

Triplet-Sensitized Bidirectional Isomerization of Bridged Azobenzene

Jussi Isokuortti[†], Thomas Griebenow[‡], Jan-Simon von Glasenapp[‡], Tim Raeker[¶], Mihail A. Filatov[§], Timo Laaksonen^{†‡}, Rainer Herges^{‡*}, Nikita A. Durandin^{†*}

[†] Faculty of Engineering and Natural Sciences, Tampere University, FI-33101 Tampere, Finland

[‡] Otto-Diels-Institute of Organic Chemistry, Christian-Albrechts-University of Kiel, 24098 Kiel, Germany

[¶] Institute for Physical Chemistry, Department for Theoretical Chemistry, Christian-Albrechts-University of Kiel, 24098 Kiel, Germany

[§] School of Chemical and Pharmaceutical Sciences, Technological University Dublin, City Campus, Grangegorman, Dublin 7, Ireland

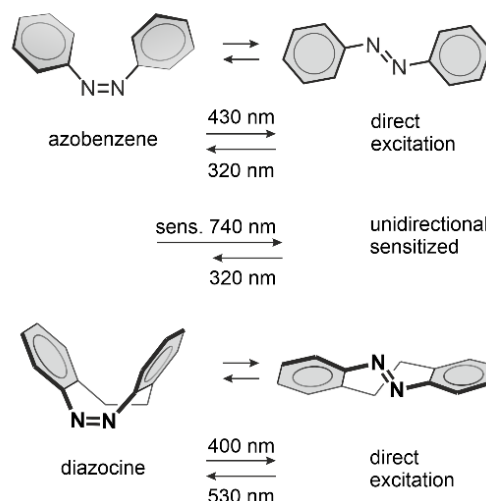
^{†‡} Drug Research Program, Division of Pharmaceutical Biosciences, Faculty of Pharmacy, University of Helsinki, FI-00014 Helsinki, Finland

ABSTRACT: Diazocine is a bridged azobenzene with both phenyl rings connected by a CH₂-CH₂ group. Despite this rather small structural difference, diazocine exhibits improved properties over azobenzene as a photoswitch, such as high switching efficiencies, very high quantum yields, switching wavelengths in the visible range, and most importantly, the fact that it is more stable in the *Z* configuration, which is particularly expedient in photopharmacology and mechanophore applications. According to our studies presented here, another advantage over conventional azobenzene is now added. In contrast to azobenzenes and other photochromes, diazocine can be switched with two different triplet sensitizers present at the same time in both directions: *Z*→*E* as well as *E*→*Z*. Experimental and theoretical (CASPT2) studies of triplet excitation energies provide an explanation for this fact. The triplet energies in *Z* and *E* azobenzene are almost equal, which prevents selective sensitization of either isomer. In diazocine, the two excitation energies are well-separated, so they can be accessed selectively. Besides offering fundamental physical insight to diazocines, an emerging class of photoswitches, our work opens up a number of potential avenues for utilizing them for example in photopharmacology and smart materials design due to the significant redshift of excitation wavelengths to from blue to green (*Z*→*E*) and green to far-red (*E*→*Z*), which triplet sensitization offers.

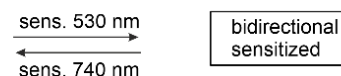
Diazocines, or bridged azobenzenes, have received considerable attention because their photoswitching behavior is inverted compared to conventional azobenzenes as their *Z* isomers are more stable than their *E* forms. Diazocines also exhibit more efficient photoswitching using longer excitation wavelengths and possess higher quantum yields.^{1–15} As a result, diazocines have found use in emerging fields, such as stimuli-responsive systems,^{14–19} photoactuation,²⁰ and most notably, photopharmacology^{21–28}.

Unlike conventional azobenzene, whose triplet state properties have been investigated since the 1960s,²⁹ no studies on the triplet states of diazocine molecules have been published. Knowledge of triplet state properties has been exploited to achieve sensitized photoswitching of conventional azobenzenes²⁰ (see Scheme 1) in addition to other classes of molecules, such as diarylethenes³¹, overcrowded alkenes³², stilbenes³³, and indigos³⁴. Compared to direct excitation of the photoswitch, triplet sensitization often enables photoswitching with red-shifted excitation wavelengths from the ultraviolet and blue, even towards near-infrared. This is paramount for most of the applications of photoswitching materials due to the harmful character and limited penetration depth of high energy excitation. Thus, we embarked to investigate the triplet state properties of diazocine and uncover whether triplet sensitization can improve its photoswitching performance.

previous work:



this work:



Scheme 1. Direct and triplet sensitized photoisomerizations of azobenzene and diazocine. In case of azobenzene, the *Z*→*E* isomerization is highly favored upon triplet sensitization in bulk.³⁵ In this work, we report on the sensitized switching of diazocine in

both directions ($Z \rightarrow E$ and $E \rightarrow Z$). Compared to direct photoisomerization, both switching wavelengths are considerably redshifted. The wavelengths leading to optimal conversions are shown.

We began investigating the diazocine triplet state properties by probing the triplet state energies (E_T) of both isomers in deoxygenated DMSO. This was performed by measuring the triplet lifetime of a sensitizer in the presence of varied concentrations of either Z or E -diazocine. The first quenching series was performed by quenching Pd(II)-tetraphenyltetrabenzoporphyrin (PdTPBP, $E_T = 1.55$ eV, see Figure S1) phosphorescence with Z -diazocine. We chose PdTPBP as the sensitizer as we expected E_T of Z -diazocine to be comparable to E_T of the Z -isomer of conventional azobenzenes, which have reported values between 1.3 and 1.6 eV.^{36,37} However, as $[Z\text{-diazocine}] = 65 \mu\text{M}$ resulted in less than 20 % quenching (see Figure S5) of PdTPBP phosphorescence, it became clear that a more potent sensitizer was required as a triplet energy donor for Z -diazocine. Thus, we chose Pd(II)-octaethylporphyrin (PdOEP, $E_T = 1.86$ eV, see Figure S2) as another sensitizer for the second quenching series. The resulting Stern-Volmer plot is shown in Figure 1A. Based on the Stern-Volmer constant (K_{SV}) and resulting rate constant of triplet energy transfer ($k_{TET} = K_{SV}/\tau_0$, where τ_0 is the unquenched triplet lifetime of the sensitizer), we calculated E_T of Z -diazocine to be $1.2 k_B T$ or 31 meV larger than PdOEP at room temperature (RT).³⁸ Thus, we derive that E_T of Z -diazocine is approximately 1.89 eV, which is considerably higher than E_T of conventional Z -azobenzenes (*vide supra*).

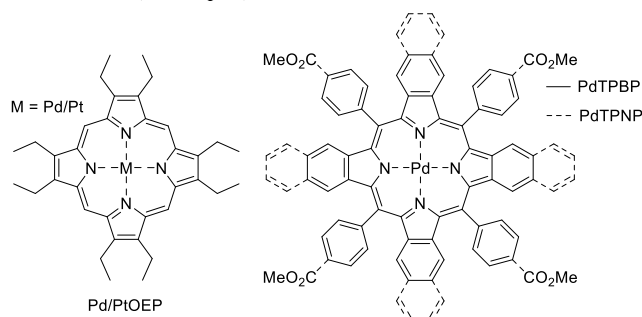


Chart 1. Triplet sensitizers used in this study.

Having determined E_T for Z -diazocine, we turned our attention to E -diazocine and decided to begin the quenching studies again with PdTPBP. Before PdTPBP phosphorescence decay measurements, the Z -diazocine was converted into the E -isomer using 385 nm light irradiation for 10 minutes. Assuming again similar behavior as conventional azobenzenes that do not exhibit large difference in E_T between the isomers,^{36,37} we expected E -diazocine to also possess a high-lying triplet state and therefore poor energy transfer efficiency from PdTPBP. To our surprise, E -diazocine was able to quench the PdTPBP triplet state effectively (see Figure 1B) as we determine E_T of E -diazocine to be approx. $0.7 k_B T$ or 18 meV (at RT) lower than that of PdTPBP i.e. 1.53 eV. As such, E_T of E -diazocine is comparable to that of the E -isomer of conventional azobenzenes.^{37,39,40} Conclusively, the triplet-state energies of Z and E -diazocine are energetically quite distinct, with the Z -isomer having a 360 meV higher triplet-state energy.

After determining the triplet energies of both isomers, we proceeded to photoswitching studies that were performed in deoxygenated DMSO with bis(methylthio)methane as an oxygen scavenger⁴¹ and $[\text{diazocine}] = 500 \mu\text{M}$. Initially, we paired diazocine again with PdTPBP. As expected, no $Z \rightarrow E$ isomerization was observed upon 640 nm excitation as E_T of Z -diazocine is over 300 meV higher than E_T of PdTPBP. Consequently, after first irradiating the system at 385 nm to drive direct $Z \rightarrow E$ isomerization

of diazocine, rapid and complete $E \rightarrow Z$ isomerization was observed under red-light (640 nm) excitation (see Figure S6). Although the absorption band of E -diazocine tails off beyond 600 nm, direct $E \rightarrow Z$ isomerization can still be driven with red-light excitation, an undisputed advantage over conventional azobenzene. Furthermore, pairing diazocine with PdTPBP affords photoswitching rates over twice as fast as those achieved with diazocine alone under red-light excitation. This rate enhancement is enabled by efficient triplet energy transfer from PdTPBP to E -diazocine and the more than two orders of magnitude higher molecular extinction coefficient of the sensitizer at 640 nm with respect to diazocine. Inspired by this improvement in the photoswitching performance at 640 nm excitation, we were determined to push the limits of this system further towards near infrared.

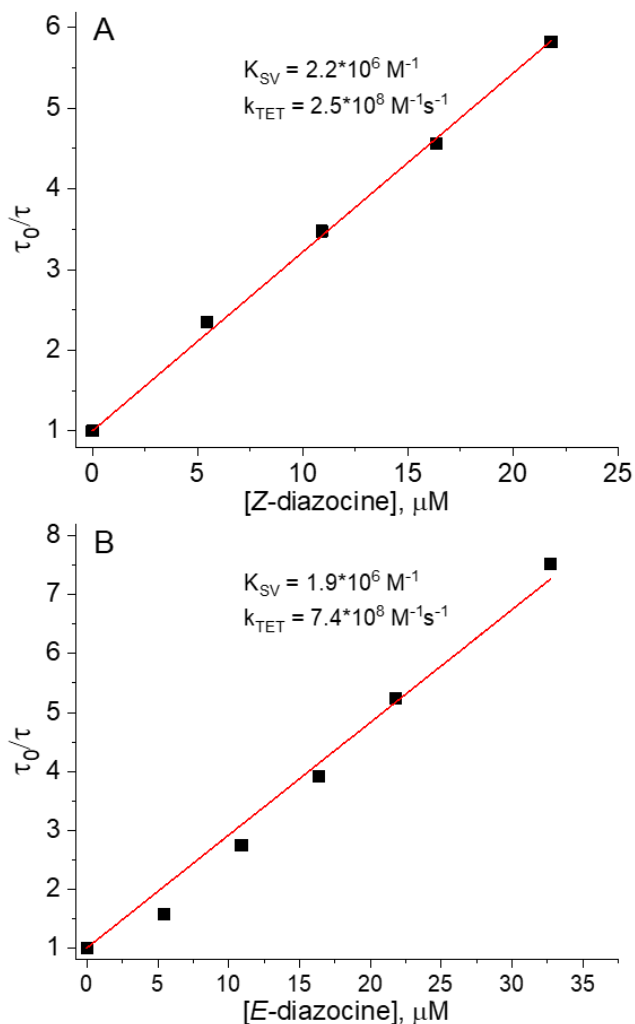


Figure 1. Phosphorescence quenching results of (A) PdOEP by Z -diazocine and (B) PdTPBP by E -diazocine as Stern-Volmer plots with linear fits for Stern-Volmer constants (K_{SV}) and rate constants of triplet energy transfer (k_{TET}).

Conventional azobenzenes are known to undergo indirect $Z \rightarrow E$ photoisomerization even if the sensitizer E_T is substantially lower than the azobenzene. This is due to the ultrashort lifetime of azobenzene triplet state and thus negligible probability of back energy transfer to the sensitizer.³⁷ To our delight, this was also the case with E -diazocine, as Pd-tetraphenyltetranaphthoporphyrin (PdTPNP, $E_T = 1.30$ eV, see Figure S3) can sensitize the $E \rightarrow Z$

isomerization under far-red 740 nm excitation (see Figure S7), which is well within the bio-optical window. In this regard, the triplet state properties of diazocine are akin to azobenzene, as low triplet energy photosensitizers can drive the isomerization from the metastable isomer to the thermodynamically stable one.

To better comprehend the triplet state properties of diazocine, we decided to perform photoswitching studies by sensitizing *Z*-diazocine with the higher triplet energy sensitizer PdOEP. Upon greenlight (530 nm) excitation, rapid *Z*→*E* isomerization was observed (see Figure S8). This resulted in approximately 25 % conversion to *E*-isomer, which is in stark contrast to conventional azobenzenes that exhibit approximately 1–2 % conversion from the thermodynamically stable isomer upon sensitization.^{36,39,40,42,43} Consequently, the triplet sensitized system also offers considerably red-shifted excitation wavelength from 402 nm to 534 nm (absorption maxima of *Z*-diazocine and PtOEP Q band, respectively) required for the isomerization when compared to the “photoswitch only” system.

After this exciting result, we sought to improve the *Z*→*E* conversion by changing the sensitizer from PdOEP to PtOEP as its higher-lying triplet state ($E_T = 1.92$ eV, see Figure S4) enables more efficient energy transfer to *Z*-diazocine. This is crucial since the energy transfer to the lower triplet energy *E*-diazocine will begin to compete immediately as it is generated upon sensitization of *Z*-diazocine. Furthermore, the large difference between the triplet energies of the isomers indicated that they could be sensitized selectively with two different sensitizers present in the system.

Thus, we decided to construct a photoswitching system consisting of three molecules: diazocine (500 μ M), PtOEP (20 μ M) and PdTPNP (1.2 μ M) in deoxygenated DMSO. The absorption spectrum of this system is shown in Figure 2A. Upon green-light (530 nm) excitation, the system reached 49 % *Z*-to-*E* conversion, and upon 740 nm excitation, >99 % *Z*-isomer (see Figure 2B). As discussed above, we attribute this more than twice improved *Z*→*E* conversion to be due to the more efficient triplet energy transfer to *Z*-diazocine from the higher triplet energy PtOEP. Altogether, this is, to the extent of our knowledge, the first demonstration of a photoswitching system where no direct excitation of the photoswitch itself is required for bidirectional isomerization.

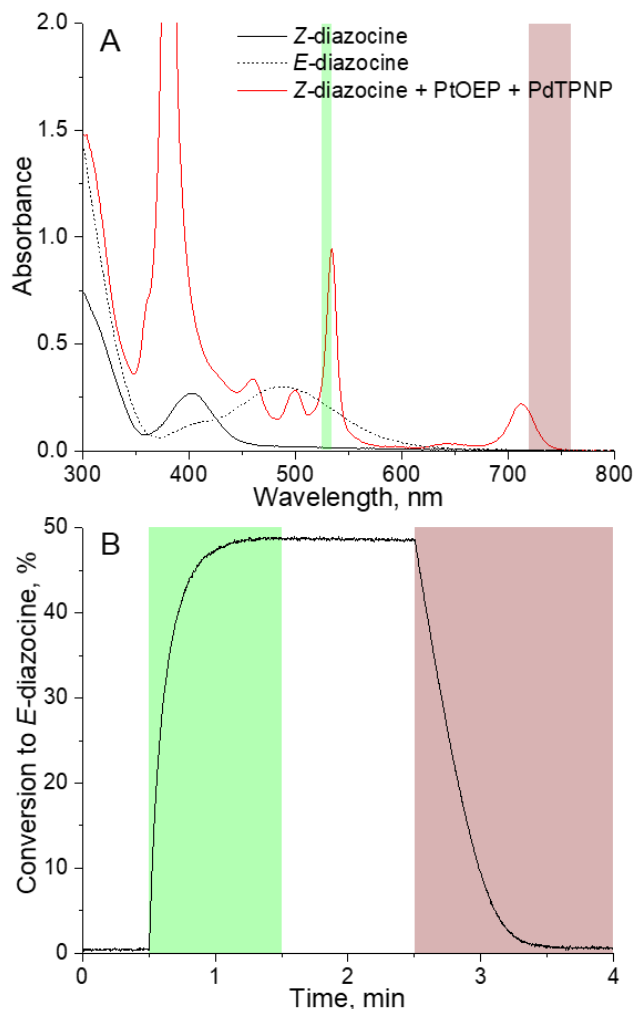


Figure 2. (A) Absorption spectra of *Z* and *E*-diazocine (after 385 nm excitation) and the photoswitching system consisting of diazocine, PtOEP and PdTPNP. The color bars indicate the excitation wavelengths to drive the triplet sensitized isomerization in both directions. (B) Diazocine photoswitching curve as the conversion percentage of *E*-diazocine. The colored areas indicate time under excitation.

To gain more insight into the photophysical properties of diazocine, we performed quantum chemical calculations at the TDDFT and CASPT2 level of theory with ORCA 5.0.1, Turbomole 7.4 and OpenMolcas (for details, basis sets and active space, see SI).^{44–49} State averaged (SA) complete active space self-consistent field (CASSCF) and second order perturbation theory CAS (CASPT2) methods are known to provide reliable energies of high spin systems and particularly CASPT2 has emerged as the standard method to calculate excited state properties.⁵⁰

The CASPT2 energies of the T_1 and S_1 excited states vertical to the S_0 ground state of azobenzene and diazocine in *Z* and *E* configuration are given in Table 1. The calculated triplet energies (T_1) are consistently about 0.3 eV higher than the measured values, which is within the usual range of accuracy.^{51–53} Both theoretical calculations and experiments predict similar triplet excitation energies for *Z* and *E* azobenzene ($\Delta\Delta E_{E-Z(\text{calc})} = 0.04$ eV, $\Delta\Delta E_{E-Z(\text{exp})} = 0.03$ – 0.27 eV). In contrast, the triplet energies of diazocine in *Z* and *E* configuration differ considerably (see Table 1). The calculated and measured energy differences are in very good agreement ($\Delta\Delta E_{E-Z(\text{calc})} = 0.38$ eV, $\Delta\Delta E_{E-Z(\text{exp})} = 0.36$ eV, Table 1). Computationally less expensive TDDFT calculations confirm the

trend for azobenzene ($\Delta\Delta E_{EZ} = 0.09$ eV) and diazocine ($\Delta\Delta E_{EZ} = 0.35$ eV).

Table 1. Experimentally determined and theoretically calculated vertical (diabatic) triplet and singlet excitation energies (eV) of azobenzene and diazocine, each in *E* and *Z* configuration. For computational details see Supporting Information.

Azobenzene	TDDFT	CASPT2	exp.
$\Delta E S_0 \rightarrow T_1$			
Z	1.99	1.83	1.30- 1.6 ^{36,37,39,40}
E	2.08	1.87 ^{52,53}	1.57 ^{36,37,39,40}
$\Delta E S_0 \rightarrow S_1$			
Z	2.98	2.58	2.82
E	2.85	2.44	2.78
Diazocine			
$\Delta E S_0 \rightarrow T_1$			
Z	2.09	2.21	1.89
E	1.74	1.83	1.53
$\Delta E S_0 \rightarrow S_1$			
Z	3.19	3.02	3.07
E	2.64	2.52	2.53 ¹⁰

The CASPT2 calculated potential energy surface of the S_0 , T_1 and S_1 states of azobenzene and diazocine as a function of the CNNC twist angle are depicted in Figure 3. Between 40° and 140° the energy surfaces of azobenzene and diazocine are almost identical. On the “*Z* side” (0° - 40°) and on the “*E* side” (140° - 180°) the energies differ. Azobenzene in its ground state (S_0) is not planar but slightly twisted into the “*E* direction” (CNNC $\sim 12^\circ$) due to the steric repulsion of the phenyl rings.⁵⁴ In contrast, the *E* configuration of diazocine is strongly distorted towards the “*Z*” form because of the high ring strain in the *E*-configured eight-membered diazocine ring (CNNC= 147° instead of 180°).

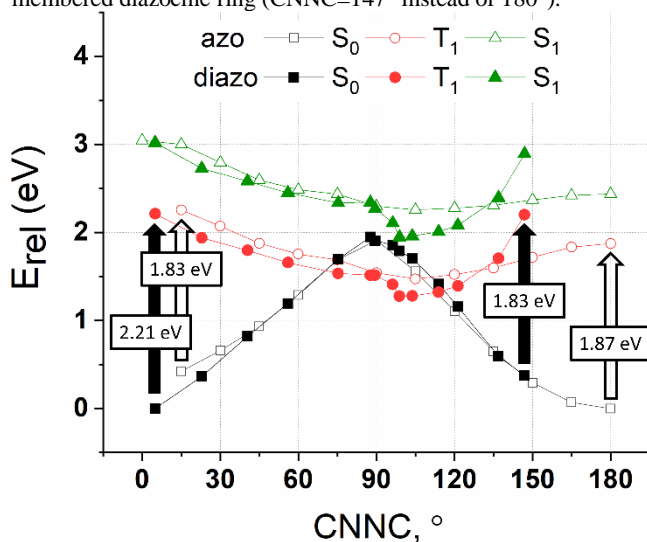


Figure 3. CASPT2 potential energies of azobenzene (“azo”) and diazocine (“diazo”) in their S_0 , T_1 and S_1 states as a function of the CNNC dihedral angle. Vertical transitions ($S_0 \rightarrow T_1$) are indicated with arrows (filled for diazocine). Energies of azobenzene and diazocine are relative to their most stable ground state (S_0) isomers (*E* azobenzene and *Z* diazocine). Note that the CNNC torsion in *Z* azobenzene is $\sim 12^\circ$ because of the non-planarity caused by steric hindrance of the two phenyl rings. The CNNC torsion in *E* diazocine deviates strongly from 180° (147°) due to the large strain

in the *trans* configured eight membered diazocine ring. Energy scans, therefore, are restricted to the range of twist angles between the corresponding ground state minima (*E* and *Z*).

In summary, we have succeeded for the first time in switching a photochromic compound with two different coinciding triplet sensitizers bidirectionally. The molecular photoswitch diazocine isomerizes upon direct irradiation at 400 nm (*Z* \rightarrow *E*) and 530 nm (*E* \rightarrow *Z*). Upon indirect, triplet-sensitized excitation, the switching wavelengths redshift to 530 and 740 nm, respectively. The *E* \rightarrow *Z* isomerization can thus be achieved with far-red light well within the bio-optical window where the penetration depth of light in tissue is largest. This is advantageous for both biological and medical applications. Technologically even more interesting is the fact that indirect electronic excitation permits additional control over the spatial addressing and the direction of the switching process. For example, upon direct irradiation with green light, an *E* \rightarrow *Z* isomerization is induced, and in the presence of a suitable triplet sensitizer (PtOEP), the process is reversed, which could be utilized for controlled chemical energy storage and release. Likewise, by employing two different sensitizers, as demonstrated herein, even more sophisticated systems can be realized.

AUTHOR INFORMATION

Corresponding Authors

* Rainer Herges – rherges@oc.uni-kiel.de

* Nikita Durandin – nikita.durandin@tuni.fi

ACKNOWLEDGMENT

The authors gratefully acknowledge financial support from the Academy of Finland (Grant No. 316893 and PREIN Flagship programme no. 320165) and the European Research Council (ERC Consolidator Grant Project PADRE, decision number 101001016).

REFERENCES

- (1) Siewertsen, R.; Neumann, H.; Buchheim-Stehn, B.; Herges, R.; Näther, C.; Renth, F.; Temps, F. Highly Efficient Reversible *Z*-*E* Photoisomerization of a Bridged Azobenzene with Visible Light through Resolved $S_1(N\pi^*)$ Absorption Bands. *Journal of the American Chemical Society* **2009**, *131* (43), 15594–15595. <https://doi.org/10.1021/ja906547d>.
- (2) Lentès, P.; Frühwirth, P.; Freißmuth, H.; Moormann, W.; Kruse, F.; Gescheidt, G.; Herges, R. Photoswitching of Diazocines in Aqueous Media. *The Journal of Organic Chemistry* **2021**, *86* (5), 4355–4360. <https://doi.org/10.1021/acs.joc.1c00065>.
- (3) Hammerich, M.; Schütt, C.; Stähler, C.; Lentès, P.; Röhrich, F.; Höppner, R.; Herges, R. Heterodiazocines: Synthesis and Photochromic Properties, Trans to Cis Switching within the Bio-Optical Window. *Journal of the American Chemical Society* **2016**, *138* (40), 13111–13114. <https://doi.org/10.1021/jacs.6b05846>.
- (4) Lentès, P.; Stadler, E.; Röhrich, F.; Brahm, A.; Gröbner, J.; Sönnichsen, F. D.; Gescheidt, G.; Herges, R. Nitrogen Bridged Diazocines: Photochromes Switching within the Near-Infrared Region with High Quantum Yields in Organic Solvents and in Water. *Journal of the American Chemical Society* **2019**, *141* (34), 13592–13600. <https://doi.org/10.1021/jacs.9b06104>.
- (5) Maier, M. S.; Hüll, K.; Reynders, M.; Matsuura, B. S.; Leippe, P.; Ko, T.; Schäffer, L.; Trauner, D. Oxidative Approach Enables Efficient Access to Cyclic Azobenzenes. *Journal of the American Chemical Society* **2019**, *141* (43), 17295–17304. <https://doi.org/10.1021/jacs.9b08794>.

- (6) Deo, C.; Bogliotti, N.; Métivier, R.; Retailleau, P.; Xie, J. A Visible-Light-Triggered Conformational Diastereomer Photoswitch in a Bridged Azobenzene. *Chemistry – A European Journal* **2016**, *22* (27), 9092–9096. <https://doi.org/10.1002/chem.201601400>.
- (7) Liu, L.; Yuan, S.; Fang, W.-H.; Zhang, Y. Probing Highly Efficient Photoisomerization of a Bridged Azobenzene by a Combination of CASPT2//CASSCF Calculation with Semiclassical Dynamics Simulation. *The Journal of Physical Chemistry A* **2011**, *115* (35), 10027–10034. <https://doi.org/10.1021/jp203704x>.
- (8) Jiang, C.-W.; Xie, R.-H.; Li, F.-L.; Allen, R. E. Comparative Studies of the Trans–cis Photoisomerizations of Azobenzene and a Bridged Azobenzene. *The Journal of Physical Chemistry A* **2011**, *115* (3), 244–249. <https://doi.org/10.1021/jp107991a>.
- (9) Carstensen, O.; Sielk, J.; Schönborn, J. B.; Granucci, G.; Hartke, B. Unusual Photochemical Dynamics of a Bridged Azobenzene Derivative. *The Journal of Chemical Physics* **2010**, *133* (12), 124305. <https://doi.org/10.1063/1.3479397>.
- (10) Siewertsen, R.; Schönborn, J. B.; Hartke, B.; Renth, F.; Temps, F. Superior Z → E and E → Z Photoswitching Dynamics of Dihydrodibenzodiazocine, a Bridged Azobenzene, by S1(Nπ*) Excitation at λ = 387 and 490 Nm. *Physical Chemistry Chemical Physics* **2011**, *13* (3), 1054–1063. <https://doi.org/10.1039/C0CP01148G>.
- (11) Joshi, D. K.; Mitchell, M. J.; Bruce, D.; Lough, A. J.; Yan, H. Synthesis of Cyclic Azobenzene Analogues. *Tetrahedron* **2012**, *68* (41), 8670–8676. <https://doi.org/10.1016/j.tet.2012.06.007>.
- (12) Klockmann, F.; Fangmann, C.; Zender, E.; Schanz, T.; Catapano, C.; Terfort, A. Substituted Dibenzodiazocines: Rapid Synthesis and Photochemical Properties. *ACS Omega* **2021**, *6* (28), 18434–18441. <https://doi.org/10.1021/acsomega.1c02524>.
- (13) Moormann, W.; Tellkamp, T.; Stadler, E.; Röhricht, F.; Näther, C.; Puttreddy, R.; Rissanen, K.; Gescheidt, G.; Herges, R. Efficient Conversion of Light to Chemical Energy: Directional, Chiral Photoswitches with Very High Quantum Yields. *Angewandte Chemie International Edition* **2020**, *59* (35), 15081–15086. <https://doi.org/10.1002/anie.202005361>.
- (14) Lee, H.; Tessarolo, J.; Langbehn, D.; Baksi, A.; Herges, R.; Clever, G. H. Light-Powered Dissipative Assembly of Diazocine Coordination Cages. *Journal of the American Chemical Society* **2022**, *144* (7), 3099–3105. <https://doi.org/10.1021/jacs.1c12011>.
- (15) Zhu, Q.; Wang, S.; Chen, P. Diazocine Derivatives: A Family of Azobenzenes for Photochromism with Highly Enhanced Turn-On Fluorescence. *Organic Letters* **2019**, *21* (11), 4025–4029. <https://doi.org/10.1021/acs.orglett.9b01215>.
- (16) Preußke, N.; Moormann, W.; Bamberg, K.; Lipfert, M.; Herges, R.; Sönnichsen, F. D. Visible-Light-Driven Photocontrol of the Trp-Cage Protein Fold by a Diazocine Cross-Linker. *Organic & Biomolecular Chemistry* **2020**, *18* (14), 2650–2660. <https://doi.org/10.1039/C9OB02442E>.
- (17) Burk, M. H.; Langbehn, D.; Hernández Rodríguez, G.; Reichstein, W.; Drewes, J.; Schröder, S.; Rehders, S.; Strunskus, T.; Herges, R.; Faupel, F. Synthesis and Investigation of a Photoswitchable Copolymer Deposited via Initiated Chemical Vapor Deposition for Application in Organic Smart Surfaces. *ACS Applied Polymer Materials* **2021**, *3* (3), 1445–1456. <https://doi.org/10.1021/acsapm.0c01312>.
- (18) Saha, M.; Chatterjee, S.; Hossain, M. S.; Ghude, A.; Bandyopadhyay, S. Modulation of Electronic Mobility of a One-Dimensional Coordination Polymeric Molecular Wire with Light. *Chemistry – An Asian Journal* **2019**, *14* (24), 4659–4664. <https://doi.org/10.1002/asia.201900956>.
- (19) Samanta, S.; Qin, C.; Lough, A. J.; Woolley, G. A. Bidirectional Photocontrol of Peptide Conformation with a Bridged Azobenzene Derivative. *Angewandte Chemie International Edition* **2012**, *51* (26), 6452–6455. <https://doi.org/10.1002/anie.201202383>.
- (20) Li, S.; Han, G.; Zhang, W. Concise Synthesis of Photoreponsive Polyureas Containing Bridged Azobenzenes as Visible-Light-Driven Actuators and Reversible Photopatterning. *Macromolecules* **2018**, *51* (11), 4290–4297. <https://doi.org/10.1021/acs.macromol.8b00687>.
- (21) Trads, J. B.; Hüll, K.; Matsuura, B. S.; Laprell, L.; Fehrentz, T.; Gördlt, N.; Kozek, K. A.; Weaver, C. D.; Klöcker, N.; Barber, D. M.; Trauner, D. Sign Inversion in Photopharmacology: Incorporation of Cyclic Azobenzenes in Photoswitchable Potassium Channel Blockers and Openers. *Angewandte Chemie International Edition* **2019**, *58* (43), 15421–15428. <https://doi.org/10.1002/anie.201905790>.
- (22) Ko, T.; Oliveira, M.; Alapin, J. M.; Morstein, J.; Klann, E.; Trauner, D. Optical Control of Translation with a Puromycin-Photoswitch. *bioRxiv* **2022**, 2022.07.12.499823. <https://doi.org/10.1101/2022.07.12.499823>.
- (23) Ewert, J.; Heintze, L.; Jordà-Redondo, M.; von Glasenapp, J.-S.; Nonell, S.; Bucher, G.; Peifer, C.; Herges, R. Photoswitchable Diazocine-Based Estrogen Receptor Agonists: Stabilization of the Active Form inside the Receptor. *Journal of the American Chemical Society* **2022**. <https://doi.org/10.1021/jacs.2c03649>.
- (24) Cabré, G.; Garrido-Charles, A.; González-Lafont, À.; Moormann, W.; Langbehn, D.; Egea, D.; Lluch, J. M.; Herges, R.; Alibés, R.; Busqué, F.; Gorostiza, P.; Hernando, J. Synthetic Photoswitchable Neurotransmitters Based on Bridged Azobenzenes. *Organic Letters* **2019**, *21* (10), 3780–3784. <https://doi.org/10.1021/acs.orglett.9b01222>.
- (25) Reynders, M.; Chaikuad, A.; Berger, B.-T.; Bauer, K.; Koch, P.; Laufer, S.; Knapp, S.; Trauner, D. Controlling the Covalent Reactivity of a Kinase Inhibitor with Light. *Angewandte Chemie International Edition* **2021**, *60* (37), 20178–20183. <https://doi.org/10.1002/anie.202103767>.
- (26) Thapaliya, E. R.; Zhao, J.; Ellis-Davies, G. C. R. Locked-Azobenzene: Testing the Scope of a Unique Photoswitchable Scaffold for Cell Physiology. *ACS Chemical Neuroscience* **2019**, *10* (5), 2481–2488. <https://doi.org/10.1021/acscemneuro.8b00734>.
- (27) Heintze, L.; Schmidt, D.; Rodat, T.; Witt, L.; Ewert, J.; Kriegs, M.; Herges, R.; Peifer, C. Photoswitchable Azo- and Diazocine-Functionalized Derivatives of the VEGFR-2 Inhibitor Axitinib. *International Journal of Molecular Sciences* **2020**, *21* (23). <https://doi.org/10.3390/ijms21238961>.
- (28) Wages, F.; Lentz, P.; Griebenow, T.; Herges, R.; Peifer, C.; Maser, E. Reduction of Photoswitched, Nitrogen Bridged N-Acetyl Diazocines Limits Inhibition of 17βHSD3 Activity in Transfected Human Embryonic Kidney 293 Cells. *Chemico-Biological Interactions* **2022**, *354*, 109822. <https://doi.org/10.1016/j.cbi.2022.109822>.
- (29) Jones, L. B.; Hammond, G. S. Mechanisms of Photochemical Reactions in Solution. XXX.1 Photosensitized Isomerization of Azobenzene. *Journal of the American Chemical Society* **1965**, *87* (18), 4219–4220. <https://doi.org/10.1021/ja01096a059>.
- (30) Ronayette, J.; Arnaud, R.; Lemaire, J. Isomérisation Photosensibilisée Par Des Colorants et Photoréduction de l'azobenzène En Solution. II. *Canadian Journal of Chemistry* **1974**, *52* (10), 1858–1867. <https://doi.org/10.1139/v74-265>.
- (31) Fredrich, S.; Göstl, R.; Herder, M.; Grubert, L.; Hecht, S. Switching Diarylethenes Reliably in Both Directions with

- Visible Light. *Angewandte Chemie International Edition* **2016**, *55* (3), 1208–1212. <https://doi.org/10.1002/anie.201509875>.
- (32) Cnossen, A.; Hou, L.; Pollard, M. M.; Wesenhagen, P. V.; Browne, W. R.; Feringa, B. L. Driving Unidirectional Molecular Rotary Motors with Visible Light by Intra- And Intermolecular Energy Transfer from Palladium Porphyrin. *Journal of the American Chemical Society* **2012**, *134* (42), 17613–17619. <https://doi.org/10.1021/ja306986g>.
- (33) Hammond, G. S.; Saitiel, Jack. Photosensitized Cis-Trans Isomerization of the Stilbenes. *Journal of the American Chemical Society* **1962**, *84* (24), 4983–4984. <https://doi.org/10.1021/ja00883a075>.
- (34) Wyman, G. M.; Zarnegar, B. M.; Whitten, D. G. Excited-State Chemistry of Indigoid Dyes. III. Interaction of Indigo and Thioindigo with Tin(IV) Tetraphenyltetrahydroporphyrin Triplets. Photosensitized Isomerization of Thioindigo. *The Journal of Physical Chemistry* **1973**, *77* (21), 2584–2586. <https://doi.org/10.1021/j100907a020>.
- (35) Gemen, J.; Church, J. R.; Ruoko, T.-P.; Durandin, N.; Białek, M. J.; Weissenfels, M.; Feller, M.; Kazes, M.; Borin, V. A.; Odaybat, M.; Kalepu, R.; Diskin-Posner, Y.; Oron, D.; Fuchter, M. J.; Priimagi, A.; Schapiro, I.; Klajn, R. Disequilibrating Azoarenes by Visible-Light Sensitization under Confinement. *ChemRxiv* **2023**. <https://doi.org/10.26434/chemrxiv-2023-gq2h0>.
- (36) Monti, S.; Gardini, E.; Bortolus, P.; Amouyal, E. The Triplet State of Azobenzene. *Chemical Physics Letters* **1981**, *77* (1), 115–119. [https://doi.org/10.1016/0009-2614\(81\)85611-4](https://doi.org/10.1016/0009-2614(81)85611-4).
- (37) Isokuortti, J.; Kuntze, K.; Virkki, M.; Ahmed, Z.; Vuorimaa-Laukkanen, E.; Filatov, M. A.; Turshatov, A.; Laaksonen, T.; Priimagi, A.; Durandin, N. Expanding Azobenzene Photoswitching into Near-Infrared via Endothermic Triplet Energy Transfer. *Chem. Sci.* **2021**. <https://doi.org/10.1039/D1SC01717A>.
- (38) Sandros, K.; Haglid, F.; Ryhage, R.; Ryhage, R.; Stevens, R. Transfer of Triplet State Energy in Fluid Solutions. III. Reversible Energy Transfer. *Acta Chem. Scand.* **1964**, *18*, 2355–2374. <https://doi.org/10.3891/acta.chem.scand.18-2355>.
- (39) Bortolus, Pietro.; Monti, Sandra. Cis-Trans Photoisomerization of Azobenzene. Solvent and Triplet Donors Effects. *The Journal of Physical Chemistry* **1979**, *83* (6), 648–652. <https://doi.org/10.1021/j100469a002>.
- (40) Monti, S.; Dellonte, S.; Bortolus, P. The Lowest Triplet State of Substituted Azobenzenes: An Energy Transfer Investigation. *Journal of Photochemistry* **1983**, *23* (2), 249–256. [https://doi.org/10.1016/0047-2670\(83\)80065-3](https://doi.org/10.1016/0047-2670(83)80065-3).
- (41) Dzebo, D.; Moth-Poulsen, K.; Albinsson, B. Robust Triplet–Triplet Annihilation Photon Upconversion by Efficient Oxygen Scavenging. *Photochem. Photobiol. Sci.* **2017**, *16* (8), 1327–1334. <https://doi.org/10.1039/C7PP00201G>.
- (42) Jones, L. B.; Hammond, G. S. Mechanisms of Photochemical Reactions in Solution. XXX.1 Photosensitized Isomerization of Azobenzene. *Journal of the American Chemical Society* **1965**, *87* (18), 4219–4220. <https://doi.org/10.1021/ja01096a059>.
- (43) Ronayette, J.; Arnaud, R.; Lebourgeois, P.; Lemaire, J. Isomérisation Photochimique de l'azobenzène En Solution. I. *Canadian Journal of Chemistry* **1974**, *52* (10), 1848–1857. <https://doi.org/10.1139/v74-264>.
- (44) Neese, F.; Wennmohs, F.; Becker, U.; Riplinger, C. The ORCA Quantum Chemistry Program Package. *The Journal of Chemical Physics* **2020**, *152* (22), 224108. <https://doi.org/10.1063/5.0004608>.
- (45) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A Consistent and Accurate Ab Initio Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu. *The Journal of Chemical Physics* **2010**, *132* (15), 154104. <https://doi.org/10.1063/1.3382344>.
- (46) Ásgeirsson, V.; Birgisson, B. O.; Björnsson, R.; Becker, U.; Neese, F.; Riplinger, C.; Jónsson, H. Nudged Elastic Band Method for Molecular Reactions Using Energy-Weighted Springs Combined with Eigenvector Following. *J. Chem. Theory Comput.* **2021**, *17* (8), 4929–4945. <https://doi.org/10.1021/acs.jctc.1c00462>.
- (47) Fdez. Galván, I.; Vacher, M.; Alavi, A.; Angeli, C.; Aquilante, F.; Autschbach, J.; Bao, J. J.; Bokarev, S. I.; Bogdanov, N. A.; Carlson, R. K.; Chibotaru, L. F.; Creutzberg, J.; Dattani, N.; Delcey, M. G.; Dong, S. S.; Dreuw, A.; Freitag, L.; Frutos, L. M.; Gagliardi, L.; Gendron, F.; Giussani, A.; González, L.; Grell, G.; Guo, M.; Hoyer, C. E.; Johansson, M.; Keller, S.; Knecht, S.; Kovačević, G.; Källman, E.; Li Manni, G.; Lundberg, M.; Ma, Y.; Mai, S.; Malhado, J. P.; Malmqvist, P. Å.; Marquetand, P.; Mewes, S. A.; Norell, J.; Olivucci, M.; Oppel, M.; Phung, Q. M.; Pierloot, K.; Plasser, F.; Reiher, M.; Sand, A. M.; Schapiro, I.; Sharma, P.; Stein, C. J.; Sørensen, L. K.; Truhlar, D. G.; Ugandi, M.; Ungur, L.; Valentini, A.; Vancoillie, S.; Velyazov, V.; Weser, O.; Wesołowski, T. A.; Widmark, P.-O.; Wouters, S.; Zech, A.; Zobel, J. P.; Lindh, R. OpenMolcas: From Source Code to Insight. *J. Chem. Theory Comput.* **2019**, *15* (11), 5925–5964. <https://doi.org/10.1021/acs.jctc.9b00532>.
- (48) Caldeweyher, E.; Ehlert, S.; Hansen, A.; Neugebauer, H.; Spicher, S.; Bannwarth, C.; Grimme, S. A Generally Applicable Atomic-Charge Dependent London Dispersion Correction. *The Journal of Chemical Physics* **2019**, *150* (15), 154122. <https://doi.org/10.1063/1.5090222>.
- (49) *TURBOMOLE | Program Package for Electronic Structure Calculations*. TURBOMOLE. <https://www.turbomole.org/> (accessed 2023-04-21).
- (50) Pulay, P. A Perspective on the CASPT2 Method. *International Journal of Quantum Chemistry* **2011**, *111* (13), 3273–3279. <https://doi.org/10.1002/qua.23052>.
- (51) Schreiber, M.; Silva-Junior, M. R.; Sauer, S. P. A.; Thiel, W. Benchmarks for Electronically Excited States: CASPT2, CC2, CCSD, and CC3. *The Journal of Chemical Physics* **2008**, *128* (13), 134110. <https://doi.org/10.1063/1.2889385>.
- (52) Gagliardi, L.; Orlandi, G.; Bernardi, F.; Cembran, A.; Garavelli, M. A Theoretical Study of the Lowest Electronic States of Azobenzene: The Role of Torsion Coordinate in the Cis–Trans Photoisomerization. *Theor Chem Acc* **2004**, *111* (2), 363–372. <https://doi.org/10.1007/s00214-003-0528-1>.
- (53) Dubecký, M.; Derian, R.; Horváthová, L.; Allan, M.; Štich, I. Disentanglement of Triplet and Singlet States of Azobenzene: Direct EELS Detection and QMC Modeling. *Phys. Chem. Chem. Phys.* **2011**, *13* (47), 20939–20945. <https://doi.org/10.1039/C1CP22520K>.
- (54) Fliegl, H.; Köhn, A.; Hättig, C.; Ahlrichs, R. Ab Initio Calculation of the Vibrational and Electronic Spectra of Trans- and Cis-Azobenzene. *J. Am. Chem. Soc.* **2003**, *125* (32), 9821–9827. <https://doi.org/10.1021/ja034433o>.

