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Unusual thermo(photo)chromic properties of some mononitro- and dinitro- substituted 3′-alkyl indolospirobenzopyrans

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This paper is dedicated to the memory of Dr Thomas G. Nevell.

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Synthesis
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ABSTRACT

Isomeric equilbria of dinitro-substituted indolospirobenzopyrans, possessing 3′-*gem*-methyl- or 3′-cyclohexyl-substitutents, have been investigated using ^{1}H NMR spectroscopy at six temperatures, ranging from 298 K to 410 K; isomerisation processes in a methanolic solution have been monitored by spectrophotometry.

For the mononitro-substituted compounds, equilibrium favoured the colourless spirocyclic isomers. Reversion of the coloured merocyanine isomers, generated by UV irradiation, followed first-order kinetics. For the dinitro-substituted compounds the coloured merocyanine isomers predominated. Following decolourisation by visible light photoirradiation, reversion towards the merocyanine structures were particularly slow, absorbances unusually increasing sigmoidally. UV. spectral observations for the *gem*-methyl- **1** and 3′-cyclohexyl-substituted systems **2** are qualitatively consistent with the simultaneous involvement of two relatively slow rate determining steps, possessing slowly forming and long-lived intermediates - postulated to be the oxygen protonated pyran-ring of the spirocyclic structure and TCC merocyanine isomer, the latter undergoing relatively slow isomerisation about the central β-alkenic bond to the TTC isomer.

1. Introduction

There is ongoing interest in the development of photochromic (photoreversible) molecular systems, including metal-chelating agents, in which chelation can be switched on- and off-by exposure to light of different wavelengths [1] (Figs. 1,2). Several research groups have made notable contributions in this area [2]. A popular molecule for such studies is 6-nitrospiro[1-benzopyran-2,2′-indole] (6-nitro-BIPS) (**1a**) and its analogues since these have well-documented photochemical properties [3,4]. Photoirradiation with UV light at ~λ = 380 nm leads to the ring-opened zwitterionic (merocyanine) coloured form (**1b**), which can be converted back to the ring-closed-form either by photoirradiation with visible light (~λ = 550 nm) or thermally. These, photocolourisation-photodecolourisation or photocolourisation–thermodecolourisation cycles may be repeated between 5 and 10,000 times – depending on the specific type of system - and have thus, importantly, formed the basis of robust light-induced ionic switches. Additionally, there are reports of specific spiropyran-based systems being utilised in the photoreversible chelation of selected metal ions [5–8]: are reports on the substituent effects in these systems [9]; including electron withdrawing groups positioned within the indole ring [10]; and photoreversible ion transportation across a solvent interface [11]. There is increasing interest in 'negative chromism' – photochromic compounds which are coloured and reversibly bleach to colourless upon irradiation [12].

We recently reported the synthesis and thermochromic evaluation of some 6-nitro-*N*-alkyl-3,3′-disubstituted-indolospirobenzopyrans, in various solvents [9]. A particular observation in this study was that changes in the type and nature of the alkyl-substituent groups - within the spirobenzopyran skeleton - were found to produce significant changes in the thermochromic properties of these molecules. In the light of this we therefore decided to investigate the expected significant effects that would be produced - on the photo-chromaticity of these molecules - by substitution

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0143-7208/

with a second powerfully inductive 8-nitro-group. To this end we synthesised and evaluated the 6,8-dinitro-*N*-methyl-3,3′-*gem*-methyl- **1** and 6,8-dinitro-*N*-methyl-3′-spirocyclohexyl- **2** indolospirobenzopyrans (depicted below in Fig. 3), in methanol at 21 °C and 40 °C. In these compounds mesomeric and inductive electronic perturbations, involving the nitro-groups, are known to induce profound variations in the mechanisms and rates of the reactions. In particular, the incorporation of an additional 8-nitro group *ortho*-to the phenoxide ion in the merocyanine will both generate maximal mesomeric and inductive effects on this moiety - which plays a primary role in the ring opening↔closing process - and, *via* conjugation, exert these electronic effects throughout the entire resultant open zwitterionic skeleton. In summary, the introduction of this second nitro-group is likely to greatly influence the rate of the colourisation reaction, and hence photochromaticity, in these systems. Therefore, investigation and comparison of these particular compounds, not only singularly, but against each other - to additionally assess the effect of varying 3′-alkyl substitution - seems particularly pertinent and worthwhile. [In fact this was the main aim and reason for instigating this work; however, in the light of the interesting results observed for the dinitro-substituted compounds, which differed significantly from those of the skeletally identical but mono-nitrated congeners, we additionally decided to undertake a comparison against the said corresponding congeners].

An understanding of these substituent effects (controlling groups) is important in 'predicting', or at least better understanding, the photochromic characteristics in these systems, which may lead to the production of more clearly defined on↔off photochemical switching devices: additionally, the use of these 'controlling groups' may enhance the design and 'fine-tuning' of structurally similar systems where the 'basic skeletal spirobenzopyran structure' forms part of more complex molecular structures. For example, it would be a practically useful capability to be able to predict (or better understand) the photochromic behavior, control, and/or biasing over ion-chelation in benzopyran structures possessing lariat-type ethers.

1.1. Syntheses of dinitro-indolobenzospiropyrans *1*–*7*

The syntheses of the substituted spirobenzopyrans **1**–**7** were undertaken using standard methods, or slight modifications thereof (Note: syntheses of the 6-nitro-spirobenzopyrans **6** and **7** has previously been reported by our group [9]). A typical synthesis is exemplified in Fig. 4, for 1′-*N*-methyl-6,8-dinitro-3′-spirocyclohexylspiro-[2*H*-1-benzopyran-2,2′-indoline] **2**: Firstly, cyclohexylmethylketone and phenylhydrazine were condensed together to yield the corresponding hydrazone (*cf.* **9**) which was then ring-cyclised to the indole (*cf.* **10**) using the Fischer indole synthesis. N-methylation of the 3,3′-cyclohexyl-2-methylindole was effected using methyltrifluoromethane sulphonate to yield the *N*-methyl-indolium triflate (**11**), from which the indolenine (*cf.* **12**) was obtained, after treatment with aqueous sodium hydroxide. The final indolospirobenzopyrans were obtained in good yields - ranging from 58% for the 3,3′-cyclohexyl-substituted compound to 63% for the *gem*-methyl-substituted compound - by condensation reactions between the appropriate indolenines and 3,5-dinitro-2-hydroxy-benzaldehyde [13] (obtained *via* treatment of 2-hydroxy-5-nitrobenzaldehyde with fuming nitric and sulphuric acids) in refluxing ethanol: the reactions typically proceeding to completion within a 24 h time period. The overall condensation yields were surprisingly good in view of the expected dinitro-group deactivation of the phenoxide-ion intermediate. (Note: 2-methylene-1,3,3′-trimethyindoline is commercially available and was utilised in the synthesis of the corresponding 6,8-dinitro-1′,3′,3′-trimethylspiro-[2*H*-1-benzopyran-2,2′-indoline]) (Fig. 5).

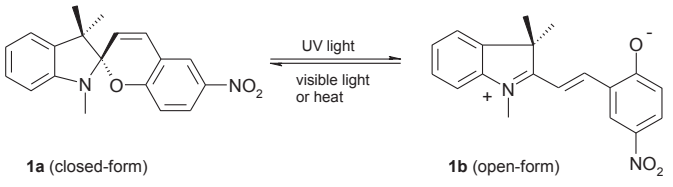


Fig. 1. Isomerisation between the spirocyclic and merocyanine forms.

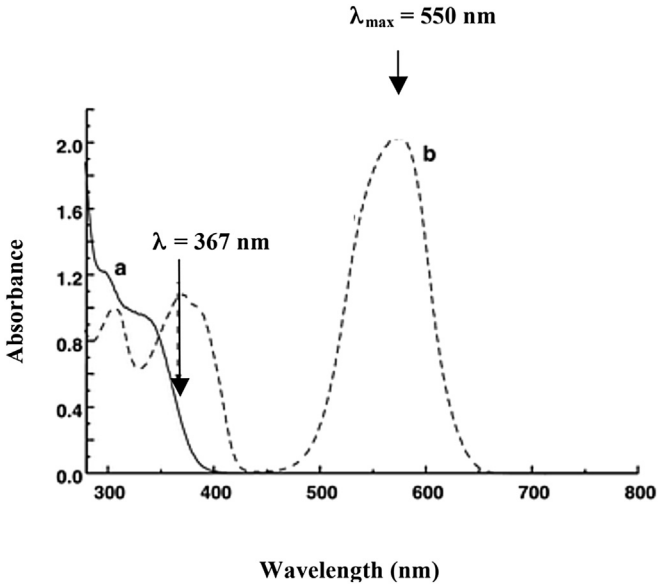
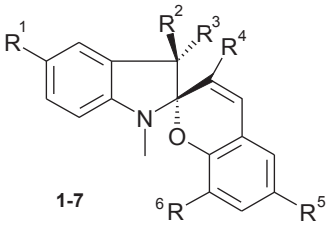


Fig. 2. Typical UV-VIS Absorption Spectra of the closed- (**1a**), and open- (**2b**) Indolospirobenzopyrans.



1 R^1=R^4=H, R^2=R^3=CH_3, R^5=R^6=NO_2
2 R^1=R^4=H, R^2/R^3=cyclohexyl, R^5=R^6=NO_2
3 R^1=H, R^2=R^3=CH_3, R^4=CH_3, R^5=R^6=NO_2
4 R^1=CF_3, R^2=R^3=CH_3, R^4=R^5=H, R^6=OMe
5 R^1=CF_3, R^2=R^3=cyclohexyl, R^4=R^5=H, R^6=OMe
6 R^1=R^4=R^6=H, R^2=R^3=CH^3, R^5=NO_2
7 R^1=R^4=R^6=H, R^2=R^3=cyclohexyl, R^5=NO_2

Fig. 3. Indospirobenzopyrans.

2. Results

2.1. ^{1}H NMR spectroscopy studies

Evaluation of the substituent effects were undertaken using ^{1}H NMR spectroscopy at six temperatures (298, 320, 340, 360,

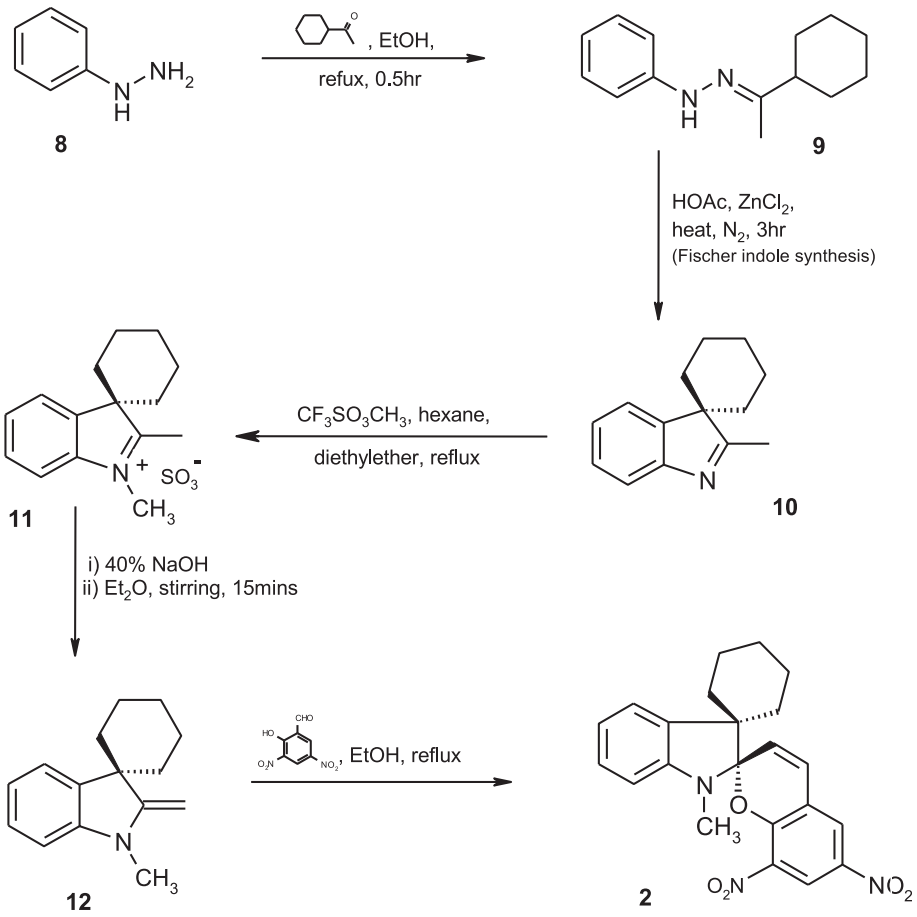
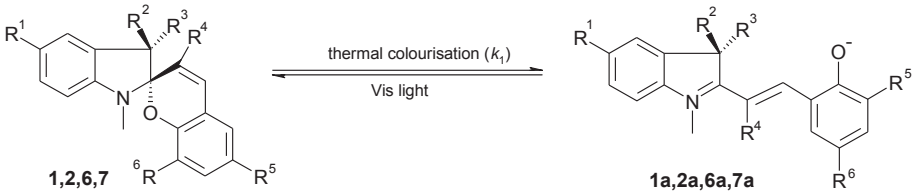


Fig. 4. Synthesis of *N′*-Methyl-6,8-dinitro-3′-spirocyclohexylspiro-[2*H*-1-benzopyran-2,2′-indoline] **2** (typical synthetic procedure used).



1 R^1=R^4=H, R^2=R^3=CH_3, R^5=R^6=NO_2
2 R^1=R^4=H, R^2/R^3= cyclohexyl, R^5=R^6=NO_2
6 R^1=R^4=R^6=H, R^2=R^3=CH_3, R^5=NO_2
7 R^1=R^4=R^6=H, R^2/R^3= cyclohexyl, R^5=NO2

Fig. 5. Conversion of the merocyanine to the closed-form by photoirradiation with broadband visible light.

380 and 410 K), selected spectra of which are reproduced herein, along with a summary of the ^{1}H NMR results (Tables 1–7): By varying the temperature and monitoring the spiropyran solution equilibrium position we have been able to ascertain a relative indication of the equilibrium-biasing (between the open↔closed states), thus enabling the thermal stability of the benzospiropyrans to be ascertained. The results are compared and contrasted to the skeletally identical but *gem*-methyl- mono-nitro-substituted compound **6**, which also served as a 'reference' system [14].

Studies, at the predefined temperatures, showed that at 298 K the potential open↔closed equilibrium of the 'reference' *gem*-methyl- substituted spiropyran system **1** in d_2-tetrachloroethane (TCE) comprises entirely of the single *trans*-open-form (merocyanine); this indicates a very facile ring-opening (Spectrum 1, Tables 1 and 2). [Note: The alkenic protons of the pyran ring possess a *cis*-coupling of J ~ 10 Hz (closed-form), whilst the same protons, in the *trans*-open-form, exhibit a coupling of J ~ 16 Hz]. Elevation of the temperature to 320 K (promotion of thermal ring-closure is expected) fails to produce any detectable amounts of the closed-form as would be evidenced by both the appearance of the *cis*-alkenic protons and the tertiary *N*-methyl group - occurring at $\delta = 6.5$, 7.5 and 2.7, respectively. At 340 K (Spectrum 2; Table 1) the appearance of the *cis*-alkenic protons, and the *N*-methyl associated with the closed-form, are observed. Further incremental increases in temperature to 360 K, and through to 380 K, continue to increase the concentration of the closed-form (Table 1), until, at 410 K (Spectrum 3, Table 1), when no further increase in the

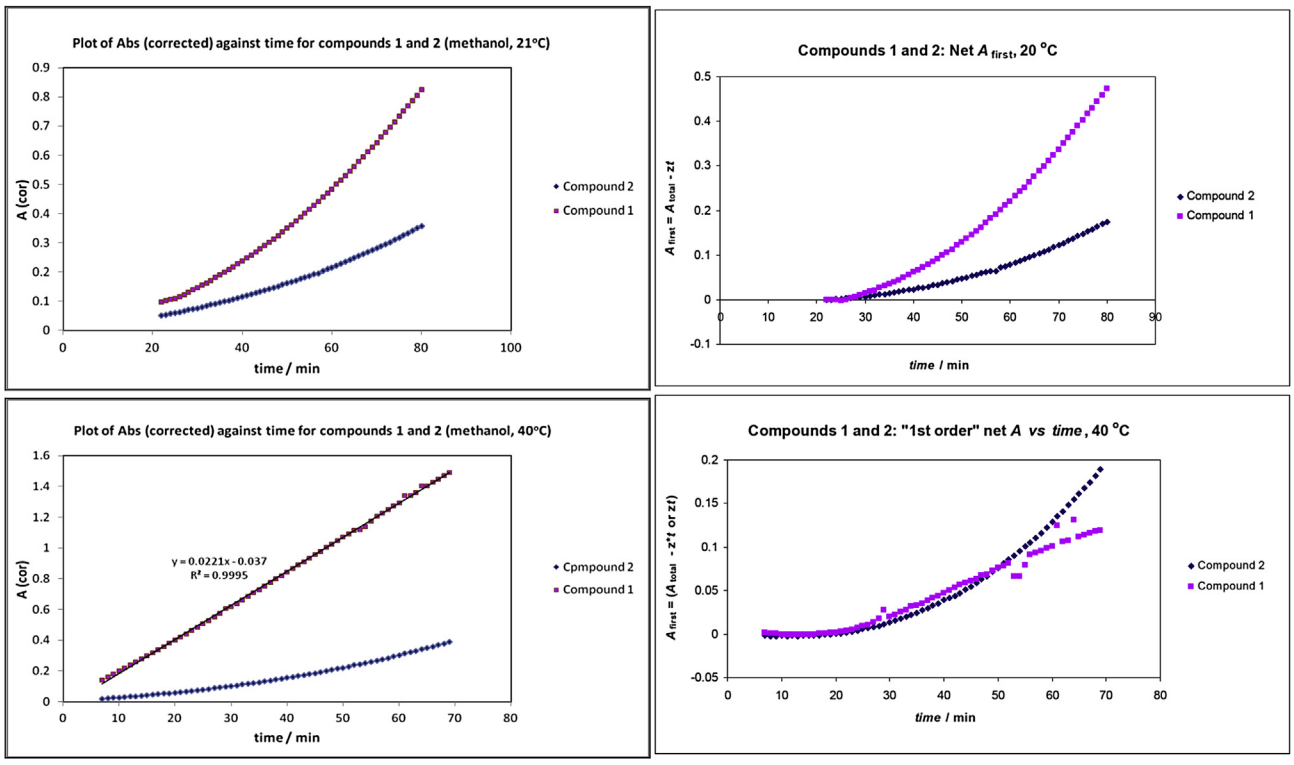


Fig. 6. Conversion of the spirocyclic forms **1** and **2** (colourless; 2×10^{-4} M in methanol, 21 °C (top left); and 40 °C (bottom left) to the zwitterionic forms **1b** and **2b** (coloured), monitored *via* increasing absorbance (550 nm, path-length 1 cm). Data re-plotted with linear contributions subtracted. 21 °C (top right) and 40 °C (bottom right).

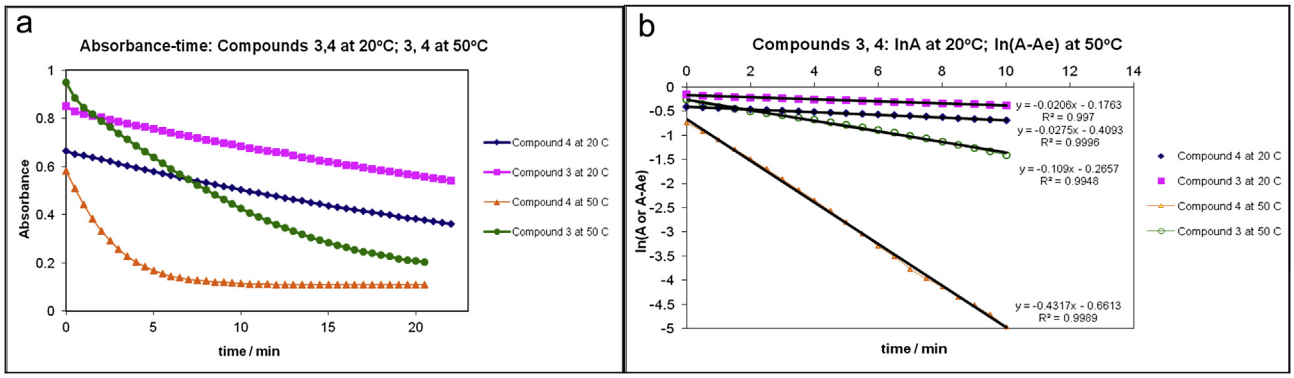


Fig. 7. The decolourisation of **6** and **7** (2.0×10^{-4} M in methanol) monitored by photometry at 550 nm **a**) Absorbance *A* vs. time, **6** and **7** (20 °C); **6** and **7** (40 °C); **b**) semi-logarithmic plots: **6** and **7** (20 °C; ln *A vs.* time); **6** and **7** (50 °C, $\ln(A - A_e)$ *vs.* time, 'e' denotes 'equilibrium').

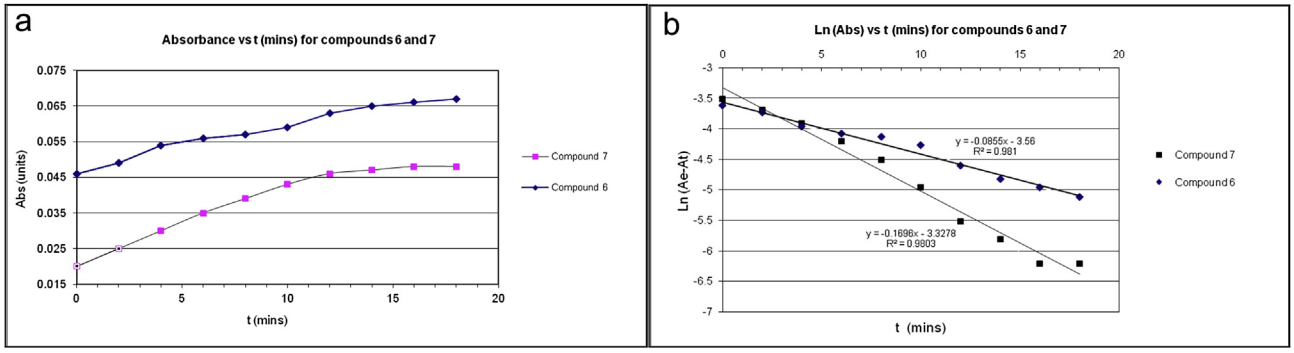


Fig. 8. Conversion of the Spirocyclic forms **6** and **7** (colourless; 2 x 10^{-4} M in methanol) to the zwitterionic forms **6b** and **7b** (coloured), monitored *via* increasing absorbance (path-length 1 cm) at 550 nm at 21 °C. a) changes in absorbance, *A*; b). First-order plots.

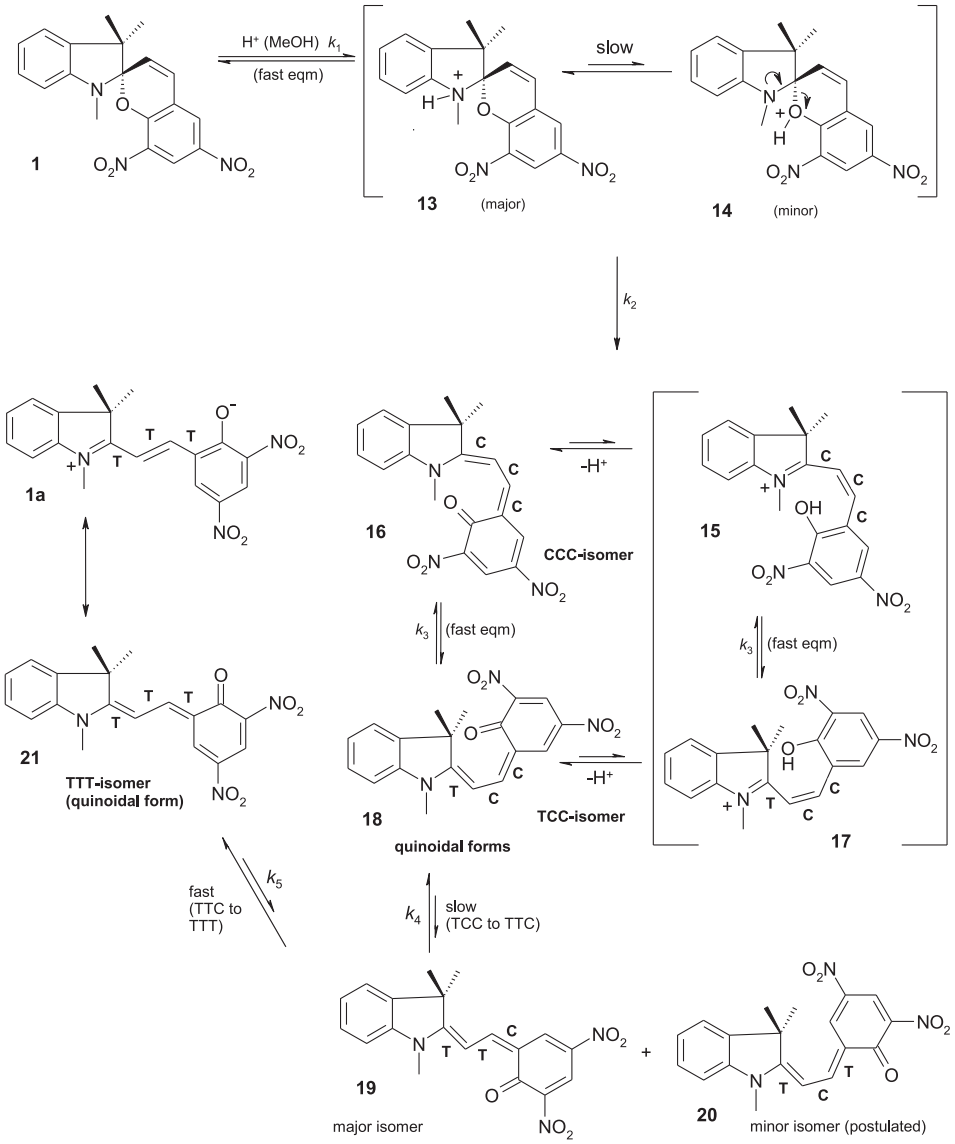
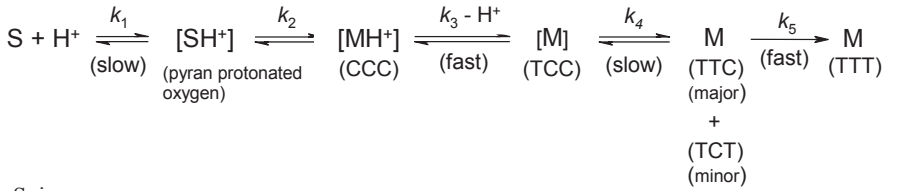


Fig. 9. Proposed reaction sequence in the sigmoidal formation of the merocyanine 1a.



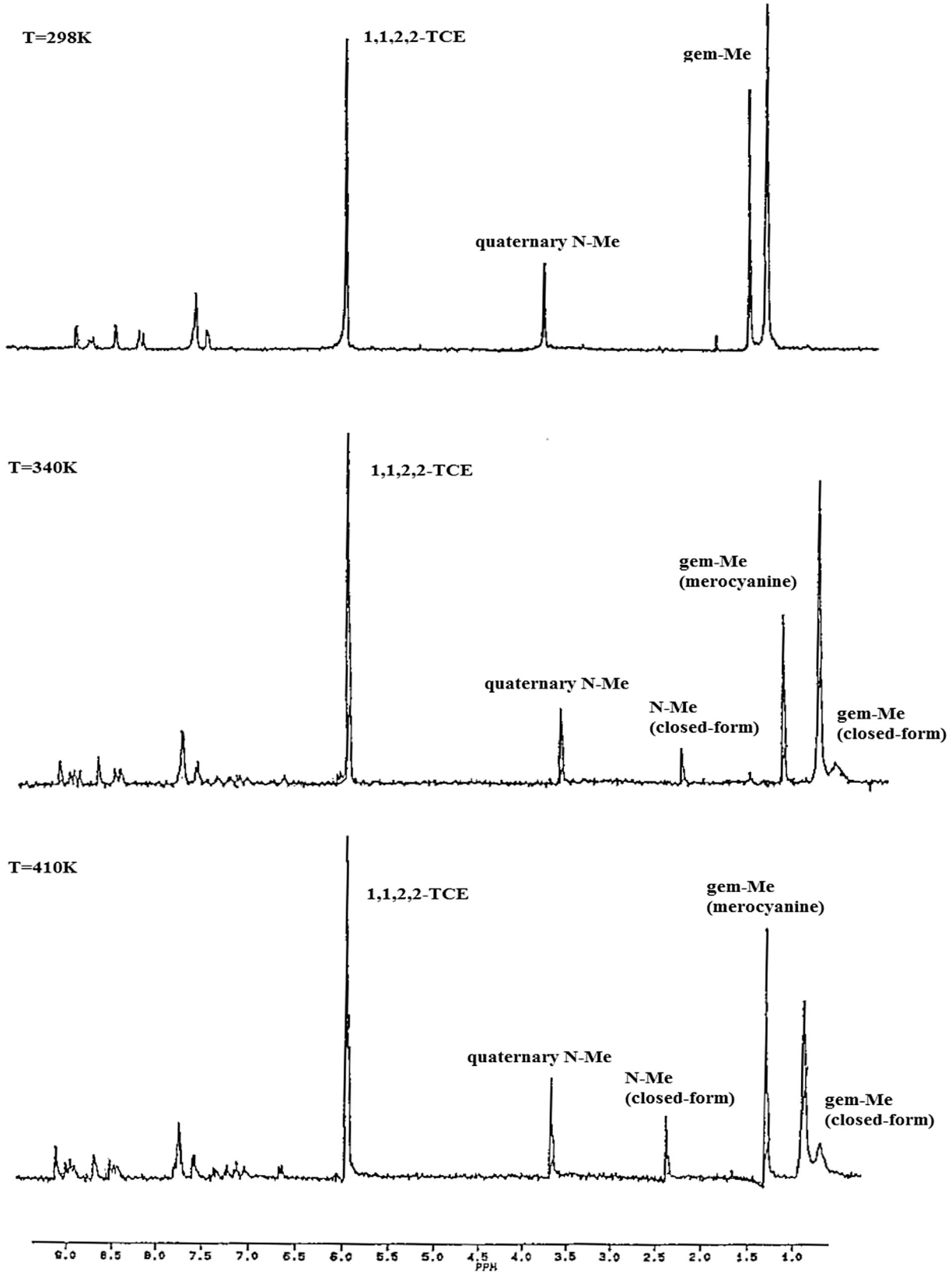
S = Spiropyran

M = Merocyanine

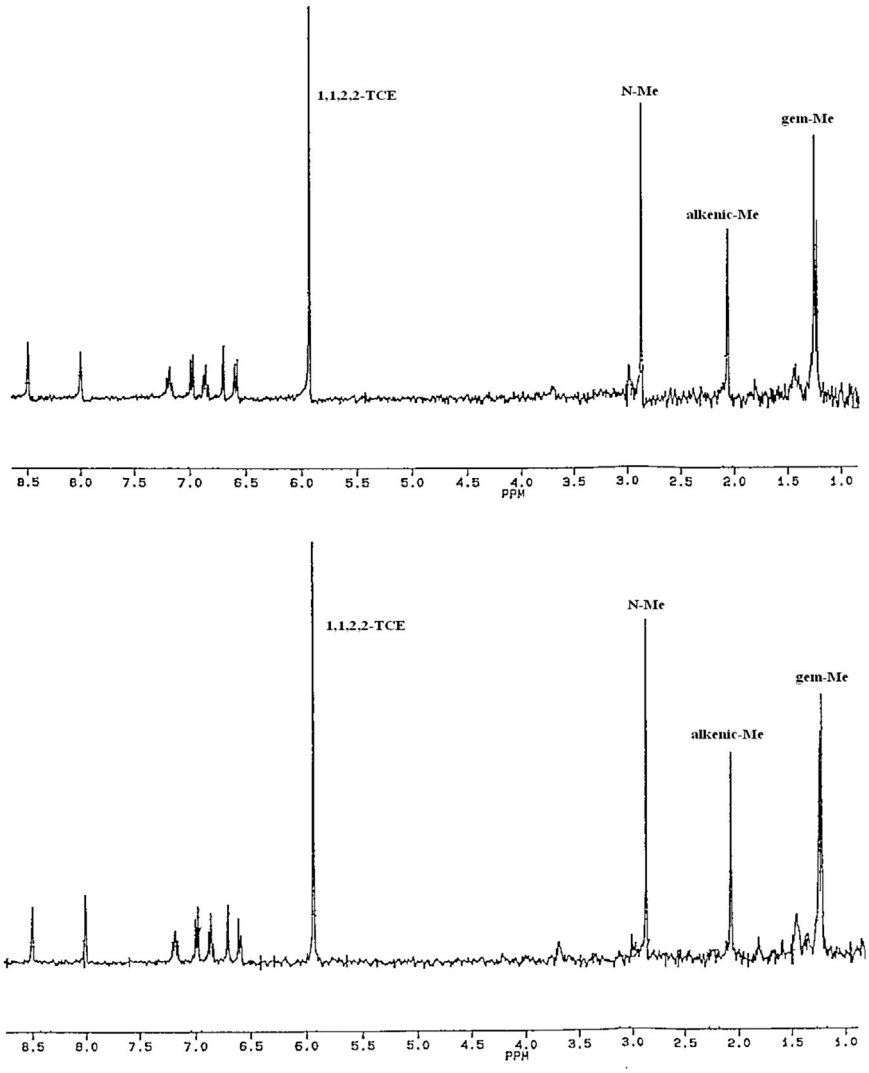
Fig. 10. Consecutive reaction sequence.

concentration of the closed-form is observed. [It was not possible to elevate the temperature much above 410 K due to the physical limitations of the solvent (TCE bp. 419.5 K)].

In order to devise a room temperature activated switchable system this facile ring-opening needs to be 'thermodynamically constrained', or controlled. The results for this compound, therefore, clearly demonstrate that increased thermodynamic inhibition of the ring-opening is required in order to produce a room temperature-activated/'photo-controllable' system.

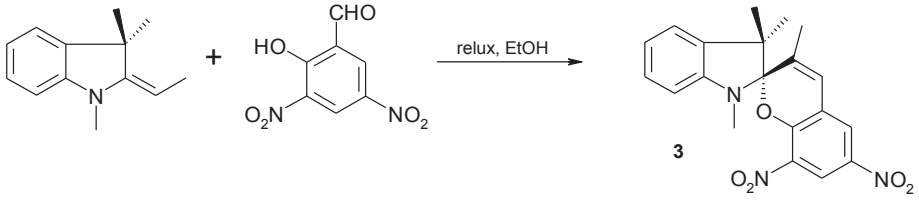


Spectra 1,2 and 3. ^{1}H NMR of compound **1** at 298 K, 340 K and 410 K.



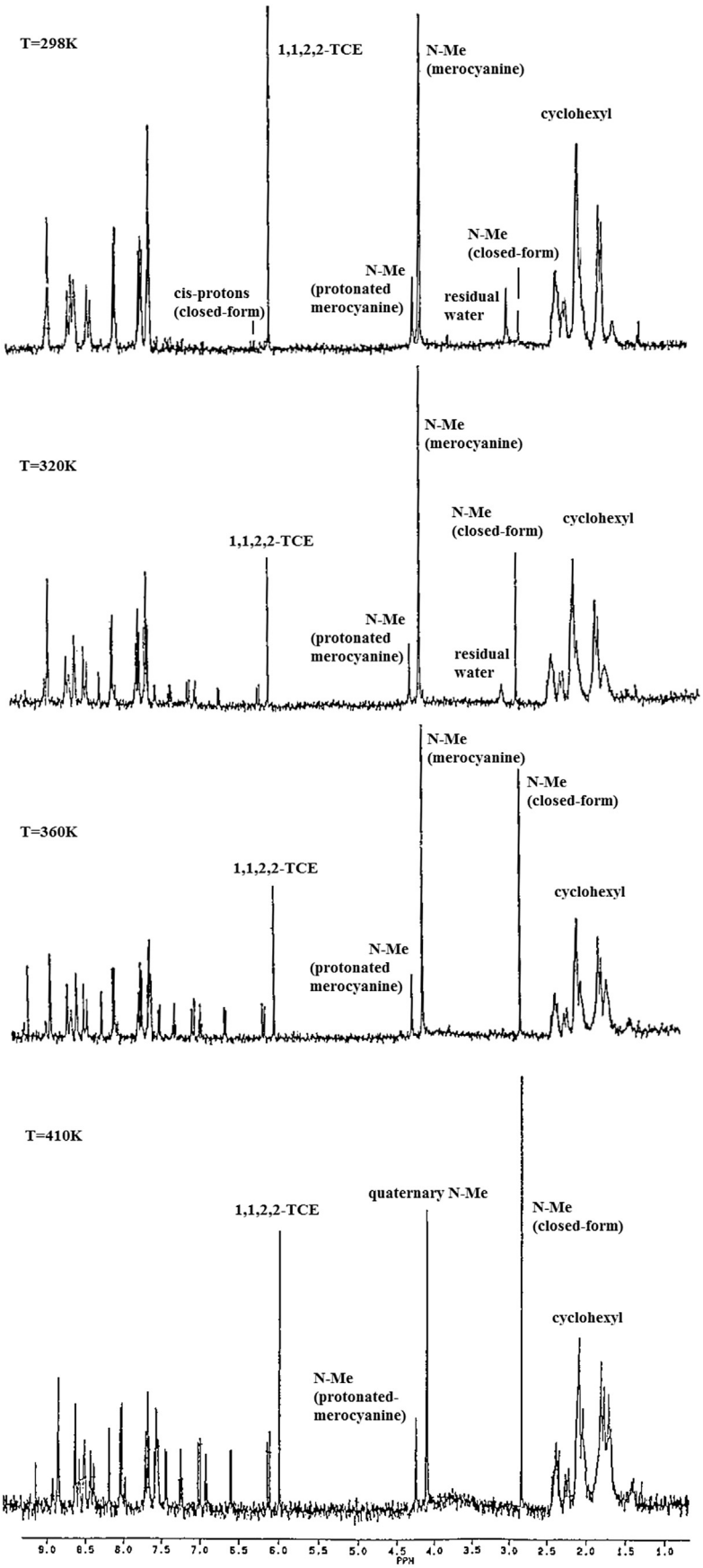
Spectra 4 and 5. ^{1}H NMR of compound **3** at 298 K and 410 K.

*2.2. Discussion for the sterically restricted 3-methyl- substituted system **3***

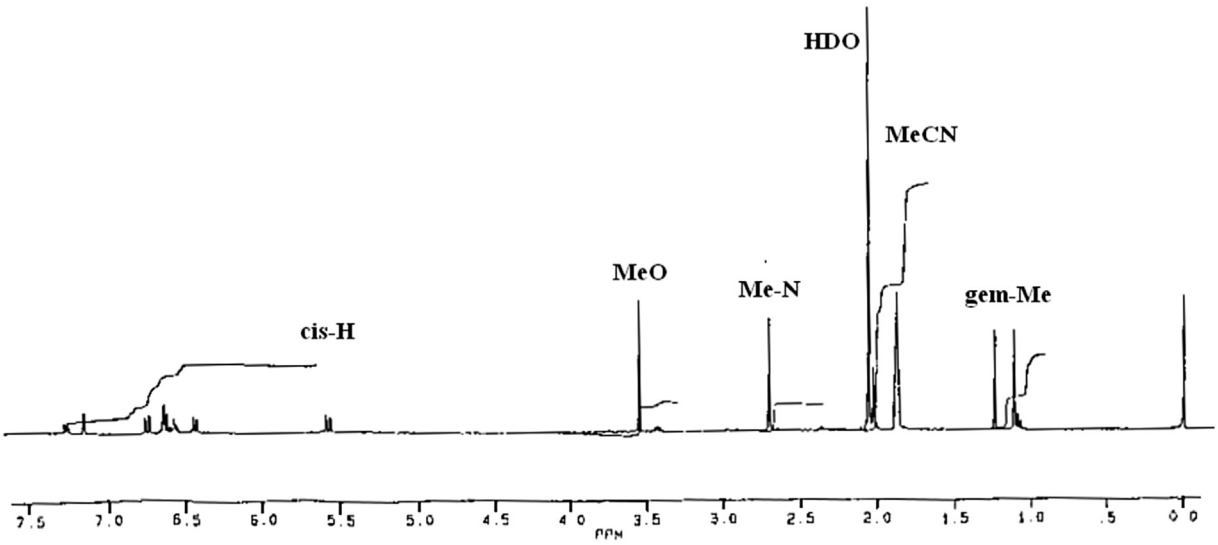


Following the observations for the *gem*-methyl- substituted spiropyran system **1** - namely that ring-opening was occurring too readily to produce a system that could significantly be thermo-, and consequently, photochromically biased at room temperature - we decided to investigate whether the placement of a sterically hindering group in the alkenic moiety of the pyran-ring would restrict ring-opening: this would potentially create a system which possessed a higher thermodynamic energy barrier to ring-opening and consequently allow greater thermodynamic solution control of the dynamic equilibrium between the open- and closed-forms: To this end we synthesisied the spirocyclic system **3**, achieved *via* modified standard methods (*cf.* Fig. 4), the final condensation step being affected by condensation between the appropriate methyl-substituted indolene and the dinitro-salicaldehyde [15].

Variable temperature studies of compound **3**, monitored using ^{1}H NMR (reference peak TCE), indicate that at room temperature (298 K; Spectrum 4, Table 5) it exists entirely as the closed-isomer; indicating that the 3-methyl- group is quantitatively effective in

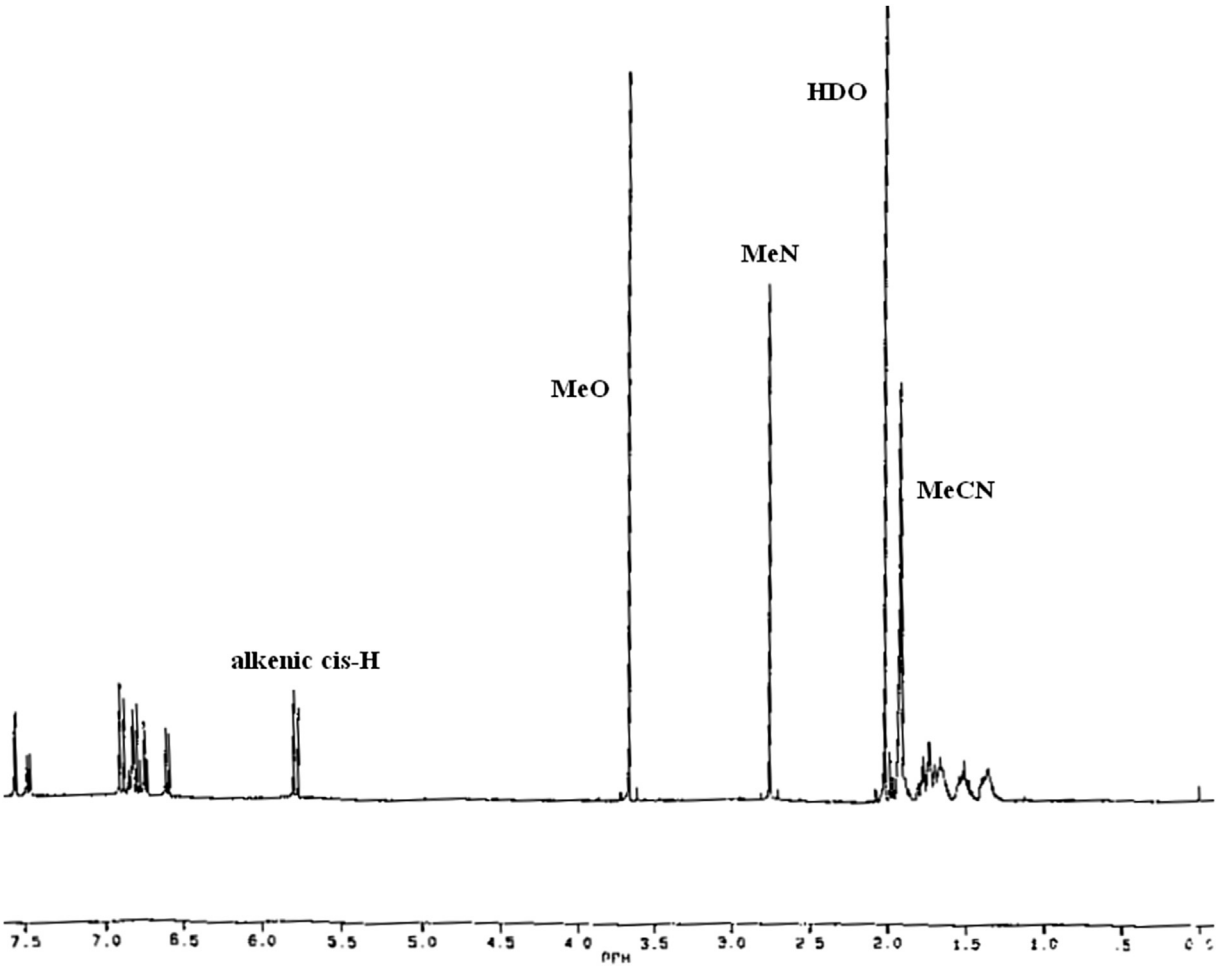


Spectrum 6,7,8 and 9. ^{1}H NMR of compound **2** at 298 K, 320 K, 360 K and 410 K.



Spectrum 10. ^{1}H NMR of compound **4** at 360 K.

prohibiting the formation of a measurable equilibrium concentration of the merocyanine form, enforcing our above hypothesis. [No proton absorbances associated with the quaternary N^{+}-Me group at $\delta \approx 3.0$ ppm, and the *trans*-coupled protons of the alkenic moiety, are observed]. Increasing the temperature by 112 °C to 410 K failed to bias the solution equilibrium to produce any measurable quantity of the open-*trans*-isomer: (Spectrum 5, Table 1). [It is noted that at this higher temperature the ^{1}H NMR signals associated with the



Spectrum 11. ^{1}H NMR of compound **5** at 360 K.

Table 1
200 MHz ^{1}H NMR spectral peak positions (ppm) and assignments for *gem*-methyl 6,8-dinitro BIPS (spiropyran) **1** in TCE at 298 K.

Solvent	C–Me	N–Me	3A	4A	5A	7A
TCE	1.3, 1.4 (b)	2.6	6.1 (J = 10 Hz)	6.6	8.2	8.7

Table 2
200 MHz ^{1}H-NMR spectral peak positions (ppm) and assignments for *gem*-methyl 6,8-dinitro BIPS (merocyanine structure) **1** in TCE at 298 K.

Solvent	C–Me	N–Me	3B	4B	5B	7B
TCE	1.6, 1.8	3.9	8.8 (J = 16 Hz)	8.2	8.2	8.8

Table 3
200 MHz ^{1}H-NMR spectral peak positions (ppm) and assignments for 3′-cyclohexyl 6,8-dinitro BIPS (spiropyran structure) **2** in TCE at 298 K.

Solvent	Cyclohexyl	N–Me	3A	4A	5A	7A
TCE	1.5–2.3	2.7	6.1 (J = 10 Hz)	6.6	8.1	9.0

Table 4
200 MHz ^{1}H-NMR spectral peak positions (ppm) and assignments for 3′-cyclohexyl 6,8-dinitro BIPS (merocyanine structure) **2** in TCE at 298 K.

Solvent	Cyclohexyl	N–Me	3B	4B	5B	7B
TCE	1.5–2.3	4.1/4.2	8.8 (J = 15 Hz)	7.95	8.0	8.9

Table 5
200 MHz ^{1}H-NMR spectral peak positions (ppm) and assignments for *gem*-methyl 6,8-dinitro 3-methyl substituted BIPS (spiropyran) **3** in TCE at 298 K.

Solvent	C–Me (*gem*)	N–Me	C–Me	4A	5A	7A
TCE	1.1, 1.2	2.7	2.1	6.7 s	8.0	8.5

gem-methyl groups coalesced to a broadened singlet, indicating equivalence – arising from a rapid interconversion between the open- and closed-forms. At the lower temperature racemisation is slower (than the NMR frequency) resulting in non-equivalence of the *gem*-methyl protons – arising from different interactions, through space, with the pyran-oxygen and alkenic-methyl groups, respectively]. Thus, it is concluded that the introduction of a 3-methyl substituent into the alkenic moiety of the pyran-ring causes a major perturbation to the thermochromic property of this system - by creating a large thermodynamic energy barrier to merocyanine formation: As a consequence, UV photoirradiation of the closed-form light failed to produce any observable quantity of the open-form, as observed by ^{1}H NMR spectrometry. In the light of the above observations we subsequently turned our attention to the investigation of an alternative substituted-spirocyclohexyl system, which would potentially possess a significant and controllable - but not totally over-biasing - substituent effect on the room temperature dynamic equilibrium position. We therefore decided to investigate whether the introduction of a sterically bulky group, but in the alternative 3′-position of the indole-ring, would produce a potentially fluxional system, which is, at room temperature, dynamically balanced, and additionally largely controllable – though external perturbation processes such as photoirradiations. To this end we synthesised the 3′-cyclohexyl-substituted indolospirobenzopyran **2**.

Table 7
^{1}H NMR spectral data for compound **5** at 360 K.

Solvent	Cyclohexyl	N–Me	OMe	4′A	3A	4A
TCE	1.5–2.3	2.7	3.7	7.6	6.9 d (J = 10 Hz)	5.8 d (J = 10 Hz)

2.3. Discussion for the sterically restricted 3′-cyclohexyl substituted system **2**

^{1}H NMR spectroscopy studies for the compound **2**, possessing a sterically 'bulky' and therefore conformationally 'directing' 3′-cyclohexyl- group in the indole ring, indicate that at room temperature (298 K) it existed as a mixture of open- and closed-forms (Spectrum 6; Tables 3 and 4). At this temperature the spectrum indicates a predominance of the *trans*-merocyanine form(s), as indicated by the ^{1}H NMR signal(s) centred at $\delta \approx 4$ ppm - for the quaternary *N*-methyl(s) [TCE reference]. Additionally, and importantly, there appears to be two absorbance peaks in the region associated with the quaternary *N*-methyl group, and in a non-equivalent ratio. Further, the ^{1}H NMR spectrum indicates extremely weak/small absorbances associated with the *cis*-isomer's ethenic protons, expected from either the spirocyclic structure, or, less likely, the open-*cis*-form (*cf.* the CCC isomer – see Fig. 9)). It is noted a residual water peak is observed ($\delta \approx 2.9$ ppm) at 298 K, which disappears at temperatures of T $\geq$ 320 K. This observation would support the simultaneous presence of two relatively stable and long-lived intermediate quaternary *N*-methyl resonances. We postulate one resonance is due to the merocyanine quaternary *N*-methyl group and the other it's corresponding, but protonated, phenoxy structure, the protonation arising from the small quantity of water present in the DCE (small chemical shift differences of ~0.1 ppm in the merocyanine *N*-methyl groups are known to occur under these conditions). As the temperature was incrementally raised – through 320 K and up to 360 K – the residual water peak begins to disappear (completely disappearing at 360 K) and the corresponding resonance due to the protonated merocyanine quaternary *N*-methyl group correspondingly increases; until, at a temperature of T $\geq$ 360 K where the is no resonance from the residual water, and only minimal detectable increases in the strength of the resonance due to the protonated *N*-methyl merocyanine structure – indicating complete exhaustion of the residual water used in this process.

It should be noted that during the process of increasing the temperature there is a concomitant process occurring; that of the expected thermal ring closure of the merocyanine to the spirocyclic structure: As the temperature was raised to 320 K (Spectrum 7, Tables 3 and 4) the appearance of both *cis*-coupled protons and a tertiary *N*–Me group – associated with the closed-spirocyclic structure – are observed in the ^{1}H NMR spectrum. Further increases in the temperature, through 320 K, and up to 340 K, resulted in an increase in the closed-form (this would be expected since thermal ring-cyclisation is increasingly favoured at elevated temperatures), as evidenced by the enhancement of the resonances for both the *cis*-coupled alkenic protons, and the tertiary *N*–Me

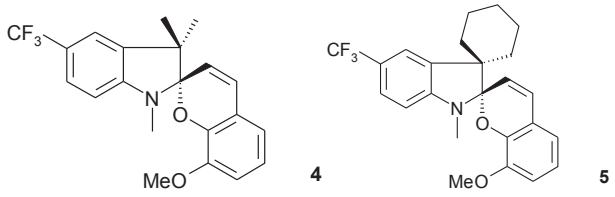
Table 6
^{1}H NMR spectral data for compound **4** at 360 K.

Solvent	C–Me (*gem*)	N–Me	OMe	4′A	3A	4A
TCE	1.1, 1.2	2.8	3.5	7.3	6.9 d (J = 10 Hz)	5.7 d (J = 10 Hz)

group, with absorbances for the merocyanine and its associated protonated congener remaining. This trend continued through to 360 K (Spectrum 8, Tables 3 and 4) and until a temperature of 410 K was attained (Spectrum 9, Tables 3 and 4): At this temperature an equilibrium situation was reached in which all three forms were present – the CCC spirocyclic closed-form, and the postulated merocyanine together with its associated phenoxide protonated structure. In addition to these observations there is, as expected, a small change in the NMR resonance pattern associated with the 3′-cyclohexyl- moiety; this is due to the differences in steric, and gross electronic interactions, exerted by the respective spirocyclic and merocyanine structures.

In summary, of the three systems studied: at room temperature, the open↔closed equilibrium position of **2** lies further towards that of the closed-form than **1**, and thus offers increased photodynamic control, particularly with regard to potential 'controllable' and 'clean' on/off 'photocontrollable' switching. Conversely, compound **3** exists entirely in the closed-form at room temperature (and above), it not being possible to bias the solution equilibrium position; thus, this system, as a 'stand-alone' structure, does not exhibit, or offer practically useable photoreversible properties: However, for example, when a crown, or other intramolecular lariate ether chelating-system - which can greatly influence the thermodynamic equilibrium in these systems (in the presence of an ion) - is incorporated into the spirobenzopyran skeleton it can thermodynamically bias the equilibrium towards the open-form, thus, potentially, making a system containing this functionality increasingly photoreversible, and thus, practically useable as an on-off switchable device.

2.4. ^{1}H NMR spectroscopy of compounds ***4*** and ***5***



In the light of the thermodynamic biasing effects we observed for the *gem*-methyl and 3′-cycohexyl- substituted compounds **1** and **2** we synthesised and investigated if similar effects could be observed for the skeletally identical and alkyl-substituted spirobenzopyrans **4** [10] and **5**, but containing strongly electron withdrawing groups in the 5′- position of the indole-ring. In these structures the 5′-trifluoromethyl- group would be predicted to destabilise the iminium ion of the open-zwitterionic structure, inhibiting its formation, potentially permitting further probing and investigation of the solution equilibrium of these systems. The ^{1}H NMR spectra obtained at both 298 K and 360 K for compounds **4** and **5** are reproduced below in Spectra 10 and 11 [Nb. Both spectra exhibited undeuterated acetonitrile peaks at $\delta \approx 1.94$ ppm (multiplicity 5; J HD = 2.5 Hz); and DHO at $\delta \approx 2.1$ ppm].

In summary; the results (Tables 6 and 7) show that at temperatures of 298 K and 360 K both compounds failed to produce any evidence of the open-forms, existing entirely as the spirocyclic structures, as observed by ^{1}H NMR spectroscopy: this might have been predicted for the 5′-trifluoromethyl- *gem*-methyl- substituted compound **4**, the strongly electron withdrawing 5′-trifluoromethyl-group being expected to destabilise the iminium ion of the zwitterionic form, consequently favouring the closed-form. However, perhaps less expectedly, the 3′-spirocyclohexyl-substituted compound - due to the predicted relief in steric strain associated with interactions between the spirocyclic 3′-cyclohexyl- group and *gem*-methyl- groups, realised on ring-opening to the merocyanine form – also remained in the closed-form, at both temperatures. Clearly, the destabilising electronic inductive effects of the 5′-trifluoromethyl- group, on the open-form - over the potential thermodynamic gain realised on the relief of the steric strain associated with ring-opening - predominates.

2.5. Photometric observations: rates of thermal colourisation and decolourisation

2.5.1. Thermal colourisation of compounds ***1*** and ***2***

To observe colourisation in solution, photoirradiation (3 min) with a broad-band visible light source (filtered to the range λ = 450–650 nm - achieved in the quartz cell) converted each compound to the spirocyclic form (colourless; Fig. 9). The subsequent spontaneous conversion towards the merocyanine isomer (dark) was followed by monitoring its visible absorption band ($\lambda_{max} \approx 550$ nm, source filtered to 450–650 nm). This procedure was undertaken at two temperatures (21 °C and 40 °C) in order to study and contrast the results, principally because significant differences in the photochromaticity of spirobenzopyran molecules, and in particular their associated ion-chelating properties (and thermochromacity), has been reported to vary with temperature [16]. Additionally, studying the reaction at 40 °C enabled possible differentiation of a thermal reaction mechanism from that of a photochemical process, since the latter is temperature independent.

Immediately following photoirradiation (450–650 nm) to produce the spirocyclic isomers, methanolic solutions of compounds (**1**,**2**,**6**,**7**), showed initial absorbances ($\boldsymbol{A}_0$ at 550 nm) in the range 0.02–0.12, probably due mainly to small proportions of the merocyanine isomers remaining. For compounds **1** and **2**, subsequent increases in absorbance were imperceptible at early stages; empirical extrapolation (linear or logarithmic) was used to estimate values of $\boldsymbol{A}_0$. In representing the results (Fig. 6), these values have been subtracted from the raw absorbance data:

$$\boldsymbol{A}_{\text{corrected}} = \boldsymbol{A}_{\text{observed}} - \boldsymbol{A}_0$$

2.6. Dinitro-substituted compounds ***1*** and ***2:*** thermal colourisation process

For the initially decoloured solutions of the dinitro-substituted compounds **1** and **2**, the plots of changes in total absorbance $A_{corrected}$ at 21 °C, Fig. 6a, showed induction periods (almost imperceptible increases; 20–25 min) followed by progressive accelerations. At 40 °C, Fig. 6c, compound **2** behaved similarly but with a shorter induction period. In contrast, colourisation of compound **1** at 40 °C: initially occurred at an almost constant rate, indicative of a slow thermal reaction of first-order kinetics. At later stages there was slight positive deviation, *i.e.* the rate of colourisation was slightly enhanced.

It appeared that, from each of these kinetic runs, the record of '$A_{corrected}$ *vs. time*' was a combination of two components, respectively linear, A_Z, and non-linear, A_F. Due to the long induction periods for the non-linear components, each linear component could be estimated from the corrected absorbance at the end of the induction period, and then could be used at each time point, t, to deduce the non-linear component by difference:

in which:

$A_Z = Initial\ gradient \times t$

The plots of A_F, Figs. 6(b) and (d), are consistent with the linear process predominating at early stages with the non-linear, accelerating, contribution becoming significant only after the induction period. These periods are similar for both compounds, namely *ca.* 25 min at 21 °C and 14 min at 40 °C. The gradients of the early linear portions were greater at the higher temperature, considerably so for compound **2**, with activation energies of 10 kJ mol^{-1} and 33 kJ mol^{-1} for **1** and **2**, respectively: Hobley reports a value for enantiomer switching of 46 kJ mol^{-1} for *gem*-methyl 6,8-dinitro-BIPS [17]. However, this is in acetone (which possesses an extremely low affinity for hydrogen bonding), our measurements being undertaken in methanol which has a strong affinity for hydrogen bonding, greatly facilitating the enantiomerisation process: in additional support of our lower observed energy values in DCE; the enantiomerisation energy is described to be extremely slow in chloroform, as compared to acetone - *i.e.* it is extremely polarity dependant.

2.7. Compounds **6** and **7**: thermal decolourisation and colourisation

Initial values of absorbance at 550 nm, immediately after UV irradiation, indicated the molar absorptivies for the merocyanine forms to be of the order of 1×10^4 dm^3 mol^{-1} cm^{-1}.

At 50 °C, decolourisations were relatively rapid (half-lives 2–8 min) and equilibria were reached with 10–20 % of the merocyanine forms remaining, Fig. 7a. Progress towards equilibrium followed first-order kinetics with no observable deviation, Fig. 7b. For both compounds at 20 °C, decolourisation followed first-order kinetics; using $A = 0$ as baseline, *ln A vs. time* plots are linear, $R^2 > 0.999$, indicating that at equilibrium decolourisation was close to being complete. From the gradients of the semi-logarithmic plots, the activation energies for decolourisation of compounds **6** and **7** are respectively 33 kJ mol^{-1} and 56 kJ mol^{-1}.

In the thermal colourisation of compounds **6** and **7**, Fig. 8, small initial absorbances mainly reflected incomplete decolourisation. Subsequent increases in absorbance were much less than for the dinitro compounds **1** and **2**, at similar concentrations, corresponding with equilibrium for **6** and **7** favouring the spirocyclic isomers. The first 60% of equilibration was close to zero-order for **7**, or not clearly established, for **6**.

3. Discussion

The implications of the unusual kinetic features observed in this study, with respect to the reaction mechanisms of colourisation↔decolourisation switches, and to their practical consequences, are considered.

3.1. Kinetic features: the physical reaction scheme

An unexpected kinetic feature of the colourisation in solution of both mononitro- and dinitro-substituted spirocyclic isomers was the contribution of zero-order processes. Such processes in dilute solution are unusual; in this case it is highly plausible that the reaction is effected by protic catalysis from the methanol solvent, with the rate contribution effectively being limited, in part (together with a slow isomer interconversion – see later), by the acidity of the methanol. This is probably because the spirocyclic form possesses a basic tertiary amine moiety which is readily protonated (due to the protic nature of the methanol) catalysing ring-opening. However, the results do show increases in rate with rising temperature (which would be expected), thereby establishing that the zero-order processes are not photochemical. The decolourisation of the mononitro-substituted compounds **6** and **7** followed first-order kinetics precisely, with no zero-order contributions.

The major feature of interest, with implications for the practical uses of the compounds studied here, is the unusual sigmoid characteristic shown by the spontaneous colourisation in a methanolic solution of the dinitro-3′-alkyl substituted indolospirobenzopyrans **1** and **2**. A suggestion, prompted by the long induction periods, that visible absorption by the coloured product (merocyanine isomer) gives rise to a photo-activated intermediate that promotes the further isomerisation of the spirocyclic isomer, may be discounted because the parallel zero-order isomerisation, leading directly to the merocyanine isomer, does not promote the observed sigmoidal process. Thus, for compound **1** at 40 °C the zero-order reaction was rapid, and predominated. If the photo-autocatalytic mechanism also occurred, its rate would have been enhanced by the production of a coloured product so that the sigmoid process would also have been more rapid and with a shorter induction period. From Fig. 6d the two parallel processes are independent at low conversions, so that an autocatalytic mechanism is unlikely.

The more likely explanation for the sigmoid plots is that the coloured products are formed by a thermal reaction mechanism involving consecutive steps possessing relatively stable reaction intermediates. For the two first-order step process, in a cuvette with path-length l, involving reactant R, intermediate X and final product P (molar absorptivity ε_R):

$$R \xrightarrow{k_1} X \xrightarrow{k_2} P$$

the variation of total absorbance A_T with time t is given by:

$$A_T = \varepsilon_P l [R]_0 \left(1 - (1 + k_1)e^{-k_1 t} + k_2 e^{-k_2 t}\right)$$

For a three-step process involving intermediates X_1 and X_2:

$$R \xrightarrow{k_1} X_1 \xrightarrow{k_2} X_2 \xrightarrow{k_3} P$$

the variation of absorbance A_T with time t is given by:

$$A_T = \varepsilon_R l\, C_A(t) + \varepsilon_{X_1} l\, C_{X_1}(t) + \varepsilon_{X_2} l\, C_{X_2}(t) + \varepsilon_P l\, C_P(t)$$

Inspection of the curves that may be generated from these equations (by substituting ranges of values for the rate constants) reveals that, in comparison with the observations, the consecutive three-step mechanism is the more likely, due to the long times taken for A_T to begin to increase, observably. The kinetic observations are therefore consistent with the intermediates being identified as X_1 = the oxygen (of the pyran ring) protonated spirocyclic structure (see Fig. 9) and X_2 = TCC isomer (see discussion).

3.2. The organic process observations for compounds **1** and **2**

3.2.1. Observations at 21 °C

At 21 °C the *gem*-methyl-substituted compound **1** produced the open-form (merocyanine) relatively faster than the corresponding 3′-cyclohexyl- substituted compound **2**. This is perhaps unexpected since ring-opening around the highly sterically crowded spirocyclic centre of **2**, additionally containing a spirocyclic cyclohexyl-group, would result in a greater relief of steric strain – a thermodynamic driving force for the ring-opening reaction ('steric acceleration') – than for the relatively less sterically hindered *gem*-methyl-substituted compound. Further, ring-opening must involve initial cleavage of the spirocyclic C–O heteratomic bond (the energy barrier to enantiomerization in spirobenzopyrans is reported [18]

to be approximately 86 kJ mol^{-1}, with the activation energies [19] of thermal interconversion ranging between 80 and 130 kJ mol^{-1}) to produce a 'distorted' planar iminium ion containing structure. However, large differences in the rates of spirocyclic ring-opening for compounds **1** and **2** are likely to arise in a strongly polar solvent such as methanol (Polarity (P) = 5.1: as a reference the most polar solvent is H_2O with a value of 10.2) due to the relatively greater thermodynamic solvation stabilization, through both dipolar and hydrogen bonding interactions with the resultant open-form (eight zwitterionic isomeric conformers are theoretically possible, although only the four *trans*-merocycanine conformers are thermodynamically likely to significantly contribute to the isomeric equilibrium mixture): Solvation differences would be particularly dominant around the relatively less sterically hindered 'planar' iminium ion of compound **1**, being flanked by the *gem*-methyl group, as opposed to the significantly more bulky 3′-spirocyclohexyl- substituent of compound **2**; thus representing a possible explanation for the relatively greater rate of merocyanine formation for this compound. Finally, some substituent-induced inductive stabilization effects from the *gem*-methyl- and 3′-cyclohexyl-groups (both being electron releasing) would be expected to play a part in the stabilization of the iminium ion; however, being separated by a single carbon–carbon bond - between the $C{=}N^+$ moiety - they would be expected to exhibit a relatively minor effect, and therefore this argument could not solely be used to explain the relative differences in merocycanine formation.

At the higher temperature of 40 °C the increasing values of absorbance commenced over a much shorter time period (7 min, against 22 min), consistent with a thermal (non-photochemical) process, and in accord with the proposed protonation; and, similar to the observations at 21 °C, continued for an extended time period (>60 min). Again, it is evident that the rate of colourisation for the *gem*-methyl-substituted compound **1** is faster than that of the 3,3′-cyclohexyl-substituted compound **2**, and additionally, formed an almost theoretically linear regression absorption plot (correlation coefficient = 0.9995) with no induction period (the data points can be extrapolated linearly to the origin), indicative of a zero-order type reaction – a first-order contribution beginning to occur after *ca.* 60 min (calculations above this point on the 'straight line' generate a slight and increasing positive curvature). This perhaps indicates the existence of a relatively long-lived transient thermal intermediate (probably the TTC isomer **19** (see Fig 9), the overall transformation of the closed-to the open-form being virtually independent of the closed-spirocyclic structure (*i.e.* that formation of the merocyanine is directly proportional to the concentration of the intermediates (*cf*: Fig. 9)). Additionally, the fact that the 3′-cyclohexyl-substituted compound **2** demonstrated a relatively slower increase in concentration of the merocyanine - over the same time period - than the *gem*-methyl compound **1** could be explained by the same arguments as for that proposed at 21 °C: primarily, the increased solvation stabilization of the resultant, relatively less sterically hindered, 'planar' iminium ion-containing merocyanine intermediate.

The higher temperature promotes: the relatively increased facile cleavage of the spirocyclic C–O heteroatomic-bond, *via* an increased rate of protonation; subsequent initial thermal isomerisation of the purely *cisoid*- (CCC) (**15**, Fig 9) transition intermediate to the relatively stable TCC (**17**, Fig 9) merocyanine (this being a relatively fast non-rate limiting step); which is followed by relatively slow isomerisation from relatively stable TCC conformer to the TTC (**19**, Fig 9) conformer (a rate second rate determining step). At 64 min the measured (uncorrected) absorbance for compounds **1** and **2** at 21 °C were 0.638 and 0.311, respectively; whilst at 40 °C they were 1.453 and 0.440, representing increases of 2.3 (1.453/0.638) and 1.4 (0.440/0.311) times, respectively; highlighting the relative differing increases in concentration of the respective merocycanines, with increasing temperature, and at identical time periods. Secondly, the increase in merocyanine concentration for compound **2** follows a progressively increasing trend, more typical of a first-order reaction; however, for compound **1** the increase in the concentration of merocyanine unusually appears to exhibit almost complete zero order characteristics: In contrast, at 21 °C both compounds exhibited a progressively increasing merocycanine concentration, perhaps indicating a relatively extremely stable intermediate, which we postulate is the relatively stable long-lived TCC conformer (**17**, Fig. 9), which slowly isomerizes about the central β-alkenic merocyanine bond, to form the TTC isomer, subsequently isomerizing to the TTT isomer – *i.e.* the formation of the TTT merocyanine being almost totally dependant on the concentration of one or more of these intermediates, but in particular the TCC isomer (this is in agreement with Hobley [17] who suggests the isomerisation of the TCC to the TTC/TTT isomer *via cis*-to *trans*-isomerisation about the central β-alkenic bond, is a slow rate determining step, indicating the CCT isomer is relatively stable).

3.3. The organic mechanistic process

Overall, it is postulated that broadband visible light photoirradiation of the solution merocyanines produces the closed-spirobenzopyran structure (expected and known to readily occur from both the *Trans- Trans- Cis-* (TTC) and *Trans- Trans- Trans-* (TTT) merocyanine isomers): On reversion to the pre-photoirradiation equilibrium position the spirocyclic structure is - in the case of these dinitro-substituted compounds – postulated to rapidly (too fast to observe in the spectrophotometer under these experimental conditions) initially form the *Cis- Cis- Cis-* (CCC) isomer, post spirocyclic heterolytic C–O bond cleavage (*via* an equilibrium mixture containing both the protonated tertiary amine spiropyran (as the major structure), but also possessing the pyran oxygen protonated spiropyran (as the minor structure) – from which spirocyclic heterolytic bond cleavage occurs). This is followed by fast pyran ring-opening to the CCC isomer, subsequently followed by relatively fast isomerisation to the relatively stable CCT isomer which undergoes slow isomerization – about the central β-alkenic merocyanine bond - to the relatively more thermodynamically stable TTC isomer, which rapidly isomerizes to form an equilibrium mixture possessing both the TTC and TTT conformers, partially explaining the sigmoidal plots - first order in transient intermediates. [On a thermodynamic basis a smaller concentration of the thermodynamically relatively less stable TCT isomer, also formed from the isomerisation of the TCC isomer, is predicted, which would undergo further isomerisation to the TTT isomer: This TCT conformer is expected to be relatively less stable than the TTC conformer since an isomer possessing a *trans*-configuration about the central β-alkenenic bond since would possess less steric strain than it's *cis*-equivalent – the largest steric effects resulting from gross interactions between the dinitro-quinone and indole moieties of **19** and **20**].

It is noteworthy, at this point, to reference work undertaken on some naphthopyrans by Coelho and co-workers [20] who found that the opposite reaction – *i.e.* fading of the ring-opened form - operated *via* a two stage process, with initial isomerisation of a *transoid* species to a *cisoid* species, which subsequently ring closes. This adds some support, albeit in a different system, and viewpoint, to our hypothesis described herein.

(Notes: in a chloroform solution of other spirobenzopyrans the TTC isomer predominates, and is identified as the most stable [17]. The intermediates are not observed in the ^1H NMR spectra due to the differing UV timescales).

To conclude, the proposed organic mechanism concurs with the postulated physical kinetics argument, with the intermediate structures being depicted in Fig. 9; and the overall mechanism consisting of a multistep step first-order sequential process (effectively ignoring the fast non-rate determining equilibrium steps), graphically shown in Fig. 10.

To our knowledge these relatively stable dinitro-substituted intermediates and extremely slow thermal isomerisation process have never been experimentally observed in such a manner as reported herein.

Lastly, at room temperature – an important factor when considering the use of substituted-spirobenzopyrans as light induced ionic switches or ion chelating systems – these dinitro-substituted compounds behave differently, to a significant and measurable degree, to the structurally identical but mono-nitro-substituted spirobenzopyrans **6** and **7**. These di-nitro-group substitution effects may also therefore prove practically useful in other (photo)thermochromic systems when incorporated into the skeleton of a larger molecule - *e.g.* lariat-ethers and crown systems *etc*. In these structures ion-chelation would thermodynamically bias the equilibrium towards the zwitterionic structure, thereby potentially allowing greater (photo)thermochromic (equilibrium) control in these systems. The latter effect offers the potential of being used in biological metal-ion sensing probes, particularly as the presence of two-nitro substituents greatly enhances the known aqueous solubility of these spirobenzopyran-based systems – necessary for their operation in biological media.

In summary, this study has clearly highlighted that the thermal formation of both the *gem*-methyl and 3′-cyclohexyl- dinitro-substituted merocyanines exhibit a previously unobserved, unusual and interesting sigmoidal absorbance phenomenon: This most probably arises from the formation of two relatively long-lived rate determining intermediates – the TCC merocyanine conformer and the oxygen-protonated pyran ring of its associated spirobenzopyran structure.

4. Experimental section

4.1. Instrumentation

^{1}H NMR assignments were carried out with a JEOL FX2000 spectrometer using deuteriochloroform, dimethyl sulfoxide-d_6 or 1,1,2,2-tetrachloroethene-d_2 (TCE) as the solvent with either tetramethylsilane (TMS) or (TCE) used as the internal reference. Multiplicities are reported as (s) singlet, (d) doublet, (t) triplet, (q) quartet and (m) multiplet. Assignments of hydroxyl and ammonium protons were verified by deuterium exchange. Mass spectra were recorded with a VG 7070H mass spectrometer interfaced with a Finnegan Incos data system. Accurate mass measurements were carried out at the EPSRC mass spectrometry service at the University of Wales, Swansea. UV spectroscopy was carried out using Perkin–Elmer Lambda 5 and Lambda 9 spectrometers; both instruments are double beamed with thermostatically controlled cell blocks. The Lambda 9 is additionally fitted with as RS 232 port, which allows remote control by PC. All UV measurements were taken at 25 °C using 3-cm^3 quartz cells with a 1-cm path length and are referenced against air. IR spectra were recorded with a Perkin–Elmer 983 spectrometer. Melting points were determined in open capillary tubes with an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were carried out in-house. Thin-layer chromatography was performed over glass plates coated with Merck silica gel 60 F254; flash chromatography was performed using Merck 7734 silica gel (20–63 μm).

Chemical intermediates were purchased from commercial sources unless otherwise stated.

4.2. Photometric processes

Solutions of compounds **1**–**7** (2.0×10^{-4} M) in dry methanol (magnesium Grignard) were prepared under dark conditions. Photometric measurements were made using thermostatted borosilicate glass cuvettes (1 cm).

To observe decolourisation, the merocyanine isomers of the mononitro-substituted compounds **6**, **7** were generated by photo-irradiating solutions (1.0×10^{-4} M) with a focussed wavelength filtered (1 M $CoSO_4$: 1 M Cu_2SO_4 solution) ultra-violet radiation (high pressure Hg–Xe source, 200 W, $\lambda = 365$ nm). Reversion towards the spirocyclic forms was followed by monitoring (intervals 30 s) the visible absorption band ($\lambda_{max} \approx 550$ nm).

4.3. Synthesis

4.3.1. Syntheses of the spirobenzopyrans

6,8-Dinitro-1′,3′,3′-trimethylspiro-[2*H*-1-benzopyran-2,2′-indoline] **1**. 2-Hydroxy-3,5-dinitrobenzaldehyde (0.20 g, 0.94 mmol) and 1,3,3-trimethyl-2-methylene indolenine (0.16 g, 0.92 mmol) were dissolved in ethanol (10 mL), and the resulting solution heated under reflux for 24 h. After this period the solvent reduced in volume by rotary evaporation to approximately 2 mL. Cooling of the remaining solution yielded a crystalline solid which was recrystallised from ethanol to yield the title compound as a bottle green crystalline solid (0.22 g, 63%). mp > 220 °C (from ethanol) (lit., [21], 280–283 °C). (Spectrum A) δ_H ($CDCl_3$) (crude); spectrum showing a mixture. Olefinic proton 5.66–5.68 (1H, d, $J = 10$), 1.16 (3H, s, CH_3), (singlet suggesting *trans*-form) also 1.35, 1.33 (6H, d, *gem*-CH_3) (suggesting *cis*-form). (Spectrum B) δ_H Sample recrystallised from ethanol producing a sharper spectrum (aromatics less complicated). No olefinic proton as in (A). 1.16 (3H, s, CH_3) (singlet suggesting *trans*-form) also 1.33, 1.35 (6H, d, *gem*-CH_3) (suggesting *cis*-form). (Spectrum C) Spectrum re-acquired after irradiating (B) with visible light: Spectrum similar to (B). Spectrum (D). UV irradiation of (C); spectrum showing mixture. Olefinic proton 5.66–5.67 (1H, d, $J = 10$) 1.16 (3H, s, CH_3), (singlet suggesting *trans*-form). Doublet at 1.33 (6H, d, *gem*-CH_3) suggesting *cis*-form. $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3020 (sat C–H), 1600 (C=C), 1220 (C–C), 1200 (C–N), 1450 (NO_2), 954 (C–O spiro), 771 (ArH, 4 adj H's). *m/z* 368 (M^++1, 31%), 367 (M^+, base peak, 100), 366 (M^+−1, 14.3). (Found: C 61.19, H 4.58, N 11.22. $C_{19}H_{17}N_3O_5$. 0.4H_2O requires C 60.93, H 4.76, N 11.22).

1′-Methyl-6,8-Dinitro-3′-spirocyclohexylspiro-[2*H*-1-benzopyran-2,2′-indoline] **2**. 1,2-Dimethyl-3-spirocyclohexyl indolium triflate (1.02 g, 2.81 mmol) was dissolved in a 40% sodium hydroxide solution (10 mL). The resulting mixture was vigorously stirred for 5 min after which time diethyether (15 mL) was added. The diethylether layer was subsequently separated, dried (anhydrous sodium sulphate), filtered and evaporated under reduced pressure to produce a yellow-orange oil (0.44 g, 2.06 mmol). The oil was isolated, dissolved in ethanol (3 mL), and added to 2-hydroxy-3,5-dinitrobenzaldehyde (0.44 g, 2.07 mmol) in ethanol (20 mL). The resulting solution was subsequently heated under reflux for 24 h. Removal of the solvent under reduced pressure to approximately 2 mL, and cooling, yielded a reddish coloured crystalline solid. Recrystallisation from the minimum quantity of ethanol yielded the title compound as a dark red coloured precipitate (0.45 g, 58%). mp > 209–211 °C. δ_H ($CDCl_3$) v. insoluble resulting in a broad spectrum. δ_H (TCE); 8.40, 8.42 (1H, d, ArH $J = 8$), 8.22, 8.24 (1H, d, ArH $J = 8$), 7.65, 7.67 (1H, d, ArH, $J = 8$), 7.39–7.41 (1H, t, ArH), 6.88, 6.90 (1H, d, CH=CH, $J = 10$), 6.85, 6.87 (1H, t, ArH), 6.74, 6.76 (1H, d, ArH $J = 8$), 6.20, 6.22 (1H, d, CH=CH, $J = 10$), 2.78 (3H, s, N–CH_3), 1.22–1.95 (10H, m, CH_2 x 5). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3020, 2930 (sat C–H), 1602 (C=C), 1430, 1330 (NO_2), 1376

(C–O), 1216 (C–N), 1092 (C–C), 774 (ArH, 4 adj H's). *m/z* 408 (M^++1, 30%), 407 (M^+, base peak, 100). $C_{22}H_{21}N_3O_5$ Acc. (CI) requires: 407.1481 Found: 407.1481.

4.3.2. Synthesis of the N-methyl indole

1,2-Dimethyl-3-spirocyclohexyl indolium triflate. 2-Methyl-3-spirocyclohexyl-3*H*-indole (3.22 g, 16.18 mmol) was added to methyltrifluoromethane sulphonate (2.66 g, 16.22 mmol) in a mixture of hexane (20 mL) and diethylether (30 mL). Instantly, a canary yellow precipitate formed which was filtered off and washed with cold diethylether to yield the title compound as pale yellow crystals (4.59 g, 78%). mp 126–128 °C. δ_H ($CDCl_3$) 7.91, 7.93 (1H, d, ArH $J = 8$), 7.66–7.68 (1H, d, ArH $J = 8$), 7.62 (1H, t, Ar $J = 8$), 7.56 (1H, t, ArH $J = 8$), 4.12 (3H, s, N^+-CH_3), 2.88 (3H, s, N^+=C–CH_3), 1.54, 2.08 (10H, m, cyclohexyl 5 × CH_2). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3020 (sat C–H), 1590 (C=C), 1325 (C–C), 1210 (C–N), ArH (760), 758 (C–F). *m/z* 233 (M^+ – (SO_3CF_3), 6.7%), 323 (M^+ – SO_3CF_3-1, 41.7), 218 (M^+-SO_3CF_3-15, 17.7), 217 (base peak, 100%) 203 (M^+-SO_3CF_3-2 x 15, 4.2). (Found: C 52.50, H 5.36, N 3.88. $C_{16}H_{20}NO_3F_3S$ requires C 52.88, H 5.55, N 3.86).

1-Methyl-3-spirocyclohexyl-2-methylene indolenine. 1,2-Dimethyl-3-spirocyclohexyl indolium triflate (1.02 g, 2.81 mmol) was dissolved in a 40% sodium hydroxide solution (10 mL) and stirred for 10 min. After this period diethylether (10 mL) was added and the solution stirred for a further 5 min. The diethylether layer was separated from the reaction mixture, dried (anhydrous sodium sulphate), filtered, and removed under reduced pressure to yield the title compound as a yellow/orange oil (0.45 g, 75%). δ_H ($CDCl_3$) 7.44 (1H, d, ArH $J = 7$), 7.14 (1H, t, ArH), 6.74 (1H, t, ArH), 6.56 (1H, d, ArH $J = 7$), 3.88 (2H, dd, C=CH_2 $J = 10, 10$), 3.02 (3H, s, N–CH_3), 1.83 (10H, m, cyclohexyl 5 × CH_2). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 2934 (sat C–H), 1644 (C=N), 1604 (C=C), 1908 (C–C), 908 (C–C), 775 (Ar–H, 4 adj H's). *m/z* 215 (M^++1, 18.5%), 214 (M^+, 46.9), 213 (M^+–1, 80.0), 158 (base peak, 100%), 306 (M^+–1, 15.8). $C_{15}H_{19}N$ Acc. (EI) requires: 213.1517 Found: 213.1517.

4.3.3. Syntheses of the 3H-Indoles

3-Cyclohexyl-2-methyl-3*H*-indole. Cyclohexylmethylketone phenylhydrazone (4.65 g, 21.53 mmol) was added to zinc chloride (1.00 g, 7.35 mmol) in glacial acetic acid (100 mL), and the resulting solution heated on a steam bath, under nitrogen, for 3 h. The resulting solution was cooled to room temperature, filtered, and the remaining glacial acetic acid removed under reduced pressure to yield the title compound as an orange oil (3.25 g, 76%). δ_H ($CDCl_3$) 7.51–7.53 (1H, d, ArH $J = 7$), 7.31 (1H, d, ArH $J = 7$), 7.15, 6.99 (2H, m, ArH), 2.7 (3H, s, N=C–CH_3), 1.25–2.31 (10H, m, cyclohexyl 5 × CH_2). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 2932 (sat C–H), 1688 (C=N), 1598 (C=C, Ar), 1216 (C–N), 1026 (C–C). *m/z* 200 (M^++1, 27.6%), 199 (M^+, base peak, 100%), 198 (M^+–1, 4.2). $C_{14}H_{17}N$ Acc. (EI) requires: 199.1361 Found: 199.1361.

3,3′-Dimethyl-2-methyl-3*H*-indole. A mixture of isopropyl methyl ketone phenylhydrazone (1.69 g, 9.60 mmol) and hydrochloric acid (30 mL) was heated under reflux for 1 h prior to stirring at room temperature for 3 h. After this period the resulting mixture was filtered and the hydrochloric acid removed under reduced pressure to yield a red oil. Column chromatography of the oil over silica using ethyl acetate as the eluent yielded the title compound as a reddish oil (1.19 g, 78%). δ_H ($CDCl_3$) 7.0–7.6 (4H, m, ArH), 2.3 (3H, s, CH_3), 1.3 (6H, s, $ArCH_3$). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3018 (sat C–H), 1450 (C=N), 1533 (C=C), 1210 (C–C), 1190 (C–N), 771 (ArH, 4 adj H's). *m/z* 159 (M^+, 11.9%), 146 (base peak, 100%).

Cyclohexyl ketone phenylhydrazone [22]. Phenylhydrazine (3.00 g, 27.77 mmol) was added to cyclohexylmethyl ketone (3.50 g, 27.77 mmol) in ethanol (100 mL) and the resulting solution heated under reflux for 0.5 h. Removal of the ethanol under reduced pressure yielded the title compound as a deep orange mobile oil (4.78 g, 79%). δ_H ($CDCl_3$) 11.0 (1H, s, NH, exchangeable D_2O), 7.25 (2H, t, ArH), 7.03, 7.05 (2H, dd, ArH), 6.79, 6.83 (1H, t, ArH $J = 8$), 1.90 (1H, m, $(CH_2)_2$CHC), 1.82 (3H, s, N=C–CH_3), 1.17–1.78 (10H, m, cyclohexyl 5 × CH_2). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3650 (N–H), 3020 (C–H), 1616 (C=C), 1520 (C–N), 1020 (C–C), 760 (ArH). *m/z* 216 (M^+, 6.6%), 215 (M^+–1, 8.1), 18 (base peak, 100%).

3,5-Dinitro-2-hydroxy-benzaldehyde. 2-hydroxy-5-nitro-benzaldehyde (0.50 g, 2.99 mmol) was stirred with fuming nitric acid (0.19 g, 3.03 mmol) and sulphuric acid (25 mL) for 3 h at room temperature. The solution was then poured over ice (50 g) and stirred for a further 10 min before being left to stand overnight. After this period the crystals that formed were filtered and washed with water to yield the title compound as very pale yellow coloured crystals (0.36 g, 57%). mp 68–70 °C (from water) (Lit., [12], 128 °C). δ_H ($CHCl_3$) 10.43 (1H, s, CHO), 9.13, 9.14 (1H, d, ArH $J = 8$), 8.98, 8.99 (1H, d, ArH $J = 8$), 3.7 (1H, bs, OH). $\nu_{(max)}$ ($CDCl_3$)/cm^{-1} 3400 (OH), 3018 (CH), 1533 (C=O), 1500 (NO_2), 1210 (C–C), 1190 (C–N). *m/z* 212 (M^++ 19.2%), 211 (M^+–1, 3.1), 194 (M^+, base peak 100%), 166 (M^+–NO_2, 3.0), 120 (M^+–2 x NO_2, 3.6). (Found: C 37.46, H 1.97, N 12.40. $C_7H_4N_2O_{36}$.0.75H_2O requires C 37.25, H 2.44, N 12.41).

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.dyepig.2015.04.027.

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