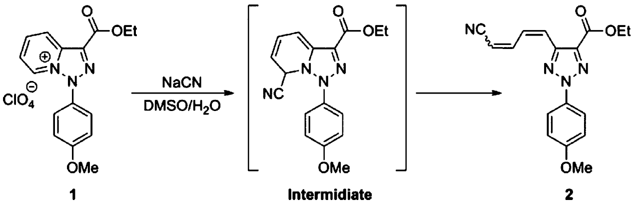
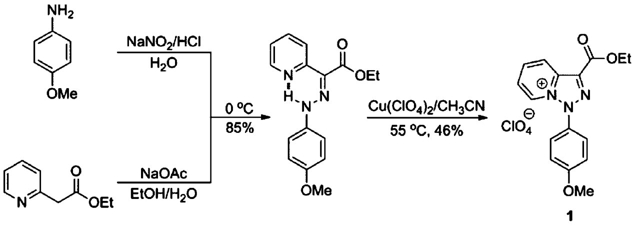
new fluorescence turn-on chemodosimeter that exhibits fast, sensitive, and selective detection of CN^- under mild conditions. The reaction-based system relies on a well established and studied ring-opening reaction of bridgehead nitrogen-containing azolopyridinium salts (Scheme 1).[12]

Scheme 1. Reaction-Based Detection of CN^- Using the Triazolopyridinium Salt **1**



We have recently reported the synthesis and photophysical properties of water-soluble triazolopyridinium salts[13] derived from our hydrazone-based switches.[14] We hypothesized that the ring-opening reaction in these systems would lead to conjugated triazole-based derivatives that can potentially be emissive[15] and, hence, used in CN^- sensing. Our choice of a sensor was based on how the emission properties of the newly formed cyano-containing triazole derivative might be best distinguished from the emission properties of the starting material. The triazolopyridinium salts emit blue light upon excitation,[13] and we anticipated that the extended π-conjugation in the cyano adduct will lead to a bathochromic shift. A recent report showed that having a *p*-OMe substituted phenyl ring at the N-2 position of the triazole ring can lead to enhanced emission.[15a] On the other hand, and based on our previous results,[13] this substituent was expected to quench the emission of the triazolopyridinium dye through charge transfer. Hence, we decided to incorporate a *p*-OMe substituent in our design (Scheme 2) to enhance the change in emission upon reaction with CN^-. Moreover, we added an ethyl ester group at position C-5 to increase the conjugation in the system. This rational design has led us to compound **1**, which was synthesized in a few simple steps (Scheme 2): *p*-Anisidine was treated with conc. HCl in H_2O and then with $NaNO_2$ at 0 °C to give the *p*-anisidenediazonium chloride salt. A solution of ethyl−2-(pyridin-2-yl)acetate that was pretreated with sodium acetate was then added to this solution to afford the hydrazone precursor. The latter was subsequently oxidized with 4 equiv of $Cu(ClO_4)_2 \cdot 6H_2O$ in CH_3CN at 55 °C to give **1** as an off-white solid in 46% yield. Both **1** and the hydrazone precursor were characterized using NMR spectroscopy and ESI-MS (Supporting Information).

Scheme 2. Synthetic Route towards the Triazolopyridinium Salt **1**



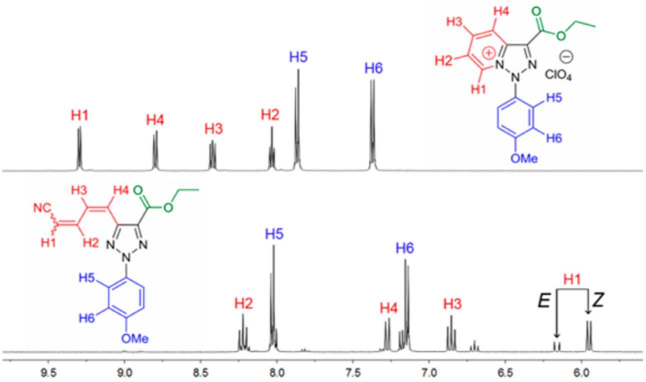


Figure 1. ^1H NMR spectra (DMSO-d_6 at 294 K) of (a) **1** and (b) a crude mixture of *E*/*Z* isomers of **2**, obtained after adding 1 equiv of NaCN to **1**.

^1H NMR spectroscopy studies in DMSO-d_6 suggest that the ring-opening reaction reported in the literature for analogous azolopyridinium salts[12] occurs rapidly with **1** as well. The ^1H NMR spectrum changes immediately upon the addition of 1 equiv of NaCN to **1** (Figure 1). The appearance of upfield alkene signals implies the formation of **2** (Scheme 1), which equilibrates over time to give an 85:15 mixture of the *Z* and *E* isomers, respectively. This assignment was inferred from the coupling constants of the signals at 5.94 and 6.17 ppm, $J = 10.9$ and 16.1 Hz, respectively (Supporting Information, Figure S4). Compound **2** was isolated as an inseparable mixture of *Z* and *E* isomers and characterized by NMR spectroscopy and ESI-MS (Supporting Information).

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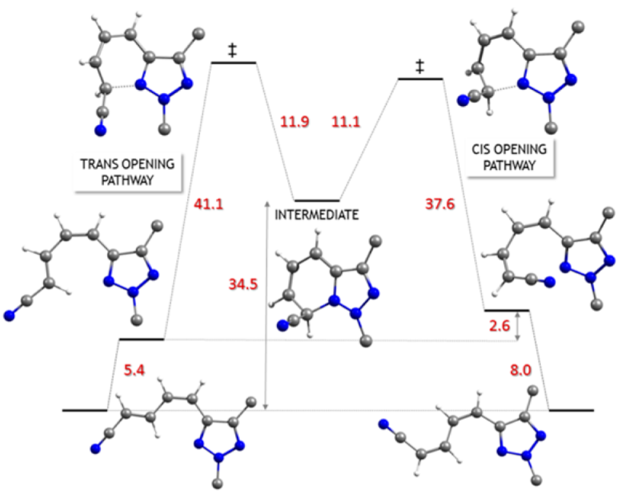
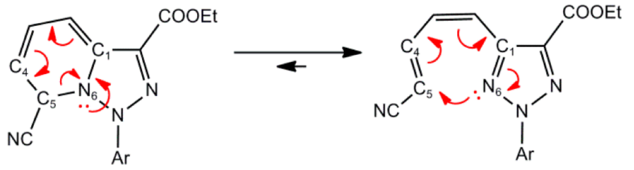


Figure 2. Free energy landscape calculated (DFT/B3LYP-D3/6-311++G**)(DMSO) for opening of cyanotriazole intermediate via pseudopericyclic pathways to give *Z*- and *E*-products. Values of ΔG are in kcal·mol^{-1}. The ester and aryl groups were removed for the sake of clarity. See Supporting Information Figure S19 for full structures.

To better understand the energetics and stereochemistry of the ring-opening reaction (Scheme 1) DFT calculations (B3LYP-D3/6311++G**) were carried out using a DMSO solvent model.[16,17] The energetics are summarized in Figure 2. The ring opening is thermodynamically favorable by 34.5 kcal/mol for both *Z* and *E* isomers. However, opening to give the *Z* isomer is kinetically favored by 0.8 kcal·mol^{-1} with very large barriers for reclosure, consistent with the observed *Z*/*E* isomer ratio of 85:15 being kinetically controlled. Application of NBO techniques (Supporting Information, Figures S28−S31 and Table S1) to the transition state illustrates that the reaction follows a pseudopericyclic pathway[18] (Scheme 3), and not a disrotatory electrocyclic ring-opening reaction as previously suggested.[12a,b] In the ring-closing direction, population of the C_4-C_5 π^* orbital occurs by depletion of electron density in the original N_6 lone pair (not the C_1-N_6 π orbital) to give the new C_5-N_6 σ-bond. The C_1-N_6 π orbital evolves into the new N_6 lone pair. Thus the transformation includes eight electrons in a cyclic orbital array and takes place in concert because it is not subject to the Woodward−Hoffmann rules. Full details of this analysis are provided in the Supporting Information.

The photophysical properties of **1** and **2** were studied in aqueous DMSO (Figure 3a). The emission intensity of **1** is much lower than that for the previously reported derivative that lacks the *p*-OMe substituent.[13] As expected this group quenches the emission of **1** by enhancing the charge transfer from the phenyl ring to the triazolopyridinium subunit. The addition of 2 equiv of NaCN to **1** affords **2**, which upon excitation at 330 nm yields a 60-fold increase in fluorescence relative to **1** at λ_{max} = 504 nm (Figure 3a). Compound **2** has a broad emission ranging from 400−620 nm and a quantum yield of 0.45 ± 0.02, which is 15 times higher than that of **1** (0.03 ± 0.02). An accurate estimation of the Stokes shift was precluded by the absorption of DMSO below 350 nm. However, when the spectroscopic analysis was carried out in acetonitrile a “mega” (larger than 100 nm)[19] Stokes shift of 177 nm (56,500 cm^{-1}) (Supporting Information, Figure S10) was measured. Such large Stokes shifts and broad emission profiles have been reported previously for other triazole-based systems.[15a]

Scheme 3. Pseudopericyclic Pathway for Ring Opening/Closing



Compound **1** exhibits a turn-on response upon the addition of NaCN, enabling its visual detection upon excitation in the UV range (Figure 3b). Because of the unique fluorescent properties of **2**, a limit of detection (LOD) of 0.2 ppm (8.46 μM) in DMSO/H_2O (99:1) was determined for CN^- (Supporting Information, Figure S7), which is at the level set by the United States Environmental Protection Agency.[3] Moreover, the reaction between **1** and

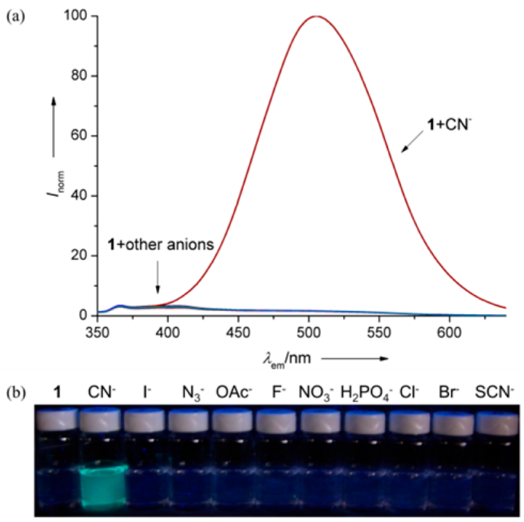


Figure 3. (a) Fluorescence intensity spectra of **1** (2.5×10^{-5} M in DMSO/H_2O (99:1)) recorded after the addition of 2 equiv of the sodium salts of various anions (**1** alone, CN^-, I^-, N_3^-, AcO^-, F^-, NO_3^-, $H_2PO_4^-$, Cl^-, Br^-, and SCN^-). (b) Fluorescence change of **1** observed upon excitation at 365 nm after the addition of various anions (conditions identical to those described above).

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2 equiv of CN^- occurs almost instantaneously (Figure S11). These results attest to the reactivity of **1** and show how it can be quickly used in the detection of low quantities of CN^-. To evaluate the selectivity of sensor **1**, 2 equiv of various potentially competing anions (studied as their corresponding sodium salts) including I^-, N_3^-, AcO^-, F^-, NO_3^-, $H_2PO_4^-$, Cl^-, Br^-, and SCN^- were each added to DMSO/H_2O (99:1) solutions of **1**. The fluorescent properties of the resulting solutions remained unaffected for days (Figure 3a and b and Supporting Information Figure S8) demonstrating the high selectivity of the ring-opening reaction toward cyanide.[22]

In conclusion we have shown that the triazolopyridinium salt **1** is an efficient reaction-based sensor for CN^-. A selective 60-fold increase in emission is observed upon the addition of NaCN to **1**, enabling the quick detection of 0.2 ppm of the analyte. The characterization of the fluorescent cyano adduct **2** confirmed that the ring-opening reaction of the bridgehead nitrogen is responsible for the observed sensing capability of **1**. This process was further elucidated using DFT/NBO calculations, which showed that it most likely proceeds via a pseudopericyclic pathway. We are currently working on further optimizing the conditions of this reaction in order to employ it in real-world applications.

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Supporting Information Available. Experimental procedures, NMR spectra, emission spectra, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.