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Surface charge inversion of self-assembled monolayers by visible light irradiation: cargo loading and release by photoreactions†

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In this study, we find that visible light can trigger both the loading and the release of *N*-alkyl substituted 4-picolinium on self-assembled monolayers (SAM). The latter process will result in surface-charge inversion of the SAM, which can be used for controlled release of molecules of interest.

Recently, photo-triggered loading–release systems have received considerable attention from scientists around the world. Light has been widely used to trigger the delivery of many kinds of substances, since it is a clean and effective remote stimulus.[1] A number of photolabile molecules can be activated using UV light irradiation, and the photoreactions can be used to load or release target substances. However, UV light may damage living cells and active substances. Compared with UV light, visible light is a greener illuminant to trigger photoreactions,[2] which has been utilized to deliver proteins, DNA, *etc.*[3]

In this study, we find that visible light can trigger both the surface loading and the release processes in one system. The two photoreactions are based on thiol–ene chemistry[4] and the photo-induced electron transfer (PET) process with a novel *N*-alkyl substituted 4-picolinium (NAP) ester.[5] Compared with other methods, this is an ideal system for rapid loading and efficient release of substances due to the utilization of those two photoreactions. Moreover, the photo-sensitizers used in this study (*i.e.*, eosin Y and $[Ru(2,2'\text{-bipy})_3]Cl_2$) have negligible cytotoxicity, so they can be used in biological systems. In addition, the surface charge of the self-assembled monolayers (SAM) is inverted after the second photoreaction, which helps in the release of other guest charged molecules.

To realize both surface loading and release of a molecule by visible light-induced photoreactions, we designed an NAP ester with an acrylic group. It is expected that *via* the first photoreaction, the NAP ester can be loaded on the thiolated substrate by the catalysis of eosin Y (hereafter referred to as eosin) *via* thiol–ene chemistry.[6] In the second photoreaction, the NAP group can be released from the substrate *via* a bond scission reaction by the catalysis of $[Ru(2,2'\text{-bipy})_3]Cl_2$ (hereafter referred to as Ru(II)). The NAP ester is synthesized *via* a two-step reaction[5b,d] (Fig. 1, ESI†): (i) the esterification reaction between acryloyl chloride and 4-pyridinemethanol, and (ii) the *N*-methylation reaction between **1** and methyl trifluoromethanesulfonate (MeOTf). The characterization results indicate the formation of the desired product **2** (Fig. S1–S5, ESI†).

Fig. 2a shows the scheme of the loading and release of the NAP ester **2** with visible light irradiation. Briefly, the thiolated substrate (**I**) (ESI†) is immersed in a solution of eosin and NAP ester **2** and exposed to green light (λ = 515 nm, 3 W LED, distance 1 cm). The NAP ester **2** is loaded onto the substrate by a covalent bond (**II**). To release the NAP, substrate **II** is immersed in a mixture of Ru(II) and ascorbic acid (Vc), and exposed to blue light (λ = 452 nm, 12 W LED, distance 1 cm). As a result, NAP is released *via* the C–O bond cleavage. Fig. 2c shows the UV-vis spectra of a thiolated quartz substrate and spectra after each photoreaction. After the first photoreaction, two significant peaks from the NAP ester **2** appear at 220 nm and 260 nm, respectively. However, the peaks disappear after the second photoreaction. Moreover, the static contact angles of the substrates are changed after each photoreaction (Fig. S6, ESI†). These results indicate that the surface photoreactions have occurred, and the visible light-induced loading (**I** → **II**) and release (**II** → **III**) of the NAP ester **2** are realized on the sample surface (ESI†).

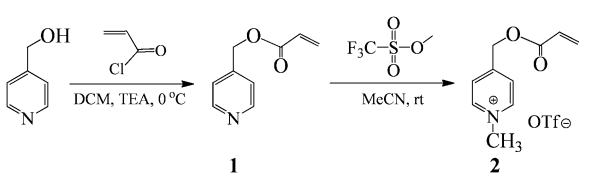

Fig. 1 Synthesis of **1** and **2**.

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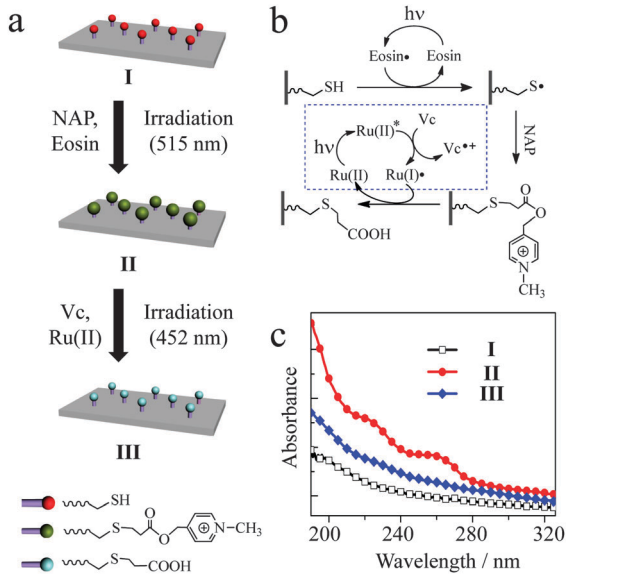

Fig. 2 The scheme (a) and reaction mechanisms (b) for the loading (**I** → **II**) and release (**II** → **III**) of the NAP ester **2**, and the UV-vis spectra (c) of three substrates (**I**, **II** and **III**).

It has been reported that for the Ru(II) catalyzed bond scission reaction of the NAP esters, there are two possible routes for the electron transfer process: direct electron transfer (DET) and mediated electron transfer (MET).[5] The Gibbs free energy (ΔG) of the bond scission reaction is estimated using cyclic voltammetry (Fig. S7, ESI†). The ΔG for the DET and MET is 9.7 kcal mol^{-1} and −1.8 kcal mol^{-1}, respectively (see ESI†).[5b,d] These results suggest that only the MET pathway is favorable for the release of the NAP group. Thus, the reaction mechanism for the loading and release of the NAP ester **2** can be briefly described as follows (Fig. 2b): (i) the eosin radicals that are generated by the irradiation of visible light (λ = 515 nm) react with thiol groups, leading to the formation of new radicals (–SH•).[6] The latter radicals then react with vinyl groups, through which the NAP ester **2** is loaded; (ii) upon visible light irradiation (λ = 452 nm), the bond scission is realized *via* the MET process in the multiple redox reactions among Ru(II), Vc and the NAP ester **2**. As a result, the ester bond is photochemically cleaved, and the NAP group is released.[5]

The loading and release photoreactions have been systematically tested in several experiments (each lacks one single parameter, see Fig. S8, ESI†). For the loading of NAP ester **2**, no significant peaks of NAP (260 nm) can be observed if any one of the components (*i.e.*, visible light irradiation, thiolated substrate or eosin) is absent (Fig. S8a, ESI†). This result reveals that the combination of all the three parameters is necessary for the loading of the NAP ester **2**.

For the release of the NAP group, the results of the control systems show that the NAP group cannot be released without Ru(II) or visible light irradiation. However, the NAP group can be partially released (28.5 ± 4.0%) even if Vc is absent (Fig. S8b, ESI†). To understand the *partial* NAP release, another control system (lacking Vc and light irradiation) is designed, which shows that the NAP group cannot be released (Fig. S8c, ESI†). These results indicate that the irradiation of blue light (~452 nm) plays an important role in the *partial* release of NAP. We notice that the NAP ester **2** does not show any pronounced absorption in the visible light region (Fig. S3, ESI†), but the Ru(II) complex shows a significant absorption at 452 nm (Fig. S9, ESI†). Considering that the yield of the first photoreaction (process **I** → **II**) would not be 100%, there should be some thiol groups remaining on substrate **II**. Thus, the possible reason for the *partial* NAP release may be that the Ru(II) complex initiates another PET process, where the thiol groups on the substrates act as electron donors in the system, leading to the bond cleavage of the NAP group with lower efficiency (Fig. S8d, ESI†). It can therefore be concluded that the release of the NAP group will be realized efficiently only when all the three conditions (visible light irradiation, Ru(II), and Vc) are applied at the same time in one system. The results of the control systems also provide strong support for the reaction mechanism of loading and release illustrated in Fig. 2.

Irradiation time and concentrations of the components also affect the loading and release of the NAP ester **2**. The UV absorbance at 260 nm increases rapidly in the first 5 min of irradiation, and then levels off after 15 min of irradiation (Fig. 3a). A smaller increase in A_{260} occurs with lower concentrations of NAP ester **2** or eosin (Fig. 3b). The comparison of two systems with lower concentrations indicates that the concentration of NAP ester **2** affects the loading efficiency more than the concentration of eosin does.

On the other hand, the release of NAP under different conditions has been monitored using UV spectroscopy (Fig. 3c and d). The absorbance gradually decreases in the first 20 min of irradiation, and then reaches the minimum after 40 min of irradiation. Also, we can observe a smaller decrease in A_{260} when lowering

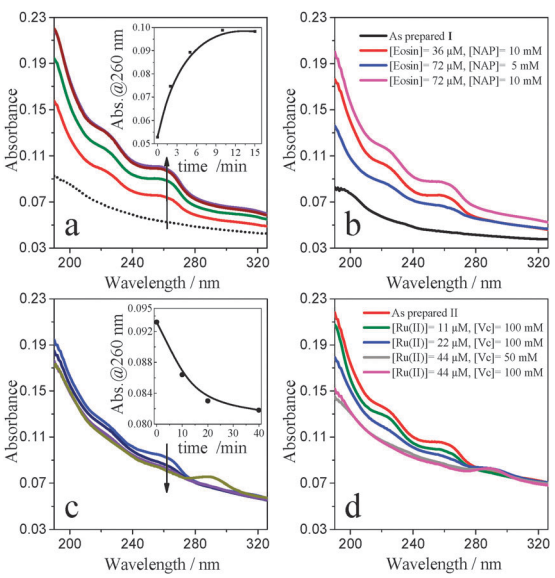

Fig. 3 The effects of various conditions on the loading (a and b) and release (c and d) of NAP ester **2**: (a) the concentrations of the NAP ester **2** and eosin are 10 mM and 72 μM, respectively; (b) the irradiation time is 15 min; (c) the concentrations of Ru(II) and Vc are 44 μM and 100 mM, respectively; (d) the irradiation time is 40 min. The insets in (a) and (c) show the absorbance at 260 nm *vs.* the irradiation time, respectively.

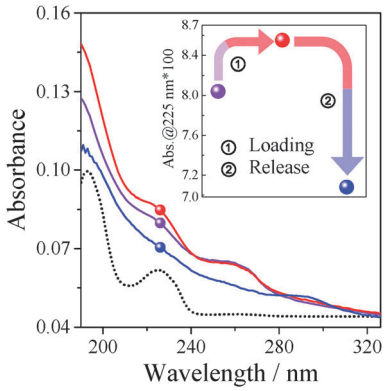

Fig. 4 The UV-vis spectra of substrate **II** (violet line), PSS-loaded (red line) and PSS-released substrate (blue line), and aqueous solution of PSS (dotted black line). Inset shows the changes of the absorbance at 225 nm within the loading and release process of PSS.

the concentration of Ru(II) and Vc. In summary, these results demonstrate that longer irradiation time and higher concentration of the components are helpful in realizing the loading and release of the NAP ester **2**. By tuning the reaction conditions, the loading and release processes can be controlled well.

After each photoreaction, new peaks can be observed at 540 and 290 nm, which are attributed to eosin and Ru(II), respectively (Fig. 3c and d and Fig. S10, ESI†). The adsorption of the photo-sensitizers is caused by the alteration of the surface charge of the substrates: (i) after the first photoreaction, the NAP ester **2** is loaded resulting in a positively charged surface, on which eosin (negatively charged) is adsorbed; (ii) after the second photoreaction, the NAP group is released resulting in a negatively charged surface, where Ru(II) is adsorbed. Our experiments show that by protonation of the carboxylic groups (from eosin and the substrate **III**) in an acid solution (pH = 3), the photo-sensitizers can be easily removed due to the weakened electrostatic interactions between the corresponding groups (Fig. S10, ESI†).

What is more interesting is that the inverted surface charge before and after the second photoreaction would be helpful in releasing other guest charged molecules. As a proof-of-concept, a polyanion, sodium polystyrene sulfonate (PSS, $M_w \sim 200\,000$, Aldrich Co.), is used as the model guest molecule to illustrate the feasibility of such a strategy. Among the substrates **I**, **II** and **III**, PSS can be well adsorbed only on substrate **II** due to the electrostatic attraction between negatively charged PSS and the positively charged substrate. When the PSS-adsorbed substrate **II** is exposed to the conditions of the second photoreaction (irradiation by λ = 452 nm, Ru(II) and Vc), the characteristic peaks of both NAP and PSS disappear, indicating that both the NAP group and PSS are released after the second photoreaction (Fig. 4). The release of PSS is due to the electrostatic repulsion from the substrate **III**, which is caused by the inversion of the surface charge of the substrate upon the second photoreaction. On the basis of the above results, we can conclude that the guest/target molecules can be successfully delivered *via* the photo-induced charge-inverted reaction.

In summary, a novel visible light-triggered loading and release system has been introduced in this study. By the visible light irradiation with λ = 515 nm, the NAP ester **2** is loaded on the surface, while by another irradiation with λ = 452 nm, the NAP group is released from the surface. The surface charge is inverted after the second photoreaction, which can be used to release other useful guest molecules. It is anticipated that many other molecules (such as drugs, fluorescent molecules and environmentally responsive molecules) can be employed to decorate 4-picolinium ester, resulting in versatile loading and release systems. We envision that this greener strategy has promising applicability in various drug-delivery systems and other processes triggered by visible light.

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