Donor-acceptor Stenhouse Adducts with Three Orthogonally Controlled Intrisic Stationary States

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Abstract

Photoresponsive molecules with more than two intrinsic stationary states are very interesting. Here, we demonstrate a series of crown ether (CE) substituted donor-acceptor Stenhouse adducts (DASAs) that can be switched between three stationary states under orthogonal control of light and metal ions. DASA-CE molecules are self-assembled into 1:1 head-to-tail supramolecular structures to form di-linear states due to strong van der Waals interactions between electron-donating and -withdrawing moieties. Furthermore, treatment with metal ions (Na+ or K+) switches the di-linear back to the linear state, which is reversible after adding free crown ether. On the other hand, green light irradiation induces linear-to-cyclic isomerization of DASA-CE, while the photoisomerization from di-linear to cyclic state is inhibited. The reverse cyclic-to-linear isomerization can occur under heating in the dark. All in all, the orthogonal switching of DASA-CE between di-linear, linear and cyclic states enables the development of smart materials in environments with complex stimuli.

Keywords: donor-acceptor Stenhouse adducts, photoresponsive, orthogonal, isomerization, supramolecular chemistry.
Donor-acceptor Stenhouse adducts (DASAs) are a new class of photoresponsive molecules, and have drawn plenty of attention in the past 5 years\(^1\)\(^-\)\(^6\). DASAs show linear-to-cyclic isomerization under visible-light irradiation, while the opposite cyclic-to-linear isomerization occurs under heating\(^7\)\(^-\)\(^10\). The molecular isomerization significantly changes the properties of DASAs in terms of molecular structure, color and polarity\(^6\)\(^,\)\(^11\)\(^-\)\(^14\), which further makes DASAs favorable in the applications of photolithography\(^15\), light-controlled molecular or macromolecular self-assembly\(^16\)\(^-\)\(^17\) and light-switched wettability on surfaces\(^6\)\(^,\)\(^18\)\(^-\)\(^19\).

However, similar to the well-studied traditional photoresponsive molecules (e.g. azobenzene (Azo)\(^20\)\(^-\)\(^22\), spiropyran\(^23\)\(^-\)\(^25\), and diarylethene\(^26\)\(^-\)\(^28\)), DASAs show only two photostationary states (i.e. linear and cyclic). In other words, the photoresponsive materials based on DASAs can only switch between two corresponding functional states, such as assembled/disassembled (in controlling molecular self-assemblies), hydrophilic/hydrophobic (in controlling surface wettability) and invisible/visible (in invisible inks). This limits the applications of DASA-based materials in environments with complex stimuli, and compounds that are switchable between multiple (n>2) functional states are urgently needed.

To achieve this, the introduction of two or more stimuli-responsive functional groups into one molecular or macromolecular system, which can be controlled in an orthogonal manner, has been reported. For example, Feringa et al demonstrated an intramolecular combination of photoswitching based on DASAs and Azo, while the isomerization of DASAs and Azo could be controlled separately\(^14\). Therefore, the resulting molecule could be switched between four independent states by controlling light and heat. This orthogonal control realized at the molecular level may open up applications for these materials in multi-stimuli environments. However, introducing more stimuli-responsive functional groups increases the complexity of the systems, which is not ideal for future developments. Instead, is it possible to realize intrinsically orthogonal switching between multiple (n>2) stationary states in a single molecule without introducing other stimuli-responsive groups? This is the question that needs to be answered.
Typical DASAs consist of electron-donating and -withdrawing moieties with a triene $\pi$-bridge in between\textsuperscript{2-3}, which makes DASAs a “push-pull” system (Scheme 1). Therefore, van der Waals interactions may exist between the electron-donating and -withdrawing moieties, which leads to the self-assembly of DASAs and induces the formation of a third state. However, this phenomenon has not been previously reported. This might be the reason of mismatched molecular geometries between the two moieties.

In the current work, we synthesized a series of new DASA derivatives (DASA-CE) using crown ethers (CEs) with different sizes (15-crown-5 and 18-crown-6) as the electron-donating moiety, while Meldrum’s acid and barbituric acid were selected for the electron-withdrawing moiety (Scheme 1). For the first time, linear DASA-CE self-assembles into a 1:1 head-to-tail supramolecular structure (di-linear state in Scheme 1) due to the strong van der Waals interaction between the crown ether (electron-rich) and the electron-withdrawing moiety.

Adding metal ions (Na\textsuperscript{+} or K\textsuperscript{+}) switches the di-linear state back to linear state, which is reversible by introducing free crown ethers into the system. Visible light irradiation with a wavelength of 530 nm induces the linear-to-cyclic isomerization of DASA-CE. However, for the di-linear DASA-CE, the photoisomerization is inhibited. Therefore, DASA-CE switching between three states (di-linear, linear and cyclic state) under orthogonal control of light and metal ions have been realized.

Scheme 1. Schematic illustration of orthogonal isomerization of DASA-CE under controlling of light and metal ions.
A series of DASA-CE were synthesized using 15-crown-5 and 18-crown-6 as the electron-donating moieties, and Meldrum’s acid or barbituric acid as the electron-withdrawing moieties (Scheme S1, see detail in Supporting Information (SI)). The synthesized DASA-CE were termed DASA-NC5, DASA-NC6, DASA-OC5 and DASA-OC6, respectively (Scheme 1). All four compounds have similar physical properties. Therefore, DASA-NC5 will be used to represent all DASA-CE in forthcoming discussions.

The three stationary states of DASA-NC5 could be clearly observed in one single $^1$H nuclear magnetic resonance (NMR) spectrum (Figure S1). The switching between the three independent states will be discussed in detail.

DASA-NC5 shows abnormally low absorbance in visible light region compared with the well-studied diethylamine-substituted DASAs (DASA-N) when dissolved in tetrahydrofuran (THF) (Figure 1a). However, the addition of NaBF$_4$ sharply increases the absorbance in the visible light region, which makes the DASA-NC5 solution strongly colored (Figure 1a). The absorbance of DASA-NC5 in the visible light region is closely and directly related to the concentration of added Na$^+$ ions, which reaches equilibrium when the Na$^+$ concentration approaches 1:1 with the DASA-NC5 (Figure S2). In addition, the absorbance in UV light region, which correlates to the electron-withdrawing moiety, shows a ~20 nm red shift after the introduction of Na$^+$ ion. On the other hand, DASA-N does not show obvious absorbance change after adding NaBF$_4$ (Figure S3). This indicates that the linear DASA-NC5 forms a centrosymmetric molecular system. The coplanarity of the centrosymmetric molecular structure is obviously reduced, leading to the “hypochromic effect”$^{29}$, which limits the absorbance of the entirely conjugated molecule in visible light region of linear DASA-NC5. The centrosymmetric self-assembly of DASA-NC5 is supposed to be a 1:1 head-to-tail supramolecular structure (di-linear state), which will be discussed in detail later in this article (Scheme 1).

After introducing NaBF$_4$ into the system, the metal ions could coordinate with the 15-crown-5 group in the electron-donating moiety, and further induce the disassembly of the centrosymmetric structure (di-linear-to-linear transition). The di-linear-to-linear
transition of DASA-NC5 does not occur in all solvents. In protic solvents (i.e. ethanol), the addition of Na$^+$ does not increase the absorbance of DASA-NC5 in visible light region, which is different to that in tetrahydrofuran (THF) and dichloromethane (Figure S4 and S5). These might be attributed to the interaction between Na$^+$ ion and 15-crown-5 in protonic solvents$^{30-31}$. DASA-OC5, DASA-NC6 and DASA-OC6 also show metal-ion induced di-linear-to-linear transition in THF (Figure S6-S9). DASA-CE with 15-crown-5 substituted electron-donating moieties are responsive to Na$^+$ ions, while 18-crown-6 substituted DASAs are sensitive to K$^+$ ions (see detail in SI).

Figure 1. (a) UV/vis spectra of linear DASA-N (black, dot) and DASA-NC5 before (red, solid) and after (blue, solid) adding NaBF$_4$ ([DASA-NC5] = [NaBF$_4$] = 0.12 mM in THF). The inset shows the color change after adding NaBF$_4$; (b) Absorbance variation at 560 (red) and 272 nm (blue) for DASA-NC5 with different concentrations after adding NaBF$_4$ solution; (c) $^1$H NMR spectra (400 MHz at 298 K) of DASA-NC5 before (red) and after (blue) adding NaBF$_4$ ([DASA-NC5] = 3 mM in THF-$d_8$). (a, b, c…(black) represent the protons in linear DASA-NC5, a’, b’, c’…(blue) represent the protons in di-linear DASA-NC5).

The absorbance variation in the visible light region caused by the addition of Na$^+$ ion was investigated on concentrations of DASA-NC5 between 0.12 and 0.015 mM (Figure 1b, red). The absorbance in the visible light region increases more upon adding Na$^+$ ions to higher concentrations of DASA-NC5 in THF, indicating more di-linear states are formed under higher concentrations. Similar changes could be noticed for the absorbance in the UV light region (Figure 1b, blue).

The di-linear-to-linear transition of DASA-NC5 was further monitored by $^1$H
NMR spectroscopy (Figure 1c). Two states of DASA-NC5 could be clearly identified before the addition of Na\(^+\) ions (Figure 1c, red). The signals of the di-linear state is broader than those of the linear state (e.g. Hb\(^-\) is broader than Hb), which is attributed to molecular aggregation. Approximately 75\% of DASA-NC5 are in the di-linear state. After the introduction of Na\(^+\) ions, all of the di-linear DASA-NC5 switches to the linear state (Figure 1c, blue). These are in good accordance with the results of the UV/vis spectroscopy investigation.

The di-linear state was further investigated by density functional theory (DFT) calculations. The electrostatic potential calculation shows a heterogeneous distribution of the electrostatic potential of the linear state, where the electron-donating moiety of the linear state is more electron rich (red) than the electron-withdrawing moiety (blue) (Figure 2a). This indicates that the van der Waals interaction between the electron-donating and -withdrawing moieties is favorable. Moreover, the other DASAs (DASA-N and other DASA-CE) show similar electrostatic potential distributions to DASA-NC5 (Figure S10-S13), which is in good accordance with the “push-pull” nature of DASAs. Linear DASA-NC5 shows a partially planar molecular structure, and the 15-crown-5 shows a slightly larger cavity than the electron-withdrawing moiety, which is ideal for the 1:1 head-to-tail self-assembly (Figure 2b). Therefore, it is possible for barbituric acid to enter the cavity of 15-crown-5 and further trigger the formation of di-linear DASA-NC5. The molecular sizes of the electron-donating and electron-withdrawing moieties are similar to the other DASA-CE (Figure S14-S16, see detail in SI).

The formation of the di-linear state was further demonstrated by 2D \(^1\)H,\(^1\)H nuclear Overhauser effect spectroscopy (2D-NOESY), and the protons on the triene \(\pi\)-bridge were investigated in detail. For the linear state, strong correlations of a-b, a-c, b-c and c-d are observed (Figure 2c, black). No correlations of d-a and d-b exist, due to the long distance between the protons (Figure 2c, blue). In contrast, a clear correlation of d’-a’ is observed for the di-linear state, indicating the formation of the head-to-tail supramolecular structure (Figure 2c, red).
Figure 2. (a) Calculated electrostatic potential distributions of linear and cyclic DASA-NC5; (b) Calculated molecular structure of linear DASA-NC5; (c) $^1$H,$^1$H NOESY spectrum (400 MHz at 298 K) of DASA-NC5 before adding NaBF$_4$ ([DASA-NC5] = 6 mM in THF-$d_8$).

The transition of DASA-NC5 between linear and di-linear states is reversible. After adding competing host molecules, the coordinated metal ions are removed from linear DASA-NC5, which further induces the linear-to-di-linear transition (Figure 3a). DASA-NC5 is mostly in the linear state after introducing Na$^+$ ions. Adding 15-crown-5 (C5 in Figure 3) sharply decreases the absorbance in visible light region. However, the absorbance can not reach the pristine value of the di-linear state when the 15-crown-5 concentration is 1:1 with the Na$^+$ ions (Figure 3b). Increasing the amount of 15-crown-5 can further decrease the absorbance of DASA-NC5, indicating that the formation of the di-linear state is promoted. This could be explained by the competition of the Na$^+$ ion between the free 15-crown-5 and DASA-NC5 (see details in SI). The absorbance in the UV light region shows similar behavior (Figure 3b, inset). The reversible transition between the linear and di-linear state was demonstrated by repeatedly treating the system with equal amounts (in molar ratio) of NaBF$_4$ and 15-crown-5 (Figure 3c). The di-linear-to-linear transition of DASA-NC5 is approximately 100% for each cycle. However, the yield of the reverse linear-to-di-linear transition decreases sharply as the cycle numbers increase, which could also be explained by the Na$^+$ ion competition (see detail in SI).
Figure 3. (a) Schematic illustration of the reversible transition of DASA-NC5 between the linear and di-linear states; (b) UV/vis spectra of DASA-NC5 before and after sequential treatment with NaBF₄ and 15-crown-5 ([DASA-NC5] = [NaBF₄] = 0.12 mM in THF). The inset shows the UV light region in detail; (c) Variation of absorbance at 560 nm of DASA-NC5 after repeated treatment with NaBF₄ and 15-crown-5 ([DASA-NC5] = 0.12 mM in THF; the amount of NaBF₄ and 15-crown-5 added are kept the same for each cycle (in molar ratio)).

The light-induced linear-to-cyclic isomerization of DASAs has been well-studied over the past 5 years. According to the previous published theory⁴⁻⁵, DASA-CE belong to the first-generated DASAs, which are mainly in the zwitterionic cyclic state after visible light irradiation (Figure 4a). DASA-NC5 does not show obvious linear-to-cyclic isomerization under 530 nm green light irradiation (40 mW/cm², 10 min) before introducing Na⁺ ions (Figure 4b, black). The slightly decreased absorbance in the visible light region is due to the residual linear state in the system. After the NaBF₄ addition, the absorbance in visible light region decreases sharply under green light irradiation, which is reversible after heating in the dark (Figure 4b, red and Figure S18). Therefore, the photoisomerization of the di-linear state is restricted. The light-induced isomerization of linear and di-linear states are further demonstrated by ¹H
NMR spectra (Figure 4c). The signals of the linear and di-linear state could be clearly identified in the same spectrum (Figure 4c, black). After green light irradiation, the signals of the linear state disappear, while the new generated signals for the cyclic state are formed, indicating the light induced linear-to-cyclic isomerization. In contrast, the signals of the di-linear state do not change after light irradiation, indicating the photoisomerization of di-linear state is restricted. These are attributed to the formed stable head-to-tail supramolecular structure.

**Figure 4.** (a) Schematic illustration of light-induced isomerization between linear, di-linear and cyclic DASA-NC5; (b) UV/vis spectra of DASA-NC5 under dark (solid) and visible light irradiation (dot) before (black) and after (red) NaBF$_4$ addition ([DASA-NC5] = 0.12 mM in THF); (c) $^1$H NMR spectra (400 MHz at 298 K) of DASA-NC5 under dark and visible light irradiation before NaBF$_4$ addition ([DASA-NC5] = 3 mM in THF-$d_8$). (a, b, c…(red) represent the protons in cyclic DASA-NC5)

In summary, we synthesized a series of crown ether-substituted DASA derivatives. The switching of the DASA-CE between di-linear, linear and cyclic states under orthogonal control of light and metal ions was realized. Taking DASA-NC5 as an example, in aprotic solvents (e.g. THF, dichloromethane), DASA-CE exist mainly in the di-linear state, which is a 1:1 head-to-tail supramolecular structure self-assembled
through the van der Waals interaction between the electron-donating and -withdrawing moieties. The addition of Na$^+$ induces di-linear-to-linear transition, while the reverse linear-to-di-linear transition occurs after adding free 15-crown-5. Similar to the reported DASAs, linear DASA-NC$_5$ isomerizes to cyclic DASA-NC$_5$ after 530 nm green light irradiation, and switches back to the linear state under heating. However, the photoisomerization of the di-linear state is inhibited. We have successfully achieved switching of multiple (n>2) stationary states in a single molecule, which is beneficial for the future development of smart materials used in environments with complex stimuli. This also leads to more intelligent photoresponsive materials, including multi-drug release systems and interpenetrating polymer hydrogels.

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**Author Contributions**

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. Y. Duan and H. Zhao contributed equally to this work.

**Declaration of Interests**

The authors declare no competing interests
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