The Photoisomerization Pathway(s) of Push-Pull Phenylazoheteroarenes

Sergi Vela and Clémence Corminboeuf*

Institute of Chemical Sciences and Engineering, École Polytechnique Fédérale de Lausanne (EPFL), Laboratory for Computational Molecular Design, CH-1015 Lausanne, Switzerland

Abstract

Azoheteroarenes are the most recent derivatives targeted to further improve the properties of azo-based photoswitches. Their light-induced mechanism for trans-cis isomerization is assumed to be very similar to that of the parent azobenzene. As such, they inherited from the controversy about the dominant isomerization pathway (rotation vs. inversion) depending on the excited state ($n\pi^*$ vs. $\pi\pi^*$). While the controversy seems settled in azobenzene, the extent to which the same conclusions apply to the more structurally-diverse family of azoheteroarenes is unclear. Here, we unravel by means of non-adiabatic molecular dynamics, the photoisomerization mechanism of three prototypical phenyl-azoheteroarenes (1, 2 and 2a) with an increasing push-pull character. The evolution of the rotational and inversion conical intersection energies, the preferred pathway, and the associated kinetics upon both $n\pi^*$ and $\pi\pi^*$ excitations can be linked directly with the push-pull substitution effects. Overall, we clarify the working conditions of this family of azo-dyes and identify a possibility to exploit push-pull substituents to tune their photoisomerization quantum yield.

Introduction

Molecular photoswitches can alter their chemical/biological function through undergoing conformational configurational or structural changes upon application of light. While nature exploits them to trigger key processes in living organisms, the synthetic analogues are increasingly used as memories,1-3 actuators4, sensitizers5, and sensors.6 Dyes based on the azo group are among the most investigated, the archetype being azobenzene (AB).7, 8 Its cis-trans photoisomerization is highly appreciated due to its significant structural change.4 Also, AB has multiple functionalization sites, which led to the development of derivatives exhibiting improved thermal stability and visible light absorption.9 All these advances fostered its application in the nascent field of photopharmacology.10 Azoheteroarenes are the most recent derivatives investigated in the quest of better azo-based photoswitches.11 Their main advantage with respect to AB relies upon their greater electronic and structural diversity, which allow for interesting functionality in their backbone. Examples are the possibility to achieve T-shaped Z-isomer structures with longer half-life times and better photostationary distributions,12 the modulation of the hydrazone tautomerism to further tune their kinetics,13 or the addition of metal-coordinating sites, which makes them ideal candidates to trigger spin transitions.14, 15

In AB, the photoswitch is triggered upon excitation to either of the productive $n\pi^*$ and $\pi\pi^*$ states (typically, $S_1$ and $S_2$). For decades, there has been controversy about its isomerization mechanism7, 16 with conflicting experimental17-21 and theoretical22-26 reports. The current consensus is that the photoisomerization occurs once the molecule is in $S_1$, through an $S_1/S_0$ conical intersection (CoIn) with either rotational or inversion character. Specifically, it has been proposed that these CoIn are the extremes of a crossing seam connecting $S_1/S_0$, with rotational-(inversion-) like structures at its lower- (higher-) energy end.24, 27 The preferred pathway depends on the excitation energy,28 solvent,28 pressure,29 temperature,30, 31 and has an impact on the quantum yield: AB photo-isomerizes with a higher quantum yield when excited to the $n\pi^*$ than to the $\pi\pi^*$ state,30 which is attributed to the increased accessibility of the rotational pathway.

Azoheteroarenes are expected to follow a similar mechanism, but the picture is much less complete.11 So far, their photoisomerization has been investigated in systems based on indole,3 pyridine,32, 33 pyrimidine14 and thiazole.35 These few cases suggest that the structural diversity of azoheteroarenes contributes to create a similar level of complexity as in the AB derivatives. A major limitation of these investigations is that the experiments do not provide direct information on the relaxation pathways, whereas computations are often limited to explore predefined regions of the ground- and low-lying excited states potential energy surfaces (PES). While this picture is informative, it is still insufficient to ascertain the effect of temperature and excitation energy on the chosen pathway, and hence on the photoisomerization quantum yield and kinetics. These are important aspects that deserve deeper computational analyses, which more closely mimic the actual experimental conditions.
In this computational work, we analyze the E-to-Z photoisomerization of three phenyl-azoheteroarenes: the unsubstituted 3-pyrazole (1) and 2-imidazole (2), and a derivative of the latter (2a), featuring DPO (2,5-diphenyl-1,3,4-oxadiazole) and thiazine as the phenyl and heteroarene substituents, respectively (see Figure 1). Heteroarenes have an increased push-pull character, by virtue of the stabilization of a resonant form. Such stabilization is progressively stronger in compounds 1, 2 and 2a, which has important consequences on their thermal stability, and on the energy and nature of their productive nπ* and ππ* transitions.

The initial assessment of the vertical nπ* (S1) and ππ* excitations (S2) of 1-2a at the respective E-isomer minima (Figure 1) shows no significant difference between 1 and 2, whereas the ππ* is significantly red-shifted in 2a by the increased charge-transfer character from the thiazine to the azo group. The shift is also clearly visible in the absorption spectra computed at the same level (i.e., ωB97X-D/6-31G(d) level, see Figure 2 and Comp. Details), which includes the conformational and vibrational transitions with the Nuclear Ensemble (NE) approach.

The ground, nπ* and ππ* states are connected with each other through CoIn. At the CASSCF (i.e., SA3-CASSCF/6-31G* level), three CoIn were identified for (unsubstituted) Phenylazoindole photoswitches. These are: (i) CoInA, characterized by a CNNC torsion angle close to 90º (corresponding to the rotation), (ii) CoInB, which involves quasi-linear NNC angles (characteristic of an inversion), and (iii) CoInC, which features an intermediate torsion, longer N=N distance, and CNN angles close to 100º. The former two (CoInA and CoInB) connect the PES of the ground (GS) and nπ* states, while the latter connects the nπ* and ππ* surfaces. CoInA was found below the nπ* excitation energy at FC, while CoInB is higher, and hence only accessible after excitation to ππ* or above. Accordingly, it was proposed that excitation to nπ* leads to CoInA, whereas excitation to ππ* leads to CoInA (ππ*/nπ*) and to CoInB (ππ*/GS) before reaching the GS. The former pathway would lead to a higher QY than the latter. Such characterization is very similar to what is known for AB, except for the proposed non-planar (i.e., twisted geometry) CoInC: the ultrafast decay from ππ* to nπ* in AB suggests a structure close to the planar FC geometry instead.
The CoInA and CoInB of 1, 2 and 2a were characterized here with TDA and ωB97X-D (see SI for complementary ADC(2) computations) using a static CoIn-search method (see Comp. Details).45 Their structures feature the characteristic CNNC torsion (close to 90°) and NNC (quasi-linear) bending, respectively (see Table S2.1). The energy of CoInA decreases by about 0.3 eV with the increase in push-pull character (see Figure 1). We associate this shift to the reduction of the azo N=N bond-order (see WI in Table S2.1) as a longer N=N distance facilitates the CNNC rotation towards CoInA. As expected (see above), CoInA is found below the S1 excitation energy at FC. In turn, CoInB lies at about 3.3 eV from the respective E-minima, and slightly above the S1 excitation energy at FC. An exception is 2a, for which CoInB and S1 are almost degenerate. That suggests the opening of the inversion pathway upon S1 excitation, in contradiction to the expected mechanism. Overall, the two sets of CoIn reported herein (A and B) present very similar structural features to those reported in the existing literature for AB and azoheteroarene derivatives.13, 33 None of the levels tested herein (i.e., ωB97X-D, ADC(2)) were able to locate the CoInC as proposed in Ref. 13, not even for the same phenylazoindole. While the identification of CoInC may be an artefact from SA3-CASSCF/6-31G* (vide infra)46, TDA-ωB97X-D describes correctly the PES regions that correspond to the two dominant photoisomerization pathways. As such, we are confident that more sophisticated simulations based on molecular dynamics can be pursued at this level (see Comp. Details).

A swarm of Non-Adiabatic Molecular-Dynamics (NAMD) trajectories based on Tully surface-hopping were initiated at the nπ* and ππ* states for 1, 2 and 2a, and propagated for a maximum of 1000 fs, or until an S1–S0 energy gap below 0.1 eV is reached (see Comp. Details). In the latter case, it is assumed that population transfer to the ground state will occur, leading to either of the two minima (E or Z). Note that while the termination criterion does not presuppose the character of S1 (nπ* or ππ*), in practice, however, S1 is the nπ* state for all terminated trajectories. In general, we favor the nomenclature nπ*/ππ* to specifically refer to these states, and use the S1–S2 nomenclature when the state character is not relevant, only the order.

Figure 3 shows the structure at which state crossings occur based on the two main variables: the CNN angle, and the CNNC torsion. In 1-2a, the relaxation from the ππ* to the nπ* state occurs at flat geometries similar to the E-isomer minimum (see grey circles). As mentioned before, flat geometries have been invoked to explain the ultrafast ππ*→nπ* decay in AB.19, 44 This point is thus reinforced by our simulations, and its validity seems to be extended to azoheteroarenes albeit in contradiction with the proposed non-planar ColIn of phenylazoindoles.13 The ColIn connecting the ππ* and ground states combine both CNN inversion and CNNC torsion (see colored circles). In fact, the distribution of ColIn describes a crossing seam (as in AB22), with ColInA- and ColInB-like structures at the extremes (see Figure 3 and S3.4). ColIn being higher in energy (see Figure 1), the inversion pathway is more often (but not exclusively) followed upon excitation at S2, while excitation to S1 predominantly leads to a rotational mechanism (see Figure 1). There are, however, many trajectories in which ColIn-like (ColInA-) are reached upon excitation to S1 (S2), which indicates that the excitation energy does not completely discriminate between photodeactivation pathways. This point might, in fact, be at the heart of the controversy about the dominant mechanism in AB and azoheteroarene derivatives, and their strong dependency on external factors such as temperature, pressure or solvent. Finally, the vast majority of ColIn in 2a are rotational (see Figure 3). The reason is that the nπ* and GS PES are no longer quasi-degenerate in a region of the crossing seam associated with the inversion pathway (see Figure S3.4). This explains why push-pull derivatives favor the rotational over the inversion pathway. Such outcome could have not been anticipated from the energy maps in Figure 1: the energy of S1 and CoInA for 2a are similar to those of 1 and 2, and the lower S2 excitation energy is counterbalanced by a more stable and, thus, equally
accessible CoIn. The low ratio of inversion-like CoIn in 2a is thus not suggested by the static picture.

In addition to the structural aspects at the crossing points, we analyze the time at which they are reached in the NAMD simulations. Overall, the CoIn connecting the nπ* and ground states in 1, 2 and 2a are reached in ca. 500 fs, with significant differences depending on the compound and excitation energy (see \( t_{CoIn} \) in Table 1). The main steps are (i) the relaxation from the \( \pi\pi^* \) to the nπ* state, and (ii) the change in CNN and CNNC angles necessary to reach the crossing seam (see discussion above). The mechanism and kinetics of each individual steps is better understood by considering four characteristic times (see Scheme 1): \( t_{CoIn} \) is the time until reaching a CoIn, \( t_{S1} \) and \( t_{S2} \) are the time spent in the \( S_1 \) and \( S_2 \) states, and \( t_{Last} \) is the time required to reach a CoIn after the last crossing to \( S_1 \). The difference between \( t_{S1} \) and \( t_{Last} \) (\( \Delta t \) in Table 1) reveals whether the system is retained in a region of the \( S_i \)-PES with frequent crossings between \( S_1 \) and \( S_2 \) states, before it reaches a CoIn (see Comp. Details).

| Initial State | 1 \( t_{CoIn} \) (ps) | 2 \( t_{CoIn} \) (ps) | Compound 2a \( t_{CoIn} \) (ps) |
|--------------|-------------------|-----------------|-----------------------------|
| \( S_1 \)    | 419               | 330             | 644                         |
| \( S_2 \)    | 530               | 373             | 483                         |
| \( t_{S1} \) | 419               | 330             | 637                         |
| \( t_{S2} \) | 250               | 260             | 413                         |
| \( t_{Last} \) | 419              | 330             | 536                         |
| \( \Delta t \) | 0                 | 0               | 100                         |

The second reason for the slower photoisomerization of 2a is that its trajectories need longer times to reach a CoIn once in the nπ* surface, as quantified by \( t_{Last} \) (Table 1). Such a behavior is surprising if one considers that the energetic profile summarized in Figure 1 places the \( S_1 \) excitation significantly higher in energy than CoIn. Along this line, the PES of the nπ* state shows no energy barrier between the FC region and CoIn (see Figure S2.1). The actual explanation for the longer \( t_{Last} \) in 2a is rooted in the CoIn structure distribution within the crossing seam. Generally, the trajectories that reach a CoIn with a pronounced rotational character display slower kinetics than those with a marked tendency toward inversion (see Figure S3.2). This difference is a manifestation of the distinct timescale associated with the rotation and inversion towards the crossing seam. In particular, the inversion-like region of the seam is explored readily after populating \( S_1 \). If a CoIn is not accessed therein, as in 2a, the system then evolves toward the rotation-like region, exhibiting slower photoisomerization kinetics. This perspective is in agreement with what has been characterized computationally for phenylazoaromatics, namely that the evolution along the nπ* surface implies an initial flattening of the CNN angle (i.e., inversion), followed by the CNN torsion (i.e. rotation). To summarize, push-pull derivatives undergo a faster decay from \( S_2 \) to \( S_1 \) but a slower evolution from \( S_1 \) to \( S_0 \) because of both the hopping back to \( \pi\pi^* \) and the longer time needed to reach the rotational CoIn. The clear preference of 2a for the rotational pathway potentially suggest that the increase in push-pull character may result in a photoisomerization process with a higher quantum yield (vide supra).

In conclusion, we have characterized the static and dynamic photoisomerization pathway of three heteroarene derivatives (1-2a). The static CoIn-search reports rotation-like (CoIn) and an inversion-like (CoIn) conical intersections connecting the nπ* and ground states at around 2.3 and 3.3 eV above the E-minima, respectively. The results from the NAMD describe a crossing seam connecting CoIn and CoIn, similar to what has been reported for AB. The decay from the nπ* to the nπ* state is more controversial. The non-planar CoIn located by CASSCF for phenylazoindoles could not be identified in 1-2a. However,
the ultrafast (ca. 100 fs) relaxation observed from the ππ* to the πσ* state that proceeds at planar geometries close to the E-isomer minimum, is in agreement with the literature on AB (100-300 fs). The existence of ColInC may thus be an artefact from SA3-CASSCF/6-31G*.

With the increase in push-pull character, the ππ* state of the heteroarene is progressively red-shifted, leading to a stronger overlap with the πσ* state that speeds up the decay towards πσ*. Once in the πσ* state, further 200-600 fs are necessary to reach the crossing seam connecting the πσ* and ground states, close to the values reported for AB and (ca. 500-1000 fs). The actual amount of time depends on which region of the crossing seam is accessed, with the rotational mechanism displaying a slower ππ*-to-GS relaxation. The unsubstituted heteroarenes (1 and 2) exploit both pathways, with rotation and inversion being slightly preferred upon excitation to the ππ* and πσ* states, respectively. In contrast, the push-pull derivative 2a exhibits a clear preference towards the rotational pathway upon excitation to both states, resulting in a slower photoisomerization than 1 and 2 as the process in 2a is further slowed down by population transfer back to the ππ* state. Overall, push-pull derivatives feature a faster decay from ππ* to πσ*, but a slower one from πσ* to the ground state.

From a design perspective, push-pull derivatives may thus represent an appealing alternative to improve the photoisomerization quantum yields by virtue of its marked preference for the rotational pathway. It is worthwhile noting that such preference could not be anticipated based on the energy maps (Figure 1). This mismatch, as well as the significant differences between the static and dynamic pictures at describing the crossing region (ColIn vs. crossing seam), highlights the risk of establishing conclusions on the photoisomerization mechanism based on the energy of the relevant points on the PES, as commonly done.

### Computational Details

Minimal energy crossing points were computed with CIOPT interfaced with Gaussian 09 (G09). Based on previous benchmarks, we used TD-DFT within the Tamm-Dancoff approximation (TDA), the ωB97X-D functional and the 6-31G(d) basis set. The Non-Adiabatic Molecular Dynamics (NAMD) simulations were performed with Newton-X interfaced with G09. Additional computations at the ADC(2)/TZVP level can be found in the SI. The initial conditions were generated from the Wigner distribution based on the harmonic oscillator, five states (So-S5), a Lorentzian broadening of 0.1 eV, an anharmonicity factor of 3, and at T=300 K. From these initial conditions, we obtain the (i) absorption spectra, and (ii) a set of the geometries and velocities that could initiate the trajectories. The selected initial conditions are those in which the S1 and S2 excitation energy is centered (and within +/- 0.1 eV) at the peak of the respective transition in the spectrum (see Figure 2). A swarm of 25 trajectories has been initiated at each S1 and S2 for 1 and 2 (see section 2.1). Due to the much larger size of 2a, we reduced the number of trajectories to 20. Hence, a total of 140 trajectories were run.

The trajectories were computed using TD-DFT (within TDA) at the ωB97X-D/6-31G(d) level. NAMD were simulated with the fewest-switches surface hopping corrected for decoherence effects (α = 0.1 hartree). Time-derivative couplings were computed for all states except S0, which is excluded due to the difficulties of TDA to describe the multi-reference character of the electronic wavefunction near a S1→S0 ColInC. Accordingly, trajectories ran for a maximum of 1000 fs or until an S1→S0 energy gap below 0.1 eV is reached. The selected time limit is sufficient to allow most of the trajectories to reach the ColInC (see Table 1). The temperature is maintained at 300 K with the Andersen thermostat. Integration was done with a time step of 0.5 (0.025) fs for the classical (quantum) equations. This setup has been successfully employed to study other small-size organic molecules.

Surface-Hopping Molecular Dynamics exploit statistics to mimic the dynamics of nuclear wavepackets and hence we analyze them as a whole. The kinetics are assessed using the characteristic times defined in Scheme 1. These are computed for each S1 and S2 excitation of 1-2a as an average using the trajectories that reach a ColInC before the time limit of 1000 fs. Should the trajectories be allowed to continue beyond 1000 fs, the associated times would change; tColInC and tS2 would increase since the slower trajectories would start counting towards the average, while the change in tS1 is harder to anticipate. As a general rule, the values are more representative when the ratio of trajectories that reached a ColInC within the time limit is closer to 1 (R in Table 1).

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### Dataset

The dataset will be available upon publication at the Zenodo and Materials Cloud repositories.

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### Conflicts of interest

There are no conflicts to declare.
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