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Substituent effects in a six-state molecular switch†

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This paper describes a series of four indolinooxazolidine molecular switches capable of accessing multiple distinct states by separately addressing photo- and stereo-isomerism. Photoswitches serve as valuable components in molecular devices owing to their ability to isomerize between distinct states using light as a non-invasive input. While most photoswitches are binary, converting between two states, multistate switches offer expanded operational capabilities and show promise for multi-bit architectures. We synthesized a series of four indolinooxazolidines with varied electronic structure and examined their switching behavior in different solvents. While electron-withdrawing substituents inhibit the photoisomerization pathway, the incorporation of an oligoethylene glycol chain enables both reversible photoisomerisation and acidochromic switching between six combinations of photo- and stereo-isomers.

Interest in stimuli-responsive materials incorporating photoswitches has exploded in recent years, with applications in multiple disciplines due to their ability to respond dynamically to external stimuli such as light, temperature, and pH.[1,2] Photoswitches have been especially useful in molecular devices, where individual molecules serve as functional components to encode information.[3–5] Operating on the fundamental electronic properties of molecules, these devices represent a cornerstone of molecular electronics, a field dedicated to minimising electronic components to the molecular scale.[6,7] Photoswitches are especially valuable in these devices as their isomers can exhibit dramatically different electronic properties, including dipole moments, conductivity, and charge density. Additionally, the use of light as a stimulus to control the change in properties is non-invasive, and can be executed with high spatial and temporal control. Many photoswitches can also be activated by other external stimuli, such as pH, temperature, or electrical current, adding versatility to molecular devices. The electronic property changes induced by photoswitch isomerisation have been used to produce diodes,[8,9] switches,[10–12] transistors,[13,14] and memories.[15,16]

Spiropyrans have been used as components of molecular devices, as their ability to switch between two states provides an "on" and "off" configuration in devices, limiting them to encoding binary information.[3–5,17,18] Multi-state switches enable the realization of a larger number of discrete states, enhancing storage or sensing capabilities and enabling the execution of more intricate logic operations.[19,20] This advancement mirrors the evolution of computing, transitioning from simple binary switches to multi-bit architectures capable of performing sophisticated operations.[21] Furthermore, these systems can be engineered to respond to distinct stimuli, allowing selective and precise control over molecular units. Orthogonal addressability, where different parts of a molecule are independently responsive to separate stimuli such as light or pH, plays a critical role in achieving targeted and reliable switching. This feature significantly expands the versatility of such systems.[22,23]

Indolinooxazolidines represent a lesser-known subclass of spiropyrans, characterized by an oxazolidine ring at the spiro carbon instead of a pyran ring.[24] Initially identified as photochromic systems, indolinooxazolidines undergo oxazolinic ring-opening (structural isomerization) upon UV irradiation, breaking the σ bond and forming a zwitterion with charge localised on the indoline, shown in the left of Fig. 1.[25] Ring-opening can also be induced by acid, shown on the right of Fig. 1, as protonation of the oxazolidine oxygen provides an additional stimulus, making these systems promising candidates for multi-responsive devices.[19] In addition to oxazolinic ring-opening, many indolinooxazolidine derivatives can undergo *cis–trans* stereo-isomerisation around the conjugated double bond, independent of the ring-opening process. Both the ring-closed and ring-open forms can access this pathway, resulting in up to six distinct isomers, from the combinations of structural- and stereo-isomerism, with unique electronic and geometric

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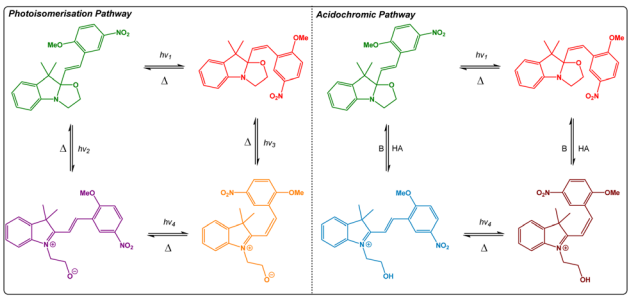

Fig. 1 The expected switching pathways of the oxazolidines. Left: Ring-opening of the oxazolidines to the zwitterionic open form; switching between the respective *cis* and *trans* forms. Right: *cis*–*trans* isomerization of the protonated open form, generated after the addition of acid. The closed form can be regenerated by deprotonation with a suitable base.

properties. Changes in molecular geometry, electronic properties, and polarity induced by photoisomerisation have been shown in other classes of photoswitch to influence the rate of tunneling charge-transport in molecular junctions.[26,27] We previously identified the change in the offset between the LUMO and Fermi level that accompanies the chemo/photo-switching of spiropyrans as the main factor affecting commensurate changes in tunneling charge-transport for that class of molecules.[3–5,28]

We present four synthetically accessible indolinooxazolidines capable of isomerizing *via* light or acid pathways to a total of six spectroscopically distinct states. By varying substituents around the aryl ring, we aimed to influence the relative stability and accessibility of specific isomers, enabling synthetic tuning to selectively access a subset of the potential states. This tunability makes indolinooxazolidines particularly promising for multi-state systems. We are particularly interested in photoswitches that incorporate triethylene glycol units, which can be used as anchors to form self-assembled bilayers that can then be incorporated into molecular ensemble junctions.[18] These junctions can then be integrated into electronic devices,[29,30] creating the possibility for independently addressable multi-state switching of conductance states. This paper focuses on the effects of substitients such as triethylene glycol and focuses on the characterization of the switching processes in solution by ultraviolet-visible (UV-Vis) spectrophotometry and nuclear magnetic resonance (NMR) spectroscopy.

The synthesis began with an established procedure to form 1-(2-hydroxylethyl)-2,3,3-trimethylindolium bromide. 2,3,3-Trimethylindoline was refluxed in dry acetonitrile with 2-bromoethanol to provide the salt as deep red crystals. The aldehydes were then functionalised prior to the formation of the indolinooxazolidines. 5-Nitrosalicylaldehyde was used in the synthesis of indolinooxazolidine 3 as received, as was 2-methoxysalicylaldehyde in the synthesis of indolinooxazolidine 2. To synthesise the aldehyde for indolinooxazolidine 1,2-hydroxy-5-nitrosalicylaldehyde was refluxed with iodomethane using potassium carbonate as a base in order to methylate the hydroxyl group, providing 2-methoxy-5-nitrosalicylaldehyde in 70% yield. A similar procedure was utilised to provide the oligoethylene

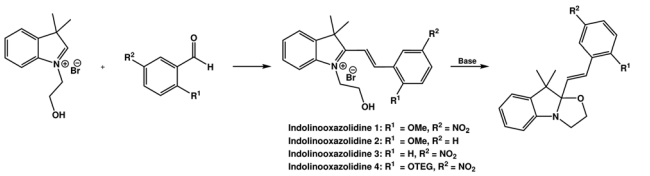

Fig. 2 The synthesis of indolinooxazolidines. A functionalized aromatic aldehyde is condensed with an indolium bromide salt, which gives a salt of the ring-opened indolinooxazolidine. The salt is then ring-closed using an inorganic base to provide the final photoswitch. Here, triethylene glycol ethyl ether is shortened to TEG.

glycol-containing aldehyde used in the synthesis of indolinooxazolidine 4 with 2-(2-(2-ethoxyethoxy)ethoxy)ethyl 4-methylbenzenesulfonate; as this compound did not form crystals, column chromatography was used to purify the product, lowering the yield to 50%.

The four indolinooxazolidines were then synthesised *via* a condensation reaction between the functionalized aromatic aldehydes and indolium bromide salts containing an ethoxy moiety at the indoline nitrogen. The resulting salts were treated with a base to precipitate the ring-closed indolinooxazolidine, as shown in Fig. 2. This synthetic approach allowed us to explore how substituents and solvents influence the photoisomerization pathways and physicochemical properties of these compounds.

Photoswitching behavior of the indolinooxazolidines was primarily characterized by UV-Vis spectrophotometry. Irradiating the compounds with UV light (λ = 365 nm or 280 nm) induced the ring-opening reaction, giving a peak centered around 385 nm in the absorption spectrum, shown in the insert in the top of Fig. 3. The ring-opening reaction is reversible in the dark, but can be sped up by irradiating with visible light. ^{1}H NMR spectroscopy was also used to confirm isomerization, as can be seen in the top of Fig. 3, where the multiplets corresponding to the oxazolidine ring (labelled H_a and H_b in blue) separate into two triplets in their open form (shown as H_a and H_b in red). Indolinooxazolidines are also acidochromic; inducing the ring-opening reaction with acid gives a broad singlet centered around 5.1 ppm corresponding to the hydroxyl group formed from the oxazolidine oxygen. Unlike in spiropyrans, the absorption spectra for the light- and acid-generated open forms are superimposable, suggesting that the two forms adopt similar geometries.[25,31] Whilst the acid- and photogenerated forms are therefore indistinguishable in their UV-Vis spectra, the differences can be clearly observed in their NMR spectra.

The *trans* to *cis* isomerization of the aryl double bond in the ring-closed form does not appear to be visible in the UV-Vis spectra; however, irradiation of NMR samples of the oxazolidines caused the spectrum to shift upfield, indicative of a *trans* to *cis* isomerization in the closed form, shown in the bottom of Fig. 3. The ethylene bond connecting to the aryl group twists out of plane in the *cis* form, causing the aryl group to shield the ethylene protons, resulting in the upfield shift seen in the NMR. Changes in the UV-Vis spectra were more apparent in the ring-opened form; the absorbance peak decreases in intensity

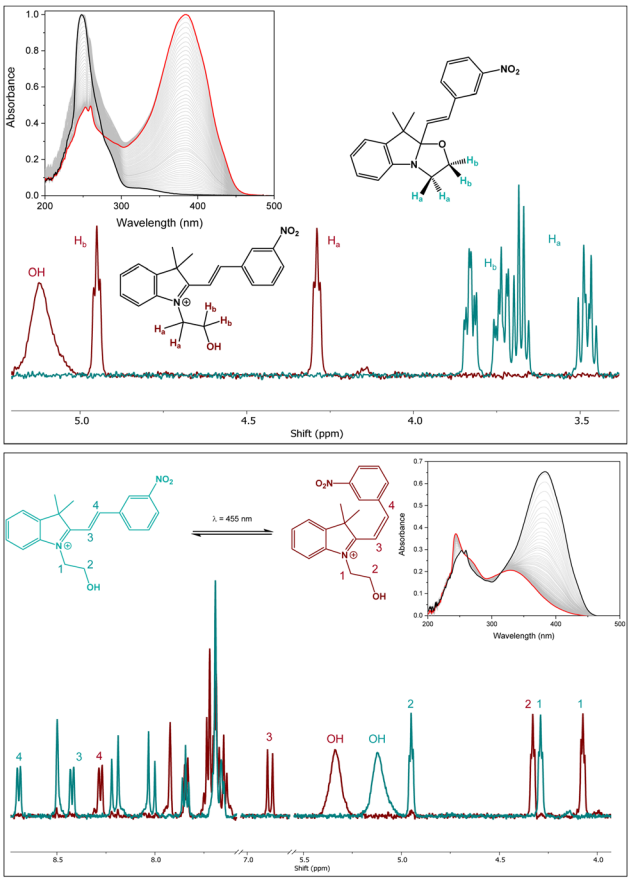

Fig. 3 Top: NMR spectrum of indolinooxazolidine 3 closed (blue) and ring-opened (red) forms following acidification, which is accompanied by an absorption band at 385 nm (inset). UV-Vis spectra were recorded every 0.5 s, with the photostationary state being reached in all cases after around 10 m. Bottom: *trans* (blue) and *cis* (red) forms with associated UV-Vis absorptions (inset) from initial (black) to final (red).

and blueshifts by around 50 nm, shown in the insert in the bottom of Fig. 3. This decrease in intensity and blueshift is characteristic of a decrease in conjugation in the overall molecule, due to a change in the torsion angle of the aromatic ring. In azobenzenes, this change in angle and loss of planarity has been associated with a decrease in conductance in molecular junctions.[32,33]

The four indolinooxazolidines studied are shown in Fig. 4a. A table summarizing the photoisomerization pathways available to each derivative is shown in Fig. 4b. The photo- and acid-generated open forms, along with their *cis*–*trans* isomerization pathways, gave six distinct species, outlined in Fig. 1. The closed and open forms both exist as *trans* and *cis* isomers, along with the two isomers of the acid-generated, protonated open form. Indolinooxazolidine 1 is a structural isomer of a well-studied spiropyran, with a methyl group attached to the phenolic oxygen to block the ring-closing of the spiro junction. This modification allows the *cis*–*trans* isomerization to be induced as a separate photochemical pathway. Altering the functional groups around the pyran ring further allowed us to synthetically tune which photoswitching pathways were

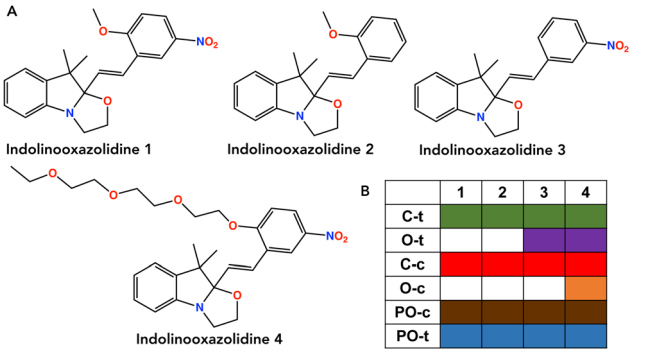

Fig. 4 a) The indolinooxazolidines studied. (b) The switching states accessible to the four indolinooxazolidines. C-*t* is closed-trans (where the oxazolidine ring is closed and the double bond is *trans*), O-*t* is open-*trans*, C-*c* is closed-*cis*, O-*c* is open-*cis*, PO-*c* is protonated open-*cis* (the oxazolidine ring is opened with acid), and PO-*t* is protonated open-*trans*.

accessible to the molecule. We removed each functional group in turn, to give indolinooxazolidine 2 and indolinooxazolidine 3. The final oxazolidine, indolinooxazolidine 4, contains an oligo-ethylene glycol chain, which can be used as an anchoring group in solid-state devices, as we have demonstrated previously.[18,29,34]

The four compounds were irradiated with either 280 nm, 365 nm, or 455 nm light in chloroform, methanol, or toluene (see the ESI,† for full UV-Vis spectra). The protonated *trans*-open form was generated with trifluoromethanesulfonic acid, and the acidic solutions were irradiated to induce the *trans* to *cis* isomerization. The reverse reaction was more favorable in methanol for all derivatives, as there was no evidence of the ring-opened forms. Previous work has reported that other indolinooxazolidine derivatives were not thermally reversible except in ethanol, demonstrating that polar, protic solvents destabilize the open form.[35] The driving force of the isomerization is relieving the ring strain of the central oxazolidine carbon, which rehybridizes from sp^3 to sp^2 upon bond cleavage, a process very sensitive to the choice of solvent.[19,35]

Indolinooxazolidine 1 was unresponsive to ultraviolet irradiation in chloroform, but addition of trifluoromethanesulfonic acid gave the protonated ring-opened form. Irradiation of the acidic solution with 455 nm light resulted in a blueshift in the absorption spectrum, indicative of formation of the *cis* protonated open form. The protonated *trans*-open form recovered in the dark, and could be accelerated with 365 nm irradiation. The UV spectrum of the closed form did not change following irradiation with 455 nm light, however the NMR spectrum shifted upfield indicating formation of the *cis*-closed isomer. The *trans*-closed isomer was regenerated in the dark.

To examine which of the two functional groups around the aromatic ring was hindering the photoisomerization of the oxazolidine ring, we removed the nitro and the methoxy group in turn. Removing the nitro group gave indolinooxazolidine 2, which again showed no evidence of the ring-opened isomer following irradiation with UV light in chloroform. The same four states attained with indolinooxazolidine 1 were also observed in indolinooxazolidine 2. Ring-opening could be induced with acid, followed by a photoinduced *trans* to *cis* isomerization.

Trans–cis isomerization of the closed form could again be detected by NMR, giving four spectroscopically distinct states accessible in both the methoxy-containing photoswitches.

The protonated open form of indolinooxazolidine 3 could be generated in all three solvents with trifluoromethanesulfonic acid. Subsequent irradiation with 455 nm light gave the protonated *cis*-open forms, which relaxed back to the *trans* forms in the dark. In chloroform, irradiation with 365 nm light provided the zwitterionic ring-opened form, but subsequent irradiation with 455 nm light caused a reduction in peak intensity without the accompanying hypsochromic shift seen in acidic solutions. This indicated that visible light irradiation accelerated the thermal back reaction rather than inducing further isomerization to the *cis* form. However, the ability of indolinooxazolidine 3 to undergo a ring-opening reaction solely with light irradiation indicates that the methoxy group in the previous two compounds was responsible for their inactivity.

We replaced the methoxy group with a triethylene glycol ethyl ether moiety to give indolinooxazolidine 4, capable of being incorporated into molecular ensemble junctions.[18] The fourth photoswitch was responsive to acid in all three solvents, with the accompanying *trans* to *cis* isomerization of the protonated open form induced with visible light irradiation. In chloroform, irradiation with 365 nm light produced the zwitterionic ring-opened form, which could be converted to the *cis* form following visible light irradiation. Generation of this zwitterionic *cis* form brings the accessible states in indolinooxazolidine 4 up to six.

We then examined the differences in absorption maxima of the compounds. Comparing the absorption maxima of the protonated ring-opened forms, we found that they do not depend strongly on solvent polarity. The difference in absorption maxima of the open forms between chloroform and toluene for indolinooxazolidine 1 was only 4 nm, and for indolinooxazolidine 3 the difference only 2 nm.

Previous work by Sanguinet *et al.* reported that the absorption maxima of indolinooxazolidines depends on the electronic effects of substituents around the aryl ring, with electron donating substituents producing a redshift in absorption.[25] Indolinooxazolidine 2 had the highest absorption maximum at 437 nm, as the most electron donating substituent. Addition of the nitro group in indolinooxazolidine 1 added electron withdrawing character, causing the absorption maximum to hypsochromically shift to 408 nm. Removing the methoxy group entirely gave a further hypsochromic shift of 24 nm in indolinooxazolidine 3 to 384 nm. Indolinooxazolidine 4 had an absorption maximum of 398 nm, as the triethylene glycol chain has more electron withdrawing character than indolinooxazolidine 1.

The four indolinooxazolidines studied explore the potential that photoswitches have for use in molecular devices by enabling multistate switching rather than a simple binary output. Their photophysical properties allow for multiple stable states, which can be precisely controlled by external stimuli, such as light or pH. In these compounds, we have shown that the substituents around the pyran ring influence the accessibility of their photoisomerization pathways by influencing the electron donating character of the molecule. In all photoswitches, a *trans* to *cis* isomerization occurs in both the closed and open isomers when they are irradiated with visible light. The compounds are also all responsive to acid, which protonates the oxazolidine oxygen and causes ring-opening. Two of the indolinooxazolidines, indolinooxazolidine 1 and indolinooxazolidine 2, do not undergo ring-opening reactions under UV light irradiation. Indolinooxazolidine 3 undergoes a ring-opening reaction, but the zwitterionic *cis* form was not formed when the zwitterionic *trans* form was irradiated with visible light. Indolinooxazolidine 4, containing an oligoethylene glycol for surface anchoring, could access six isomers through acid addition and light irradiation. This multistate functionality opens avenues for creating more complex data storage, logic operations, and signal processing at the molecular level, making indolinooxazolidines promising components for advanced, multifunctional molecular devices. Additionally, in this paper we have shown how synthetic tuning allows the activation or deactivation of photoswitching pathways by altering the electronic structure of the compounds, and highlights the need to explore the behavior of photoswitches in solution prior to incorporating them into devices.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the ESI.†

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