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Simple Hydrazone Building Blocks for Complicated Functional Materials

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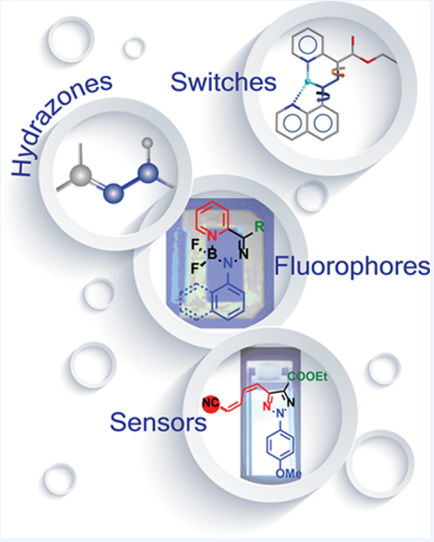
CONSPECTUS: The ability to selectively and effectively control various molecular processes via specific stimuli is a hallmark of the complexity of biological systems. The development of synthetic structures that can mimic such processes, even on the fundamental level, is one of the main goals of supramolecular chemistry. Having this in mind, there has been a foray of research in the past two decades aimed at developing molecular architectures, whose properties can be modulated using external inputs. In most cases, reversible conformational, configurational, or translational motions, as well as bond formation or cleavage reactions have been used in such modulations, which are usually initiated using inputs including, irradiation, metalation, or changes in pH. This research activity has led to the development of a diverse array of impressive adaptive systems that have been used in showcasing the potential of molecular switches and machines. That being said, there are still numerous obstacles to be tackled in the field, ranging from difficulties in getting molecular switches to communicate and work together to complications in integrating and interfacing them with surfaces and bulk materials. Addressing these challenges will necessitate the development of creative new approaches in the field, the improvement of the currently available materials, and the discovery of new molecular switches.



This Account will describe how our quest to design new molecular switches has led us to the development of structurally simple systems that can be used for complicated functions. Our focus on the modular and tunable hydrazone functional group was instigated by the desire to simplify the structure and design of molecular switches in order to circumvent multistep synthesis. We hypothesized that by avoiding this synthetic bottleneck, which is one of the factors that hinder fast progress in the field, we can expedite the development and deployment of our adaptive materials.

It should be noted though that designing structurally simple switches cannot be an end goal by itself! Therefore, we showed that our molecules can be used in applications that are beyond a simple molecular switching event (i.e., the control of the photophysical properties of liquid crystals and multistep switching cascades). While focusing on these switches, we discovered that the hydrazones can be easily transformed, using straightforward one-step reactions, into visible light activated azo switches, and two different families of fluorophores that can be used in sensing applications. These findings demonstrate that our approach of developing simple systems for sophisticated functions is not limited to the field of molecular switches and machines but can also encompass other adaptive materials.

INTRODUCTION

Research in the area of stimuli responsive molecules[1] attracts a great deal of interest because such systems can potentially lead to smart materials that can be used in applications ranging from nanotechnology to pharmacology. Common switchable molecular motifs include azobenzenes,[2] diarylethenes,[3] spiropyrans,[4] and catenanes and rotaxanes,[5] just to name a few. These molecules undergo structural changes in response to specific stimuli that include light, electrochemical potential, and chemical input, which can be used in modulating not only their properties but also of those of their environment. The research in this area yielded numerous molecular architectures that work as muscles, ratchets, and walkers, among others.[1] However, and as highlighted in a recent review by Stoddart et al.,[5a] numerous challenges in the field (e.g., difficulties in interfacing and integrating switches with bulk materials, controlling the directionality of their motion, and getting them to work together) preclude us from mass producing real molecular machines, i.e., materials that can drive systems out of equilibrium, and produce work. With this in mind, we set out to develop a family of easily accessible molecular switches with the hope that the simplification of the molecular framework will facilitate and expedite the understanding of the basic science required for the development of molecular machines.

The choice of the hydrazone framework as the basis of our molecular switches stems from its modularity, straightforward synthesis, functional diversity, and stability.[6] These properties

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have enabled the utilization of hydrazones in various fields, ranging from medicinal to supramolecular chemistry. What makes the hydrazone group especially suitable for switching applications is its incorporation of an imine bond that can undergo stimuli responsive E/Z isomerization (i.e., configurational switching). The light induced activation of this process was already known in the literature[7] when we started working with these molecules. However, its chemical modulation was still uncharted until we showed that it can be accomplished with pH.[8] This dual control over E/Z isomerization is unique to the hydrazone functional group and will be important in our quest to expand the types of intricate motions that we can modulate externally.

In this Account, we will describe our recent progress in employing the hydrazone functional group in the development of adaptive materials. After a brief overview of hydrazone-based light activated switches, we will focus on chemically controllable systems. We will first discuss the pH induced configurational switching of our systems and then delve into the importance of the intramolecular H-bond in defining the isomerization mechanism. Next, we will show how a cholesteryl-containing hydrazone switch can be used in manipulating the photophysical properties of a bulk liquid crystal. We will also discuss the development of a hydrazone that can be induced to undergo both conformational and configurational switching. We will then shift gears and show how metal coordination can be used in a multistep switching cascade that involves coordination coupled deprotonation (CCD) and proton relay. Finally, we will discuss how the hydrazones can be converted in a single step (i.e., oxidative cyclization or coordination with BF_2) into two families of light emitting materials, visible-light activated azo switches and chemical sensors.

LIGHT INDUCED CONFIGURATIONAL SWITCHING

It has long been known that irradiation of hydrazones can induce $E \rightarrow Z$ isomerization around the imine C=N bond;[7] however, the obtained Z isomer is usually thermodynamically unstable and thus short-lived (Figure 1a). Using 1,2,3-tricarbonyl-2-arylhydrazones (TCAHs) derived from β-diketones and β-ketoesters, Courtot et al. showed[9] that intramolecular hydrogen bonding can kinetically stabilize the Z isomers formed by irradiation (Figure 1b). Moreover, they showed that a different light source can be used to drive the $Z \rightarrow E$ isomerization process, thus opening the way for using these systems as light activated molecular switches.[10] Lehn et al. later showed that pyridyl phenyl and bispyridyl hydrazones could also be converted from the E to the Z isomers using light.[11] The intramolecular H-bond in the Z configuration "locks" the switch in place, only to be released back to the E form by heating at 45 °C with 20 mol % trifluoroacetic acid (TFA) in methanol for 2 h (Figure 1c).

pH INDUCED CONFIGURATIONAL SWITCHING

It has been long established that TCAHs can undergo acid or base catalyzed equilibration that can change their E and Z isomer ratio in solution (Figure 2).[12] We hypothesized that replacing the 1,2,3-tricarbonyl rotor of TCAH with 2-pyridyl ethyl acetate will convert the hydrazones into efficient switches that can be toggled from one configuration to another using acid and base (Figure 3).[8] The pyridyl-containing switch can be easily synthesized using the Japp–Klingemann reaction

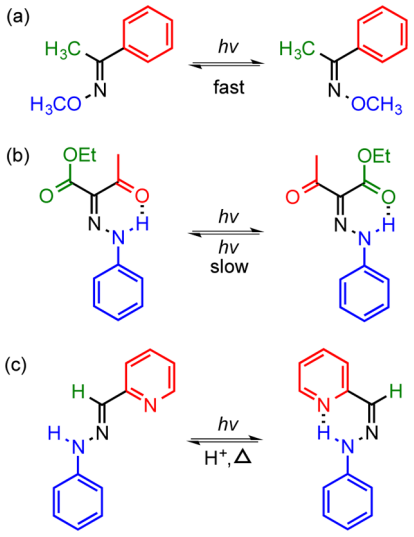

Figure 1. Isomerization in hydrazone-based switches. (a) The $E \rightarrow Z$ isomerization in imines occurs upon irradiation with UV light; however, the system quickly reverts to the thermodynamically stable E isomer. (b) After irradiation TCAHs are able to stabilize the Z configuration via intramolecular hydrogen bonds. (c) Pyridyl phenyl hydrazones can also form stable Z isomers after irradiation, which yield the E configuration after the addition of acid and heating.

(Scheme 1). The existence of an intramolecular H-bond in these systems can be confirmed by the diagnostic NH proton signal that resonates between 11 and 15 ppm, depending whether it originates from the E or Z isomers. These signals are convenient probes for the analysis of thermodynamic stability of the isomers and studying their interconversion kinetics. The strong H-bond between the pyridyl ring and hydrazone NH proton yields high E/Z ratios for **1** and **2** (Figure 3) in solution (93:7 and 97:3, respectively). Protonation of these compounds with TFA completely converts their E forms into the protonated Z-H^+ species. Subsequent addition of base, triethylamine (Et_3N), or passing the solution over potassium carbonate (K_2CO_3) affords the thermodynamically less stable **1**-Z and **2**-Z species that isomerize with time to the corresponding E configurations, thus completing a switching cycle. Unlike TCAHs, **1** and **2** fully convert between the E and Z isomers with the addition of acid and base. Clearly the replacement of one of the carbonyl groups with a pyridyl one converted the sluggish equilibration process (Figure 2) into an effective switching cycle. The difference in the H-bonding capability of the pyridyl group and the ester moiety in **1** and **2** plays a crucial role in optimizing the isomerization process. We found[13] that the secondary H-bonding motif (e.g., ester group) has to be strong enough to provide an energetic impetus for the isomerization to occur; however, if it is too strong then the isomer ratio becomes unfavorable for efficient switching (i.e., more Z isomer in solution).

The uncatalyzed isomerization of the imine C=N bond has been postulated to proceed through two different mechanisms, either rotation or lateral inversion (Figure 4a).[14] In the case of rotation, the isomerization proceeds through a polar, zwitterionic transition state. In contrast, the inversion mechanism goes through a nonpolar transition state. These differences make the two mechanisms discernible by monitoring the effect of solvent polarity on the E/Z isomerization rate. Surprisingly, we discovered that in intramolecularly H-bonded

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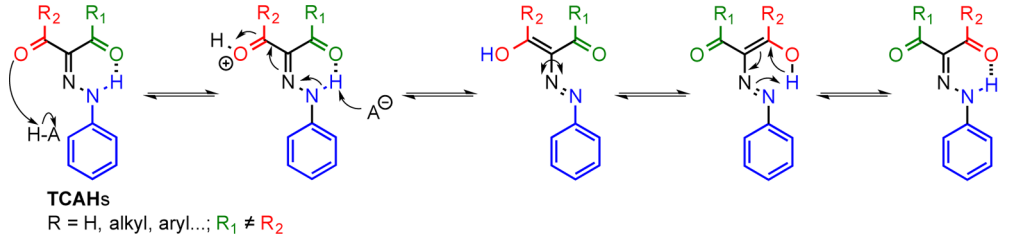


Figure 2. Acid induced equilibration in TCAHs.

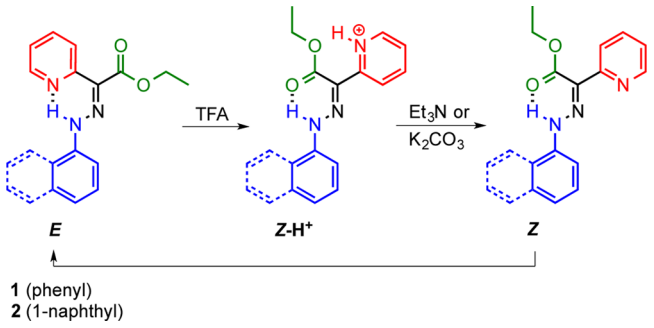
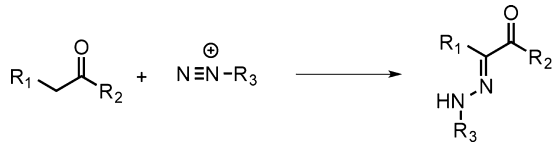


Figure 3. Acid/base switching cycle of hydrazones **1** and **2**.

Scheme 1. Synthesis of Hydrazones via the Japp–Klingemann Reaction



hydrazones a third pathway exists, involving hydrazone–azo tautomerization (Figure 4a).

Mechanistic studies of the $E \rightarrow Z$ switching process of hydrazones **1** and **2** revealed that the addition of TFA results in a rapid equilibration between the E and E-H$^+$ forms.[15] The rate limiting step of the switching process was found to be the isomerization from E-H$^+$ to the Z-H$^+$ species, with rate constants of $2.7(3) \times 10^{-2}$ s^{-1} and $5.2(3) \times 10^{-2}$ s^{-1} for compounds **1** and **2**, respectively. Kinetic and thermodynamic studies of the E-H$^+ \rightarrow Z$-H$^+$ and $Z \rightarrow E$ isomerization steps indicate that the switching process proceeds through a polarized transition state. Based on earlier precedence,[14] this finding should have led us to conclude that isomerization proceeds through out-of-plane rotation (Figure 4a). However, DFT calculations showed that the dependence of isomerization rates on solvent polarity originates from an increase in the dipole moment, which stems from the reorganization of the π-electronic framework going from the ground to the transition state (Figure 4b). Paired with computational studies, the kinetic and thermodynamic analyses of the switching processes revealed that the isomerization occurs via a new mechanism that we called tautomerization followed by rotation. We postulate that the intramolecular H-bond is responsible for this new mechanistic pathway.[16]

AMPLIFICATION OF MOTION THROUGH A LIQUID CRYSTAL

Having established that the E/Z isomerization process in the hydrazone switches involves rotation, we were interested to see whether we can use this motion to effect changes in bulk materials. Drawing inspiration from previous studies[17] that used light activated switches in the photochemical modulation of

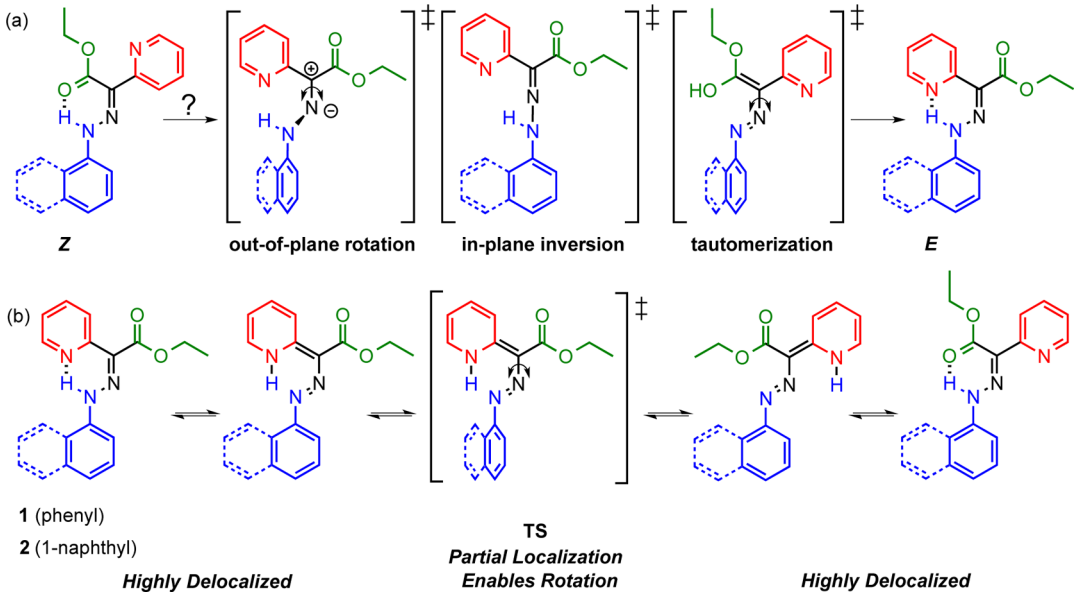


Figure 4. Mechanistic considerations of hydrazone isomerization. (a) The three possible mechanisms for the $Z \rightarrow E$ isomerization of the hydrazone-based switches. (b) Experimental evidence along with DFT calculations confirm that the tautomerization followed by rotation mechanism is the preferred one in intramolecularly H-bonded hydrazones.

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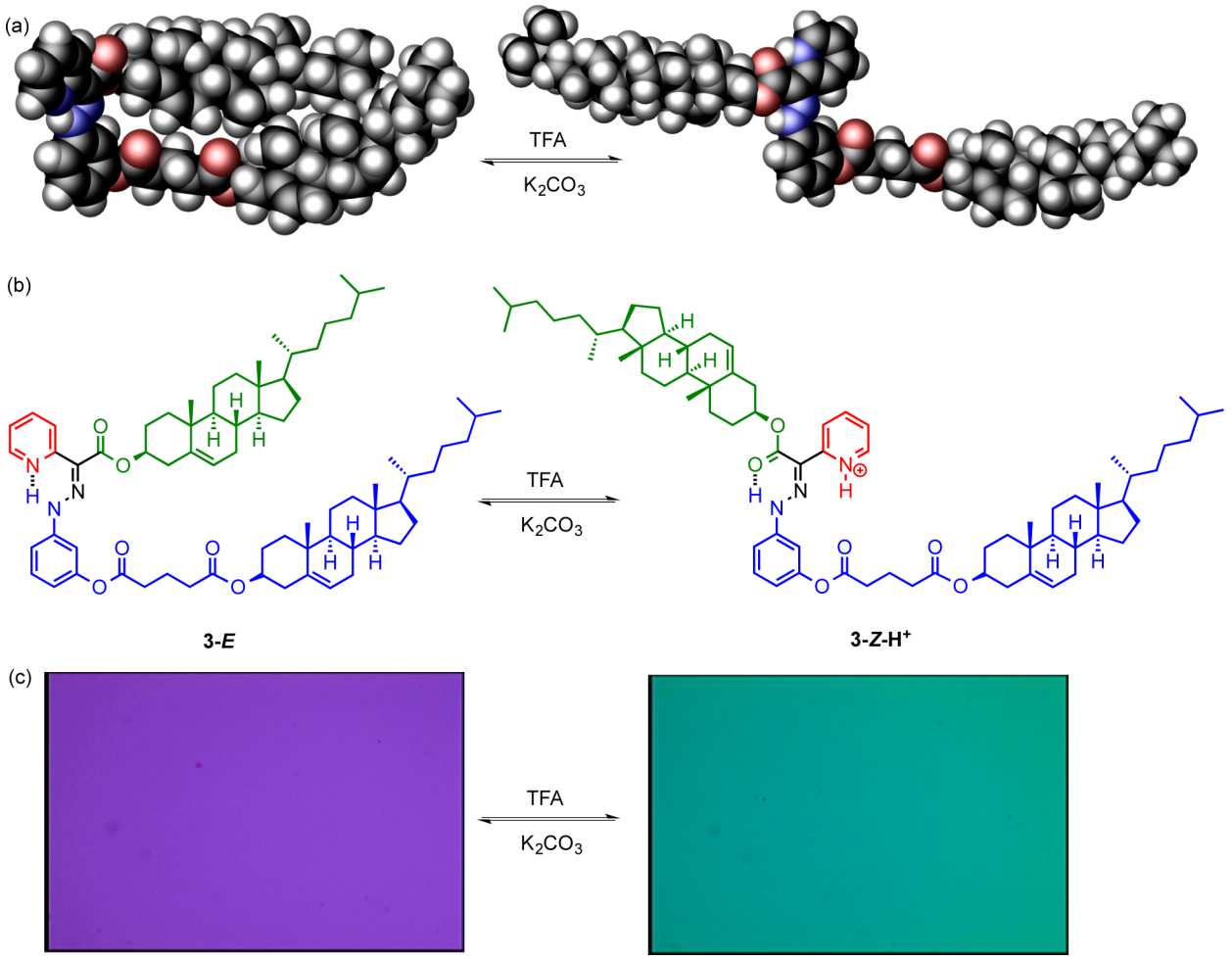

Figure 5. Incorporation of a hydrazone switch in a liquid crystal. (a) The DFT calculated structures of **3**-*E* and **3**-*Z*-H$^+$. (b) The acid/base induced switching of **3**-*E*. (c) Polarized optical micrographs of **3**-*E* and **3**-*Z*-H$^+$ doped NP5.

liquid crystals (LCs), we decided to convert our hydrazone switches into liquid crystalline materials.

This goal was achieved by synthesizing hydrazone **3**, which contains chiral cholesteryl groups in both the rotor and stator of the switch (Figure 5).[18] When **3** is doped (5 wt %) into an achiral liquid crystal (nematic phase 5, NP5), it induces chirality in the bulk mesophase. Upon addition of the **3**/NP5 mixture to a 90° twisted cell, the system displays a purple color (Figure 5b). The helical twisting power (HTP) of **3** was determined to be 56 μm^{-1} (wt %) using Cano's wedge cell method.[19] After exposure to TFA, the reflected color from the cell changes to green, which corresponds to a decrease in the HTP from 56 to 46 μm^{-1} (wt %). Exposure to Et_3N reverts the system back to the original purple color, thus completing a switching cycle. DFT calculations using the B3LYP-D3 (6-31G*) hybrid gave minimum energy structures whereby the cholesterol units orient in a *syn*-fashion in **3**-*E* and an *anti*-manner in **3**-*Z*-H$^+$ (Figure 5a). This change in cholesterol orientation upon protonation increases the solvent accessible surface area by 10.4%, which can lead to the observed modulation in HTP and subsequent color change. This example represents the first use of the molecular level structural changes in our hydrazone-based switches in effecting microscopic/mesoscopic level responses. More importantly, this example shows that our structurally simple switches can be used in complicated functions!

COMPLICATED ROTARY MOTIONS

The control over different types of motions in a single molecular switch can increase the depth of capabilities of such a system and allow it to perform complicated functions. Having this in mind, we synthesized switch **4** (Figure 6), which has an additional protonation/binding site in the stator,[20] in order to test whether a combined manipulation of configurational and conformational changes in hydrazone switches is possible. We took advantage of the pK_a difference between the pyridyl and quinolinyl groups to effect configurational and conformational changes as a function of the sequence and amount of TFA and Et_3N added to the solution. Such control of different rotational motions in a single molecule has not been accomplished so far in molecular switches!

The incorporation of the quinolinyl stator had an unexpected side effect: slowing of the $Z \rightarrow E$ isomerization rate by 2 orders of magnitude (relative to **2**). We hypothesize that this effect results from the extra intramolecular H-bond with the quinolinyl ring, which can inhibit the hydrazone−azo tautomerization process. Recently,[21] we replaced the quinolinyl ring with a bipyridyl one (**5**) and showed that zinc(II) coordination with the latter can turn "off" the extra intramolecular H-bond (Figure 7), leading to a 10^6 fold acceleration of the $Z \rightarrow E$ isomerization rate.

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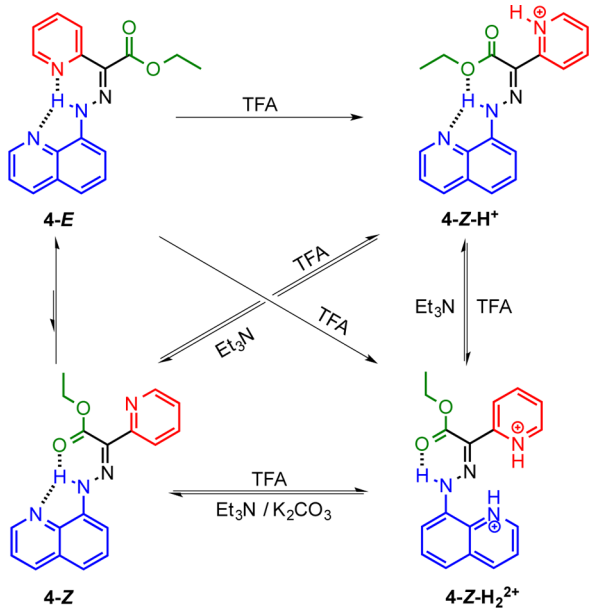

Figure 6. The quinolinyl stator in **4** allows for the acid/base control over the rotary motion around the CN double and single bonds.

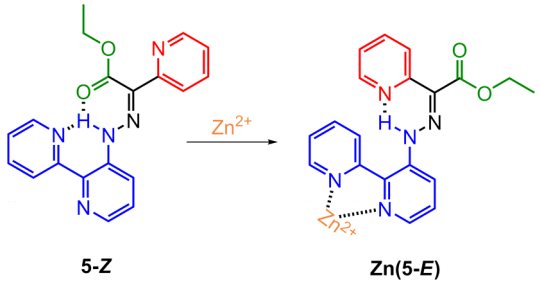

Figure 7. The Zn(II) induced accelerated $Z \rightarrow E$ isomerization of a bipyridyl-containing hydrazone switch.

COORDINATION INDUCED SWITCHING

The coordination of transition metals with protein residues sometimes leads to the release of protons to the environment. This process, which is called coordination-coupled deprotonation (CCD),[22] has also been shown to alter the pK_a of neighboring amino acids.[23] We have been interested in this process because it opens the door for activating our hydrazone switches under mild conditions, that is, without the addition of strong acids.

Hydrazone switch **4**, which contains a quinolinyl stator, can be viewed as an η^3 ligand (Figure 8), and so we studied its interaction with Zn(II), in order to assess whether coordination

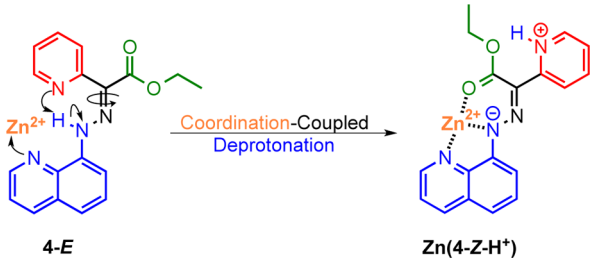

Figure 8. The activation of **4** through zinc(II)-initiated coordination-coupled deprotonation.

can lead to $E \rightarrow Z$ isomerization.[24] Upon titration with zinc perchlorate ($Zn(ClO_4)_2$), the UV/vis absorption of **4** undergoes a hyperchromic shift, from λ_{max} of 393 to 452 nm, because of the formation of Zn(**4**-*Z*-H$^+$). After removal of Zn(II) with tetra-*n*-butylammonium cyanide (*n*-Bu_4NCN), the UV/vis absorption returns to its original state (λ_{max} = 393 nm), thus completing a switching cycle.

The zinc(II) initiated switching of **4** was established using NMR spectroscopy and X-ray crystallographic analysis. Based on these studies, the switching mechanism involves CCD: Upon coordination with zinc(II), the hydrazone NH is deprotonated, and the proton is subsequently transferred to the pyridyl nitrogen (Figure 8). In order to avoid electrostatic repulsion, as well as to fulfill the coordination sphere of the metal, the pyridinium group rotates about the C=N bond allowing for the ester carbonyl to coordinate with the zinc(II). Interestingly, the pyridinium N–H proton of Zn(**4**-*Z*-H$^+$) could not be deprotonated using potassium carbonate, and tributylamine had to be used, indicating a drastic change in its pK_a as a result of coordination.

CCD INITIATED PROTON RELAYS

Complex biological functions such as photosynthesis and enzymatic catalysis rely on proton relays between cellular compartments.[25] The imidazolyl group of histidine plays a crucial role in such processes,[26] and hence we incorporated it into the design of the hydrazone switch **6** (Figure 9). Based on the CCD process described above, we envisioned a multistep switching cascade in which a single input, in this case Zn(II), could initiate a series of configurational transformations in structurally different switches through CCD initiated proton relay.[27]

In the presence of zinc(II), the hydrazone proton in **6** is transferred to the imidazolyl nitrogen leading to the expected $E \rightarrow Z$ isomerization (Figure 9), and the protonated imidazolium, Zn(**6**-*Z*-H$^+$). This acidic species can now act as a proton donor that can be used in activating (through proton relay), an orthogonally initiated (i.e., noncoordinating) switch, such as **1**. Based on DFT calculations, the crucial step in the switching process is the lowering of the pK_a of the imidazolium ring upon binding with zinc(II), which results from the electrostatic repulsion between it and the metal cation. Having a weakly H-bonded proton is also important; otherwise the proton relay does not occur. This is evident by the comparison between Zn(**6**-*Z*-H$^+$) and Zn(**4**-*Z*-H$^+$): In the former, the imidazolium ring is not coplanar with the rest of the molecule because of the methyl group, and hence the proton is weakly H-bonded and available for proton relay. On the other hand, in the latter, the pyridinium ring is coplanar with the rest of the molecule, leading to a strongly H-bonded proton that does not participate in proton relay.

This multistep switching cascade is the first instance of a dynamically switched compound acting as the input to another and a first step toward an ultimate goal in the field of molecular switches and machines:[1] controlling the collective behavior of molecular switches, so as to bring about biological level complexity.

BF_2–HYDRAZONE COMPLEXES

Derived from dipyrromethenes through BF_2-coordination, boron-dipyrromethenes, or BODIPY dyes,[28] are highly efficient light emitters that are broadly used in imaging applications. The

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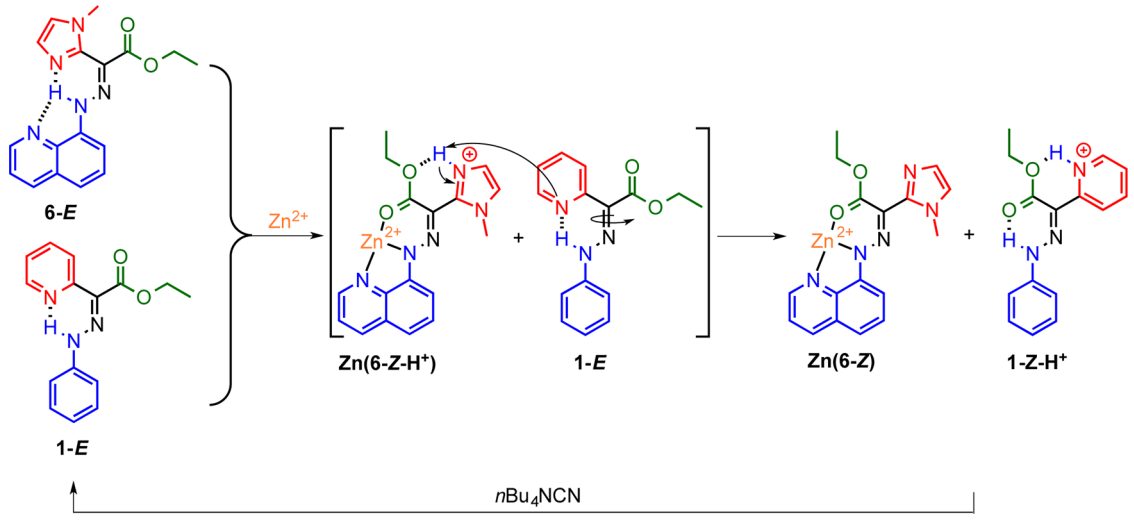

Figure 9. CCD mediated proton relay leads to the activation of two different hydrazone switches using a single input.

hydrazone switches developed in our group are structurally similar to dipyrromethenes, and therefore we envisioned that the BF_2-coordination of deprotonated hydrazones might lead to a novel class of borondifluorohydrazone (BODIHY) fluorophores.[29]

The BODIHY dyes (**7**−**12**, Figure 10) were obtained by the reaction between the appropriate hydrazones and boron

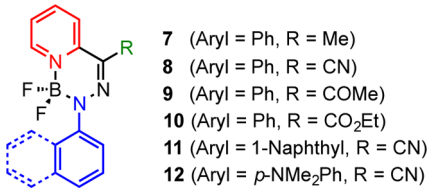

Figure 10. The structures of BODIHY dyes **7**−**12**.

trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$) in the presence of Hünig's base (*N*,*N*-diisopropylethylamine, iPr_2EtN). Complexes **7**−**11** exhibit rigidification induced emission:[30] their emission quantum yields are higher in the solid state than in solution (e.g., 0.52 and 0.06, respectively, for **8**). This phenomenon is attributed to a number of factors that obviate nonradiative decay pathways; the main one being the restriction of the aryl ring rotation in the solid state. Analysis of the crystal structures of **7**−**11** showed that the planarity of these complexes, defined as the dihedral angle between the BODIHY core and the aryl group, in addition to the number of CH···π and π−π interactions also contribute to their emission efficiency. While the later interactions contribute to the rigidification of the dyes,[30a,b] planarity leads to better conjugation, which in turn gives rise to higher quantum yields. However, the more planar the complexes, the more π−π interactions they will have in the solid state, which eventually diminishes emission. Hence, a fine balance has to be struck between planarity and number of π−π interactions in the solid state to ensure high quantum yields.

The protonatable *N*,*N*-dimethylamino (NMe_2) group in complex **12** allows for the control of its solid state photophysical properties. This can be accomplished by toggling the charge transfer (CT) from the NMe_2 group (which quenches the emission of **12** in the solid state) "on" and "off" using acid and base, respectively. When a sample of **12**, which is smeared on a silica gel plate support, is exposed to HCl vapor, its emission is greatly enhanced because of the protonation of NMe_2 (**12**-H^+) and suppression of the CT (Figure 11). This process can be reversed by exposing **12**-H^+ to NH_3 vapor. This simple gaseous phase sensing experiment showcases a potential solid state application for the BODIHY dyes.

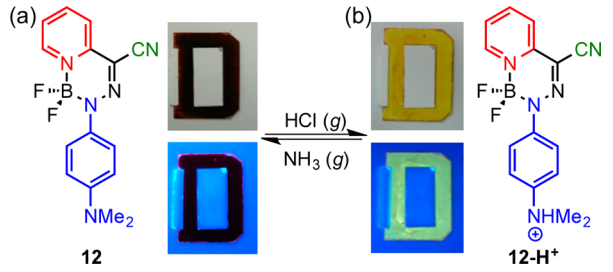

Figure 11. BODIHY fluorescence. (a) **12** on a silica support under ambient (top) and UV light (bottom). (b) **12**-H^+ under ambient (top) and UV light (bottom).

■ BF_2−AZO COMPLEXES

In an effort to red-shift the emission of the BODIHY dyes, we replaced the pyridyl ring with a quinolinyl one, which yielded an unexpected and new BF_2−azo complex (**13**) as the major product (Figure 12).[31] Instead of forming a six-membered coordination ring with the deprotonated hydrazone nitrogen as in **14**, the boron atom forms a five-membered ring by coordinating to an azo nitrogen. The azo nature of complex **13** was unambiguously characterized from its crystal structure, which showed a N=N bond length of 1.278 Å, which is

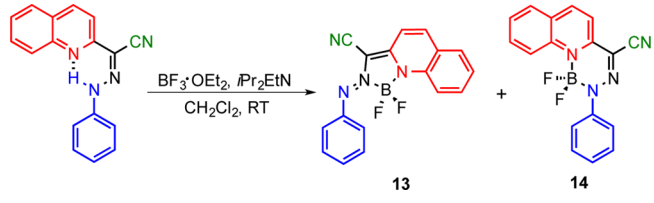

Figure 12. The synthesis of the BF_2 complexes **13** and **14**.

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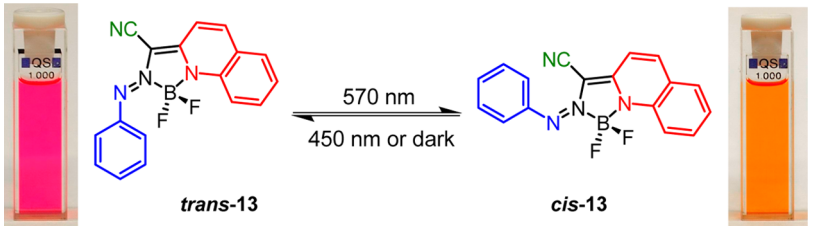

Figure 13. Visible light-induced *trans*/*cis* isomerization of the BF_2–azo complex **13**.

comparable to the average N=N bond length (1.25 Å) of azobenzene.[32]

Unlike most azo compounds in the literature,[2] the *trans* → *cis* isomerization process in **13** can be activated using visible light (Figure 13). This feature is of great practical significance because UV light, which is commonly required for this transformation, is not biocompatible and can lead to complications (i.e., photodamage[33]) especially for *in vivo* applications (e.g., strong scattering[34] and apoptosis[35]). This is the reason why there is a great push in the community to shift the activation wavelengths of these systems to the visible spectrum. This activity has led to a handful of systems that can be modulated with visible light;[33,36] however, most of them rely on forbidden n–π^* transitions that are in the visible range for their function. DFT calculations (B3LYP/6-311++G**) showed that the n–π^* and π–π^* transitions in our system are reversed on the energy scale (relative to other azo-compounds), which is the reason it can be efficiently activated by visible light. For example, complex **13** shows quantum yields of 48% and 67% for the *trans* → *cis* and *cis* → *trans* processes, respectively, with photostationary states as high as 97% and 80% for the *cis* and *trans* isomers, respectively. Based on the DFT calculations, increasing the electron density in **13** through appropriate derivatization will red shift the activation wavelength further. We are currently investigating this hypothesis.

TRIAZOLOPYRIDINIUM SALTS

It is well established that hydrazones can be transformed into [1,2,3]triazolo[1,5-*a*]pyridinium salts through oxidative cyclization.[37] Various reagents or methods have been developed to perform this transformation; however, most lead to non-negligible side products (e.g., bromination when NBS is used as oxidant[38]) or require toxic reagents (e.g., $SbCl_5$[39]). While studying the coordination properties of various transition metals with our hydrazone switches, we discovered that Cu(II) in acetonitrile (MeCN) can also lead to oxidative cyclization.[40] The use of MeCN is critical for this transformation, because no reaction occurs in methanol or acetone!

The triazolopyridinium salts have been used as intermediates for various reactions;[41] however, we were surprised to find that their photophysical properties have not been explored before. We studied the photophysical properties of **15** and **16** in water (Figure 14), as well as polar organic solvents such as acetone, MeCN, and ethanol, and observed no solvatochromism. In water, **15** emits green-blue light with a quantum yield of 5%, whereas **16** shows deep-blue emission with a significantly increased quantum yield of 30%. This enhancement in fluorescence efficiency going from **15** to **16** can be attributed to a decrease in charge transfer from the phenyl group to the triazolopyridinium core, which results in the quenching of the former. Interestingly, **15** and **16** have broad emission profiles that cover almost the entire visible spectrum, with full widths at

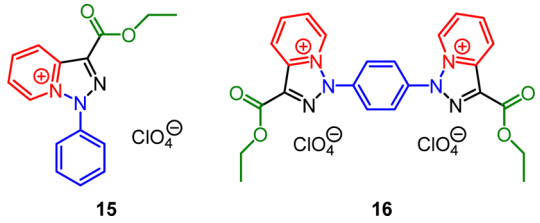

Figure 14. The structures of triazolopyridinium salts **15** and **16**.

half-maximum of 6008 and 5097 cm^{-1}, respectively. Moreover, they both exhibit mega-Stokes shifts (>100 nm), which are not commonly observed for simple organic dyes. We are presently conducting an in-depth study of the photophysical properties of these dyes, and will use the gained insights in controlling their properties so they can be used in energy related applications, such as OLEDs.

The positively charged pyridinium ring in these salts is susceptible to nucleophilic attack that yields highly conjugated dienes through a pseudopericyclic ring-opening reaction.[42] We hypothesized that this reaction can be used in the fluorescence turn-on sensing of CN^- as long as there is a large difference in the emission properties of the sensor and reaction product. For this reason, we synthesized the triazolopyridinium **17** (Figure 15), which is weakly fluorescent in DMSO/water (99:1)

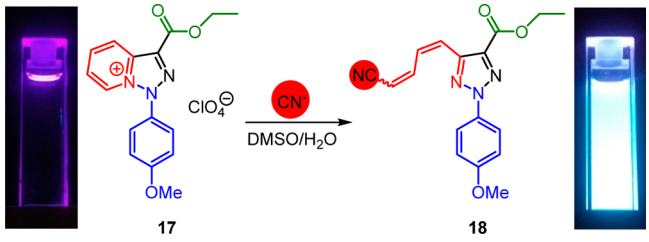

Figure 15. The cyanide induced ring-opening of the triazolopyridinium salt **17**, accompanied by enhanced fluorescence emission.

because of the quenching effect of the *p*-OMe phenyl group. Upon reaction with cyanide, a highly conjugated triazo diene species (**18**) is obtained that exhibits 60-fold enhancement in emission. This reaction is very fast, highly selective, and has a limit of detection of 0.2 ppm (8.46 μM), which is the maximum contaminant level goal of this toxic pollutant as set by the US Environmental Protection Agency.[43] These properties show that the triazolopyridinium compounds are a promising platform for the sensing of CN^- and other highly reactive anions.

CONCLUSION AND OUTLOOK

The straightforward synthesis and functional diversity of the hydrazone functional group enable its use in various stimuli responsive materials. In this Account, we focused on our recent

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efforts in converting hydrazones into chemically activated molecular switches that can be used in addressing some of the challenges in the field: controlling multistep switching cascades and the photophysical properties of bulk materials. In order to achieve these goals, we had to conduct structure−property analyses that helped us unravel the isomerization mechanism in the intramolecularly H-bonded systems and understand how to control motion around different types of bonds. We also showed that the same systems can be easily converted into two families of fluorophores (i.e., BODIHY and triazolopyridinium dyes), which can be used in sensing applications. Moreover, we demonstrated how coordination to BF_2 can convert the hydrazone switches into visible light activated azo-compounds. These and other applications showcase the multifacetedness of hydrazones and how this structurally simple group can be used in complicated functions.

There are still a myriad of challenges to address before these (and other) molecular switches can be efficiently used in driving systems out of equilibrium and producing work, among other targeted applications. With the knowledge that we have gained through the past few years, we are now poised to tackle these obstacles. We intend to do this by (i) developing "waste management" strategies (i.e., how to deal with the byproducts of each switching cycle), (ii) controlling cross-talk between different families of switches in order to further complicate the switching cascades, (iii) using the switches in controlling catalytic cycles that can lead to signaling, signal amplification, and feedback loops, (iv) controlling the alignment of the switches in polymers so they can be used as actuators, (v) controlling the timing of the switching events (i.e., temporal control) in order to develop molecular timers, and (vi) using compartmentalization in order to activate parallel and non-compatible switching events. We are confident that these synthetically accessible hydrazones will facilitate and expedite the discovery of complicated switching schemes that when appropriately combined will lead to complexity.

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Notes

The authors declare no competing financial interest.

Biographies

Luke Tatum received his B.Sc. degree in Biology-Chemistry from Point Loma Nazarene University (2009), where he worked with Professor Victor Heasley. He completed his Ph.D. studies working with Professor Benjamin King at the University of Nevada, Reno (2013), where he developed liquid crystals for use in electronics as well as porous membranes. His current research in the Aprahamian group focuses on molecular switch-based liquid crystals and polymers.

Xin Su received his B.Sc. degree in Chemistry from Nankai University (2009), where he worked in the Liu group on the recognition and assembly of water-soluble calixarenes. He joined the Aprahamian group at Dartmouth College in 2009 and worked on the development of novel hydrazone-based molecular switches and switching systems thereof. He received his Ph.D. degree at the end of 2013 and is currently a postdoctoral researcher at the National Energy Technology Laboratory.

Ivan Aprahamian received all his degrees (B.Sc., 1998; M.Sc., 2000; Ph.D., 2005) from the Hebrew University of Jerusalem, Israel. His doctoral research was conducted under the supervision of Professors Mordecai Rabinovitz and Tuvia Sheradsky. He started his independent career at Dartmouth College in 2008, after finishing his postdoctoral research with Sir Fraser Stoddart (UCLA). His research focuses on using structurally simple, modular, and tunable hydrazone-based building blocks in the development of adaptive functional materials.

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