Exploring coordination chemistry and reactivity of formazanate ligands
Travieso Puente, Raquel

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Chapter 5

Arylazoindazole photoswitches: facile synthesis and functionalization via $S_{\text{NAr}}$ substitution

A straightforward synthetic route to arylazoindazoles via nucleophilic aromatic substitution is presented. Upon deprotonation of the NH group, a C$_6$F$_5$-substituted formazan undergoes facile cyclization as a result of intermolecular nucleophilic substitution ($S_{\text{NAr}}$). This new class of azo photoswitches containing an indazole five-membered heterocycle shows photochemical isomerization with high fatigue resistance. In addition, the $Z$-isomers have long thermal half-lives in the dark of up to several days at room temperature. The fluorinated indazole group offers a handle for further functionalization and tuning of its properties as it is shown to be susceptible to a subsequent, highly selective nucleophilic displacement reaction.

This chapter has been published:
5.1 Introduction

Photoswitchable organic compounds are of fundamental importance for applications ranging from data storage\textsuperscript{1,2} and catalysis\textsuperscript{3} to molecular biology\textsuperscript{4} and photopharmacology.\textsuperscript{5,6} Of the several classes of photoswitches that have been studied, those based on azobenzenes are popular due to their synthetic versatility and desirable properties including large geometrical changes accompanying isomerization, high quantum yields and fatigue resistance.\textsuperscript{7} Azobenzene (PhN=NPh) shows a planar conformation in the most stable \textit{E}-isomer; photochemical isomerization upon irradiation with UV light (\(\pi\rightarrow\pi^*\) transition) leads to a photostationary state (PSS) that predominantly contains the \textit{Z}-isomer. This isomer is unstable and reverts to the \textit{E}-isomer either thermally or with irradiation in the visible range of the spectrum (\(n\rightarrow\pi^*\) transition). Due to overlap between the absorption spectra of the two isomers, the visible irradiation often leads to incomplete conversion. While a large variety of substituted azobenzenes have been prepared to tune the (photo)chemical properties, these systems often suffer from low thermal stability of the \textit{Z} isomer. This is problematic for applications such as optical data storage.\textsuperscript{1} Recently, substituted azobenzenes have been reported that combine significantly higher thermal stability with excellent photoswitching.\textsuperscript{8–10} In contrast, heterocyclic analogues of azobenzenes have been so far largely ignored. Some examples of azopyridines\textsuperscript{11–13} and azoimidazoles\textsuperscript{14–16} were reported to behave as photodissociable ligands, leading to changes in spin state upon photoisomerisation of metal porphyrins bearing these ligands.\textsuperscript{17–19} Fuchter and co-workers recently reported arylazopyrrole and –azopyrazole photoswitches, which in some cases show long thermal half-lives and quantitative \(Z\rightarrow E\) photoswitching.\textsuperscript{20,21} Related arylazopyrazoles were used by Ravoo and co-workers in switchable supramolecular host-guest systems.\textsuperscript{22} Although several methods have been reported for the synthesis of (substituted) azobenzenes,\textsuperscript{23–25} high-yielding entries into new classes of azoheterocycles are desirable. In previous chapter we reported a novel method that leads to the formation of indazole derivatives, which contain an azo moiety. The azo moiety is installed via a standard diazonium coupling to give a formazan derivative containing a C\textsubscript{6}F\textsubscript{5} group. In a subsequent step, base-induced nucleophilic aromatic substitution\textsuperscript{26,27} is used to form the indazole heterocycle in excellent overall yield (94%). The resulting arylazoindazoles show good switching behavior and, in addition, cleanly undergo a subsequent S\textsubscript{n}Ar reaction to afford substituted derivatives.
5.2 Photoswitching studies of arylazoindazoles

5.2.1 Arylazoindazoles 4.3 and 4.4

The azoindazoles 4.3/4.4 belong to the class of azoheteroarenes and are similar to the azoimidazoles14–16 and azopyrroles/-pyrazoles,20 which were recently reported to be efficient photoswitches. Similarly, 4.3 and 4.4 show photochemical switching behavior. While no changes are observed in the dark, an NMR sample of the mixture (in C₆D₆ solution) kept under ambient light for several days shows formation of two new compounds. A mixture containing the 4 components was analyzed by GC/MS, which showed that all have the same mass (413.11 m/z), suggesting that photochemical isomerization is taking place. UV/Vis spectroscopy of pure E-4.3 in toluene shows a broad absorption at 355 nm and a weaker, very broad band around 457 nm which are attributed to π→π* and n→π* transitions, respectively (Figure 5.1). Irradiation in the high-energy band (λ_{irr} = 365 nm) results in photochemical isomerization with formation of a photostationary state (PSS) that consists of 80% of the Z-isomer (based on integration of the 19F NMR resonances). The π→π* transition in Z-4.3 is blue-shifted by 36 nm with a reduction in extinction coefficient, while the n→π* band of the Z- and E-isomer overlap significantly. As a consequence, the reverse (Z→E) photoswitching by irradiation at 420 nm results in a PSS that shows incomplete conversion (49% of E-4.3). For compound 4.4, the Z-isomer likewise has a lower molar extinction coefficient and a blue-shifted π→π* absorption band with respect to E-4.4. However, the larger shift (50 nm) leads to a more efficient photoisomerization (PSS at 365 nm: 92% Z-4.4). In addition, the absorption for Z-4.4 and E-4.4 show more pronounced differences in the visible range, leading to a higher PSS upon irradiation at 420 nm (70% of E-4.4). The quantum yields for the photochemical reactions were determined as 0.16/0.11 (E→Z; λ_{irr} = 355 nm) and 0.60/0.47 (Z→E; λ_{irr} = 457 nm) for 4.3/4.4, respectively (see experimental section 5.5.2 for details).
Chapter 5

Figure 5.1 UV/Vis spectra of E-4.3 and E-4.4 in toluene at 25 °C, and photostationary states (PSS) obtained upon irradiation of the samples at 365 nm (4.3, 80% Z-isomer; 4.4, 92% Z-isomer).

The thermal stability of Z-4.3 and Z-4.4 was probed by monitoring the changes in the UV/Vis spectrum at several temperatures between 60 and 105 °C in DMSO solution. Figure 5.6 in section 5.5.2.3 shows the UV/Vis absorption changes by conversion from trans to cis upon irradiation at 355 nm (left), and cis to trans upon irradiation at 457 nm (right) for compounds 4.3 and 4.4.

A global fit of the kinetic traces afforded the activation parameters for the thermal Z→E isomerization as ΔH° = 100.0 ± 1.3 / 96.9 ± 1.1 kJ.mol⁻¹ and ΔS° = -24 ± 4 / -21 ± 3 J.mol⁻¹.K⁻¹ for 4.3/4.4, respectively. These values extrapolate to free energies of activation at 25 °C of 107.1 / 103.3 kJ.mol⁻¹ and thermal half-lives of 7.7 / 1.6 days. High thermal stabilities are important for applications such as information storage, or in vivo uses. The slightly larger activation enthalpy for 4.3 (with the more hindered mesityl-substituted azo moiety) is consistent with the notion that increasing the size of the ortho-substituents in azobenzenes leads to larger barriers. For 4.3, thermal isomerization kinetics were additionally measured in toluene to probe the influence of solvent polarity. These data lead to activation parameters (ΔH° = 97.6 ± 1.6 kJ.mol⁻¹ and ΔS° = -31 ± 5 J.mol⁻¹.K⁻¹) that are very similar to those in DMSO. The fatigue resistance of photochromic switches 4.3 and 4.4 was evaluated by repeating several isomerization cycles, which shows that they are robust: no photobleaching takes place (Figure 5.2), even upon irradiation over 20 days.
Figure 5.2 Switching cycles of 4.3 and 4.4 in DMSO, monitored by following the absorbance at λ = 350 nm, after irradiation at λ = 365 nm and λ = 420 nm.

5.2.2 Arylazoindazoles 4.3OMe and 4.3SC8H17

The absorption maxima do not change appreciably upon going from 4.3 to 4.3OMe/4.3SC8H17. Irradiation of E-4.3OMe at 365 nm in C6D6 results in photochemical isomerization and formation of a PSS that consists of 75% of the Z-isomer of 4.3OMe. The back-reaction was monitored by irradiation at 420 nm and shown to result in the re-formation of 46% of E-4.3OMe. Similar results are obtained for 4.3SC8H17. Evaluation of the stability of Z-4.3OMe in DMSO solution leads to similar activation parameters for the thermal Z/E isomerization as those found for the precursor 4.3 (ΔH‡ = 99.2 ± 1.5 kJ·mol⁻¹ and ΔS‡ = -26 ± 4 J·mol⁻¹·K⁻¹; half-life at 25 °C of 7.3 days). These data indicate that substitution of F for O- or S-alkyl groups does not significantly affect the photochemical and thermal switching behavior in this class of compounds. The facile nucleophilic aromatic substitution on compound 4.3 suggests that this reaction may present a more general strategy toward functionalized arylazoindazole photoswitches, for example for incorporation into biomolecular scaffolds or attachment to surfaces.

5.3 Computational studies

The flexible molecular skeletons of the compounds and the X-ray diffraction study (Figure 4.6, chapter 4) support the existence of several rotamers in addition to the two N=N bond isomers of azobenzene. Indeed, for the E isomer of each molecule, theoretical calculations lead to two rotamers that have similar energies (E2 - E1 = 1.2 kJ/mol). Both E rotamers are separated by a relatively small barrier of ca. 20 kJ/mol in the ground-state, so their
interconversion at room temperature should be facile. For the Z isomer, one of the rotamers (Z₂) is preferred by 14.2 kJ/mol, probably due to favourable C-H−π and CH₃−π interactions (Figure 5.3). As expected, the global energy minimum is the E isomer, which is ca. 32 kJ/mol more stable than the Z form for 4.3. This difference is smaller than in azobenzene, where we found a difference between E and Z as large as 54 kJ/mol at the same level of theory.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Figure</th>
<th>Relative ΔG (M06-2X/TZVP) [kJ/mol]</th>
</tr>
</thead>
<tbody>
<tr>
<td>E₁-GS</td>
<td><img src="image" alt="E₁-GS" /></td>
<td>0.0</td>
</tr>
<tr>
<td>E₂-GS</td>
<td><img src="image" alt="E₂-GS" /></td>
<td>1.2</td>
</tr>
<tr>
<td>TS₁ (Rot)</td>
<td><img src="image" alt="TS₁ (Rot)" /></td>
<td>135.3</td>
</tr>
</tbody>
</table>
For azobenzene, rotation and inversion mechanisms are discussed in the literature as possible thermal reaction paths from \( Z \) to \( E \). Transition state calculations for 4.3 indicate that thermal \( Z \rightarrow E \) isomerization follows the rotation pathway as this presents the lowest barrier, \( \Delta G^\ddagger = 104 \text{ kJ/mol} \) according to theory, in very good agreement with the experimental value of 107.1 kJ/mol (see transition state in Figure 5.4). The inversion mechanism is slightly less favourable with \( \Delta G^\ddagger = 124 \text{ kJ/mol} \). These DFT results agree well with CASPT2 calculations that provide activation energies of 137 kJ/mol (rotation) and 142 kJ/mol (indazole inversion) (Table 5.1). We underline that for 4.3, DFT predicts a positive (negative) value of the activation entropy for the inversion (rotation) mechanism, further...
supporting that rotation is dominant (experimentally, $\Delta S^{\ddagger}$ is negative; see section 5.2.1). Similarly, the calculations for $4.4$ and $4.3^{\text{OMe}}$ indicate that the rotational pathway presents the lowest activation energies. This contrasts with recent results for other azoheteroaryl switches where DFT calculations favoured the inversion mechanism.²¹

**Figure 5.4** Calculated structure of the most accessible transition state for the thermal $Z\rightarrow E$ isomerization of $4.3$.

**Table 5.1** Activation parameters for thermal isomerization in compounds $4.3$, $4.4$ and $4.3^{\text{OMe}}$.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Mechanism</th>
<th>$\Delta E^{\ddagger}$ (CASPT2) (kJ.mol$^{-1}$)</th>
<th>$\Delta E^{\ddagger}$ (M06-2X) (kJ.mol$^{-1}$)</th>
<th>$\Delta G^{\ddagger}$ (298 K) (kJ.mol$^{-1}$)</th>
<th>$\Delta S^{\ddagger}$ (J.mol$^{-1}$.K$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$4.3$</td>
<td>Mesitylene inversion</td>
<td>154.7</td>
<td>131.1</td>
<td>123.8</td>
<td>4.9</td>
</tr>
<tr>
<td>$4.3$</td>
<td>Indazole inversion</td>
<td>142.1</td>
<td>131.4</td>
<td>126.9</td>
<td>10.2</td>
</tr>
<tr>
<td>$4.3$</td>
<td>Rotation</td>
<td>137.1</td>
<td>110.9</td>
<td>103.8</td>
<td>-10.0</td>
</tr>
<tr>
<td>$4.4$</td>
<td>Benzene inversion</td>
<td>131.7</td>
<td>122.7</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td>$4.4$</td>
<td>Indazole inversion</td>
<td>127.5</td>
<td>120.5</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>$4.4$</td>
<td>Rotation</td>
<td>107.4</td>
<td>96.7</td>
<td>-1.6</td>
<td></td>
</tr>
<tr>
<td>$4.3^{\text{OMe}}$</td>
<td>Mesitylene inversion</td>
<td>134.1</td>
<td>128.9</td>
<td>-2.2</td>
<td></td>
</tr>
<tr>
<td>$4.3^{\text{OMe}}$</td>
<td>Indazole inversion</td>
<td>133.3</td>
<td>128.9</td>
<td>-1.4</td>
<td></td>
</tr>
<tr>
<td>$4.3^{\text{OMe}}$</td>
<td>Rotation</td>
<td>113.2</td>
<td>106.9</td>
<td>-12.9</td>
<td></td>
</tr>
</tbody>
</table>
Theoretical calculations reveal two low-lying excited-states for the $E$ isomer which present $n\rightarrow\pi^*$ (E-S$_1$) and $\pi\rightarrow\pi^*$ (E-S$_2$) character in all molecules modelled. The $n$ orbital is an out-of-phase combination of lone pairs on the two azo nitrogen atoms. As the photoswitches are not perfectly planar, the first singlet excited-state has non-zero oscillator strength due to the admixture of $\pi$-orbitals from aromatic rings (TD-DFT: 468 nm, $f = 0.06$ for 4.3). The second excited-state is strongly allowed (350 nm, $f = 0.88$ for 4.3). The $\pi$ and $\pi^*$ orbitals involved in the two lowest excited-states are bonding/antibonding orbitals centred mostly on N=N moiety. The vertical excitation energies of the different rotamers differ quite significantly (Table 5.3, section 5.5.3) and because their Boltzmann weights are comparable, both contribute to the experimentally measured broad UV/Vis spectrum. The situation is slightly different for the $Z$ isomer where we found two $n\rightarrow\pi^*$ excited-states with low oscillator strengths (for 4.3, S$_1$: 479 nm, $f = 0.04$; S$_2$: 340 nm, $f = 0.05$) below the weak $\pi$(mesitylene)$\rightarrow\pi^*$ excitation (S$_3$: 337 nm, $f = 0.04$) and a significantly dipole-allowed state (S$_4$: 328 nm $f = 0.13$). The two lowest excited-states have mostly $n\rightarrow\pi^*$ character, comparable with $E$-S$_1$, while transitions in Z-S$_3$ involve orbitals combining the lone pairs from the azo nitrogen atoms and $\pi$ orbitals from aromatic rings. In agreement with experiment, theory predicts a decrease of the oscillator strength for the allowed state when going from $E$ to $Z$. The photochemical reaction inducing the $E\rightarrow Z$ conversion is initiated by high energy irradiation at 365 nm with population of the $E$-S$_2$ state. Assuming a behaviour following Kasha’s rules, S$_2$ rapidly relaxes to the S$_1$ state. On the S$_1$ potential energy surface of azobenzene, several structurally different S$_1$/S$_0$ conical intersections exist (following inversion/rotation motions),$^{38}$ and recent molecular dynamics studies of azobenzene and derived photoswitches found that mostly rotational motion of the central N=N moiety brings the molecule towards a state-hopping geometry.$^{39-42}$ For the present compounds, the rotation around the N=N bond also brings the S$_1$ and S$_0$ states close to each other ($\sim 0.55$ eV at CASPT2 level in TS$_{rot}$ geometry), which supports a (photo)isomerization mechanism similar to the one found in "classical" azobenzene switches. Our calculations furthermore reveal that, in the lowest excited-state, the two $E$ rotamers can reach a similar conical intersection by a barrierless path, whereas the excited-state interconversion between the two rotamers involves a small barrier (16 kJ/mol). As a result, the interconversion between the two rotamers in the excited state should be a minor process and should not strongly influence the observed quantum yields of photoconversion.$^{43}$
The existence of multiple isomers of similar stabilities can influence the quantum yield of photo-isomerisation in two different ways. On the one hand, some of the excited-state "nuclear momentum" can be lost in the inter-conversion process. We therefore calculated the barrier for the inter-conversion between the two rotamers in the excited state, and this barrier is relatively low (16 kJ/mol). Therefore, this rotational pathway is potentially open in the excited-state which can lead to a loss of energy and, possibly, more effective non-radiative vibrational deactivation. On the other hand, each rotamer could in principle proceed via a different photochemical pathway (in an extreme case, only one of the two could be photochemically active, which would obviously be detrimental for the photochemical conversion). Therefore, we investigated this aspect as well and we found that, for both rotamers, a barrierless pathway to a specific conical intersection exists. This pathway mainly involves the rotation around C(mes)-N=N-C(ind)dihedral angle. Having made these two observations, we can conclude that the CI route should be favored over the rotamer interconversion (barrierless process versus small barrier), though of course some small amount of excited-state interconversion could still appear as a minority process. Therefore, photochemical transformation of the E₁-4.3 rotamer will lead to Z₁-4.3 rotamer and analogously E₂-4.3 to Z₂-4.3. Since Z₂-4.3 is more stable (14 kJ/mol difference) and as the barrier for Z₁-4.3 → Z₂-4.3 rotation is small (6 kJ/mol) on the ground-state surface, the final equilibrium will be dominated by Z₂. The total quantum yield is therefore mainly influenced by the non-radiative pathways and the efficiencies of each conical intersection explored by the system, rather than by excited-state rotameric interconversions. We expect comparable photochemical efficiencies for both isomers, based on the structural similarity and same character of the first excited-state. Quantitative modeling of the QY would require excited-state dynamics, but due to the size of the systems investigated here, this is beyond reasonable reach. Recently, Thiel and coworkers studied chiral pathways for the excited relaxation in arylazopyrazole switches where the barrier is as small as 2 kJ/mol. Such small barrier was found to significantly penalize one of the chiral excited-state relaxations. This supports our conclusion that for our systems each rotamer will relax by its own conical intersection without significant mutual transformations in excited state. In short, the observed rather small quantum yield can be the result of the flexible structure of the switch allowing vibrational relaxation of the excited-state but none of the described rotamers blocks the photoreaction.
5.4 Conclusions

In conclusion, arylazoindazoles and their corresponding substituted via nucleophilic aromatic substitution are shown to be photochromic switches that have moderate to high photoconversion in both directions, long thermal half-lives and good fatigue resistance. These new azoindazoles could be useful as (switchable) bidentate ligands in coordination chemistry and catalysis, an avenue that we will pursue in future work. The possibility to further react the fluorinated ring with nucleophiles allows late-stage functionalization of this new class of photoswitches, which is potentially useful for their incorporation into biological scaffolds and functional materials.

5.5 Experimental

5.5.1 General methods

Routine NMR spectra were recorded on Varian Gemini 400 or Varian Inova 500 spectrometers. $^{19}$F, $^{19}$F-COSY and $^{19}$F, $^{19}$F-NOESY NMR spectra were recorded on Agilent 400MR or Varian Inova 500 spectrometers. For the $^{19}$F, $^{19}$F-NOESY experiments, long mixing times (2 s) were used to avoid spurious correlations due to zero-quantum artifacts. $^{1}$H, $^{19}$F-HOESY NMR spectra were recorded on an Agilent 400MR spectrometer (with OneNMR probe) or a Varian 400 MHz VNMRJ system (with an Auto Switchable (ASW) probe, with tuning optimized for both $^{1}$H and $^{19}$F). The standard $^{1}$H, $^{19}$F-HOESY experiment present in the VNMRJ software was applied, using $^{19}$F detection. The $^{1}$H and $^{13}$C NMR spectra were referenced internally using the residual solvent resonances and reported in ppm relative to TMS (0 ppm); $J$ is reported in Hz. Photostationary states were determined by using NMR spectroscopy (Varian Inova 500). Samples were irradiated inside the NMR spectrometer using an optical fiber cable inside of the NMR tube, which was connected to 365 nm and 420 nm LEDs for photo-conversion from $E\rightarrow Z$ and $Z\rightarrow E$, respectively. UV/Vis absorption spectra were measured on an Analytik Jena Specord S600 diode array or a Hewlett-Packard 8453 spectrometer in a 1 cm quartz cuvette. Kinetics of thermal $Z\rightarrow E$ isomerization are measured and analyzed as described in more detail below (section ‘thermal isomerization kinetics’).
5.5.2 Photoisomerization quantum yields

5.5.2.1 Actinometry

The absolute quantum yield was determined with reference to the actinometer potassium ferrioxalate. Laser flux was determined by the method of total absorption using 2 mL of 6 mM (for 355 nm) and 0.15 M (for 457 nm) potassium ferrioxalate in a 1 cm path length cuvette with stirring. The actinometer was irradiated for 90 s (at 355 nm) and 45 s (at 457 nm), respectively. A reference cuvette was held apart from the excitation source. After irradiation, 1 mL of each solution was added to buffered aqueous phenanthroline (0.1 M, 2 mL), and diluted 10 fold with water and left to stand in the dark for at least 30 min and the absorbance determined at 510 nm. The photon flux was calculated using equation (E1):

$$\frac{(N h \nu / t)}{L} = \frac{A}{\varepsilon_{\lambda_{max}} \phi \times 20} \quad (E1)$$

Where $L$ is the path length of the cuvette, $\varepsilon$ is the molar absorptivity of iron(II) tris-phenanthroline (11100 L mol$^{-1}$ cm$^{-1}$ at $\lambda_{max}$ 510 nm), $\phi$ is quantum yield of the actinometer at 355 nm and 457 nm, $t$ is the irradiation time, $F$ is the fraction of the light the actinometer absorbed.

5.5.2.2 Equations used for quantum yield calculations

The arylazindazole trans-to-cis isomerization was calculated as previously reported.

$$-V \frac{dC_1}{dt} = \phi_1 \frac{\varepsilon_{C_1}}{D} I(1 - 10^{-D}) - \phi_2 \frac{\varepsilon_{C_2}}{D} I(1 - 10^{-D}) \quad (E2)$$

$-V \frac{dC_2}{dt}$ is the change of species A in mole; $I(1 - 10^{-D})$ is the light absorbed by the whole system; $\frac{\varepsilon_{C_1}}{D}$ is the fraction of light absorbed by A; $C_1, C_2$ are the concentrations of trans and cis isomers (M); $\varepsilon_1, \varepsilon_2$ are the absorption coefficients of trans and cis isomers at $\lambda_{irr}$; $D$ is the absorbance when using a 1 cm path length cuvette; $\phi_1, \phi_2$ are the quantum yields for reactions trans to cis, and cis to trans; $I$ is the photon flux determined by actinometry.

Using mole fractions $X = \frac{C}{C_0}$, $C_0 = C_1 + C_2$ is the total concentration, defining $K = \varepsilon_1 \phi_1 + \varepsilon_2 \phi_2$,

$$\frac{dX_1}{dt} = \frac{\theta}{10^{-D}} l \left( KX_1 - \frac{\varepsilon_2 C_2}{C_0} \right) \quad (E3)$$

Using $R = \frac{\varepsilon_2 C_2}{C_0}$,

$$\frac{dX_1}{dt} = \frac{\theta}{10^{-D}} l \left( KX_1 - R \right) \quad (E4)$$
Using \( f = \int_0^1 \frac{1 - 10^{-D}}{D} \, dt \) and integrating the equation, then

\[
\ln \left( \frac{(X_1 - R)}{(X_0 - R)} \right) \frac{Kf}{V} = \frac{\epsilon_1}{\epsilon_2} \left( \frac{X_1 - X_0}{X_1} \right)
\]

(ES)

When the photostationary state is reached, \( \frac{dX_1}{dt} = 0 \),

\[
\left( KX_1 - \frac{\epsilon_1 \epsilon_2}{\epsilon_2} \right) \frac{X_1 - X_0}{X_1} = 0, \quad KX_1^* = R
\]

So,

\[
\ln \left( \frac{(X_1 - KX_1^*)}{(X_0 - KX_1^*)} \right) = \frac{Kf}{V} \ln \left( \frac{(X_1 - X_0)}{(X_0 - X_1^*)} \right) \frac{Kf}{V},
\]

at the photostationary state,

\[
-V \frac{dX_1}{dt} = \phi_1 \frac{\epsilon_1 \epsilon_2}{\epsilon_2} \left( 1 - 10^{-D} \right) - \phi_2 \frac{\epsilon_2 \epsilon_2}{\epsilon_2} \left( 1 - 10^{-D} \right) = 0
\]

\[
\epsilon_1 \phi_1 X_1^* = \epsilon_2 \phi_2 X_2^*
\]

because \( K = \epsilon_1 \phi_1 + \epsilon_2 \phi_2 \),

\[
\phi_1 = \frac{K X_1^*}{\epsilon_1}, \quad \phi_2 = \frac{K X_2^*}{\epsilon_2}
\]

(6)

### 5.5.2.3 Quantum yield measurements

**Extinction coefficients**

The extinction coefficient at 355 and 457 nm for trans isomers was measured by linear fitting of absorbance at a series of known concentrations of the pure compounds (Figure 5.5). The trans:cis isomer ratio was determined by NMR integration of the PSS solution obtained by irradiation with a 355 nm laser. The extinction coefficient for cis isomers at 355 nm and 457 nm is calculated using equation E7.

\[
\epsilon_{cis} = \frac{\epsilon_{pss} - (\text{trans} \times X_1)}{1 - X_1}
\]

(7)

Where \( \epsilon_{pss} \) is the extinction coefficient of the mixture at the photostationary state, and \( X_1 \) is the fraction of trans isomer in the mixture.
Figure 5.5 Extinction coefficients determined by linear fitting of absorbance vs. concentration at 355 nm and 457 nm for both trans and cis isomers for 4.3 and 4.4.

Determination of constant $K$

Figure 5.6 shows the UV/Vis absorption changes by conversion from trans to cis upon irradiation at 355 nm (left), and cis to trans upon irradiation at 457 nm (right) for compounds 4.3 and 4.4.
Figure 5.6 Changes in UV/Vis absorbance at 20 °C for 4.3 (top) and 4.4 (bottom) under irradiation at 355 nm (left) and 457 nm (right).

According to the absorbance changes, the plot of $\ln\left(\frac{X_f - X_0}{X_0 - X_f}\right)$ vs $f$ (Figure 5.7) was fitted to a linear equation to get the slope $K$ from equation (E5), then the constant $K$ can be calculated.

Figure 5.7 Constant $K$ determined by linear fitting of $\ln\left(\frac{X_f - X_0}{X_0 - X_f}\right)$ with $f$ according to equation (E5).
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Quantum yield

The quantum yields were calculated by equation (E6); results are listed in Table 5.2.

Table 5.2 Extinction coefficients (ε) and quantum yields (Φ) for 4.3 and 4.4.

<table>
<thead>
<tr>
<th></th>
<th>Extinction coefficient ε</th>
<th>Quantum Yield</th>
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<tr>
<td></td>
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<td>cis</td>
</tr>
<tr>
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<tr>
<td></td>
<td>457 nm</td>
<td>1531.8</td>
</tr>
<tr>
<td>4.4</td>
<td>355 nm</td>
<td>20847.4</td>
</tr>
<tr>
<td></td>
<td>457 nm</td>
<td>835.5</td>
</tr>
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</table>

5.5.3 Computational studies

Our main methodology relies on an implicit solvation picture based on the Polarizable Continuum Model (PCM)\textsuperscript{46} in combination with Density Functional Theory (DFT) and its Time-Dependent counterpart (TD) for electronic excited-states. All DFT/TD-DFT calculations were performed with the Gaussian software\textsuperscript{47} using the M06-2X\textsuperscript{48} exchange-correlation functional for geometry optimizations and thermodynamic calculations while PBE0\textsuperscript{49} functional was used for excited-state calculations. In all cases we applied a so-called ultrafine DFT integration grid (99,590 points). The TZVP atomic basis set\textsuperscript{50} was used for all calculations as a compromise between size and the accuracy. The optimized geometries and vibrational frequencies were obtained in toluene solvent and the perturbative corrected linear response (cLR) method\textsuperscript{51} was applied to determine the transition energies in the same solvent. The barrier for excited state rotation around the C-N(indazole) bond was obtained by constrained ES optimization at several values of this dihedral angle at PBE0 level. The angle C(mes)-N=N-C(ind) was fixed at its GS value to avoid collapse of the ES and GS, due to the barrierless pathway of photochromism.
Transition states for the $E$ to $Z$ isomerization involve breaking of a double bond, and to describe this phenomenon in a physically sound way, we have used broken-symmetry (BS) approach within DFT calculations. The transition state character of located minima was systematically confirmed by frequency calculation (one imaginary frequency found with value ca. $370i$-$430i$ cm$^{-1}$). Single-point energies were additionally calculated by CASPT2 (complete active space self-consistent field with second order multiconfigurational perturbation theory) with the TZVP atomic basis set. In CASPT2 we considered 16 electrons in 11 orbitals as an active space and used state-averaged wavefunction over the ground and the excited-states (equal weights) for excitation energies. Minimal active space for the compounds under study includes two combinations of lone pairs from aza nitrogen atoms and the $\pi$, $\pi^*$ orbitals for N=N bond. Using this active space in preliminary calculations, we build the final active space by adding the interacting $\pi$, $\pi^*$ orbitals having occupations inside the 0.05-1.95 interval, as well as orbitals close in energy to the minimal active space (Figure 5.10). In the calculation of thermal activation energies, the focus is the ground-state only, and we optimized the corresponding wavefunction in a similar state-specific approach. Dynamical correlation effects were included using multi-state (MS) CASPT2 calculations, here the zero-order Hamiltonian was modified using a standard shift of 0.25 au.\textsuperscript{52}

The Molcas software\textsuperscript{53} was used for multireference calculations. In order to speed up the calculations Cholesky decomposition of two-electron integrals was used with threshold $10^{-4}$ au.
**Table 5.3** Vertical excitation energies (VEE) and oscillator strengths calculated at PBE0 and CASPT2 levels of theory for the isomers of 4.3, 4.4 and 4.3OMe.

<table>
<thead>
<tr>
<th>Isomer-state</th>
<th>Oscillator strength $f$</th>
<th>TD-PBE0 VEE [nm]</th>
<th>CASPT2 VEE [nm]</th>
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<tbody>
<tr>
<td>4.3</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>E1-S1</td>
<td>0.06</td>
<td>468</td>
<td>443</td>
</tr>
<tr>
<td>E1-S2</td>
<td>0.88</td>
<td>350</td>
<td>279</td>
</tr>
<tr>
<td>E2-S1</td>
<td>0.04</td>
<td>500</td>
<td>475</td>
</tr>
<tr>
<td>E2-S2</td>
<td>0.86</td>
<td>370</td>
<td>308</td>
</tr>
<tr>
<td>Z-S1</td>
<td>0.04</td>
<td>479</td>
<td>428</td>
</tr>
<tr>
<td>Z-S2</td>
<td>0.05</td>
<td>340</td>
<td>270</td>
</tr>
<tr>
<td>Z-S3</td>
<td>0.04</td>
<td>337</td>
<td>258</td>
</tr>
<tr>
<td>Z-S4</td>
<td>0.13</td>
<td>328</td>
<td>262</td>
</tr>
<tr>
<td>4.4</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>E1-S1</td>
<td>0.001</td>
<td>452</td>
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</tr>
<tr>
<td>E1-S2</td>
<td>0.81</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>Z1-S1</td>
<td>0.05</td>
<td>445</td>
<td></td>
</tr>
<tr>
<td>Z1-S2</td>
<td>0.12</td>
<td>339</td>
<td></td>
</tr>
<tr>
<td>Z2-S1</td>
<td>0.04</td>
<td>452</td>
<td></td>
</tr>
<tr>
<td>Z2-S2</td>
<td>0.08</td>
<td>340</td>
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</tr>
<tr>
<td>4.3OMe</td>
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</tr>
<tr>
<td>E1-S1</td>
<td>0.004</td>
<td>481</td>
<td></td>
</tr>
<tr>
<td>E1-S2</td>
<td>0.70</td>
<td>380</td>
<td></td>
</tr>
<tr>
<td>Z1-S1</td>
<td>0.05</td>
<td>469</td>
<td></td>
</tr>
<tr>
<td>Z1-S2</td>
<td>0.12</td>
<td>340</td>
<td></td>
</tr>
</tbody>
</table>
Figure 5.8 Ground state energy profile for the indazole rotation around C-N(aza) bond as obtained with DFT

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>( E_{1-S_1} )</td>
<td>0.003</td>
<td>492</td>
</tr>
<tr>
<td>( E_{1-S_2} )</td>
<td>0.60</td>
<td>389</td>
</tr>
<tr>
<td>( Z_{1-S_1} )</td>
<td>0.05</td>
<td>469</td>
</tr>
<tr>
<td>( Z_{1-S_2} )</td>
<td>0.06</td>
<td>357</td>
</tr>
</tbody>
</table>

\[ 4.3 \text{cm}^{-1} \]
Figure 5.9 Singly occupied orbitals for the lowest excited states of the Z and E isomers of 4.3 (TD-PBE0).
Figure 5.10 Molecular orbitals of 4.3 included in the active space during CAS calculation.
5.6 References

(36) Cattaneo, P.; Persico, M. PCCP 1999, 1, 4739.


Chapter 5