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# One-Pot Synthesis of Pyranocoumarins via Microwave-Assisted Pseudo Multicomponent Reactions and Their Molecular Switching Properties

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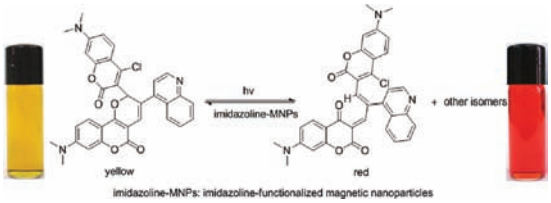
## ABSTRACT




**Two new pyranocoumarins were synthesized via one-pot, microwave-assisted pseudo multicomponent condensations of coumarin and 4-methylquinoline to investigate their molecular switching properties. Both are light-sensitive and have a distinct change of color upon UV irradiation. The reaction can be reverted by treating the photogenerated products with imidazoline-functionalized magnetic nanoparticles, which can be swiftly recycled with an external permanent magnet.**

Molecular systems capable of changing state reversibly have attracted considerable attention since they conceptually provide a pathway for the development of molecular scale devices such as molecular switches/shuttles[1] and molecular information processing/storage devices.[2] Typical molecular switches consist of two stable states distinguishable by physical or chemical properties (response), which are interchangeable through the alteration of controllable parameters (stimuli) such as temperature, light, pH, redox potential, and metal ions. For molecular switches using pH as the external stimulus, the added acid (or base) needs to be removed from reaction media before the system can proceed to the next switching cycle. Normally, it is done by neutralizing the acid with a base, but the repeated neutralization process and accumulation of the resulting salt in the system may potentially be detrimental to the reversibility of the switch. One way to overcome this problem is to immobilize the acid on the surface of a solid support, which can be separated from the reaction media via a simple filtration or centrifugation step.[3] Indeed, this heterogenization method on solid supports works well for most conventional reactions. For molecular switching systems, however, repeated filtration or centrifugation in each switching cycle becomes cumbersome and unrealistic. Therefore, a faster, easier separation method to remove the added stimulus from the switching system remains desired.

The use of magnetic nanoparticles (MNPs) as a solid support for catalysts has recently emerged to be a promising field mainly due to their high surface area to volume ratios.[4] One of the major advantages of the functionalized MNPs over the traditional catalysts is that they can be

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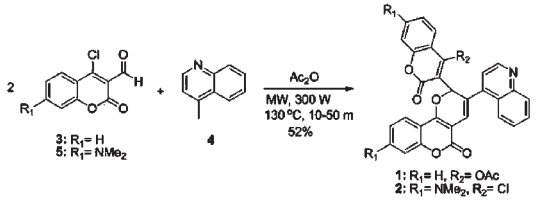
separated from the reaction media by a permanent magnet without the need for filtration or centrifugation or a tedious workup procedure.[5] While recent studies primarily focused on their potential synthetic applications,[6] utilization of the derived MNPs to function as an external stimulus in molecular switching systems has never been reported. Here, we describe a one-pot, microwave-assisted, pseudo multicomponent synthesis of two new pyranocoumarins to investigate their ring-opening properties using UV light as controllable parameters. The feasibility of accelerating the reverse ring-closing reaction with the imidazoline-functionalized MNPs was also explored.

Scheme 1 shows the one-pot synthesis of pyranocoumarins **1** and **2**. An acetic anhydride-mediated, pseudo three (or four) component condensation of 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde (**3**)[7] or 4-chloro-7-dimethylamino-2-oxo-2*H*-chromene-3-carbaldehyde (**5**)[8] with 4-methylquinoline (**4**) in acetic anhydride under microwave irradiation conditions (300 W) at 130 °C gives **1** and **2**, respectively. The molecular structures of **1** and **2**

**Scheme 1**




were elucidated by $^{1}H$ and $^{13}C$ NMR spectroscopy and X-ray crystallography (Figure 1), clearly revealing a quinoline substituted pyranocoumarin skeleton. Scheme 2 depicts the proposed mechanism for the formation of **2**. It begins with the reaction of 4-methylquinoline with acetic anhydride to yield 1-acetyl-4-methylene-1,4-dihydroquinoline (**6**). The coupling of **6** with aldehyde **5** gives intermediate **7**, which subsequently loses a molecule of $Ac_2O$ to afford alcohol **8**. **8** then reacts with acetic anhydride again to give the 4-methylene-1,4-dihydroquinoline **9**. The coupling of **9** with a second molecule of **5** generates the zwitterion **10**. Final cyclization of **10** following by dehydration furnishes the final product **2**. Essentially, this one-pot, microwave-promoted, $Ac_2O$-mediated multicomponent reaction provides a quick access to the bulky substituted pyranocoumarin skeleton, which generally requires several synthetic steps to accomplish.[9]

With the availability of **1** and **2**, their photochemical properties were then investigated. Both compounds were

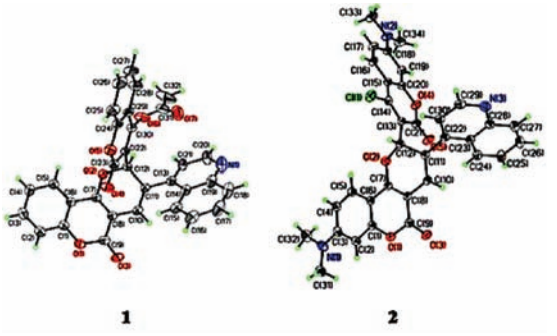
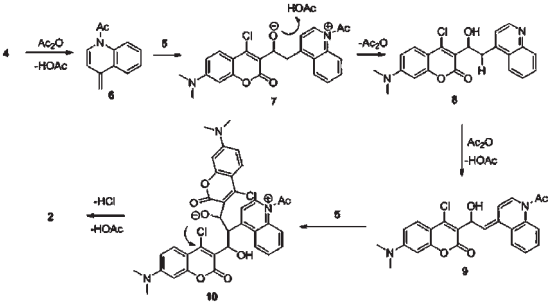



**Figure 1.** ORTEP crystal structures of **1** and **2**.

**Scheme 2**




found to be sensitive to light. For instance, the yellow solution of **2** turned red within seconds upon UV irradiation (306 nm). Figure 2 shows the UV−vis absorbance changes of **2** in chloroform prior to and after irradiation. With the increase of exposure time, a new absorption band with the peak wavelength at ~504 nm gradually emerged, along with the appearance of two isosbestic points at 362 and 429 nm. Although the proposed photogenerated products **11**−**14** (Scheme 3) were not stable enough to be isolated and characterized, their formation was partially supported by the $^{1}H$ NMR spectra of **2** in deuterated chloroform after irradiation, which exhibited a time-dependent downfield shift of $H_a$ and $H_b$ absorption peaks (see Scheme 3 for H-atom labeling and Figure S4, Supporting Information (SI)). The discernible downfield shift of $H_a$ (from 6.982 to 7.186 ppm) and $H_b$ (from 7.344 to 7.570 ppm) after irradiation presumably resulted from

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the structural change on the pyran moiety of **2** during the ring-opening reaction.

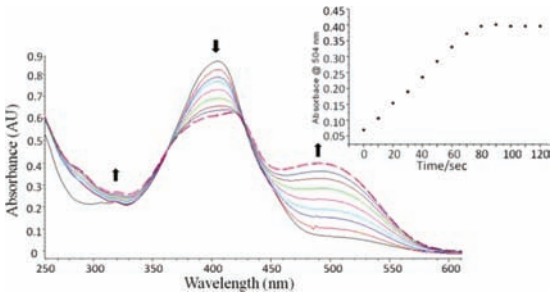
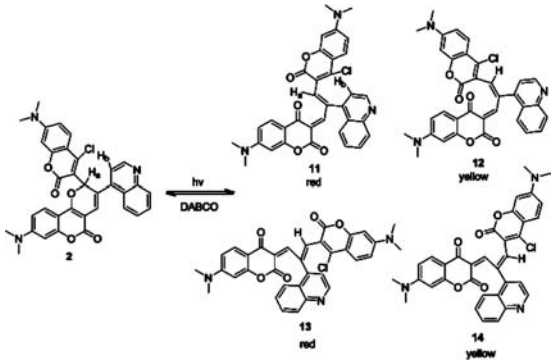



**Figure 2.** Absorption spectra of **2** ($1.5 \times 10^{-5}$ M in $CHCl_3$) obtained with different exposure times (306 nm), 0−130 s, in increments of 10 s. Inset: Increase of absorbance at 504 nm with respect to irradiation time.

**Scheme 3**




To gain more evidence for this light-induced ring-opening reaction and subsequent *trans*−*cis* isomerization, compound **15**, whose structure resembles the ring-open product **11**, was prepared by the same procedure as that of **2** except under heating rather than microwave irradiation. Similarly, the yellow **15** turned red instantly upon UV irradiation (Figure 3). The absorption at 504 nm upon UV irradiation of **15** presumably resulted from a light-induced *trans*−*cis* isomerization which facilitated the donor−acceptor charge-transfer process from coumarin to quinoline (Scheme 4). Indeed, the $^1$H NMR experiments of **15** in $CDCl_3$ after prolonged irradiation did provide evidence for the formation of the *cis* isomer, that is, the observation of two new doublets at 7.348 and 6.783 ppm, which were assigned to the two *cis* olefin hydrogen absorptions of the *cis* isomer (Figure S5, SI).

Since **11** and **13** share the same *cis* conformation (i.e., the coumarin and quinoline moieties) of **16**, we speculate that the color variation of **2** (the observation of absorption at 504 nm) upon UV irradiation was due to a light-induced electrocyclic pyran ring opening, which brought the coumarin and quinoline moieties of the resulting *cis* isomer

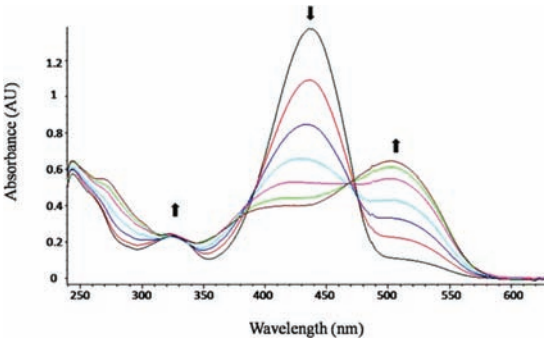
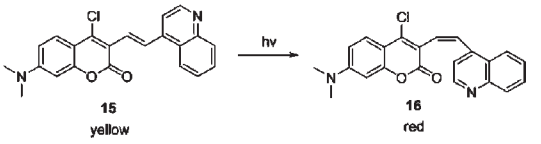



**Figure 3.** Absorption spectra of **15** ($3.1 \times 10^{-5}$ M in $CHCl_3$) obtained with different exposure times (306 nm), 0−60 s, in increments of 10 s.

into close proximity for an efficient donor−acceptor charge-transfer process. Yet, **12** and **14** share the same *trans* conformation of **15**; the observation of the residual peak at ~407 nm (Figure 2) after irradiation is likely due to the formation of the *trans* isomers **12** and **14**. In addition to the color change, UV irradiation of **2** also exhibited a second output property, that is, emission variation. While **2** was weakly fluorescent in chloroform ($\lambda_{max} = 450$ nm), the fluorescence intensity at 598 nm increased with increasing exposure time (Figure S6, SI).

**Scheme 4**




This light-induced color variation of **2** was reversible when the photogenerated products were kept in the dark at rt for ~2 weeks. This slow reverse process can be accelerated substantially by adding 1,4-diazabicyclo[2.2.2]octane (DABCO).[10] Figure 4 shows the UV−vis spectra of the photogenerated products in the presence of excess DABCO. With the increase of DABCO concentrations, the photogenerated products swiftly reverted back to **2**. Scheme 5 depicts a plausible mechanism for this DABCO-mediated cyclization process. It presumably involves the zwitterion **17** as an intermediate, which is formed by the conjugate addition of DABCO to **11**. Our studies suggest that the ring-closed form **2** and ring-open form **11** are interchangeable and can be converted from one to the other using UV light and DABCO as external stimuli.

To avoid the repeated neutralization process, DABCO was replaced with the imidazoline-functionalized $Fe_3O_4$ MNPs, so the latter can be removed from the system

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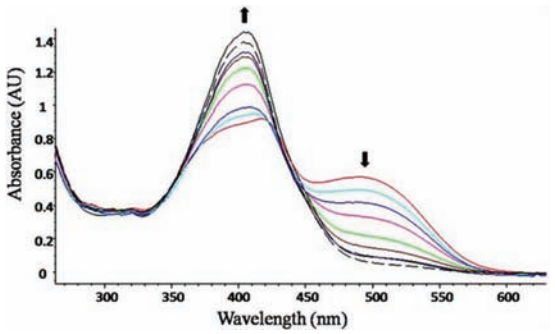
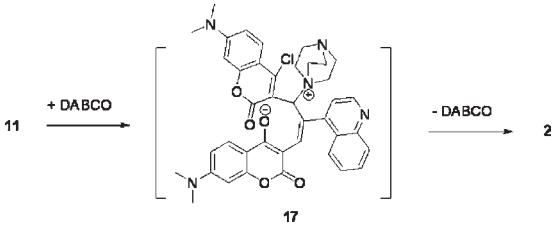


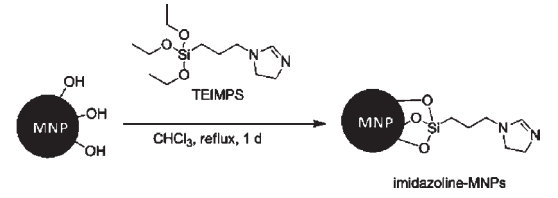

**Figure 4.** Absorption spectra of **11** ($2.5 \times 10^{-5}$ M in $CHCl_3$) obtained in the presence of different equivalents of DABCO (0.5 $\mu$mol), 0−7 equiv, in increments of 1 equiv.

**Scheme 5**




magnetically vs chemically. The functionalized MNPs were readily accessed by coupling of triethoxy-3-(2-imidazolin-1-yl)propylsilane (TEIMPS) with the active OH groups on the $Fe_3O_4$ particles' surface (Scheme 6).[11]

**Scheme 6**




The functional groups grafted on the magnetic materials were then characterized by TGA and FT-IR spectroscopy (Figures S7 and S8, SI). Figure 5 shows the time-dependent absorption spectra of **11** in chloroform with different exposure times to the prepared imidazoline-MNPs (2 equiv of imidazoline). To our delight, the red **11** turned yellow again with the appearance of the 407 nm absorption band characteristic of **2**, along with an isosbestic point at 431 nm. The reversible switching process between **2** and **11** by UV irradiation and imidazoline-MNPs was repeated 10 times without significant changes in the UV−vis spectra (Figures S9 and S10, SI). Note that the recycled imidazoline-MNPs were reused in the next cycle with almost consistent activity. When imidazoline-MNPs were replaced with the unfunctionalized MNPs as the external stimulus, no reversible switching process between **2** and **11** was observed (Figure S11, SI). This result provides strong evidence to support that cyclization of **11** was indeed promoted by the imidazoline moiety attached to the MNPs. To the best of our knowledge, the switching system reported here represents the first example employing UV light and functionalized MNPs as external stimuli to facilitate interconversion between two states.

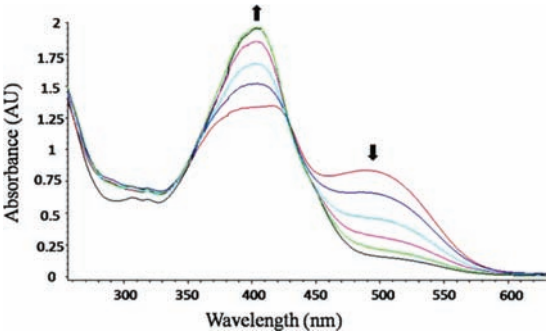



**Figure 5.** Time-dependent absorption spectra of **11** ($3.5 \times 10^{-5}$ M in $CHCl_3$) in the presence of imidazoline-MNPs (3.0 mg), 0−50 s, in increments of 10 s.

In summary, two new pyranocoumarins **1** and **2** were efficiently synthesized and characterized via one-pot, microwave-assisted condensations of coumarin and methylquinoline. We have demonstrated that the switching between **2** and its corresponding ring-open forms can be realized by two external stimuli, that is, UV irradiation and imidazoline-functionalized MNPs. The latter can be not only swiftly recycled from the system with a permanent magnet but also reused with consistent activity.

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**Supporting Information Available.** Synthesis of compounds **1**, **2**, and **15**, experimental details, and additional spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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