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Summary of the Doctoral Thesis:

Expanding Heteroaryl Azo Toolbox - Synthetic Approaches of Novel Molecules and Evidence of their Photoswitching Ability

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2026

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Introduction

The field of molecular photoswitches has received significant attention over the past decades, stemming from the vast potential these dynamic chemical systems hold across numerous areas of activity. The possibility of interconverting a compound between two or more states in a spatio-temporal manner, each state bearing its own set of physico-chemical properties, creates many opportunities ranging from compounds with controllable biological activity, to alternative data-storage solutions, innovative materials and novel approaches to the current energy crisis.[1–5]

However, the development of such technologies depends critically on fundamental research, particularly chemistry, which is currently in need of molecular designs capable of being implemented into practical uses. Fundamental research, whether through the development of synthetic methodologies or the physico-chemical characterisation of obscure and ignored structural scaffolds, acts as the foundation for all implementations, providing applied scientists with the tools to rapidly develop and test their ideas without the struggles of developing synthetic methodologies or understanding the intricacies of the molecular scaffolds they require.

The field of heteroaryl azo photoswitches has proven this point multiple times over the last decade.[6,7] As old and forgotten structural motifs started reappearing in the literature due to their potential, this brought to light the lack of available research on synthetic methods for obtaining these compounds, on their spectral properties and even on their chemical properties. This gap is significant, as heteroaromatic compounds are known for sometimes unpredictable reactivities and difficult synthetic methodologies. With this in mind, we set out to develop and describe novel heteroaryl azo structural scaffolds, with the aim of providing the scientific community with approachable synthetic strategies alongside thorough characterisation of structure-property correlations for photoswitching performance.

The thesis is structured in five chapters. The first chapter provides a deep dive into the current state of the art of molecular photoswitches, including azobenzenes and heteroarylazo photoswitches. The second and third chapters present our original experimental contributions on arylazopyrazole, arylazo-1,3,4-oxadiazole and arylazo-1,3,4-thiadiazole scaffolds, describing novel synthetic methodologies, structural characterisation and evaluation of photoswitching performance. The fourth chapter describes a large-scale implementation of the Briggs-Rauscher oscillating reaction commissioned for a contemporary art installation at Hamburger Bahnhof in Berlin. The fifth chapter contains the experimental section.

Chapter 1. State of the Art in the Field of Photoswitches

Molecular switches are dynamic chemical systems capable of interconverting between two states by means of physical or chemical stimuli; when light is used as the stimulus, the molecules are called photoswitches and the fundamental property they present is photochromism due to the spectroscopic differences between the two states.[8] In the context of this thesis, unimolecular photoswitches based on the azo N=N chromophore represent the central focus, which specifically interconvert between thermodynamically stable *E* and metastable *Z* isomers through irradiation with light of appropriate wavelengths.

The performance of a photoswitch is described by a set of parameters proposed by van Dijken *et al.*:[9] addressability, the spectral separation between the absorption bands of the two isomers that allows selective excitation; reliability, also termed fatigue resistance, describing the capacity of the system to sustain multiple switching cycles without degradation; stability, quantified through the thermal half-life ($t_{1/2}$) of the metastable state; and efficiency, reflecting the extent of photoconversion at the photostationary state (PSS). These parameters, alongside modularity, which describes the ease with which the photoswitching core can be integrated into larger molecular architectures, define the suitability of a photoswitch for a given application (Figure 1).

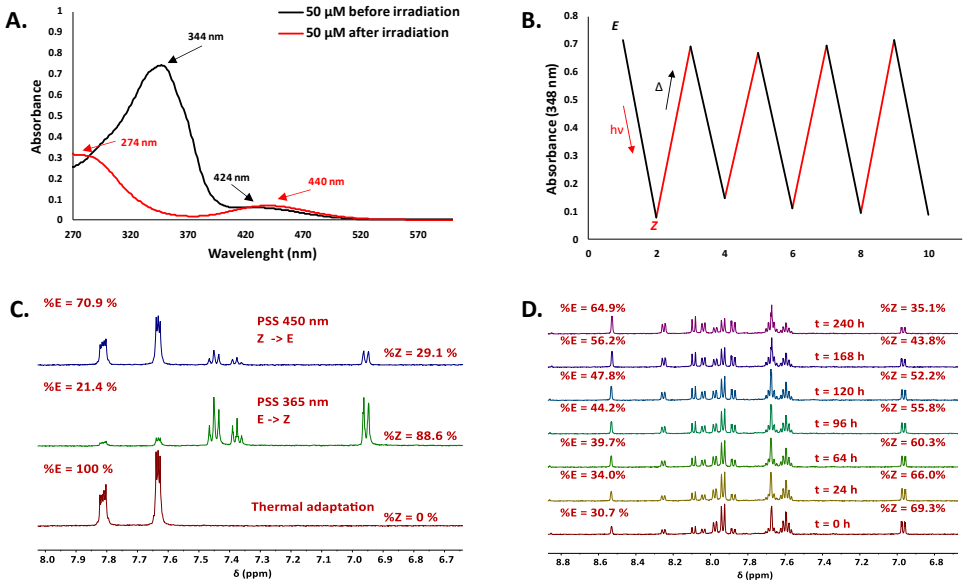


Figure 1. Key parameters describing photoswitching performance, addressability **(a)**, reliability **(b)**, efficiency **(c),** and stability **(d)**. **(a)** UV-Vis absorption spectra of an arylazopyrazole photoswitch before and after irradiation at 365 nm, displaying the spectral differences between the two isomers. **(b)** Fatigue resistance experiment through UV-Vis spectroscopy, measuring change in absorbance over multiple switching cycles of an arylazopyrazole photoswitch. **(c)** PSS quantification of isomer content through ^{1}H NMR spectroscopy after irradiation at specific wavelengths. **(d)** Kinetic monitoring of back-isomerization reaction of a metastable (*Z*)-arylazopyrazole derivative using ^{1}H NMR spectroscopy. The figures represent personal results.

Azobenzene quickly became one of the most popular molecular systems for studying the dynamics of photoswitches and managed to prove its usefulness in developing applications which involve spatiotemporal control of properties, from biological activity to catalysis, data storage and molecular movement.[2,10,11] Given this potential, we conducted a thorough survey of the existing literature on azo-bearing photoswitches, presenting their advantages and limitations alongside the physico-chemical phenomena and mechanisms governing their photoswitching capabilities.

The large palette of synthetic methodologies and comprehensive research on its structure-property relationships established azobenzene as a robust and efficient scaffold in the field of photoswitches. However, its intrinsic limitations with regards to addressability and stability, briefly explained as a trade-off between red-shifting absorption bands and thermal stability of the metastable state, pushed scientists to develop molecular design strategies such as *ortho*,*ortho'*-substitution with fluorine or methoxy groups, push-pull designs and even indirect photoexcitation through attachment of photosensitising motifs.[11–13] While efficient for their scope, azobenzenes clearly possess limited structural possibilities since most strategies revolve around grafting various motifs onto the aryl fragments, an approach which intrinsically introduces molecular complexity and could impede the development of applications due to toxicity, solubility and stability issues.

The rise of heteroaryl azo photoswitches as an alternative to azobenzene proved to be a key turning point for this field of research. Through the substitution of one aryl fragment with a heteroaryl one, a wide door opened to new molecular scaffolds which present exciting properties and are mostly unexplored, the diverse and numerous classes of heteroaromatic systems generating what seems to be a world of infinite photoswitching possibilities.[2,7] Thus, we further surveyed the literature on heteroaryl azo photoswitches as alternatives to azobenzenes, extracting the most relevant examples regarding synthetic strategies, structure-property relationships and applications, while identifying the significant gaps in both synthetic methodologies and photoswitching characterisation, which motivated the work described in the following chapters.

Novel interactions inside the photoswitching scaffold, such as the case of arylazopyrazoles with their favourable C–H···π interactions and excellent band separation between *E* and *Z* forms, proved capable of breaking the limits of azobenzene, this specific class achieving record-breaking thermal stabilities in the order of years and near-quantitative bidirectional photoconversion.[14–16] Such discoveries, combined with the continuous development of applications in fields such as photopharmacology and materials sciences, creates an urgent need for fundamental research onto novel azoheteroarene systems.[2,5]

Despite extensive research on heteroaryl azo photoswitches, the literature still presented significant gaps regarding synthetic methodologies for a large number of azoheteroarene systems, most of them not being evaluated for their photoswitching potential, but treated as mere dyes, some of them being completely unexplored synthetically. Computational chemistry has also emerged as a valuable complement to experimental work in the field of photoswitches, particularly for rationalising structure-property relationships from first principles.[17] With this in mind, we performed a background literature survey on the application of density functional theory and related methods in the study of organic and supramolecular systems, with particular emphasis on their utility in elucidating the mechanisms governing thermal back-isomerisation, conformational analysis of metastable states and the prediction of spectral properties.

With this in mind, we marched in developing and investigating novel heteroaryl azo photoswitches based on underexplored heteroaromatic scaffolds, with the aim of providing approachable synthetic strategies and characterising their structure-property correlations for photoswitching performance.

Chapter 2. Arylazopyrazole Photoswitches

2.1. Objectives and Molecular Design

At the time when this research was considered, the evaluated structural palette of arylazopyrazole photoswitches was limited despite the remarkable performance delivered by the 4-arylazopyrazole scaffold.[14–16] We identified three specific gaps in the structural space of arylazopyrazoles:

i. the influence of 3,5-bis(trifluoromethyl) substitution on the pyrazole ring, considering the remarkable properties fluorine atoms have proved to induce on photoswitching performance;[13]
ii. the effect of extending the conjugated system through naphthyl and 1,3,4-oxadiazole motifs, considering the electron-rich nature of the naphthyl ring and the intrinsic π-deficient nature of the 1,3,4-oxadiazole ring;[18] and
iii. the essentially uncharted territory of *N*-aryl substitution at the pyrazole nitrogen.

Thus, we designed eighteen novel derivatives (**2.1a-o** and **2.2a-c**) to address these perspectives.

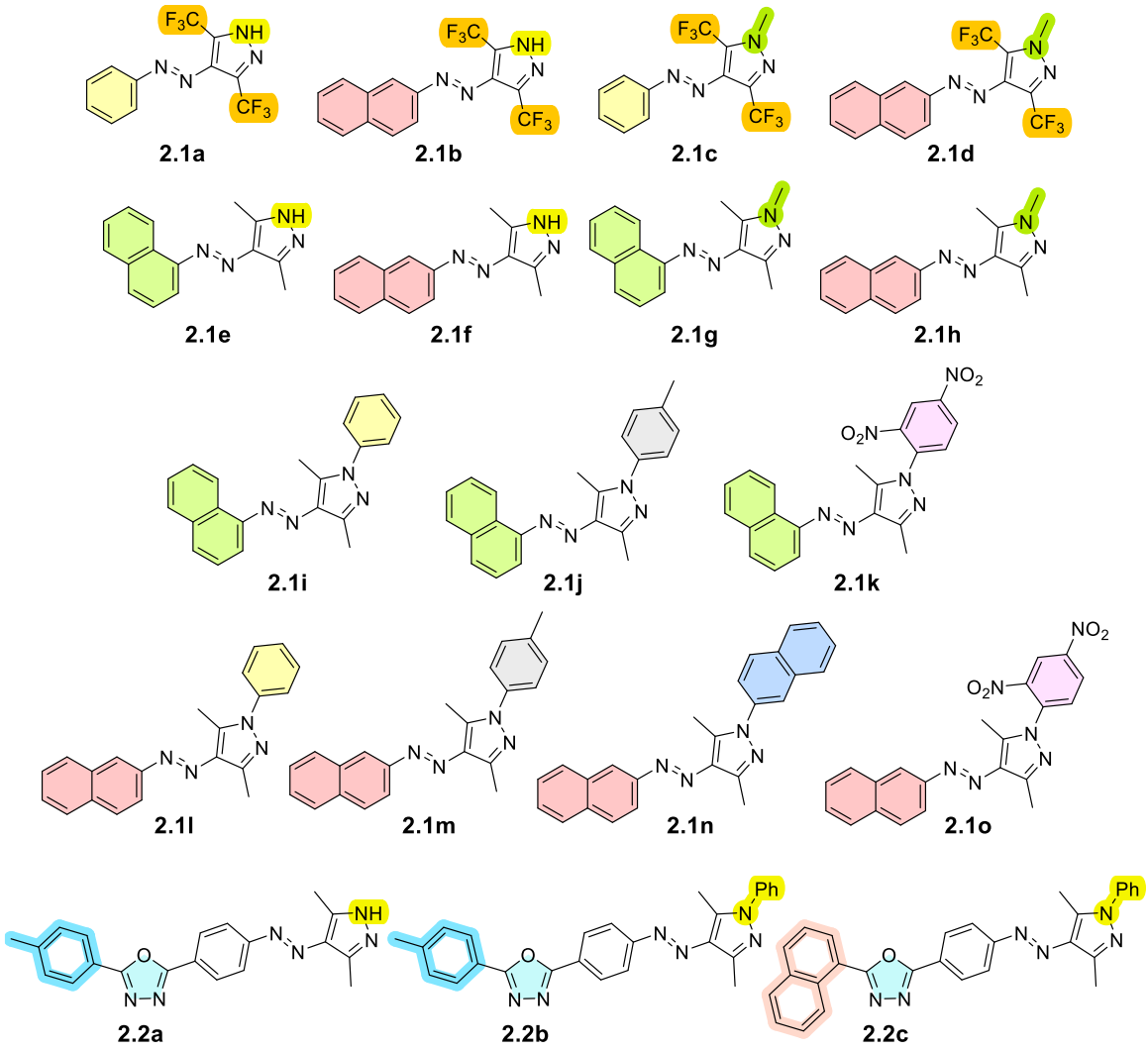
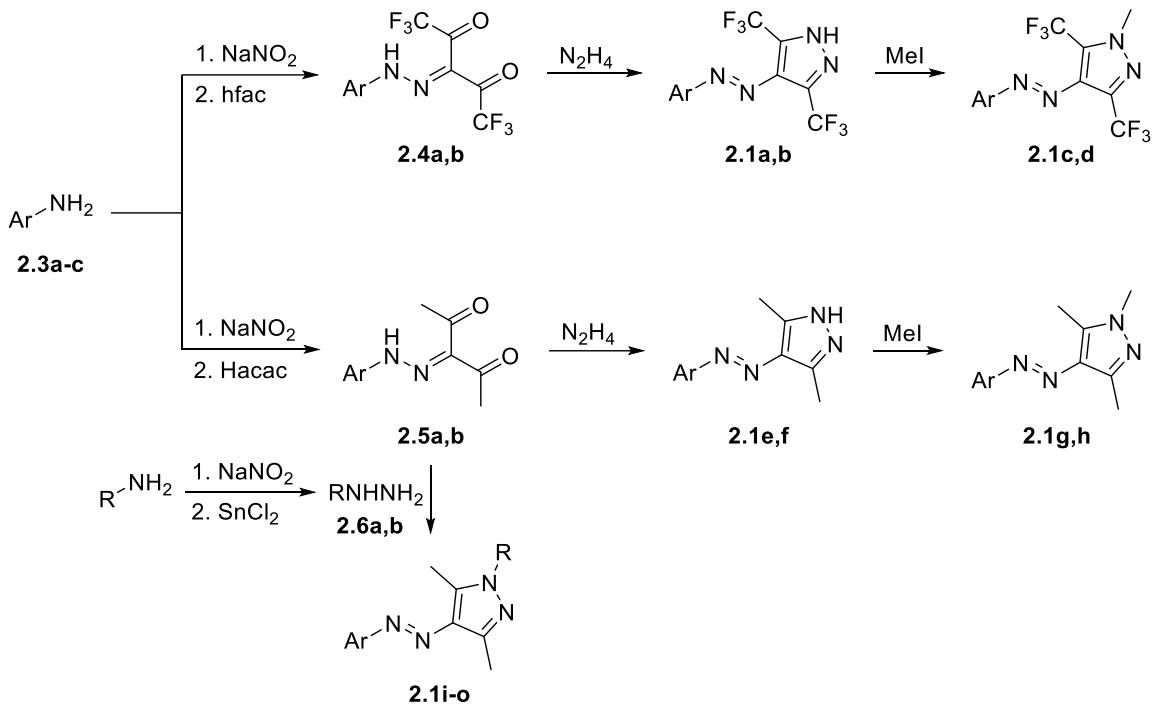


Figure 2. Molecular design for the target compounds.

2.2. Synthesis

All target compounds were accessible through a two- or three-step approach based on diazotisation-coupling of aromatic amines with hexafluoroacetylacetone or acetylacetone, followed by dehydrative cyclisation with the appropriate hydrazine and methylation for some. Purification was performed exclusively through recrystallisation, and global yields ranged from 16% to 60%, confirming the synthetic accessibility of this scaffold for broad structural diversification (Scheme 1).



Scheme 1. Simplified representation of the synthetic approach for obtaining target arylazopyrazole compounds.

Structural characterisation through single-crystal X-ray diffraction and NMR spectroscopy provided valuable insights at both the intermediate and product stages. The hydrazone intermediates presented magnetic non-equivalence of the methyl/trifluoromethyl groups, traced to an intramolecular N–H···O=C hydrogen bond confirmed crystallographically (Figure 3) and sustained by VT-NMR experiments yielding a conformational exchange barrier $\Delta G^{\ddagger} > 16.5$ kcal/mol.

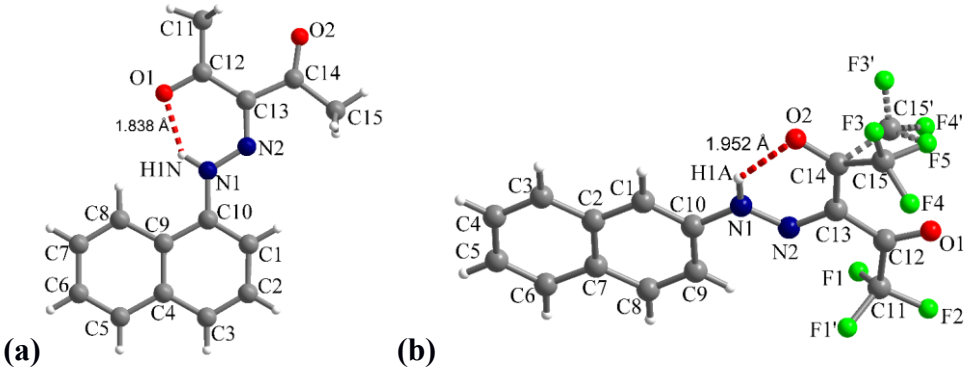


Figure 3. Structures of compounds **2.5a (a)** and **2.4b (b)** revealed by single crystal X-ray diffraction. In **2.4b**, one CF_3 group is disordered on two crystallographic positions with site occupancy factors of 0.5 (symmetry code: ' = x, 1.5-y, z)

2.3. Photoswitching Performance

2.3.1. Trifluoromethyl series

The 3,5-bis(trifluoromethyl) arylazopyrazole series delivered the most significant results of this chapter. The phenyl *N*-unsubstituted derivative **(*Z*)-2.1a** displayed a half-life of $t_{1/2}$ ~ 22 days, largely suppressing the tautomerisation-assisted back-isomerisation pathway that notoriously affects *N*-unsubstituted arylazopyrazoles. The phenyl *N*-methyl derivative **(*Z*)-2.1c** reached $t_{1/2}$ ~ 146 days (Figure 4), representing a 15-fold enhancement over the parent **4pzMe** scaffold and the longest half-life reported for 3,5-disubstituted arylazopyrazoles at the time of publication.[19] The UV-Vis absorption profiles of **(E)-2.1a** (λ_{max} = 344 nm, π→π*; 424 nm, n→π*) and **(E)-2.1c** (λ_{max} = 320 nm, π→π*; 428 nm, n→π*) confirmed good band separations ($\Delta\lambda_{\pi\rightarrow\pi^*}$ = -70 and -36 nm, respectively), and photostationary state compositions exceeded 70% in both switching directions as determined by ^{1}H NMR spectroscopy. This stabilising effect was maintained upon extension of conjugation to the 2-naphthyl motif in **2.1b** and **2.1d**, confirming the robustness of the trifluoromethyl strategy.

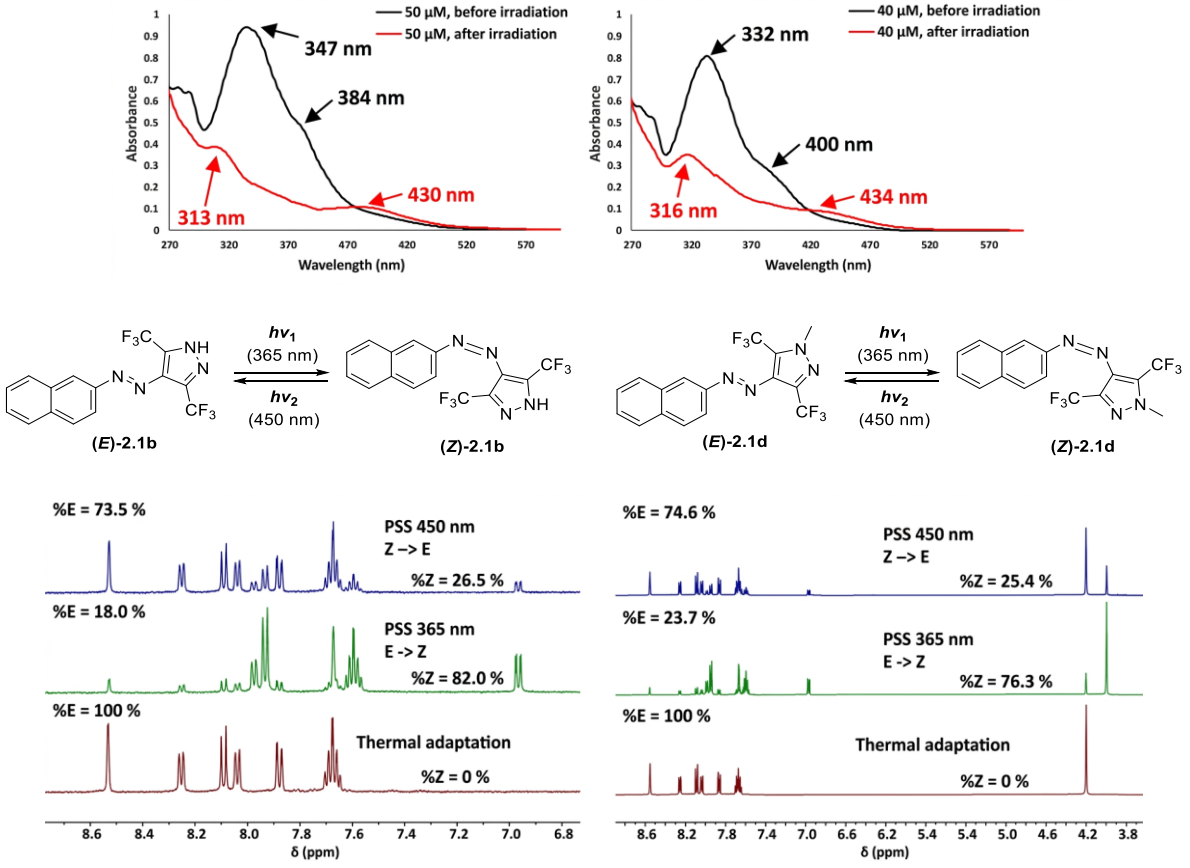


Figure 4. **(Top)** UV-Vis spectra of thermally adapted **(*E*)-2.1b** (left) and **(*E*)-2.1d** (right) and their corresponding photostationary states PSS_{365} after irradiation, marked with red. Arrows point to corresponding absorption maxima for π→π* and n→π* transitions of both isomers. **(Bottom)** ^{1}H NMR spectra of the photostationary states PSS_{365} and PSS_{450} and isomer quantifications for compounds **2.1b** (left) and **2.1d** (right) in DMSO-d_6 (1.5 mM).

2.3.2. Extended conjugation series.

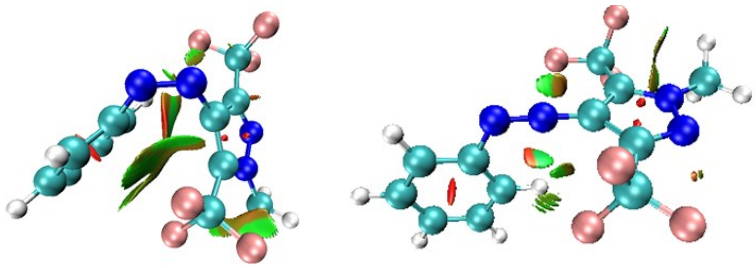
Extension of the conjugated system through 1-naphthyl and 2-naphthyl groups (**2.1e-h**) provided the expected bathochromic shifts ($\Delta\lambda \sim$ 13-42 nm relative to parent analogues), generating the largest $\pi \rightarrow \pi^*$ band separations in our series; compound **(*Z*)-2.1e** presented $\Delta\lambda_{\pi\rightarrow\pi^*} = -75$ nm, the largest in our entire work. The 2-naphthyl derivatives showed particularly high PSS compositions, **2.1f** achieving 91% *Z* and **2.1h** reaching 94% *Z*, at the cost of reduced thermal stability compared to the trifluoromethyl series ($t_{1/2}$ = 56.4 h for **(*Z*)-2.1h**). In a parallel line of structural exploration, the 1,3,4-oxadiazole-decorated derivatives **2.2a-c** roughly doubled the molar extinction coefficients relative to the naphthyl analogues (ε = 4.14-4.43 × 10^4 M^{-1} cm^{-1}), positioning them as particularly efficient light-absorbing photoswitches, with PSS values of 86–87% *Z* and moderate half-lives of 8.6–15.7 h.[20]

2.3.3. *N*-aryl series

The *N*-aryl series (**2.1i-o**) revealed that variation at the pyrazole nitrogen atom exerts minimal influence on position of the absorption bands, yet strongly affects efficiency and stability. Derivatives with electron-neutral or -donating substituents (*N*-phenyl, *N*-4-tolyl) preserved high PSS values (up to 93% *Z*), whereas electron-withdrawing 2,4-dinitrophenyl groups drastically reduced photoconversion yields to ~33% *Z*, yet the half-lives of the dinitrophenyl derivatives were comparable to or longer than those of the *N*-phenyl counterparts (**(*Z*)-2.1o**, $t_{1/2}$ = 70.7 h *vs.* **(*Z*)-2.1l**, $t_{1/2}$ = 59.8 h). All compounds displayed excellent fatigue resistance over at least five switching cycles.

2.4. Computational Chemistry

Theoretical calculations at the PBE0-D4/def2-TZVP level of the theory corroborated the experimental trends, confirming the inversion mechanism for thermal back-isomerisation and revealing that bis(trifluoromethyl) derivatives present higher activation barriers arising from increased N=N double-bond character in the *Z* isomer and reduced dispersive stabilisation of the transition state (Figure 5); MEP and NBO analysis further showed that these derivatives uniquely favour a TS type-II pathway, a preference traced to electron density redistribution induced by the $–CF_3$ groups.



(*Z*)-2.1c **(*TS*)-2.1c**

Figure 5. Calculated NCI surfaces for isomer *(Z)* and transition states (TS) of azopyrazoles **2.1c**. Attractive dispersive intramolecular effects are marked by green surface, whereas repulsive ones are marked by red surface.

2.5. Conclusions

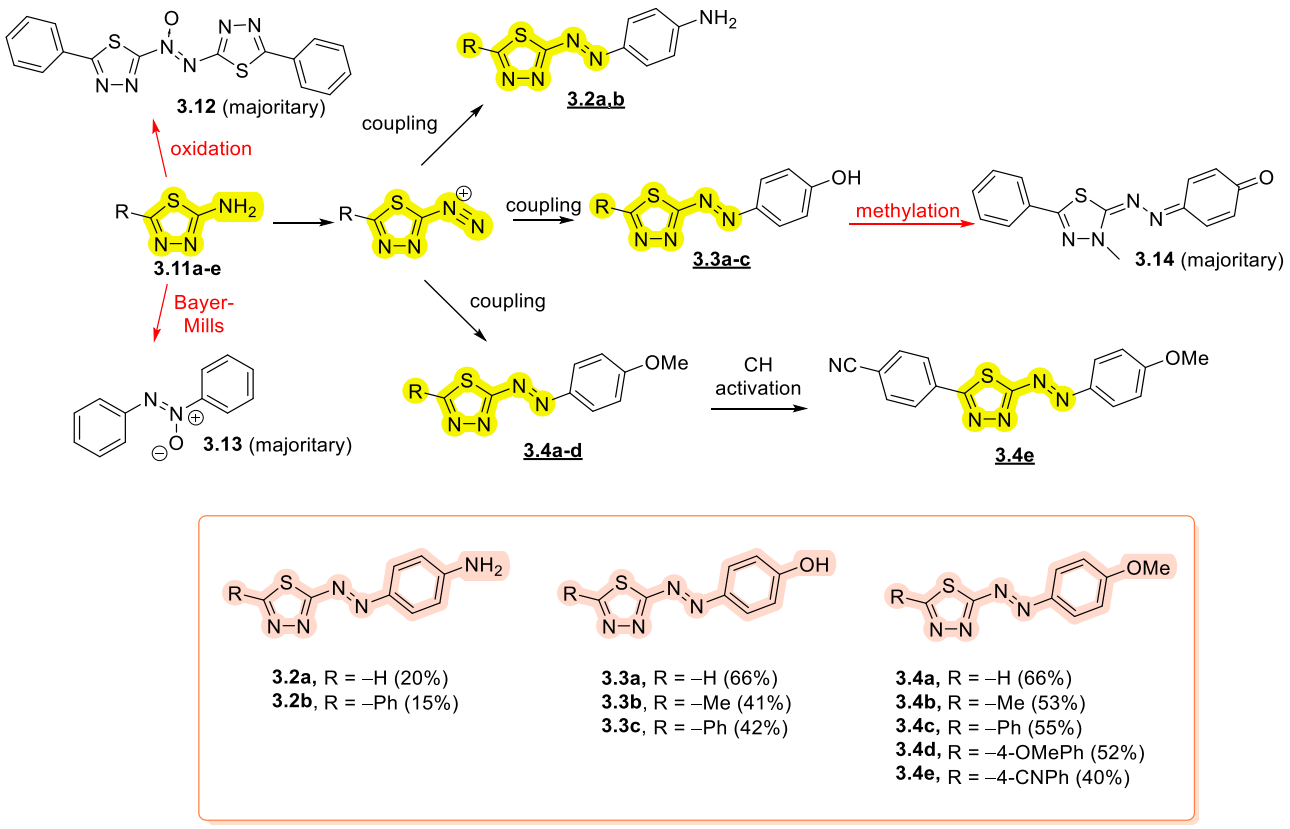
Taken together, the results expand the structural toolbox of arylazopyrazole photoswitches along three previously unexplored dimensions and demonstrate that the photoswitching parameters of the parent scaffold can be independently modulated and fine-tuned through structural choices: trifluoromethyl groups for stability enhancement, naphthyl and oxadiazole motifs for red-shifting and absorptivity gains, and *N*-aryl substitution for fine-tuning of half-lives and photoconversion yields. Results from this chapter were published in *ACS Omega* and *Synthesis*.[19,20]

Chapter 3. Arylazothiadiazoles

3.1. Objectives and Molecular Design

The third chapter follows a mostly uncharted territory within the heteroaryl azo space, as the 1,3,4-oxadiazole and 1,3,4-thiadiazole azo scaffolds had received virtually no attention as photoswitching platforms prior to our work. Among the five-membered heteroaromatic systems, two closely related yet distinct systems attracted our attention due to their intrinsic electronic properties and widespread utility in medicinal chemistry and materials sciences: the 1,3,4-thiadiazole and 1,3,4-oxadiazole rings.[18,21] On one hand, both share a π-deficient character; on another hand, they present distinct physico-chemical properties through their difference at the chalcogen atom (sulphur or oxygen), which could allow for interesting and unique spectral and photoswitching characteristics when incorporated into an azo system. An exhaustive literature survey revealed a clear lack of research on the dynamics of such systems as heteroaryl azo photoswitches, further justifying the need for experimental and computational work in this area.

We envisaged series of arylazo-1,3,4-oxadiazole and arylazo-1,3,4-thiadiazole derivatives decorated with various structural motifs ranging from aliphatic to aromatic, varying also the substitution pattern on the aromatic fragment of the azo bond so as to create an opportunity of thoroughly evaluating the scope of these novel classes with regards to photoswitching performance.

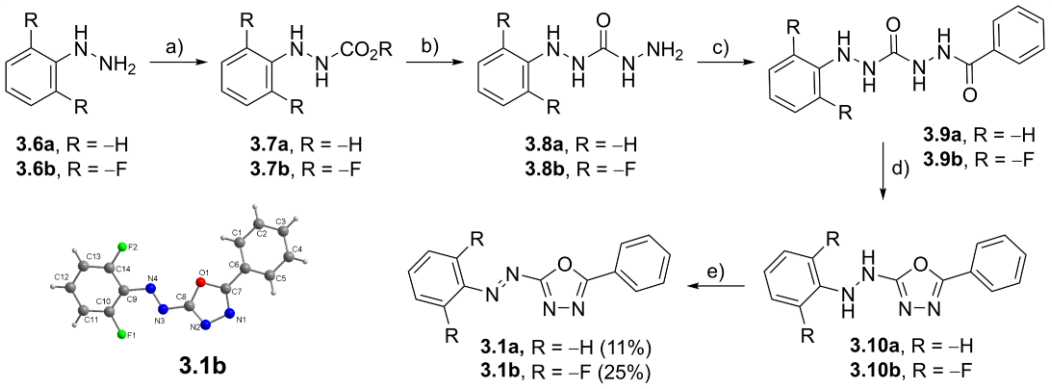


Scheme 2. Synthetic approaches for 1,3,4-thiadiazole azo derivatives.

3.2. Synthesis

3.2.1. Arylazo-1,3,4-oxadiazoles

Direct synthetic approaches proved unsuccessful for the oxadiazole series, likely due to the low aromaticity of the 1,3,4-oxadiazole ring and the poor nucleophilicity of its 2-amino derivatives. We eventually managed to reach the target azo derivatives through an adapted indirect approach[22] comprising six steps starting from substituted arylhydrazines, reporting the synthesis of an *ortho,ortho'*-difluorophenyl-decorated compound (**3.1b,** Scheme 3). During characterisation, this derivative showcased an intriguing intramolecular S_NAr-type cyclisation reaction, revealing the intriguing chemical reactivity of this system.



Scheme 3. Synthesis of compounds **3.1**. a) alkyl chloroformate (R=Et for **3.6a**, R=*i*-Pr for **3.6b**), pyridine, MeCN, rt. b) hydrazine hydrate (neat), 70 °C, c) benzoyl chloride, toluene, $NaHCO_3$ (aq.), rt., d) $POCl_3$, 80 °C, e) MnO_2, DCM, rt. Compound **3.6b** was obtained from its corresponding amine through diazotization ($NaNO_2$, conc. HCl, 0-5 °C) followed by treatment with a reducing agent ($SnCl_2$, conc. HCl). Reported yields are global. (inset) Structure of **3.1b** determined through single-crystal XRD.

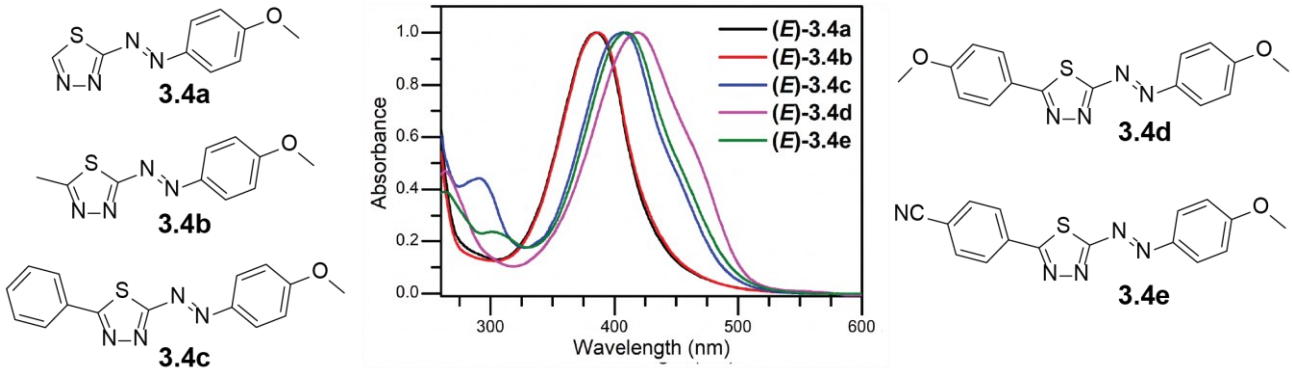
3.2.2. Arylazo-1,3,4-thiadiazoles

We saw greater success in the case of the sulphur analogues, which also responded better in preliminary photoswitching experiments. We synthesised three series of compounds bearing as the aryl segment 4-aminophenyl (**3.2a-c**), 4-hydroxyphenyl (**3.3a-c**) and 4-methoxyphenyl (**3.4a-e**) groups. The 4-aminophenyl and 4-hydroxyphenyl derivatives were envisaged to serve as intermediates, but due to intricate reactivity the 4-aminophenyl series was just structurally characterized, whereas the 4-hydroxyphenyl series, while not photoswitchable due to competitive tautomerisation processes, presented intriguing solvatochromic and pH-sensing properties (pK_a = 7.30 ± 0.03 for **3.3c** in aqueous buffers) consistent with reported literature values.[23] The 4-methoxyphenyl series **3.4a–e** proved photoswitchable and represented the core of our photoswitching investigation.

3.2.3. Photoswitching Performance

Through this work we identified a small and robust push-pull photoswitching scaffold, 4-methoxyphenylazo-1,3,4-thiadiazole, which presents visible-light addressability and, most importantly, stable metastable states. The spectral profiles of the *E* isomers present a single highly red-shifted absorption band (λ_{max} = 385–419 nm for the π→π* transitions), with extinction coefficients ranging from ε = 1.76 × 10^4 to 3.02 × 10^4 M^{-1} cm^{-1} across the series. The parent unsubstituted derivative **(*E*)-3.4a** and the methyl-substituted **(*E*)-3.4b** display an anomalously small separation between the π→π* and n→π* bands (Δλ = 8 and 9 nm, respectively); extension of

conjugation through 5-aryl substitution in **3.4c-e** progressively separated the two bands ($\Delta\lambda$ = 44–52 nm). This spectral behaviour is characteristic of a strong push-pull system comprising the electron-donating methoxy motif on the aryl side and the intrinsic electron-deficit of the 1,3,4-thiadiazole ring on the heteroaryl side; analogous azo compounds with similar spectral features are often termed pseudostilbenes.[11]



Compound	3.4a	3.4b	3.4c	3.4d	3.4e
ε (10^4 M^{-1} cm^{-1})	1.76 ± 0.08	2.45 ± 0.11	2.54 ± 0.08	3.02 ± 0.11	2.98 ± 0.25

Figure 6. Normalized UV-Vis spectra of *E* isomers of derivatives **3.4a-e**.

Photoconversion efficiency was found to be strongly concentration-dependent, particularly for the 5-aryl-substituted derivatives. *E*→*Z* PSS compositions ranged from 93% *Z* (**3.4b**) to 51% *Z* (**3.4c**), whereas the *Z*→*E* direction proved to be >98% *E* in all cases, confirming efficient bidirectional switching.

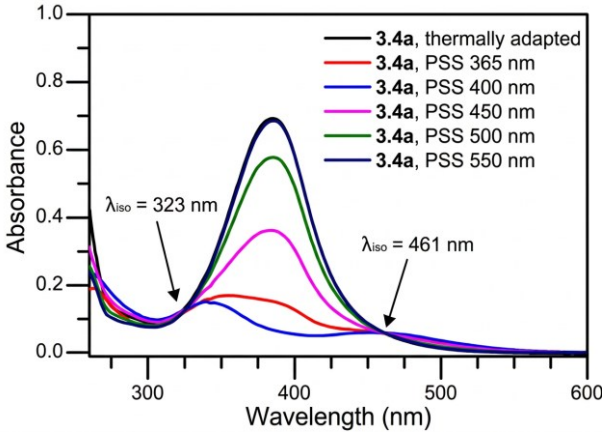


Figure 7. UV-Vis (right) spectra of the photostationary states for **3.4a** in DMSO (3 × 10-5 M) obtained through irradiation at various wavelengths.

The thermal back-isomerisation kinetics proved intriguing, as all compounds presented complex concentration-dependent behaviour likely attributed to aggregation phenomena in solution.

For **(*Z*)-3.4a**, kinetic measurements at five concentrations (2–10 mM) revealed apparent half-lives ranging from $t_{1/2,\,app}$ = 3.7 h to 6.4 h; analysis of residuals showed that a biexponential decay model provides a statistically superior fit over the monoexponential model, confirmed through the F-test, exposing a faster aggregation-mediated pathway ($t_{1/2,\,fast}$ ~ 1.7‑3.0 h) and a slower monomeric pathway ($t_{1/2,\,slow}$ ~ 9 h). The 5-aryl-substituted derivatives **3.4c** and **3.4d** presented even more pronounced concentration-dependent kinetics, with apparent half-lives at 5 mM concentration in the range of minutes ($t_{1/2,\,app}$ = 8.6 min for **3.4c**; 11.2 min for **3.4d**), attributed to enhanced π-π stacking interactions. All compounds displayed excellent fatigue resistance over multiple switching cycles in both DMSO and MeOH.

3.3. Computational Chemistry

Computational chemistry served as an indispensable tool throughout this work. Through a validated DFT/TD-DFT protocol with ORCA at the PBE0-D4/def2-TZVP level of theory and activation barrier correction at the ωB97X-D4/def2-QZVPP level, we achieved excellent correlation between calculated and experimental absorption spectra and activation barriers for the thermal $Z \rightarrow E$ back-isomerisation. The computational results confirmed the inversion mechanism as the dominant pathway for this class and provided molecular-level rationalisation for the observed substituent effects on half-lives through favourable LP···π stabilising interactions in the *Z* isomers (Figure 8).

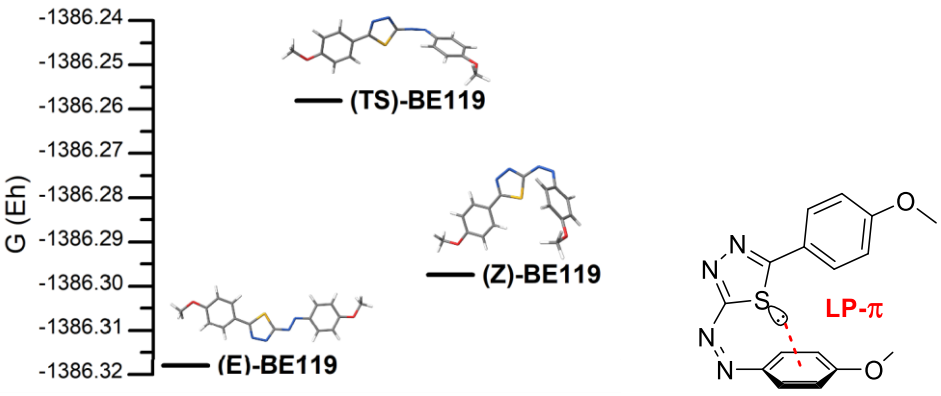


Figure 8. (Left) Energy diagram and structures for lowest-energy (*E*)-, (TS)- and (*Z*)-conformers for compound **3.4d**. Represented energies were Boltzmann-averaged. (Right) Representation of the lowest-energy conformer of (*Z*)-**3.4d**, showcasing the LP···π stabilizing interaction.

3.4. Conclusions

Considering the properties described herein, the parent structure **3.4a** emerges as the key structural entry point for this class, as alkyl derivatisation preserves the spectral and kinetic

performance it presents, while aryl derivatisation opens the room for fine-tuning properties through red-shifting and modulation of kinetics and photoconversion efficiency. The ease of its synthesis and the possibility of derivatisation in the 5th position through C–H activation render it a conveniently attachable photoswitching fragment for any molecular architecture. Considering the pharmacophore nature of the 1,3,4-thiadiazole ring and the specific resistance of the arylazothiadiazole scaffold to the action of glutathione,[23] this novel class of push-pull photoswitches presents great potential for applications. Results from this chapter are currently in the process of publishing.

Chapter 4. How Chemists Contribute to Artworks

In 2024, an opportunity appeared to collaborate with the Romanian artist Alexandra Pirici on her performative installation *"Attune"*, commissioned by Audemars Piguet Contemporary and exhibited at Hamburger Bahnhof – Nationalgalerie der Gegenwart in Berlin.[24] Pirici's artistic vision drew heavily from the philosophical framework described by Prigogine and Stengers in *Order out of Chaos*,[25] which describes how complex, self-organising structures can spontaneously emerge from systems driven far from thermodynamic equilibrium. With this philosophical underpinning, the artist envisioned a living installation in which chemical, biological and human performers would coexist in a shared choreographic space. The centrepiece of the chemical choreography was an element referred to as *"the Organ"*, a sculptural metallic structure bearing multiple suspended glass cylinders, each hosting a different chemical or physical phenomenon: chemical gardens grown from metal salts in sodium silicate, Rayleigh–Bénard convection cells visualised with mica powder in heated oil, and a single, fully automated cylinder dedicated to the Briggs–Rauscher oscillating reaction.

The Briggs-Rauscher (BR) oscillating reaction, first reported by Briggs and Rauscher in 1973,[26] represents one of the most visually striking demonstrations in chemistry: upon mixing three colourless solutions containing potassium iodate with sulphuric acid, malonic acid with manganese(II) sulphate and starch, and hydrogen peroxide, the system oscillates rhythmically between amber, dark blue and colourless states through two competitive redox processes before reaching equilibrium as a deep blue mixture.[27] The reaction was planned to occur in a custom-made glass cylinder (d = 12 cm, h = 120 cm) at a scale of ~7-8 L. We designed a system in which the cylinder bore four inlets, each dedicated to a specific solution to avoid cross-contamination, with volume control handled by peristaltic pumps and sequence automation achieved through an in-house Arduino approach by a dedicated engineering collaborator. Following each oscillation cycle, a two-stage cleaning protocol operated through a single sprinkler line ensured complete neutralisation of residual iodine through sodium thiosulphate and subsequent washing with distilled water, with all drained liquids collected in a waste vessel containing a pre-calculated excess of thiosulphate solution.

Figure 9. Live snapshots of the yellow-blue (left) and blue-colourless (right) transitions of the Briggs–Rauscher reaction.

The automated system ran throughout the exhibition period delivering reproducible oscillation cycles at the discussed scale without any incidents. Beyond the technical accomplishment, this collaboration touched upon something far more personal: a recalibration, a reminder of the beauty and the magic which reside at the core of our field. As Roald Hoffmann argued in *Molecular Beauty*,[28] the aesthetic dimension of molecular science is not a superficial ornament, but a genuine driver of scientific intuition and creativity. Jean-Marie Lehn, in his perspective *Steps towards Complex Matter*,[29] described the evolution of matter from divided to condensed, to organised, to living, to thinking, all driven by self-organisation, a narrative that resonates with the Briggs–Rauscher reaction's own capacity to generate temporal order from an apparently disordered mixture.

Performing chemistry outside the walls of the laboratory, within the public space of a major museum, provides the general public with direct exposure to scientific phenomena,[30] acts as a vehicle for attracting young minds towards the sciences,[31] and provides the scientist with a deeper, more reflective understanding of the very phenomena they study,[32] positioning such work within the broader framework of transdisciplinary research as articulated by Nicolescu.[33]

Chapter 5. General Conclusions

The doctoral thesis titled *"Expanding Heteroaryl Azo Toolbox — Synthetic Approaches of Novel Molecules and Evidence of their Photoswitching Ability"* presents the design, synthesis and study of the photoswitching properties of novel heteroaryl azo derivatives built upon three structural scaffolds: arylazopyrazoles, arylazo-1,3,4-oxadiazoles and arylazo-1,3,4-thiadiazoles. These molecular platforms share the azo N=N chromophore as the main photochromic motif, yet each heterocyclic fragment introduces its own set of electronic, steric and supramolecular features which modulate photoswitching performance in distinct and, at times, unexpected ways.

All synthesised compounds were characterised through NMR spectroscopy, HRMS, single-crystal XRD, UV-Vis spectroscopy and DFT/TD-DFT computational chemistry using a validated protocol with ORCA. A large-scale implementation of the Briggs–Rauscher oscillating reaction within Alexandra Pirici's installation "Attune" at Hamburger Bahnhof was also presented, illustrating the broader interdisciplinary capabilities of chemistry.

The first chapter surveys the physico-chemical phenomena underlying molecular photoswitches and the framework employed to quantify their performance, tracing the evolution from azobenzenes to heteroaryl azo photoswitches and identifying the significant gaps in the literature which motivated the original contributions described herein.

The second chapter describes a systematic investigation of arylazopyrazole photoswitches, where eighteen novel derivatives were designed to address three specific gaps in the structural space. The trifluoromethyl series delivered the longest half-lives reported for 3,5-disubstituted arylazopyrazoles at the time of publication ($t_{1/2}$ ~ 146 days), the naphthyl and oxadiazole motifs provided the largest band separations and doubled the molar extinction coefficients, and the *N*-aryl series revealed that substitution at the pyrazole nitrogen strongly modulates efficiency and stability. Results were published in ACS Omega[19] and Synthesis.[20]

The third chapter ventures into a mostly uncharted molecular territory, reporting the development of synthetic methodologies for arylazo-1,3,4-oxadiazole and arylazo-1,3,4-thiadiazole derivatives. We identified 4-methoxyphenylazo-1,3,4-thiadiazole as a small and robust push-pull photoswitching scaffold presenting visible-light addressability, stable metastable states and complex concentration-dependent kinetics attributed to aggregation phenomena. Results from this chapter are currently in the process of publishing.

The fourth chapter describes a large-scale implementation of the Briggs–Rauscher oscillating reaction within Alexandra Pirici's installation "Attune" at Hamburger Bahnhof, illustrating the broader interdisciplinary capabilities of chemistry.

Through this work we demonstrated that the vast and largely uncharted molecular space of azoheteroarenes holds considerable potential for the discovery of photoswitches with tailored properties, and that a combination of classical organic synthesis, modern spectroscopic tools and computational chemistry can efficiently pin-point the intricate physico-chemical features which govern their molecular dynamics.

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List of publications and conferences

Publications

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Arylazopyrazoles with Long Half-Lives and near-Quantitative Bidirectional Photoswitching. *ACS Omega* **2022**, *7*, 39122–39135. DOI: 10.1021/acsomega.2c04984 .

2. Enache, B.-C.; Simene, A. F.; Hanganu, A.; Tablet, C.; Mădălan, A. M.; Popescu, C. C.; Matache, M. Light-Responsive Oxadiazole-Based-(Hetero)aryl-Azobenzenes. *Synthesis* **2025**, *57*. DOI: 10.1055/a-2675-3787.
3. Enache, B.-C. *et al.,* Arylazothiadiazoles – a new class of stable push-pull photoswitches, *Manuscript in preparation.*
4. Enache, B.-C. *et al.,* Beyond switching – photochemical conversion of arylazooxadiazoles into triazinone scaffold, *Manuscript in preparation.*

Conferences

1. Enache, B. C., Hanganu, A., Tablet, C., Anghel, C. C., Mădălan, A. M., Popescu, C. C., Paun, A., Hădade, N. D., Matache, M., Synthesis of novel 3,5-bis(trifluoromethyl)-4-arylazopyrazole photoswitches. *Student Scientific Communications Session*, Bucharest, 2024. (Presentation)

2. Enache, B. C. Exploring novel azoheteroarene scaffolds towards more versatile photoswitches. *Scientific Communications Session — Chemistry Day*, Bucharest, 2024. (Presentation)

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4. Enache, B. C., Dobre, A.F., Hanganu, A., Mădălan, A.M., Popescu, C.C., Păun, Anca, Matache, M., Synthetic challenges in preparation of novel oxadiazole and pyrazole-based (hetero)arylazo compounds. *KAUST Research Conference — Advances in Sustainable Catalysis*, Jeddah, Saudi Arabia, 2023. (Poster)

5. Enache, B. C., Dobre, A.F., Hanganu, A., Mădălan, A.M., Popescu, C.C., Păun, Anca, Matache, M., Influence of electronic effects on performance of novel arylazopyrazole photoswitches. *8th EuChemS Chemistry Congress*, Lisbon, Portugal, 2022. (Poster)

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