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J. Am. Chem. Soc., **Just Accepted Manuscript** • DOI: 10.1021/jacs.9b00341 • Publication Date (Web): 10 Apr 2019

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ACS Publications

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Taming the complexity of donor–acceptor Stenhouse adducts: IR motion pictures of the complete switching pathway

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ABSTRACT: Switches that can be actively steered by external stimuli along multiple pathways at the molecular level are the basis for next-generation responsive material systems. The operation of commonly employed molecular photoswitches revolves around one key structural coordinate. Photoswitches with functionalities that depend on and can be addressed along multiple coordinates would offer novel means to tailor and control their behaviour and performance. The recently developed donor–acceptor Stenhouse adducts (DASAs) are versatile switches suitable for such applications. Their photochemistry is well understood, but is only responsible for part of their overall photoswitching mechanism. The remaining thermal switching pathways are to date unknown. Here, rapid-scan infrared absorption spectroscopy is used to obtain transient fingerprints of reactions occurring on the ground state potential energy surface after reaching structures generated through light absorption. The spectroscopic data are interpreted in terms of structural transformations using kinetic modelling and quantum chemical calculations. Through this combined experimental-theoretical approach, we are able to unravel the complexity of the multi-dimensional ground-state potential energy surface explored by the photoswitch, and use this knowledge to predict – and subsequently confirm – how DASA switches can be guided along this potential energy surface. These results break new ground for developing user-gated DASA switches, but also shed light on the development of novel photoswitches in general.

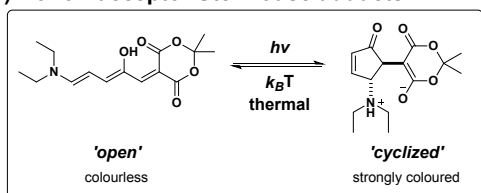
INTRODUCTION

Photochemical tools rely on light as external stimulus to manipulate chemical, biological, and materials systems with high spatiotemporal control and without contaminating the sample.^{1,2} Molecular photoswitches³ have been particularly successful in this respect as they can be switched reversibly between isomers⁴ whose distinct properties can be harnessed

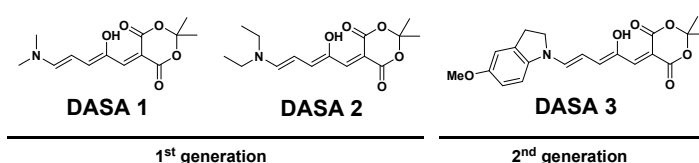
in applications ranging from receptors⁵ and molecular muscles⁶ to machines^{7–9} and ‘smart’ materials.^{10,11} More recently, they have been used for biological and medicinal applications, with photopharmacology attracting tremendous interest.^{12–18} Switches such as azobenzenes,¹⁹ stilbenes, hemithioindigos,²⁰ and diarylethenes²¹ rely, for all practical purposes, on a simple transformation, that is, the key step for their functioning involves one reaction coordinate such as *E–Z* isomerization or electrocyclization. Going beyond the possibilities offered by these ‘simple’ systems requires photoswitches that undergo addressable transformations along multiple possible reaction pathways. Such switches open novel avenues for tailor-made, user-oriented chemical systems whose functionalities can be manipulated by directing the mechanistic pathway.

The recently introduced donor–acceptor Stenhouse adducts (DASA),^{22–27} which have already found a wide range of applications,²⁷ feature in this respect favourable characteristics. The visible-light-triggered transformation starts from a strongly coloured, linear triene (‘open’) that cyclizes into a colourless²⁸ cyclopentenone (‘closed’, Fig. 1a) – whose structure depends on the generation of DASAs used^{24,25} (Fig. 1b) – and then thermally reverts to the original form. It has become clear (*vide infra*) that the functional use of DASAs along a productive photoswitching pathway depends on at least two key steps (see Fig. 1c for mechanistic proposal):^{23,29} a photoinduced *Z–E* isomerisation within the triene and a thermal electrocyclization. Whereas the actinic step of the reaction has been previously investigated in detail,^{29–32} insight into the thermal part of the pathway is as yet largely lacking. Here, using time-resolved infrared absorption spectroscopy and quantum chemical calculations, we show that competing photoswitching pathways are indeed far more complicated than one would have assumed *a priori*, and that a rational control over it requires ‘turning knobs’ that one normally would not consider.

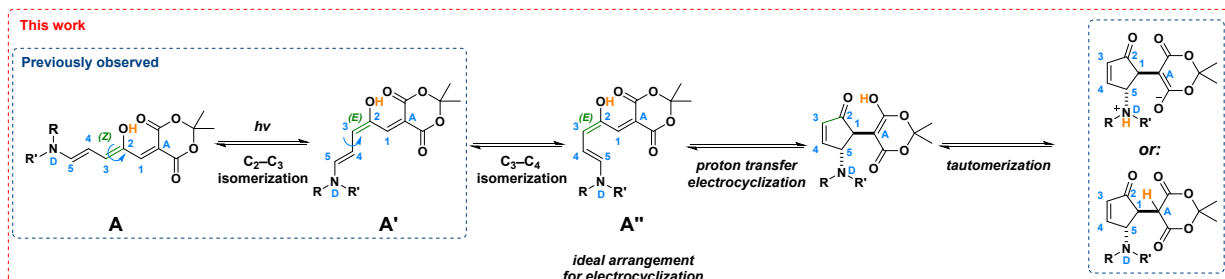
a) Donor–acceptor Stenhouse adducts



b) Photoswitches studied herein:



c) Mechanistic proposal



d) Overview of possible thermal interconversions

* experimentally observed (previously)

* experimentally observed (this work)

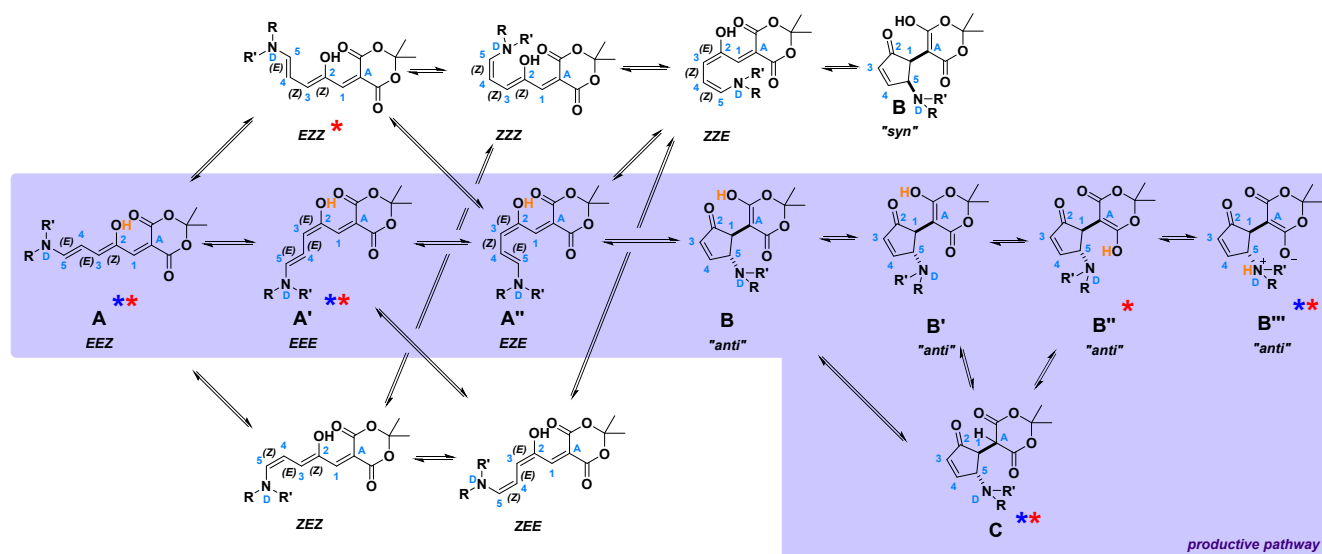


Figure 1. Donor–acceptor Stenhouse adducts: (a) overall photochemical transformation; (b) photoswitches studied in this work; (c) current mechanistic proposal for the photoswitching mechanism; and (d) all possible thermal interconversions.

Previous mechanistic studies of DASAs in solution have only focused on the initial photochemical step by means of ultrafast pump-probe spectroscopy and density functional theory (DFT) calculations, in combination with temperature-dependent steady-state UV/Vis spectroscopy and photoaccumulation experiments at low temperature.^{29–31,33} These investigations suggested *Z*–*E* isomerization happening on a picosecond timescale (from **A** to **A'** in Fig. 1c).^{30,31,33} The presence of a hydroxy group on the triene chain seems to favour the productive photochemical isomerization pathway around the C_2 – C_3 bond,³¹ but many different 'non-productive' isomers can potentially be obtained by thermal rotation or photochemical isomerization along the conjugated bridge³² before and after photoactivation (Fig. 1d). This increases the complexity of the switching process tremendously. In addition, gas-phase studies have suggested that the step following the initial photoisomerization could also be photochemical in nature, with **A'** absorbing a second photon yielding **A''**.³² This finding can be relevant for 'real-life' applications of DASA switches for which usually

continuous wave light sources are used as opposed to the pulsed laser sources employed in high-end spectroscopic studies.

In analogy to the Piancatelli rearrangement^{34,35} and related (*iso*-)Nazarov-type³⁶ chemistry, it has been postulated that a productive mechanistic pathway involving a thermally allowed 4π -electrocyclization starting from **A''** (Fig. 1c) is followed by a proton transfer and tautomerization.^{23,29} Although the primary photochemical step determines the immediate photoresponse, the thermal steps that occur on much longer timescales are far more important for understanding and controlling DASA-photoswitching. To characterize this thermal part of the switching mechanism we employ a combination of rapid-scan IR absorption spectroscopy,³⁷ quantum chemical computations, and kinetic modelling. This approach offers the necessary time-resolution (milliseconds to hours) and structural information to come for the first time to a complete picture of the thermal reaction pathways in DASAs in terms of calculated and observed intermediates, as well as their IR absorption

spectra, energies, and possible ground-state interconversions. At the same time, it allows us to fill the gap between our ultrafast spectroscopy studies^{29,30} and the photoswitching outcomes. We then show that the complicated reaction mechanisms are in fact governed by a few simple but sometimes counterintuitive principles that provide detailed design suggestions and guidelines for next-generation DASAs, and that are applicable beyond the presently studied class of photochromes.

RESULTS AND DISCUSSION

Herein, we focused on three molecules (Fig. 1b) representing both first- (**1** and **2**)^{22,23} and second-generation (**3**)^{24–26} DASA photochromes (SI section 1.1, 2 and 7). To elucidate the molecular basis of the thermal interconversions and overall photoswitching mechanism, we identified the structures of the various isomers formed upon continuous wave illumination using rapid-scan FT-IR spectroscopy and kinetic modelling. Interpretation and assignment of the time-resolved spectra requires the comparison with computed FTIR spectra of all possible intermediates. We therefore optimized the structure of all ground-state minima and computed the corresponding vibrational spectra using DFT at the B3LYP^{38,39}/maug-cc-pVDZ⁴⁰ level and an implicit SMD⁴¹ solvent model. For the evaluation of the energy profile, we employed instead the M06-2X functional,⁴² since B3LYP is known to describe incorrectly the ring-closure step⁴³ even though it produced better spectra for our systems (see SI Fig. S5.33).

Photoinduced thermal reaction pathways of DASA 1

Rapid-scan FT-IR spectra of DASA **1** in dichloromethane (DCM) are shown in Fig. 2. Visual inspection of the time evolution makes immediately clear that most of the intense bands from the linear form **A** strongly decrease once light is switched on. As illumination progresses, new low-intensity bands appear as a result of cyclization, in particular in the carbonyl stretching region (1650–1750 cm⁻¹). Cyclization under continuous illumination is also observed by steady-state UV/Vis spectroscopy (see SI section 3), manifesting itself in the disappearance of the intense absorption band in

the visible spectral region, characteristic of the open form, and the increasing absorption in the UV region attributed to the closed form. Time-resolved IR experiments provide kinetic traces (Fig. 2b) that allow to distinguish three different phases in the reaction. Immediately after irradiation is started with broadband white light (see SI section 1.2), a quick response of the system occurs, producing a new equilibrium within the experimental time resolution of the experiment (96 ms). Subsequently, an exponential behaviour is observed both in the decay of the starting compound and the concurrent formation of a product. Importantly, time traces of bands in the carbonyl stretching region show different kinetics that suggests the delayed formation of another final product (see for instance the kinetic behaviour of red trace in Fig. 2b as compared to the yellow trace).

To identify the minimum number of kinetic components needed to describe the time-dependent behaviour of the spectra, we analysed the rapid-scan FT-IR data using singular-value decomposition⁴⁴ (see SI section 1.7 for more details). Subsequently, we used a global analysis procedure⁴⁴ that fits the kinetic traces recorded at all frequencies simultaneously with a combination of exponential decay functions. Global analysis requires the specification of a kinetic scheme, allowing to write the differential equations describing the change in the concentration of reactant and products and determine the associated kinetic constants. In view of the multitude of intermediate structures that may be formed during the reaction, and the resulting complexity of the kinetic scheme describing their interconversion, the analysis was performed applying a simplified sequential reaction scheme shown in Fig. 3a that nevertheless allows us to identify the timescale of formation of the main products.⁴⁴ The reaction scheme describes the time evolution of the system in terms of compartments (boxes S1–S4 boxes in Fig. 3a) representing the state of the system at a given time. The different compartments are connected by the kinetic constants determined from the fit of the kinetic traces. Apart from the kinetic constants, the analysis also determines the spectral component associated with each compartment. We loosely name these components “Species Associated Differential Spectra” (SADS) even though they do not reflect the

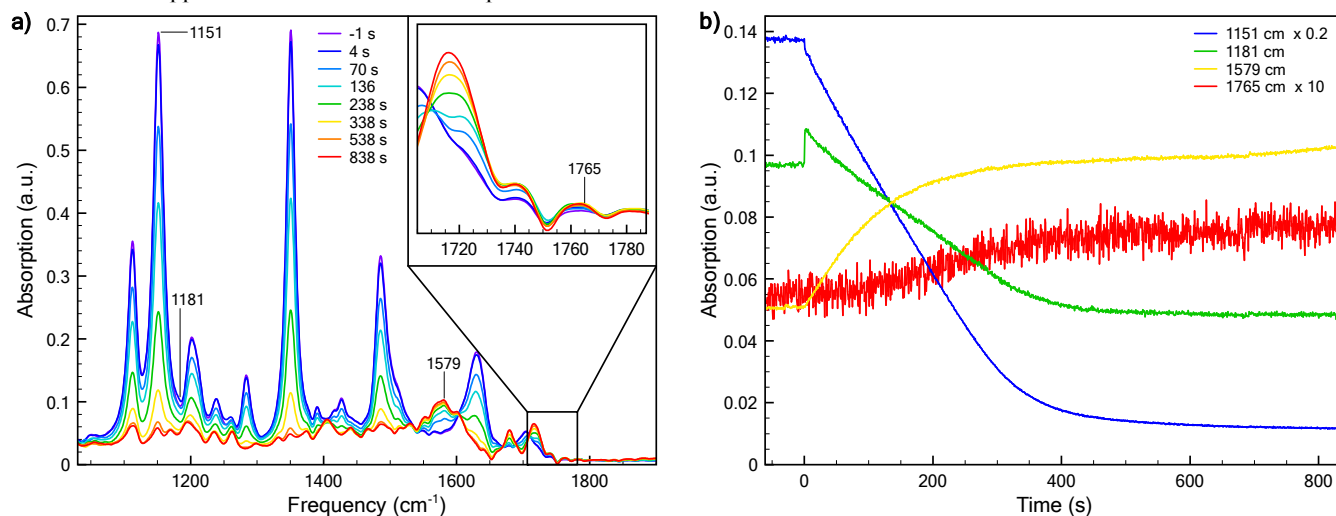


Figure 2. Rapid-scan FT-IR spectra of DASA 1. (a) Snapshots of spectra before and after switching on the light (broadband white light; at $t = 0$) in the rapid-scan FT-IR experiment. (b) Time-dependent behaviour of key bands during the rapid-scan FT-IR experiment. For the

1765 cm^{-1} trace, absorption is taken relative to the absorption at 1779 cm^{-1} in order to eliminate the change in absorbance due to other bands in the spectrum.

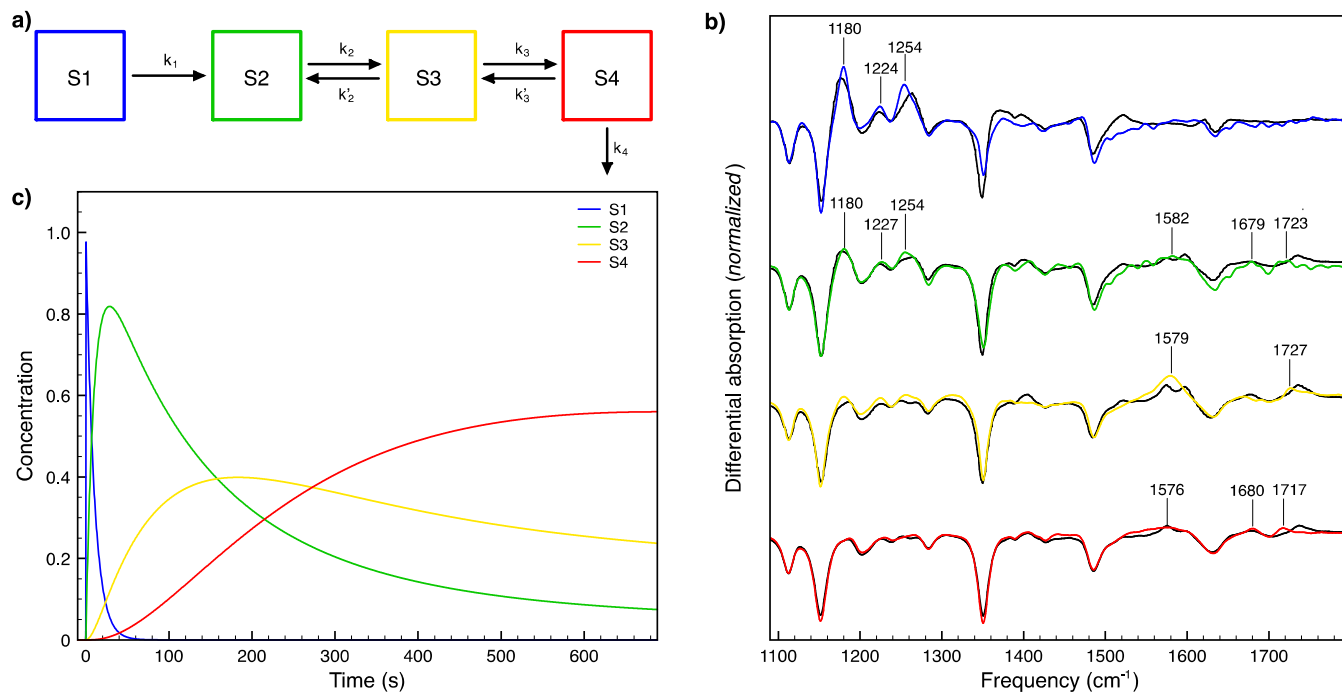


Figure 3. Kinetic scheme and modelling of the rapid-scan FT-IR measurement of DASA 1. (a) Schematic representation of the kinetic model. (b) Resulting SADS (black) and their fits with computed spectra with SADS1 to SADS4 from top to bottom. The spectrum of the elongated form **A** has been subtracted before fitting the data, producing the differential signals shown in panel b. The four SADS have respectively been fitted as (see Figure 1d for isomer notation): SADS1 a 37:63 mixture of **A'**:**EZZ**, SADS2 a 14:18:34:34 mixture of **A'**:**EZZ**:**B''**:**B'''**, SADS3 a 58:31:11 mixture of **B''**:**B'''**:**C** and SADS4 a 74:26 mixture of **B''**:**B'''**. (c) Concentration profile of the four SADS in time.

differential spectra of pure intermediates (as in the case of a complete reaction scheme) but rather of mixtures due to the simplification here introduced. The four SADS resulting from the kinetic analysis with estimated lifetimes of $t_1=10$ s, $t_2=88$ s, $t_3=201$ s, and $t_4=14 \times 10^3$ s are shown in Fig. 3b. Assigning the positive/negative vibrational bands of each SADS to appearing/disappearing isomers during the course of the reaction requires knowledge of the energy profile of the productive lowest-energy pathway and the vibrational spectra of all intermediates along this pathway, which for clarity we split into three steps:

1. From **A** to **A''** (Fig. 4a): Our previous studies have shown that the primary photochemical step consists of photoisomerization around $\text{C}_2\text{—C}_3$ to form **A'**. This isomer can then thermally isomerize around $\text{C}_3\text{—C}_4$ to form **A''**, so that the molecule is spatially arranged for a thermally allowed, conrotatory 4π -electrocyclization step (Fig. 1b).^{30,33} Importantly, our calculations indicate that, beside the three open isomers (**A**, **A'** and **A''**) put forward from the mechanistic proposal, one has to consider at least the isomer **EZZ** among the remaining five possible open isomers of Fig. 1d (**EZZ**, **ZZZ**, **ZZE**, **ZEZ** and **ZEE**), **EZZ** being the second most stable structure. ¹H-NMR experiments confirm this finding as they show that the elongated triene form **A** is in thermal equilibrium with a minor amount of **EZZ** in solution at room temperature in the dark (see SI section 8).
2. From **A''** to **B** (Fig. 4b): For a successful ring-closure step, the electrocyclization of **A''** should be

accompanied by a concomitant proton-transfer reaction (Figs. 1c and 4) which breaks the extended conjugation and results in the formation of the colourless isomer **B**. An alternative electrocyclization without such an associated proton transfer is only possible in the absence of the intramolecular hydrogen bond. This pathway would involve a cyclized intermediate **I7** also involved in the pathway from **B** to **C** (see Fig. 4c) that is high in energy (see SI Fig. S6.4) and is thus unlikely to occur. Another possible, but energetically disfavoured electrocyclization pathway starting from the **ZZE** isomer (Fig. 1d) would lead to a sterically encumbered *syn*-configuration in contrast to the energetically favoured and experimentally observed^{23,25,45} *anti*-configuration.

3. From **B** onwards (Fig. 4c): To reach the lowest energy products, tautomerization of **B** to **B''** or **C** needs to occur. While a solvent-assisted process was previously postulated,³³ it appears that a fast, intramolecular proton-transfer pathway is possible without direct involvement of solvent or another DASA molecule. Our calculations find that the system follows three consecutive steps to reach the zwitterionic final product **B'''**: a nitrogen inversion (**B'**), a rotation around $\text{C}_1\text{—C}_A$ (**B''**), and a $\text{C}_5\text{—N}_D$ bond rotation with a concomitant transfer of a proton to the nitrogen atom. We note that this path is energetically preferred among the many possible routes resulting from the combination of the above

four processes, also when the possible ring-flip of the Meldrum's acid moiety is considered (see SI Figs. S6.5-S6.7). The enol-keto tautomerization pathway from either **B** or **B'** to **C** (which is the primary cyclized product of DASA **3** as observed by $^1\text{H-NMR}$

in CD_3CN and $\text{DMSO}-d_6^{25}$ and in crystal structures^{24,25}) proceeds with a proton transfer mediated by the oxygen of the cyclopentenone

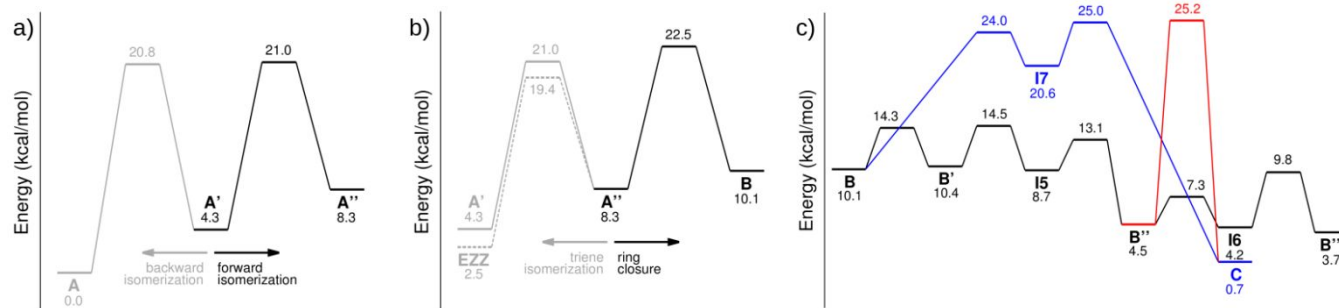


Figure 4. Possible isomers and calculated low-energy productive pathway: Energy profiles of DASA **1** in DCM for (a) backward (gray) and forward (black) isomerizations of the initial photoproduct **A'**, (b) triene isomerization (gray) and ring closure (black) of **A''**, and (c) the competing tautomerization pathways of **B** to **B'''** (black) and **C** (blue) and of **B''** to **C** (red).

ring, without any need for a catalyst, external acid, or base. Alternatively, the amine group on the cyclopentenone ring can facilitate the tautomerization from **B''** to **C** without any intermediates.

After identifying the lowest-energy pathway connecting the open and closed forms, the SADS obtained from the kinetic analysis of the experimental time-resolved IR spectra have been interpreted using the calculated IR spectra of the species reported in Fig. 4. To this end, we fitted the SADS with combinations of the calculated spectra (reported in SI section S5.1.4) using an in-house developed genetic algorithm (see SI section S1.8).

Surprisingly, the first SADS **S1** (Fig. 3b), which describes the species formed within the time resolution of the rapid-scan measurement (96 ms), shows a large contribution of **EZZ** which was not observed in our previous femtosecond time-resolved infrared (fs-TRIR) experiments that explored time delays up till the nanosecond timescale.⁴⁶ In particular, the two positive bands at 1224 and 1254 cm^{-1} observed in **S1** are missing in the fs-TRIR spectrum, which was previously assigned exclusively in terms of the formation of **A'** (SI Fig. S5.20). Although the presence of a large amount of **EZZ** fits well with the energy of this isomer in comparison with **A'** and **A''**, the mechanism by which it is generated is not immediately clear, as the aforementioned TRIR experiments exclude photochemical generation from **A**. One possible explanation could be that a second photon absorption takes place, as recently put forward by Bieske and co-workers.³² However, rapid-scan FTIR experiments in which a band-pass filter (HQ510/80m-2p, Chroma) was used to inhibit absorption of a second photon by either **A'** or **A''**, which are both red-shifted with respect to **A**, show that this does not occur, since under these conditions **EZZ** is still formed and with the same temporal behaviour as without filter (see SI Figs. S5.5 and S5.6). We therefore conclude that **EZZ** is generated along a thermal reaction path from **A'** (obtained photochemically within the time resolution of the experiment) to **A''** and then back to **EZZ**. Considering the inherent uncertainties in calculated energy barriers, this path is energetically very well possible and in line with the observed time scales.

The second component (**S2** in Fig. 3b) is formed on a 10 s timescale. Importantly, the IR spectra of closed isomers, in particular **B''** and **B'''**, needed to be included for an

adequate fit. Notably, we observed bands at 1582 and 1723 cm^{-1} that are distinctive signatures of **B'''**, while the band at 1679 cm^{-1} can only be explained by **B''** (see SI Fig. S5.17). The presence of the latter isomer is further supported by the observation of bands associated with its N-H bending and stretching modes at 1579 cm^{-1} and 2200 cm^{-1} (see SI Figs. S5.7 and S5.17), which are significantly broadened and shifted as a result of the internal hydrogen bond in **B''**. We therefore conclude that after the 'instantaneous' photoinduced transformation of **A** into other open isomers, ring closure can occur on a timescale of 10 s. In terms of Eyring's equation, this implies a Gibbs activation energy of 18.5 kcal/mol, which is in excellent agreement with the calculated Gibbs energy difference between **A'** and the transition state connecting **A''** to **B** (18.2 kcal/mol). Once the molecule has overcome this barrier, there is a downward energy path from **B** via **B'** that populates **B''** and **B'''**. The fact that **S2** shows contributions of **A'** and **EZZ** is due to the continuous generation of these isomers.

Subsequently, formation of **S3** occurs with a time constant of about 90 s (Fig. 3b). What distinguishes this component from **S2** is the presence of the most stable closed isomer **C** – which is evidenced by the appearance of three characteristic carbonyl stretching bands in the spectrum (highlighted in Fig. 2a) – and the absence of open isomers. The fact that the formation of **C** occurs on a much longer time scale and that a delayed ingrowth is observed (Fig. 2b, red trace) implies that tautomerization towards **C** starts from the closed **B**-type forms and is associated with a higher energy barrier. These conclusions are in good agreement with our calculations (Fig. 4c) which show that after isomer **B** is formed, the tautomerization path with the lowest barrier is the one leading to **B'''** via **B''**. However, once these two isomers have been populated, a thermal reaction from **B''** to **C** is possible, albeit with a higher Gibbs activation energy which explains its slower rate of formation.

The presence of a further component **S4** (Fig. 3b) showing the presence of only **B''** and **B'''** and not of **C** may in first instance seem puzzling. Important to notice is that, in the sequential kinetic scheme adopted in Fig. 3c, a particular SADS reports the changes that occur in the concentrations of the pertaining components with respect to the previous SADS. This implies that in going from **S3** to **S4** the contribution of **B''** and **B'''** is affected to a major extent,

while the contribution of **C** is much less affected. In our experiments on DASA **1**, dissolved in DCM, we have observed that precipitation occurs (see SI Fig. S5.1). Such a precipitation does not occur when DASA **1** is dissolved in dimethyl sulfoxide (DMSO). Moreover, analyses of the rapid-scan FT-IR data on DASA **1** in DMSO do not show a fourth component (*vide infra*). The major difference between the two solvents is that in DMSO the zwitterionic **B'''** isomer is the end product and is very well soluble, while in DCM the solubility of **B'''** is considerably lower. We therefore conclude that the presence of **S4** for DASA **1** in DCM is due to the precipitation of **B'''**. This is in line with the observation that the concentration of **C** hardly changes in going from **S3** to **S4**, and that the dominant changes occur in **B''** and **B'''**, with **B''** being influenced because it is on the pathway from **C** to **B'''** and has a nearly equal energy as **B'''** (Fig. 4c). Such conclusion is also in agreement with the time scale on which **S4** decays (14×10^3 s), which, in turn, is in line with the Gibbs energy difference between **C** and the highest transition state leading to **B'''** (24.5 kcal/mol, Fig. 4c).

The detailed studies presented above for DASA **1** in DCM have led to a series of remarkable and unexpected findings, highlighting the importance of thermal reaction pathways in determining both the rate and the efficiency of DASA photoswitching. The isomer **EZZ** is clearly observed and plays a key role in the early phase of photoswitching. Moreover, the cyclization occurs on a 10 s timescale consistent with the computed thermal barriers to produce **B**, which rapidly isomerizes to **B'** and then to **B''** and **B'''**. Subsequently, on a longer timescale, the most stable isomer **C** is formed.

Tailoring DASA's reaction pathways

Our experiments and calculations on DASA **1** show that the photoswitching process – although operationally simple – is in reality a picture of complex interconversions among different open and closed isomers where different tuneable ‘knobs’ allow controlling the overall photoswitching behaviour. The experimental insights gained on the contribution of thermal interconversions and the developed theoretical model enable us to account for previously observed differences in the kinetic behaviours of DASA, which could depend on solvents or on the nature of donor or acceptors groups. Rationally addressing the key steps of the reaction by tuning the stability of selected isomers or the

energetic barriers which regulate their thermal conversions, allows us to deliberately steer efficacies, rates, and switching characteristics of DASAs, as will be shown in the following.

The reaction scheme depicted in Fig. 4 predicts the stability of the transition states from **A'** to **A''** and back from **A'** to **A** to be a key means to control the reaction rate of DASAs conversion. With the electrocyclization being the rate-limiting step, this is counterintuitive. A simple way to tune the energy of transition states is to change the solvent. Indeed, calculations with DMSO as a solvent show that the transition state between **A'** and **A** is 3.4 kcal/mol lower than in DCM, while the transition state to **A''** is only slightly higher by 0.7 kcal/mol (Fig. 5a). In agreement with these findings, we observe experimentally that in DMSO full conversion of DASA **1** does not occur even after 3 h of irradiation, while in DCM ring closure proceeds in the order of minutes. As the energy profile of the ring-closure step (**A''** to **B**) is practically the same in both solvents, the lower conversion rate can only be attributed to a quicker thermal back conversion from **A'** to **A** in addition to a possible influence of band overlap.³³ This is confirmed by rapid scan FT-IR studies (Sections S5.1.2 and S5.1.3) that show almost no evidence for the presence of **A'** on the milliseconds timescale, in agreement with the calculations that predict the half-life of **A'** to drop to around 1 ms in DMSO.

Further support for the importance of the stabilities of the transition states from **A'** to **A''** and back to **A** is found by analysing the photoswitching behaviour of DASA **1** in toluene. Here, faster photoswitching than in DCM is observed, in line with the lower/higher barrier for the forward/backward thermal conversion of **A'** predicted by the calculations (Fig. 5a). The relative energy of the barriers can simply be explained by analysing the bonding characteristics in different solvents (SI Fig. S6.8). As the solvent polarity increases, the zwitterionic resonance contribution gains more importance and, consequently, the bond order of C_2-C_3/C_3-C_4 decreases/increases, thereby hindering/favouring isomerization around these bonds. The same consideration applies to the stability of the transition state from **A''** to **EZZ**: higher barriers are found in toluene preventing the formation of the non-productive **EZZ** isomer (SI Fig. S6.9). From all these findings, we thus conclude that to increase the forward switching rate both the transition state from **A''** to **EZZ** and from **A'** to **A** should be destabilized as much as possible to minimize unproductive backward reactions.

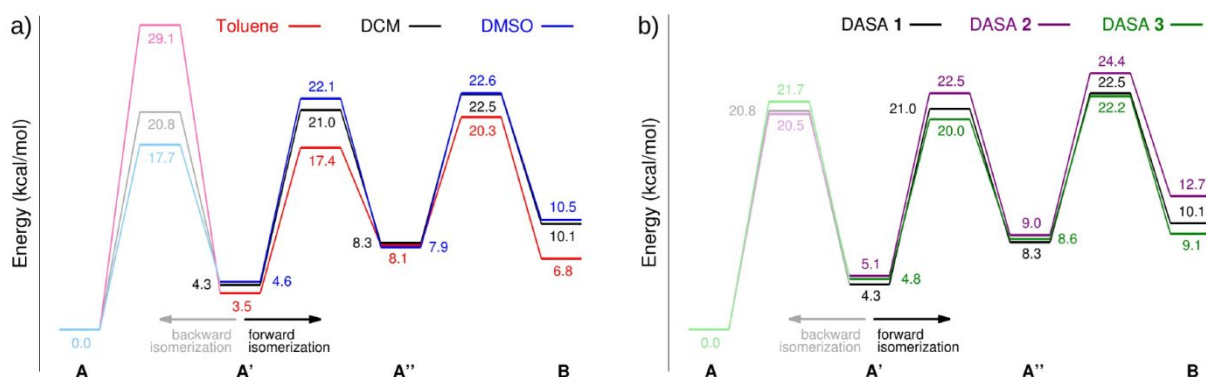


Figure 5. Role of solvent and substituent in the ring-closure reaction: Energy profiles for backward (lighter color) and forward (darker color) isomerization pathways of isomer **A'** of (a) DASA **1** in toluene (red), DCM (black) and DMSO (blue) and of (b) all studied DASAs (**1** in black, **2** in purple, and **3** in green) in DCM.

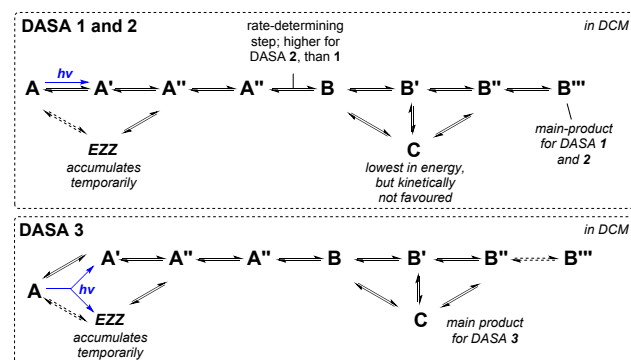


Figure 6. Overview of photoswitching behaviour of DASA 1–3 in DCM.

Being able to control the composition of photostationary states is highly desirable when dealing with photoswitches. Although the use of different substituents on a particular donor is an obvious means to target this issue for DASAs – as exemplified by the recent studies of Beves and co-workers⁴⁵ – it is quite unexpected that replacing the methyl groups in DASA **1** by ethyl groups in DASA **2** leads to major changes in photoswitching behaviour (for DASA **2** cyclization is much reduced, see SI section 3.2). Rapid scan FT-IR spectra of DASA **2** in DCM recorded directly after switching on the light are very similar to those of DASA **1** in the same solvent, indicating comparable early steps (SI Fig. S5.20). Hence, differences in the overall photoswitching behaviour should be a result of differences in energies at later stages. Our calculations find indeed that the ring-closure step (from **A''** to **B**) is responsible for the slower photobleaching in DASA **2** (Fig. 5b), which can be related to the steric hindrance arising from the bulkier ethyl groups. This seems to hold for different solvents as well, since switching experiments in toluene (SI section S3.2) found that DASA **2** converts more slowly to the cyclized product than DASA **1** (see also the energy profile in SI Fig. S6.18). Fine-tuning of steric interactions thus appears to be more instrumental in regulating DASA's switching pathways than expected. Thus, substitutions at the triene unit could very well be another useful means to obtain further control over DASA's photoswitching behaviour, and this is indeed one of the directions we are presently exploring.

By now, several generations of DASAs have been developed that aim for further control by modifying the electronic properties of the donor and acceptor groups. Our studies on DASA **3** (see SI sections S5.3 and S6.4), an example of a second-generation DASA, demonstrate how the present investigations allow for rationalizing in much more detail how specific donors influence the switching behaviour. Importantly, already the actinic step is dramatically influenced by a change in donor: excitation of isomer **A** of DASA **3** leads to the formation of both **A'** and **EZZ** in equal amounts, in contrast to the first-generation DASAs (compound **1** and **2**) where only **A'** is formed. Using a combination of ¹H-NMR, ultrafast TRIR, rapid-scan FTIR experimental data and DFT calculations we find that most likely a forked photochemical reaction pathway is responsible for this behaviour (see Fig. 6). ¹H-NMR *in situ*-irradiation experiments support this finding as both **A'** and

EZZ accumulate rapidly (see SI section 9). The fact that upon irradiation **EZZ** is easily formed in DASA **3** can help explain previously observed differences³³ in the behaviour of first- and second-generation DASAs. In these ultrafast time-resolved IR spectroscopic studies, it was observed that for nanosecond delays the spectra of compound **2** showed solvent-dependent changes, while for compound **3** the same spectral features were observed for all solvents. This observation can now be understood: in first-generation DASAs the interconversion between **A'** and **EZZ** is a thermal process whose barrier depends on the employed solvents whereas for second-generation DASAs the formation of **EZZ** is photoinduced and solvent independent. We expect the photochemical forked pathway of DASA **3** to be a direct result of a further weakening of the double bonds in the triene due to the aromaticity of the indoline group. Since **EZZ** is not part of the productive switching pathway, the efficacy of such switches is in principle reduced.

Our rapid-scan FT-IR studies on DASA **3** (SI section S5.3) further show that in DCM only **C** is formed as suggested previously,^{24,25} in line with the prediction that this isomer is considerably more stable than the **B** forms. However, what in first instance would not have been expected – but is in excellent agreement with the calculated higher energy barrier between **B** and **C** – is that several forms of **B** can be observed as intermediates, except **B'''** which is markedly destabilized, most likely due to the decreased basicity of the donor. The destabilization of the zwitterionic **B'''** helps preventing the formation of precipitated products for DASA **3** as compared to DASA **1** in chlorinated solvents.

Overall, thermal interconversions between isomers thus prove to be essential for DASA photoswitching (Fig. 6). First generation DASAs **1** and **2** predominantly produce **A'** through light absorption, but the unproductive **EZZ** isomer can be accumulated *via* a solvent dependent thermal interconversion through **A''**. In contrast, DASA **3** exhibits a forked photochemical reaction to produce both **A'** and **EZZ**. With a complete understanding of the thermal reaction steps involving the electrocyclization, proton transfer and tautomerizations leading to the cyclized forms, we now can start acting on the molecular structure to deliberately steer the outcome and kinetics of DASA photoswitching and to produce application-tailored switches.

CONCLUSIONS

Photoswitching of DASAs **1–3** has been studied using rapid-scan FT-IR to elucidate the structural transformations at work after photoexcitation and their timescales. Key to the interpretation of these data has been a complete mapping of the reaction pathway with all possible intermediates and transition states. This has led to a detailed understanding of the switching pathways, the energies and barriers governing the thermal equilibrium. Overall, a picture has emerged in which thermal interconversions play a crucial role in the photoswitching of DASAs.

While the primary photochemical step provides an initial means to kick-start the process, the rate-limiting thermal steps govern the overall behaviour of these switches.

Unexpectedly, thermal interconversions not only play a central role in the electrocyclization and proton-transfer/tautomerization steps, but also in the arrangement of the DASA structure for electrocyclization as has been outlined above for the role played by the **EZZ** isomer. The photochemical step gives access to high-energy open intermediates, and it is the control over the lifetime of these intermediates that allows one to steer the reaction towards a targeted outcome. Once electrocyclization takes place, rapid interconversion of the primary closed species **B** to other **B**- and **C**-type closed forms is possible, with a product distribution that can be directed according to the specific application at hand. The herein presented results have clarified for the first time where modifications need to take place to achieve a particular photoswitching behaviour, enabling operators to steer DASA's photoswitching outcome along multiple switching pathways.

DASAs have entered the molecular nanotechnology field only recently, but have evolved tremendously over the past few years. The beauty of these switches relies on their complex reaction pathway that allows tuning of their photoswitching and overall behaviour with interventions in structure and environment. The 'IR motion pictures' recorded in the present work together with elaborate quantum chemical calculations that supply crucial 'subtitles' have provided the insight necessary to do so in a rational manner, at any point, and at a level that was not possible before.

EXPERIMENTAL SECTION

Rapid-scan FT-IR: The samples were prepared in a dark room. Subsequently 10–15 min. rapid-scan FT-IR measurements have been performed using a Nicolet iS50 FT-IR spectrometer at a resolution of 8 cm⁻¹ and a sampling rate of 10.4 s⁻¹. For samples which did not fully convert within 15 min. a 3–3.5 h kinetics measurement was performed with the same spectrometer using a resolution of 4 cm⁻¹ and a sampling rate of 1 s⁻¹. After 30–60 s a ThorLabs OSL2 high-intensity fiber light source was switched on at maximum power at <3 cm in front of the sample. More detailed information about the experiments is given in the Supplementary Information (SI section 1).

ASSOCIATED CONTENT

Supporting Information

All experimental procedures and characterization of compounds, steady-state UV/Vis spectra and ultrafast visible and mid-IR spectra, kinetic analysis, measured and calculated vibrational absorption spectra and full computational details are available in the Supplementary Information. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

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Notes:

The authors declare no competing financial interest.

Acknowledgements

This work was supported financially by the Netherlands Organization for Scientific Research (NWO–CW, Top grant to B.L.F., VIDI grant no. 723.014.001 for W.S., NWO Chemical Innovations Project Nr. 731.014.209 to W.J.B.), the European Research Council (ERC; Advanced Investigator Grant, no. 694345 to B.L.F.) and the Ministry of Education, Culture and Science (Gravitation program, no. 024.001.035). The computational work was carried out on the Dutch national supercomputer Cartesius with the support of the SURF Cooperative. Furthermore, the authors acknowledge support from: Laserlab-Europe (LENS002289, grant no. 654148) and the Royal Netherlands Academy of Arts and Sciences (KNAW). The Swiss Study Foundation is acknowledged for a fellowship to M.M.L.. We thank P. van der Meulen for support with the temperature dependent NMR *in situ*-irradiation studies and T. Tiemersma-Wegman for ESI-MS analyses.

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- (46) In SI section 4 we report for completeness fs UV/vis transient absorption studies on DASA 1 in DCM that have not been reported in our previous work.^{30,33}

Table of Content Graphic

