Photochromic molecular switches
Robertus, Jort

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2015

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Here we report a study of the photochemical isomerisation and thermal relaxation reaction of a double azobenzene system, in which two azobenzene photochromic units are connected via a phenyl ring. Upon UV irradiation, three thermally unstable isomers are formed. Kinetic studies using arrayed $^1$H-NMR spectroscopy revealed four distinct barriers for the thermal reversion to the stable isomer. The double isomerised Z,Z-2 can revert thermally to the E,E-2 isomer via either of two isomerisation pathways. The thermal Z to E isomerisations are not significantly affected by the state of the neighbouring azo-switching unit in the meta position. These findings are supported by quantum chemical calculations on the thermal Z to E isomerisation.

Chapter 3 has been published as:

3.1 Introduction

Recently organic multi-component materials based on photochromic switches\textsuperscript{1,2} (such as stilbenes, azobenzenes, diaryethenes, spiropyrans, and overcrowded alkenes) have attracted increasing attention due to their possible use in data storage devices\textsuperscript{3} and sensors.\textsuperscript{4} Addressable multi-component systems based on several photochromic components are of interest to the fields of optical computing, such as in logic gates, field-effect transistors, and high density data storage.\textsuperscript{1}

Single molecule systems have potential advantages over systems derived from mixtures in solution, polymer matrices, or single crystals.\textsuperscript{1} These advantages include high resolution and multi-frequency single molecular memories.\textsuperscript{5} Many examples have been reported of systems containing one\textsuperscript{6} or several\textsuperscript{7} addressable diarylethene units. Other models include overcrowded alkenes,\textsuperscript{8} dihydropyrenes,\textsuperscript{9} bisnaphthopyrans,\textsuperscript{6d} stilbenes,\textsuperscript{10} spiropyrans,\textsuperscript{11} and azobenzenes.\textsuperscript{12}

Double azobenzenes (Scheme 3.1) are systems with a discrete number of azobenzene units connected in a meta orientation relative to one another and are generally used as dyes in the textile and colour industry. Azobenzene oligomers contain two\textsuperscript{13,14,15} or three\textsuperscript{16,17} azobenzene switching units that share a central phenyl ring, have been reported; however, their switching behaviour has only scarcely been studied.

The proximity of two or more photochromic components in a multi-component system can lead to unexpected interactions that enhance their function or render the nano-scaled system inoperative. These interactions include photochemical quenching, energy transfer, steric interactions and dipole-dipole interactions. Some examples of changes to the photochemical and thermal behaviour of meta substituted bisazobenzenes have been reported.\textsuperscript{12} For instance, Spada and co-workers\textsuperscript{18} have shown that irradiation ($\lambda = 345$ nm) of a (E-E)-m-bisazobenzene leads to a mixture of three isomers $E,E$, $E,Z$ and $Z,Z$ at the photostationary state (PSS). Analysis of the quantum yield of the $E$ to $Z$ photo-isomerisations revealed that the isomerisation of the first azo-unit quenches the photo-isomerisation of the second azo-unit.

An open question, however, is how the individual units interact in the thermal reversion, \textit{i.e.} does the thermal switching of one unit influence the second unit’s ability to switch thermally. In the development of complex multicomponent systems it is important to understand whether the large dipole change that accompanies switching is in fact sufficient to control switching pathways.
In this chapter we describe the thermal relaxation mechanism of a photochromic double switch, based upon an asymmetric *meta*-bisazobenzene (Scheme 3.1), observed after photochemical isomerisation. The asymmetry in the bisazobenzene switch is due to the phenol ester moiety, which is either in the *ortho* or *para* position relative to the azo switching units. In contrast to bisazobenzene systems described previously the asymmetry allows for distinguishing between the two switching units and to study them individually. Bisazobenzene switch 2 exhibits photochromic behaviour similar to monoazobenzene switch 1 upon irradiation with UV light. Upon photochemical formation of the thermally unstable *Z,Z* isomer there are two possible thermal isomerisation pathways back to the stable *E,E* isomer. Pathway (A) goes from the *Z,Z* isomer to *ortho*-Z,E (relative to the butanoate moiety), followed by a final isomerisation to the *E,E* isomer, while in pathway (B) the *Z,Z* isomer thermally isomerises to the *para*-Z,E (relative to the butanoate moiety) isomer first (Figure 3.1).
3.2 Synthesis and characterization

3.2.1 Synthesis

Azobenzene $E$-1 and bisazobenzene $E,E$-2 were synthesised using the procedure described below (see experimental section for details).19,20 Aminobenzoic acid tert-butyl ester 4 was diazotised in a dilute aqueous HCl solution containing NaNO₂ at 0°C. Subsequently, the 4-diazo benzoic acid tert-butyl ester 5 was treated with phenol and KOH in MeOH at 0°C to obtain azobenzene switch $E$-6 (Scheme 3.2) and bisazobenzene switch $E,E$-3 in 68% and 9% yield, respectively. The ester derivatives $E,E$-2 and $E$-1 were prepared by introducing a butyric acid moiety via $N,N'$-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) coupling21 providing the desired switches $E,E$-2 and $E$-1 in 93% and 97% yield, respectively.22

![Scheme 3.2 Synthesis of phenol substituted azobenzene switch 3 and 6 and butanoate functionalised azobenzene switch 1 and 2.](image-url)
3.2.2 Characterisation of photochemical and thermal isomerisation

Photochemical investigation of switch 3

The photochemical properties of bisazobenzene switch 3 were studied by UV/Vis absorption spectroscopy. Irradiation ($\lambda_{\text{exc}}$ 355 nm, at 20°C) of a solution of 3 in acetonitrile ($\approx 10^{-5}$ M) did not result in changes in the UV/Vis spectrum (Figure 3.2a). This is probably due to the phenol substituent on the central phenyl ring. The azo-double bond in this case can be drawn as a single bond in one of its resonance structures. The photochemical properties were further investigated under basic (to increase electron donation) and acidic conditions (to limit electron donation).

Addition of NaOH to deprotonate the phenol moiety led to a red shift in the UV/Vis spectrum (Figure 3.2). The band at $\lambda_{\text{max}}$ 345 nm disappears and two new bands at 325 nm and 430 nm appear. Irradiation at $\lambda_{\text{exc}}$ 355 and 455 nm did not lead to significant changes in the UV/Vis absorption spectrum (Figure 3.2). To exclude irreversible phenol oxidation under basic conditions NaOH was added to a solution of 3, subsequently perchloric acid was added to reprotonate the phenol. The UV/Vis absorption spectrum of 3 reverted to its initial shape. Irradiation of the acidic solution of 3 did not result in changes in the UV/Vis absorption spectrum.
Photochemical investigation of switch 2

Esterification of the phenolic group as in bisazobenzene 2, restores the switching functionality of the bisazobenzene. Additionally the introduction of the butanoate moiety allows for the kinetic study of the thermal isomerisation mechanisms of each of the azobenzene switching units using $^1$H-NMR spectroscopy (Figure 3.12).

Figure 3.3: a) Changes in the UV/Vis absorption spectra of E-1 (3.87 × 10^{-5} M in CH$_2$Cl$_2$) upon irradiation at $\lambda_{exc}$ 365 nm at -10°C. Spectra were recorded at indicated time increments. b) Changes in the $^1$H-NMR spectrum of E-1 (1.63 × 10^{-5} M in CD$_2$Cl$_2$) upon irradiation ($\lambda_{exc}$ 365 nm, at -10°C). PSS was determined by integration of the signals for proton b.

Under irradiation at $\lambda_{exc}$ 365 nm the UV/Vis absorption spectrum of 1 undergoes a hypsochromic shift with the band at $\lambda_{max}$ = 332 nm decreasing and a new band appearing at $\lambda_{max}$ = 261 nm (Figure 3.3a). Additionally new bands appear up-field from
the E-2 isomer in the $^1$H-NMR spectrum (Figure 3.3b). At the photostationary state (PSS) the signal of proton b shifts from 2.581 ppm (b$^E$) to 2.495 ppm (b$^Z$). From the integration of these signals the Z/E ratio was determined to be 81:19.

![Figure 3.4: Changes in the UV/Vis absorption spectra of E,E-2 as a function of irradiation time. Irradiation at $\lambda_{exc}$ 365 nm in CH$_2$Cl$_2$ at -20°C.](image)

The switching behaviour of bisazobenzene 2 was studied using $^1$H-NMR and UV/Vis absorption spectroscopy in order to gain an understanding of its photochemical and thermal behaviour. E,E-2 was irradiated at $\lambda_{exc}$ 365 nm, in CH$_2$Cl$_2$, (Scheme 3.1) at -20°C to prevent the reverse thermal isomerisation from the thermally unstable isomers to stable E,E isomer. Upon irradiation, the intensity of the long wavelength band decreased ($\lambda_{max} = 331$ nm) and a new band appeared at $\lambda_{max} = 268$ nm. This hypsochromic shift is characteristic for azobenzene systems (Figure 3.4).$^{25}$ The initial isosbestic point at 284 nm was not retained upon irradiation, indicating that several photochemical processes take place (Figure 3.4 insert).

Irradiation ($\lambda_{exc}$ 355 nm) of E,E-2 in C$_2$D$_4$Cl$_2$ at 20°C led to an up-field shift in the signals in the aliphatic region of the $^1$H-NMR spectrum of 2. The signal for proton b$^{E,E-1}$ (Figure 3.5) at approximately 2.69 ppm diminished in intensity and three new signals appeared at 2.60, 2.53 and 2.48 ppm for the para-Z,E, ortho-Z,E, and the Z,Z isomers (Figure 3.5b), respectively. $^1$H-NMR spectroscopy revealed that UV irradiation results in the formation of three thermally unstable isomers at the PSS; para-E,Z-2 (13%), ortho-Z,E-2 (15%), and Z,Z-2 (33%). Thermal-reversibility of the switching was demonstrated by $^1$H-NMR spectroscopy (Figure 3.5b); heating of the PSS mixture at 40°C leads selectively to thermal reversion to the stable E,E isomer.
Figure 3.5: a) Structure and ¹H-NMR spectrum in dichloromethane-d₂ of the aliphatic region of switch E,E-2. b) ¹H-NMR spectroscopy study of switch 2. The chemical shifts for proton b (see Figure 3.6) in the E,E, p-Z,E, o-Z,E and Z,Z isomers are shown; UV (λ<sub>ex</sub> 355 nm) irradiation of stable E,E-2 in dichloroethane-d₄ leads to a PSS mixture containing E,E, para-Z,E, ortho-Z,E, and E,E. The mixture reverts back to stable E,E isomer thermally.

The isomers in the PSS mixture of E,E-2 were separated by preparative TLC.²⁶ The four isomers were isolated²⁷,²⁸ and studied by ¹H-NMR and NOE-spectroscopy.²⁹ The E,E-2 (2.69 ppm, R<sub>f</sub> = 0.44) and Z,Z-2 (2.48 ppm, R<sub>f</sub> = 0.12) isomers could be identified by ¹H-NMR spectroscopy (Figure 3.5b).

The para-Z,E and ortho-Z,E isomers were identified using three methods. First, the chemical shifts in the ¹H-NMR spectra of switch 1 (4,4'-substitution pattern) were compared with those in the ¹H-NMR spectra of the isomers para-Z,E and ortho-Z,E. The change in chemical shift between the signal for proton 2-b<sub>p-Z,E</sub> and 2-b<sub>E,E</sub> equals 0.083 ppm while the change between protons 2-b<sub>o-Z,E</sub> and 2-b<sub>E,E</sub> equals 0.123 ppm (Figure 3.5b). This change corresponds well to the change in chemical shift observed between 1-b<sub>p-Z,E</sub> and 1-b<sub>E,E</sub> which is 0.086 ppm (Figure 3.3b). Therefore, the signal at 2.60 ppm is representative of a 4,4'-substitution pattern and corresponds to the para-Z,E-2 isomer while the signal at 2.56 ppm corresponds to the ortho-Z,E-2 isomer.
The second method for the identification of the \textit{para-Z,E} and \textit{ortho-Z,E} isomers involved the calculation of the $^1$H-NMR chemical shifts of the four isomers of \textit{2} with
the Gaussian 09 QC package\textsuperscript{31} using density functional theory (Figure 3.6). Each molecular geometry was first optimised in the gas-phase with the OPBE functional and a 6-311G(d,p) basis set. The subsequent \textsuperscript{1}H-NMR simulation was then performed with the GIAO method, using the same functional and basis set, and with the IEFPCM solvation model (solvent: dichloroethane). The relative chemical shifts in the calculated \textsuperscript{1}H-NMR spectra are in good agreement with the experimentally obtained spectra – both absolute and relative position of the calculated signals for the aromatic protons show especially good correspondence. This provided further evidence for the assignment of the \textit{o}-\textit{Z},\textit{E}-\textit{2} and \textit{p}-\textit{Z},\textit{E}-\textit{2} isomers.

### 3.2.3 Identification of the PSS mixture of switch 2

![Figure 3.7: A) \textsuperscript{1}H-NMR spectrum of \textit{Z},\textit{Z}-\textit{2}, isolated by PTLC chromatography (R\textsubscript{f}: 0.12). Sample contains small amount of the \textit{para}-\textit{Z},\textit{E}, \textit{ortho}-\textit{Z},\textit{E} and \textit{E},\textit{E} isomers.\textsuperscript{32} B) \textsuperscript{1}H-NMR spectrum of \textit{para}-\textit{Z},\textit{E}-\textit{2}, isolated by PTLC chromatography (R\textsubscript{f}: 0.33). Sample contains an equal amount of the \textit{E},\textit{E} isomer.\textsuperscript{32} C) \textsuperscript{1}H-NMR spectrum of \textit{ortho}-\textit{Z},\textit{E}-\textit{2}, isolated by PTLC chromatography (R\textsubscript{f}: 0.20). Sample contains small amount of the \textit{E},\textit{E} isomer.\textsuperscript{32} D) \textsuperscript{1}H-NMR spectrum of PSS mixture of \textit{2}.](image)
Finally, a distinction between the different isomers could also be made based on the retention factor \((R_f)\) of each of the isomers on silica gel TLC plates (Figure 3.9). We observed that the \(Z\)-isomers generally displayed a lower \(R_f\) than the \(E\)-isomers. A rationale for this is that, for a \(Z\)-azo group, the lone pairs on the nitrogen atoms are situated on the same side of the molecule and thereby lie relatively unexposed on the periphery of the molecule. This allows for more interaction with the silica gel phase. For an \(E\)-azo group, however, the nitrogen atoms are less easily accessible due to steric hindrance from the neighbouring phenyl groups, which makes it more difficult for them to interact with the silica gel phase. The exposed \(Z\)-azo groups could be visualised by mapping the electrostatic potential (ESP) for each molecule (Figure 3.10). In these maps, the \(Z\)-azo groups are visible while the \(E\)-azo groups are somewhat obscured.

In agreement with the above rationale, we found that the thermally unstable \(Z,Z-2\) isomer, which contains two \(Z\)-azo groups, displayed the lowest \(R_f\) value of the four isomers. The stable \(E,E-2\) isomer on the other hand displayed the highest \(R_f\) value.
Figure 3.9: PTLC chromatography of a PSS λ= 355 nm mixture of switch 2. PLC: SiO₂ eluted with pentane/ethyl acetate (10:1).

Figure 3.10: Front and rear views of the ESP maps for a) ortho-Z,E-2, b) para-Z,E-2, c) Z,Z-2 and d) E,E-2. These maps were generated from the DFT ¹H-NMR calculations and were drawn with an isovalue of 0.0002.

The significant difference in Rf value between ortho-Z,E-2 and para-Z,E-2 (0.20 and 0.33) is remarkable as both isomers contain one Z-azo and one E-azo group. The sole difference between these isomers is the position of the Z-azo bond relative to the butanoate moiety on the central phenyl ring. The ESP maps indicate that with the ortho-Z,E-2 isomer the carbonyl group of the butanoate moiety is more exposed than is the case with the para-Z,E-2 isomer where it is shielded by one of the phenyl groups attached to the Z-azo group. This indicates that the isomer with the lower Rf of 0.20 is the ortho-Z,E-2 isomer while the Rf of 0.33 is of the para-Z,E-2. This conclusion is in full agreement with the experimentally obtained and calculated ¹H-NMR spectroscopic data described above.

3.2.4 Photochemical Z to E isomerisation of switch 2

The photo-reversibility of the switching was demonstrated by UV-Vis absorption spectroscopy (Figure 3.11). A sample containing a PSS mixture of 2 (Figure 3.11) in
CH₂Cl₂, could be reverted to the E,E-2 isomer by irradiation with visible light (λ_{exc} 450 nm), confirming the photo-reversibility of switch 2.

3.2.5 Thermal behaviour of Z to E isomerisation of switch 1

The thermal Z to E isomerisation of a PSS_{365 nm} mixture of switch 1 was studied at four temperatures in dichloroethane-d₄ (50, 65, 70 and 75°C) and DMSO-d₆ (60, 70, 80 and 85°C) by ¹H-NMR spectroscopy using a thermal array experiment. A first order exponential decay could be fitted to the collected traces, from which the rate constant k for the thermal Z to E isomerisation could be determined. The thermodynamic parameters ΔG°, ΔH° and ΔS° for the thermal isomerisation are shown in table 3.1 and were calculated using the Eyring equation.

\[
k = \frac{k_B T}{h} e^{-\Delta H^o / R} e^{\Delta S^o / R}
\]

Table 3.1: Thermodynamic data for the thermal Z to E isomerisation of 1

<table>
<thead>
<tr>
<th>Solvent</th>
<th>ΔG°</th>
<th>ΔH°</th>
<th>ΔS°</th>
</tr>
</thead>
<tbody>
<tr>
<td>dichloroethane-d₄</td>
<td>24.9</td>
<td>22.5</td>
<td>-8.1</td>
</tr>
<tr>
<td>DMSO-d₆</td>
<td>25.5</td>
<td>25.8</td>
<td>0.9</td>
</tr>
</tbody>
</table>
3.2.6 Thermal behaviour of Z to E isomerisation of switch 2

The photochemically generated thermally unstable $Z,Z$-$2$ isomer has two possible thermal isomerisation pathways to the stable $E,E$-$2$ isomer. Pathway (A) goes from the $Z,Z$ isomer to $Z,E$, followed by a final isomerisation to the $E,E$ isomer, while in pathway (B) $Z,Z$-$2$ isomerises to the $E,Z$ isomer followed by isomerisation to $E,E$-$2$ (Figure 3.1). A kinetic study of pure $Z,Z$-$2$ proved experimentally inaccessible.\(^{34}\) However, using thermal array $^1$H-NMR spectroscopic experiments at five temperatures ($28.1$, $45.0$, $54.5$, $64.6$ and $68.7$°C) a kinetic study of the thermal reversion of $Z,Z$-$2$, $ortho-Z,E$-$2$ and $para-Z,E$-$2$ could be carried out simultaneously (Figure 3.12).

Figure 3.12 a) $^1$H-NMR spectroscopic thermal array of unstable isomers $Z,Z$-$2$, $para-Z,E$-$2$ and $ortho-Z,E$-$2$ at $55^\circ$C. b) Kinetic traces of thermal reversal of PSS mixture of $2$ at $55^\circ$C, determined by $^1$H-NMR spectroscopy. $E,E$-$2$ (□), $o-Z,E$-$2$ (○), $p-Z,E$-$2$ (△) and $Z,Z$-$2$ (○).\(^{35}\)

3.2.7 Fitting model for the kinetic analysis of thermal Z to E isomerisation of switch 2

Our aim was to extract the four rate constants ($k_1$ to $k_4$) for Z to E isomerisation of the thermally unstable isomers of switch $2$ from the kinetic traces in Figure 3.12. Each of the four kinetic traces is described by two rate constants, as shown in Figure 3.1. Each state is associated with a function $A(t)$, $B(t)$, $C(t)$ and $D(t)$, which describes the relative concentration of each isomer ($Z,Z$, $o-Z,E$, $p-Z,E$ and $E,E$) as a function of time (equation 3.2-3.5). These functions depend on the rate constants $k_i$ as well as the initial concentrations $A(0) = A_0$, $B(0) = B_0$, etc (equation 3.10-3.13).

\[
\frac{dA(t)}{dt} = A'(t) = -k_1A(t) - k_2A(t) \quad (3.2)
\]
\[
\frac{dB(t)}{dt} = B'(t) = k_1A(t) - k_2B(t) \quad (3.3)
\]
The model parameters were obtained by a least squares fit to the available data.
The rate constants $k_1$, $k_2$, $k_3$ and $k_4$, are extracted from the fits at each of the temperatures (28, 49, 55, 65 and 69°C, respectively). The statistical error is set at $1 \sigma$ as coming from the fit. We estimate the systematic error by varying the end time of the fit. As at high temperatures, the reaction proceeds more rapid than at the lower temperatures. Especially at 28°C, the reaction has not been completed by the time the kinetic analysis is terminated. Since the termination time-point might influence the fitted coefficients, we estimate the systematic error as a result of the termination time of data collection. This is done using a fit that utilizes various termination times. As can be expected we see that at higher temperatures the variation of the termination times of the fit has a relative small effect on the results of the fit (Figure 3.13).

### Table 3.2: Determined rate constant $k$ for the thermal isomerisation pathways thermal $Z,Z$-2 to $E,E$-2 isomerisation at 28.2°C

<table>
<thead>
<tr>
<th>Rate constant $k$ for thermal $Z$ to $E$</th>
<th>Value $k$</th>
<th>Statistical error</th>
<th>Systematic error</th>
<th>Total error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>4.811e-06</td>
<td>± 8.5e-08</td>
<td>± 1.7e-07</td>
<td>± 1.9e-07</td>
</tr>
<tr>
<td>$k_2$</td>
<td>1.840e-06</td>
<td>± 8.9e-08</td>
<td>± 2.3e-07</td>
<td>± 2.5e-07</td>
</tr>
<tr>
<td>$k_3$</td>
<td>2.814e-06</td>
<td>± 6.0e-08</td>
<td>± 2.3e-07</td>
<td>± 2.4e-07</td>
</tr>
<tr>
<td>$k_4$</td>
<td>3.232e-06</td>
<td>± 8.8e-08</td>
<td>± 3.9e-07</td>
<td>± 4.0e-07</td>
</tr>
</tbody>
</table>

### Table 3.3: Determined rate constant $k$ for the thermal isomerisation pathways thermal $Z,Z$-2 to $E,E$-2 isomerisation at 49.0°C

<table>
<thead>
<tr>
<th>Rate constant $k$ for thermal $Z$ to $E$</th>
<th>Value $k$</th>
<th>Statistical error</th>
<th>Systematic error</th>
<th>Total error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>6.762e-05</td>
<td>± 7.4e-07</td>
<td>± 3.4e-07</td>
<td>± 8.2e-07</td>
</tr>
<tr>
<td>$k_2$</td>
<td>2.527e-05</td>
<td>± 7.7e-07</td>
<td>± 6.2e-07</td>
<td>± 9.9e-07</td>
</tr>
<tr>
<td>$k_3$</td>
<td>3.459e-05</td>
<td>± 2.8e-07</td>
<td>± 6.1e-07</td>
<td>± 6.7e-07</td>
</tr>
<tr>
<td>$k_4$</td>
<td>4.034e-05</td>
<td>± 5.0e-07</td>
<td>± 5.0e-07</td>
<td>± 7.0e-07</td>
</tr>
</tbody>
</table>

### Table 3.4: Determined rate constant $k$ for the thermal isomerisation pathways thermal $Z,Z$-2 to $E,E$-2 isomerisation at 54.5°C

<table>
<thead>
<tr>
<th>Rate constant $k$ for thermal $Z$ to $E$</th>
<th>Value $k$</th>
<th>Statistical error</th>
<th>Systematic error</th>
<th>Total error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>1.176e-04</td>
<td>± 2.1e-06</td>
<td>± 8.4e-07</td>
<td>± 2.3e-06</td>
</tr>
<tr>
<td>$k_2$</td>
<td>5.174e-05</td>
<td>± 2.1e-06</td>
<td>± 8.0e-07</td>
<td>± 2.3e-06</td>
</tr>
<tr>
<td>$k_3$</td>
<td>5.842e-05</td>
<td>± 5.9e-07</td>
<td>± 4.1e-07</td>
<td>± 7.2e-07</td>
</tr>
<tr>
<td>$k_4$</td>
<td>7.755e-05</td>
<td>± 1.2e-06</td>
<td>± 6.2e-07</td>
<td>± 1.4e-06</td>
</tr>
</tbody>
</table>
Table 3.5: Determined rate constant $k$ for the thermal isomerisation pathways thermal $Z,Z$-2 to $E,E$-2 isomerisation at 64.6°C.

<table>
<thead>
<tr>
<th>Rate constant $k$ for thermal $Z$ to $E$</th>
<th>Value $k$</th>
<th>Statistical error</th>
<th>Systematic error</th>
<th>Total error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>3.750e-04</td>
<td>± 1.0e-05</td>
<td>± 1.8e-06</td>
<td>± 1.1e-05</td>
</tr>
<tr>
<td>$k_2$</td>
<td>2.022e-04</td>
<td>± 1.0e-05</td>
<td>± 5.6e-06</td>
<td>± 1.2e-05</td>
</tr>
<tr>
<td>$k_3$</td>
<td>1.896e-04</td>
<td>± 2.6e-06</td>
<td>± 2.1e-06</td>
<td>± 3.4e-06</td>
</tr>
<tr>
<td>$k_4$</td>
<td>2.361e-04</td>
<td>± 4.4e-06</td>
<td>± 2.0e-06</td>
<td>± 4.8e-06</td>
</tr>
</tbody>
</table>

Table 3.6: Determined rate constant $k$ for the thermal isomerisation pathways thermal $Z,Z$-2 to $E,E$-2 isomerisation at 68.7°C.

<table>
<thead>
<tr>
<th>Rate constant $k$ for thermal $Z$ to $E$</th>
<th>Value $k$</th>
<th>Statistical error</th>
<th>Systematic error</th>
<th>Total error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>3.997e-04</td>
<td>± 1.0e-05</td>
<td>± 6.4e-06</td>
<td>± 1.2e-05</td>
</tr>
<tr>
<td>$k_2$</td>
<td>2.355e-04</td>
<td>± 9.8e-06</td>
<td>± 1.3e-05</td>
<td>± 1.7e-05</td>
</tr>
<tr>
<td>$k_3$</td>
<td>1.965e-04</td>
<td>± 2.0e-06</td>
<td>± 3.5e-06</td>
<td>± 4.1e-06</td>
</tr>
<tr>
<td>$k_4$</td>
<td>3.191e-04</td>
<td>± 4.7e-06</td>
<td>± 7.6e-06</td>
<td>± 9.0e-06</td>
</tr>
</tbody>
</table>

Figure 3.13: Eyring plots for thermal $Z$ to $E$ isomerisation of 2. a) $Z,Z$ to ortho-$Z,E$ b) $Z,Z$ to para-$Z,E$ c) ortho-$Z,E$ to $E,E$ and d) para-$Z,E$ to $E,E$. 

91
From the fitted data\textsuperscript{36} (Figure 3.12b) the rate constant for thermal \( Z \) to \( E \) isomerisation of each of the thermally unstable isomers can be determined (Tables 3.2 to 3.6).\textsuperscript{37} The activation barrier (\( \Delta G^\ddagger \), Table 3.7) for each thermal isomerisation can be calculated using the Eyring equation (1).

### Table 3.7: Thermodynamic data for the thermal isomerisation of \( Z,Z \)-2 to \( E,E \)-2 at 20°C

<table>
<thead>
<tr>
<th>Thermal ( Z ) to ( E )</th>
<th>( \Delta G^\ddagger ) (Kcal/mol)</th>
<th>( \Delta H^\ddagger ) (Kcal/mol)</th>
<th>( \Delta S^\ddagger ) (cal/K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( k_{(Z,Z \rightarrow o-Z,E)} )</td>
<td>24.8 ± 4.9</td>
<td>22.2 ± 3.7</td>
<td>-9.0 ± 11.2</td>
</tr>
<tr>
<td>( k_{(O-Z,E \rightarrow E,E)} )</td>
<td>25.6 ± 4.8</td>
<td>24.7 ± 3.6</td>
<td>-2.5 ± 10.9</td>
</tr>
<tr>
<td>( k_{(Z,Z \rightarrow p-Z,E)} )</td>
<td>25.1 ± 6.3</td>
<td>21.1 ± 4.7</td>
<td>-13.6 ± 14.3</td>
</tr>
<tr>
<td>( k_{(p-Z,E \rightarrow E,E)} )</td>
<td>25.2 ± 2.2</td>
<td>22.9 ± 1.7</td>
<td>-7.8 ± 5.0</td>
</tr>
</tbody>
</table>

3.2.8 Quantum chemical study of thermal \( Z \) to \( E \) isomerisation of switch 2

Quantum chemical calculations were carried out on the \( E,E \)-2, \( para-Z,E \)-2, \( ortho-Z,E \)-2, and the \( Z,Z \)-2 isomers, with the Firefly QC package,\textsuperscript{38} which is based partially on the GAMESS (US)\textsuperscript{39} source code. Geometry optimisations and energy calculations were performed using the B3LYP hybrid functional (using VWN formula 1 RPA correlation) and a 6-31G(d,p) basis set. The validity of the transition state geometries found during this study was verified by both a vibrational analysis and an IRC analysis.

For this study, we presumed that \( Z \) to \( E \) isomerisation would take place via the inversion mechanism.\textsuperscript{40,41} In this mechanism the lowest energy pathway passes through a virtually linear N-N-C transition state. Thermal relaxation of \( Z,Z \)-2 can take place through four distinct inversion pathways. Inversion can take place over either of the four nitrogen atoms contained in the diazo-double bonds \( N^1 \), \( N^2 \), \( N^3 \) or \( N^4 \). The thermal barrier over each of the four nitrogen atoms was calculated to determine the lowest energy pathway over the barrier to the thermal \( Z \) to \( E \) isomerisation (Table 3.8).

![Diagram](image)

<table>
<thead>
<tr>
<th>( ZZ )-2 ( \rightarrow ) ortho-( Z,E )-2</th>
<th>( ortho-Z,E )-2 ( \rightarrow ) ( EE )-2</th>
<th>( ZZ )-2 ( \rightarrow ) para-( Z,E )-2</th>
<th>para-( Z,E )-2 ( \rightarrow ) ( EE )-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>inversion</td>
<td>Kcal/mol</td>
<td>inversion</td>
<td>Kcal/mol</td>
</tr>
<tr>
<td>( N^1 )</td>
<td>26.8</td>
<td>( N^2 )</td>
<td>25.6</td>
</tr>
<tr>
<td>( N^2 )</td>
<td>26.2</td>
<td>( N^3 )</td>
<td>22.2</td>
</tr>
<tr>
<td>( N^3 )</td>
<td>25.5</td>
<td>( N^4 )</td>
<td>22.6</td>
</tr>
<tr>
<td>( N^4 )</td>
<td>26.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.3 Discussion

The thermal isomerisation behaviour of the individual switching units in switch 2 can be analysed by comparison with the thermal behaviour of switch 1 (Table 3.1) and the calculated quantum chemical data for switch 2 in table 3.8. However, before considering the influence of the interactions of the neighbouring azobenzene units on the thermal Z to E isomerisation, we must determine if a change in the mechanism of the isomerisation of switches 1 and 2 occurs.

There are two known mechanisms for azobenzene Z to E isomerisation; a rotation mechanism wherein a 180° rotation takes place around the N=N double bond and the inversion mechanism, which proceeds via a dipolar transition state (Scheme 3.3).42,43,44 Quantum mechanical and experimental investigations suggest that the nature of the substituents on the phenyl rings determines the pathway taken.49,45,46,47

Scheme 3.3: Mechanism of thermal relaxation via in plane inversion (upper) and out of plane rotation (lower). It is proposed that the mechanism of thermal isomerisation in azobenzenes containing electron donating and electron withdrawing functionalities on opposite sides of the switch (known as push-pull systems) takes place via rotation in highly polar solvents.48,49

Experimental50 and quantum mechanical calculations49 have shown that in unsubstituted, neutrally substituted azobenzenes and sterically constrained azobenzenes50 the thermal Z to E isomerisation takes place via the inversion mechanism. Calculations by Hecht, Saalfrank, and co-workers have revealed that the isomerisation barrier of azobenzenes is lowered more effectively by electron withdrawing groups than by electron donating groups. The groups have the same effect whether in the 2-position (ortho) or 4-position (para) of the azobenzene.49 In both cases strong electronically active groups (EDG or EWG) induce enhanced lowering of the thermal barrier than lesser donating or withdrawing groups. Substituents in the meta position only give rise to small changes in the barrier to isomerisation.
In push-pull azobenzenes, the *para* and *ortho* substituted positions lower the barrier to the greatest extent. Azobenzene I contains *t*-butyl ester groups in the 4’ and the 4” positions (Scheme 2.4). The *t*-butyl ester is moderately electron withdrawing (A), whereas the butanoate group in the 4”-position is moderately electron donating (D). Consequently, both of the azo-switching units resemble a push-pull system (Scheme 3.4). The transition state (TS) of thermal isomerisation via the rotation mechanism has a zwitterionic character and might be stabilised by resonance in push-pull systems. This would result in a change of mechanism for the thermal Z to E isomerisation.

However, the *t*-butyl ester and the butanoate group are far weaker electron withdrawing and electron donating groups than the -NO₂ and -NH₂ respectively. Therefore smaller changes to the barrier are to be expected compared to 4-((4-nitrophenyl)diazene)aniline push-pull systems.⁴⁰,⁴¹

An isokinetic relation has previously been reported for the thermal Z to E isomerisation for a number of variously substituted azobenzene switches (ΔH° = βΔS° + ΔH°;⁴⁰,⁴² Wherein β is the constant of proportionality (ΔH° vs. ΔS°) and ΔH° (kcal mol⁻¹) is constant regardless of the substituent.⁵¹ When the determined enthalpy of activation (ΔH°) is plotted against the entropy of activation (ΔS°) for each Z to E thermal isomerisation step in table 3.1 and 3.2 (Figure 3.14), the data points fall in line with the previously reported data (unfunctionalised azobenzene, crown ether bridged azobenzene, morpholinomethanone functionalized azobenzenes, and azobenzene in zeolites) for the inversion mechanism.⁴³
From the isokinetic plot it can be concluded that there is no change in the mechanism of thermal relaxation, going from $Z,Z$-$2$ to $E,E$-$2$ regardless of which of the two pathways is taken. As a consequence we can exclude that the preferred pathway of the thermal isomerisation is the result of a change in the thermal $Z$ to $E$ isomerisation mechanism of the azo-double bond. Kinetic measurements of the $Z$ to $E$ isomerisation of switch 1 in dms-o-$d_6$ also exclude the rotation mechanism in polar solvents, indicating that the mechanisms of $Z$ to $E$ of 1 and 2 are not solvent dependent. The determined $\Delta S^\ddagger$ values for the thermal $Z$ to $E$ isomerisation (Table 3.2) are of the same order as reported previously.$^{42,50}$ The variation in $\Delta S^\ddagger$ between isomerisation via different pathways is small as expected. The experimental uncertainty of $\Delta S^\ddagger$ is relatively large as a result of method used for the kinetic analysis. Therefore no conclusions can be drawn on basis of the absolute $\Delta S^\ddagger$ values.

From the data in Table 3, it is apparent that, although the azo-units share a phenyl ring, significant interaction does not occur between the thermal $Z$ to $E$ isomerisations of the azo-units. The pathways described in Figure 3.1 contribute equally to the thermal relaxation from $Z,Z$-$2$ to $E,E$-$2$. The difference in relative speed of depletion of the ortho and para-$Z,E$-$2$ isomers, which can be seen in Figure 3.12, was found not to be significant. No significant differences could be determined for any of the activation barriers to each of the four isomerisation steps described in Figure 3.1. Changes in the polarity of the neighbouring azo-group do not have an effect on the thermal relaxation of meta substituted bisazobenzene switches. This is possibly due to the position of the switching units relative to one and another, i.e. meta. This is also evident by comparison of the UV/Vis spectra of switches 1 and 2 (Figures 2.3a and 2.4) in which only minor
differences are observed, indicating that the electronic structure of the azo switching units are not perturbed significantly by introducing a second azo-unit meta relative to its position. As described above, substitution in the meta position only gives rise to small changes in the barrier to thermal Z to E relaxation. These findings correlate well with quantum mechanical modelling (vid supra). It should be noted that quantum mechanical calculations were performed in the gas-phase. This is most likely due to the use of CH₂Cl₂, which, being an apolar solvent, would result in little additional stabilization of the dipolar-like transition state.

3.4 Conclusions

Herein we described the kinetic behaviour of a meta bisazobenzene system. This system serves as a model to study the effect of more complex azobenzene switching systems. Our results indicate that the thermal Z to E isomerisations of one of the switching units does not affect the second unit significantly. Both units in 2 function independently from each other and behave as individual switches. Furthermore, it was shown that the thermal behaviour of bisazobenzene 2 is comparable to that of azobenzene 1. It can be expected that bisazobenzenes containing two switching positioned meta relative from each other show similar thermal relaxation behaviour.

Additionally, we determined that the weakly electron donating group (EDG) and electron withdrawing group (EWG) groups do not change the mechanism of the thermal Z to E isomerisation of switches 1 and 2. This is advantageous as the t-butyl esters are easily deprotected and can be used for further functionalisation and the introduction of bio- or photo-active groups via ester synthesis, without having a major electronic effect on the mechanism of thermal helix inversion and therefore their function when incorporated in to more complex systems.

3.5 Experimental section

General remarks

For synthesis all chemicals were obtained from commercial sources and used as received unless stated otherwise. Solvents were reagent grade. For column chromatography, silica gel (Silicycle Siliaflash P60, 40-63 μm, 230-400 mesh) was used in all cases. Separation was determined on Merck TLC silica gel 60, kieselguhr F254. ¹H and ¹³C NMR spectra were recorded on a Varian Gemini-200 (operating at 200 and 50 MHz), a Varian VXR-300 (operating at 300 and 75 MHz) and a Varian AMX400 (operating at 400 and 100 MHz) spectrometer. Kinetic and temperature dependant ¹H-
NMR studies were recorded on a Varian Unity Plus (500 MHz) in CD2Cl2, C2D4Cl2 and DMSO-d6. Chemical shifts are reported in δ values (ppm) relative to CDCl3 (1H δ = 7.24, 13C δ = 77.2), CD2Cl2 (1H δ = 5.32, 13C δ = 54.0), C2D4Cl2 (1H δ = 3.72), and DMSO-d6 (1H δ = 2.50, 13C δ = 39.5). For 1H-NMR the signals were assigned as following: singlet (s), doublet (d), double doublet (dd), triplet (t), quartet (q), and multiplet (m). For 13C-NMR, the signals were designated as: primary carbon (CH3), secondary carbon (CH2), tertiary carbon (CH), quaternary carbon (C). MS spectra were obtained on a Hewlett-Packard HP 6890 GC with HP 5973 mass selective detector, containing an Agilent 5%-(phenyl)methylpolysiloxane column (25 m × 0.25 mm × 0.25 μm). MS (ESI, APCI) and HRMS (ESI, APCI) spectra were obtained on a Thermo scientific LTQ Orbitrap XL. Melting points were recorded using a Buchi melting point B-545 apparatus. UV/Vis absorption spectra were recorded on a Hewlett-Packard HP 8453 FT spectrometer using UVASOL grade solvents. Irradiation experiments were performed with a spectroline ENBC-280C/FE UV lamp (365 nm) or an Innolas Spotlight 400 Nd: YAG laser (excitation at 355 nm, 6 nm FWHM, 10 Hz, 40 mW).

Synthesis of *tert*-butyl-4,4′-(1E,1′E)-(4-hydroxy-1,3-phenylene)bis(diazene-2,1-diyldibenzate) (3)

4-Aminobenzoic acid *tert*-butyl ester 4 (5.00 g, 26 mmol) was dissolved in a stirred aqueous solution of dilute hydrochloric acid (1 mM, 60 mL). The resulting solution was cooled to 0 °C. Compound 3 was diazotized by a dropwise addition of 5 mL solution of NaNO2 (1.79 g, 26 mmol) in water at 0 °C. Upon addition of NaNO2, the solution became intensely yellow. The yellow solution was diluted with chilled methanol (100 mL), subsequently the coupling was performed by slow addition of the diazotized mixture to a mixture of phenol (2.35 g, 25 mmol), KOH (2.81 g, 50 mmol), and MeOH (25 mL) at 0 °C. The mixture was neutralized with aqueous 10% HCl solution and subsequently extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with brine (2 × 200 mL) and dried over MgSO4. The organic solvent was removed under reduced pressure and an orange-red oil was obtained. The oil was dry loaded onto celite and purified by column chromatography (SiO2, pentane / ethyl acetate = 4:1, Rf = 0.79). The excess of organic solvent was removed in vacuo to yield a red solid, which was recrystallized from *n*-hexane. Compound 3 was obtained as red crystals (1.17 g, 18 mmol, 9 %). m.p.: 141-142 °C. 1H NMR (200 MHz, CDCl3) δ: 1.63 (s, 18H), 7.15 (d, J = 8.8 Hz, 1H), 7.92 (m, 4H), 8.04 (d, J = 8.8 Hz, 2H), 8.14 (m, 4H), 8.59 (s, 1H), 13.24 (s, 1H); 13C NMR (100 MHz, CDCl3) δ: 28.4 (CH3), 81.6 (C), 81.9 (C), 119.3 (CH), 122.3 (CH), 122.6 (CH), 127.9 (CH), 130.6 (CH), 130.9 (CH), 133.7 (C), 134.6 (C) 152.6 (C) 154.9 (C) 156.2 (C) 165.0 (C) 165.4 (C; m/z (APCI pos.) = 503 (+H)+; HRMS (EI): calcd. for C28H31N4O5 H+: 503.2216, found 503.2289.
Synthesis of tert-butyl-4,4'-((E,E)-(4-(butyryloxy)-1,3-phenylene)bis(diazen-2,1-diyl) dibenzoate (2) A solution of DCC (812 mg, 3.9 mmol) in DCM (2 mL) was added dropwise to a solution of 3 (789 mg, 1.6 mmol), butyric acid (277 mg, 0.3 mL, 3.1 mmol), and DMAP (46 mg, 0.4 mmol) in DCM (3 mL) at 0°C under an argon atmosphere. The reaction mixture was stirred for 20 min at 0°C. The colour of the reaction mixture changed from dark red to bright orange. Subsequently the solution was allowed to warm to rt and stirred for 1 h. The solvent was removed in vacuo and the orange solid obtained was further purified by column chromatography (SiO2, pentane / ethyl acetate = 10:1, Rf = 0.44) to afford 2 as orange crystals (837 mg, 1.5 mmol, 93 %). m.p.: 146-147°C. 1H NMR (500 MHz, CD2Cl2) δ: 1.05 (t, J = 7.3 Hz, 3H), 1.61 (s, 18H), 1.78-1.82 (m, 2H), 2.69 (t, J = 7.3 Hz, 2H), 7.42 (d, J = 8.6 Hz, 1H), 7.93 (dd, J = 7.8, 11.4 Hz, 4H), 8.12 (d, J = 9.3 Hz, 1H), 8.14 (d, J = 8.6 Hz, 1H) 8.30 (s, 1H); 13C NMR (100 MHz, CD2Cl2) δ: 14.2 (CH3), 19.0 (CH2), 28.5 (CH3), 36.4 (CH2), 81.9 (C), 82.0 (C), 112.2 (CH), 123.2 (CH), 123.3 (CH), 125.0 (CH) 127.2 (CH), 130.9 (CH), 134.9 (C), 135.2 (C), 145.2 (C), 151.1 (C), 152.2 (C), 155.1 (C), 155.3 (C), 165.3 (C), 165.4 (C), 172.3 (C); m/z (EI, %) = 573, (100); HRMS (EI): calcd. for C32H36N4O6 + H: 573.2635, found 573.2716.

Synthesis of (E)-4-((4-hydroxyphenyl)diazenyl)benzoic acid (6) E-4-(4-hydroxyphenylazo)benzoic acid tert-butyl ester 6 was obtained during the synthesis of compound 3. Compound 6 was purified using column chromatography (rf: SiO2, pentane / ethyl acetate = 4:1, Rf = 0.57). The excess of organic solute was removed in vacuo and a red solid was obtained and recrystallized from n-hexane. Compound 6 was obtained as red crystals (5.22 g, 18 mmol, 68 %). m.p.: 145-146°C. 1H NMR (400 MHz, CDCl3) δ: 1.64 (s, 9H), 6.47 (s, 1H), 6.98 (d, J = 8.8 Hz, 2H), 7.89 (q, J = 1.8, 6.6 Hz, 4H), 8.12 (d, J = 8.4 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ: 28.4 (CH3), 82.0 (C), 116.1 (CH), 122.6 (CH), 125.6 (CH), 130.6 (CH), 133.1 (C), 147.2 (C), 155.3 (C), 159.5 (C); m/z (APCI, pos) = 299; HRMS (APCI, pos): calcd. for C17H19N2O3 +H+: 299.1317, found 299.1390.

Synthesis of tert-Butyl-4-((4-(5-(1,2-dithiolan-3-yl)pentanoyloxy)phenyl) diazenyl) benzoate (1) Compound 1 was synthesized as described for 2, and purified by column chromatography (SiO2, pentane: ethyl acetate = 4:1, Rf = 0.70) to afford orange crystals (55 mg, 0.14 mmol, 79 %). (caution: butyric acid is extremely putrid) m.p.: 101-102°C. 1H NMR (300 MHz, CDCl3) δ: 1.10 (t, J = 7.3 Hz, 3H), 1.66 (s, 9H), 1.83-1.86 (m, 2H), 2.61 (t, J = 7.3 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H), 7.99 (dd, J = 8.4, 11.4
Kinetic analysis of the thermal isomerisation pathways in a double azobenzene switch

\[ \text{Hz, 4H), 8.17 (d, } J = 8.4 \text{ Hz, 1H)} \]

\[ ^{13} \text{C NMR (100 MHz, CDCl}_3^\text{)} \delta: 13.9 (\text{CH}_3), 18.6 \]

\[ (\text{CH}_2), 28.4 (\text{CH}_2), 36.4 (\text{CH}), 81.6 (\text{C}), 122.5 (\text{CH}), 122.7 (\text{CH}), 130.6 (\text{CH}), 134.0 \]

\[ (\text{C}) 150.3 (\text{C}), 153.4 (\text{C}), 154.9 (\text{CH}), 165.3 (\text{C}), 171.9 (\text{C}); m/z (\text{APCI, pos}) = 299; \]

\[ \text{HRMS (APCI, pos): calcd. for C}_{21}\text{H}_{24}\text{N}_2\text{O}_4 +H^+: 369.1736, found 369.1789. } \]

**Photochemical E to Z isomerisation**

Samples used for arrayed $^1$H-NMR experiments were prepared as following. A 1 mL solution of $E,E$-1 ($4 \times 10^{-5}$ M in C$_2$H$_4$Cl$_2$, at 20°C) was irradiated at $\lambda_{\text{exc}}$ 355 nm (10 Hz, 5-6 ns pulse, 30 mW) in a quartz cuvette (pathlength 1 mm) for 9 min. Thermal array $^1$H-NMR experiments were carried out on a Varian Unity Plus (500 MHz). Separation of the isomers was achieved by irradiating a sample containing $E,E$-2 in 1 ml CH$_2$Cl$_2$ at 20°C, at $\lambda_{\text{exc}}$ 355 nm in a stirred 1 mL quartz cuvette (d = 1 cm) for 9 min. The PSS mixture was subsequently applied to a Merck PLC plate (Silica gel 60, 3 mm, 20 × 20 cm) and eluted with pentane / ethylacetate, 10:1 ($R_f$: $E,E$-2 = 0.44, ortho-$Z,E$-2 = 0.33, para-$Z,E$-2 = 0.20, $Z,Z$-2 = 0.12).

**Photochemical Z to E isomerisation**

The Z to E photoisomerisation was performed by irradiating a PSS solution of 1 (2.50×10$^{-5}$ M in CH$_2$Cl$_2$) at $\lambda_{\text{exc}}$ 450 nm (5 min, at 20°C) in a 1 cm quartz cuvette.

**Thermal Z to E isomerisation**

Changes in the UV and $^1$H-NMR spectra upon thermal reversion were determined by irradiating ($\lambda_{\text{exc}}$ 355 nm) a sample of $E,E$-2 ($4 \times 10^{-5}$ M in C$_2$H$_4$Cl$_2$, at 20°C) to the PSS as previously indicated. Subsequently the sample was heated at various temperatures in the Varian Unity Plus (500 MHz) spectrometer $^1$H-NMR experiments used Varian software (VNMRJ version 2.2 revision D 2008 inova).

**3.6 Acknowledgment**

Thomas C. Pijper is gratefully acknowledged for the quantum mechanical calculations of the $^1$H-NMR spectra$^{52}$ and the mapping of the electrostatic potential$^{53}$ of the isomers of 2 in sections 2.2.2 and 2.2.3, as well as calculating the theoretical barriers of $Z$ to $E$ isomerisation$^{54}$ of $Z,Z$-2 to $E,E$-2.

Siebren F. Reker and Albert Deuzeman are gratefully acknowledged for developing the data fitting model in section 2.2.3.
3.7 References

20 Proton b will be used throughout this Chapter to identify the individual isomers.
The data is fitted for all the isomers simultaneously.

After separation of the photochemically generated isomers using PLC the Z,E-2 and para-Z,E-2 after thin layer chromatography (SiO₂, 1:10 ethyl acetate / pentane). The organic solvents were removed in vacuo (30°C), however due to the thermal Z to E isomerisation, the isomers cannot be heated under reduced pressure for an extended period. During removal of the organic solvent ortho-Z,E-2 and para-Z,E-2 partially revert back to the thermally stable E,E-2 isomer.

Statistical outliers were removed using the Grubbs test.

We list the coefficients $k_1$, $k_2$, $k_3$ and $k_4$, as extracted from the fits at each of the temperatures (28.1, 45.0, 54.5, 64.6 and 68.7°C), respectively. We give a statistical error (1σ) as coming from the fit. The systematic error is estimated by varying the end time of the fit.

The data is fitted for all the isomers simultaneously.

Traces of ethyl acetate remain in the 1H-NMR sample of ortho-Z,E-2 and para-Z,E-2 after thin layer chromatography (SiO₂, 1:10 ethyl acetate / pentane). The organic solvents were removed in vacuo (30°C), however due to the thermal Z to E isomerisation, the isomers cannot be heated under reduced pressure for an extended period. During removal of the organic solvent ortho-Z,E-2 and para-Z,E-2 partially revert back to the thermally stable E,E-2 isomer.

After separation of the photochemically generated isomers using PLC the Z,Z-2 can only be obtained as mixtures of Z,Z-2 and ortho or para E,Z-2 as a result of the rapid thermal revision of Z,Z-2.

Statistical outliers were removed using the Grubbs test.

We list the coefficients $k_1$, $k_2$, $k_3$ and $k_4$, as extracted from the fits at each of the temperatures (28.1, 45.0, 54.5, 64.6 and 68.7°C), respectively. We give a statistical error (1σ) as coming from the fit. The systematic error is estimated by varying the end time of the fit.

The data is fitted for all the isomers simultaneously.

Traces of ethyl acetate remain in the 1H-NMR sample of ortho-Z,E-2 and para-Z,E-2 after thin layer chromatography (SiO₂, 1:10 ethyl acetate / pentane). The organic solvents were removed in vacuo (30°C), however due to the thermal Z to E isomerisation, the isomers cannot be heated under reduced pressure for an extended period. During removal of the organic solvent ortho-Z,E-2 and para-Z,E-2 partially revert back to the thermally stable E,E-2 isomer.

After separation of the photochemically generated isomers using PLC the Z,Z-2 can only be obtained as mixtures of Z,Z-2 and ortho or para E,Z-2 as a result of the rapid thermal revision of Z,Z-2.

Statistical outliers were removed using the Grubbs test.

We list the coefficients $k_1$, $k_2$, $k_3$ and $k_4$, as extracted from the fits at each of the temperatures (28.1, 45.0, 54.5, 64.6 and 68.7°C), respectively. We give a statistical error (1σ) as coming from the fit. The systematic error is estimated by varying the end time of the fit.

The data is fitted for all the isomers simultaneously.

Traces of ethyl acetate remain in the 1H-NMR sample of ortho-Z,E-2 and para-Z,E-2 after thin layer chromatography (SiO₂, 1:10 ethyl acetate / pentane). The organic solvents were removed in vacuo (30°C), however due to the thermal Z to E isomerisation, the isomers cannot be heated under reduced pressure for an extended period. During removal of the organic solvent ortho-Z,E-2 and para-Z,E-2 partially revert back to the thermally stable E,E-2 isomer.
The $^1$H-NMR chemical shifts (Figure 2.6) were calculated with the Gaussian 09 QC package using DFT. Each molecular geometry was first optimised in the gas-phase with the OPBE functional and a 6-311G(d,p) basis set. The subsequent 1H-NMR simulation was then performed with the GIAO method, using the same functional and basis set, and with the IEFPCM solvation model (solvent: dichloroethane).

ESP maps were generated from the DFT $^1$H-NMR calculations and were drawn with an iso value of 0.0002.

Quantum chemical calculations were performed with the Firefly QC package, which is based partially on the GAMESS (US) source code. Geometry optimisations and energy calculations were performed using the B3LYP hybrid functional (using VWN formula 1 RPA correlation) and a 6-31G(d,p) basis set. The validity of the transition state geometries found during this study was verified by both a vibrational analysis and an IRC analysis.