

Tuning the Conformational Properties of Dithienylbenzene Photoswitches for Solid-State Applications

OTDK paper by

David Dorian Nemeth

Supervisor: *Gábor London*

Co-supervisor: *Attila Kunfi*

HUN-REN TTK,
Functional Organic Materials Research Group



and



ELTE Eötvös Loránd University, Budapest, Hungary
Faculty of Science, Institute of Chemistry

Budapest, 2024.12.29.

**THIS PAPER IS SUPPORTED BY
THE EKÖP-24 UNIVERSITY EXCELLENCE SCHOLARSHIP PROGRAM OF THE
MINISTRY FOR CULTURE AND INNOVATION FROM THE SOURCE OF THE
NATIONAL RESEARCH, DEVELOPMENT AND INNOVATION FUND.**



Table of contents

Acknowledgements.....	5
Abbreviations	6
1. Introduction.....	7
2. Scientific background	8
2.1 Historical overview	8
2.2 Photoswitch properties	9
2.3 Dithienylethenes.....	9
2.3.1 Conformation of dithienylethenes and its effect on photoswitching	9
2.4 Dithienylbenzenes.....	10
2.4.1 Conformation of dithienylbenzenes in the literature.....	11
2.5 Virtual screening of potential photoswitches with conformational analysis	14
3. Goals	18
4. Results and discussion	19
4.1 Synthesis of the photoswitches	19
4.1.1 Synthesis of the reversible photoswitch (1)	19
4.1.2 Synthesis of the irreversible photoswitch (31).....	22
4.1.3 Synthesis of the modified reversible photoswitch (7).....	25
4.2 Photochemical measurements	27
4.2.1 Photoswitching of the reversible photoswitch (1) in solution.....	27
4.2.2 Photoswitching of the irreversible photoswitch (31) in solution	29
4.2.3 Photoswitching of the modified reversible photoswitch (7) in solution	29
4.3 Single crystal structure of the reversible photoswitch (1).....	30
4.4 Synthetic modification of the reversible photoswitch (1).....	31
4.4.1 Methylation	31
4.4.2 Metal-organic frameworks	33
4.4.3 Organometallic complexes.....	34

5.	Summary of the results	36
6.	Experimental section.....	37
6.1	Materials and equipment.....	37
6.2	Synthesis of 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene (1).....	37
6.2.1	3,5-dibromo-2-methylthiophene (23).....	37
6.2.2	(4-bromo-5-methylthiophen-2-yl)boronic acid (24)	38
6.2.3	4-(4-bromo-5-methylthiophen-2-yl)pyridine (25)	38
6.2.4	1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene (1)	38
6.3	Synthesis of 1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene (31)	39
6.3.1	(4-bromothiophen-2-yl)boronic acid (28).....	39
6.3.2	4-(4-bromothiophen-2-yl)pyridine (29)	40
6.3.3	Alternative synthesis of 4-(4-bromothiophen-2-yl)pyridine (29)	40
6.3.4	(5-(pyridin-4-yl)thiophen-3-yl)boronic acid (30)	40
6.3.5	1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene (31)	41
6.4	4,4'-((4,5-dimethoxy-1,2-phenylene)bi(5-methylthiophene-4,2-diyl))dipyridine (7).....	41
6.5	Synthesis of the methylated reversible photoswitch (32)	42
6.6	Synthesis of MOF	42
6.7	Synthesis of the organometallic complex	42
	Summary	43
	Összefoglalás	44
	References.....	45

Acknowledgements

I want to thank Gábor London, head of the Functional Organic Materials Research Group at HUN-REN TTK, for giving me the opportunity to work in the lab and for providing me with many useful tips.

I would also like to thank János Daru for guiding me through the theoretical chemistry part and for his willingness to answer my questions any day of the week.

I owe a lot to Attila Kunfi and Tamás Gazdag, who were my mentors during my lab work and taught me how to work safely and effectively.

I thank all the members of the research team for their help whenever I had a problem, and I would also like to thank the other staff at the Institute for their contribution, especially Tamás Holczbauer, who carried out the X-ray diffraction measurements and helped me with the literature search.

Last but not least, I would like to thank my family and friends for supporting me in achieving my goals.

Abbreviations

BuLi	butyllithium
DCM	dichloromethane
DFT	density functional theory
DMF	dimethylformamide
dppf	1,1'-bis(diphenylphosphino)ferrocene
EtOAc	ethyl acetate
GC-MS	gas chromatography - mass spectrometry
HRMS	high resolution mass spectrometry
MOF	metal-organic framework
NMR	nuclear magnetic resonance spectroscopy
TEA	triethylamine
THF	tetrahydrofuran
UV-Vis	ultraviolet-visible

1. Introduction

Nature has always been a great source of inspiration for chemists. We make medicines by synthesizing compounds originally found in plants¹; we create hydrophobic surfaces by reproducing the structure of lotus leaves², and we are developing molecular machines similar to the nanomotors in our bodies³. Photoswitches are also inspired by nature, with a function similar to retinal (Figure 1). This molecule, which plays a crucial role in our vision, undergoes an extremely rapid *cis-trans* isomerization in response to light⁴ and reverts back to its original form in the dark within minutes⁵.

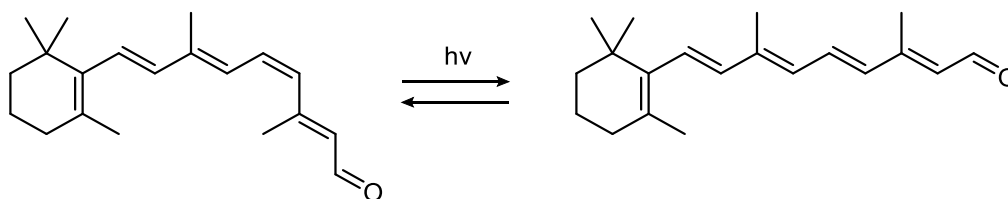


Figure 1. Isomerization of 11-*cis*-retinal by light.

Most of the recent researches⁶⁻⁸ are aiming to develop photoswitches, where both the initial and the photogenerated forms can be reversibly transformed into each other by using light of a specific wavelength. These photoswitches offer high level thermal and spatial control, and can be used as photopharmacological compounds⁹, or as storages for optical data¹⁰ as well as solar energy¹¹. Nevertheless, there are cases, where back conversion by light stimulus is not advantageous, just like in the case of retinal, where biochemical processes are responsible for that. Therefore, the aim of my research was to synthesize new type of photoswitches that are capable of ultrafast thermal back conversion, and I also wanted to test their properties in solid state, which is crucial to get a deeper understanding of the possible future applications.

2. Scientific background

2.1 Historical overview

Photoswitches are molecules whose structure, and therefore some of their properties, change in response to light with specific wavelength. The first photochromic compound was discovered by Fritzsche in 1867, who noticed that the orange crystals of tetracene (Figure 2) lost their color in daylight and regained it at night¹². In the following decades, similar phenomena were observed in other molecules but did not receive much attention.

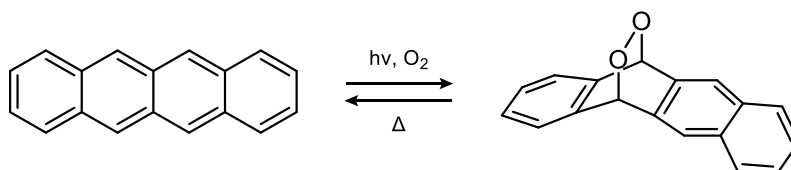


Figure 2. Reversible transformation of tetracene by light in the presence of oxygen¹³.

In the 1930s, an azo compound, called prontosil, was launched as the first commercially available antibiotic¹⁴, and at the same time it was discovered that two conformers of azo compounds, cis and trans, could be converted into each other by light⁶ (Figure 3). Hirschberg and Fischer then began to actively research the field and photoswitching became more widely known.

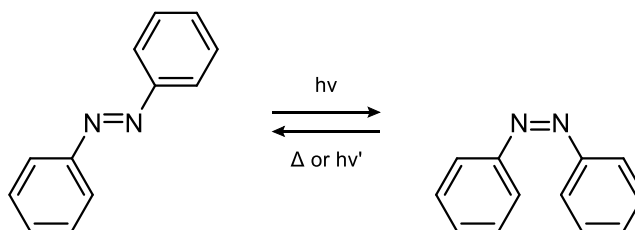


Figure 3. Light-induced cis-trans isomerization of azobenzene¹⁵.

The real breakthrough, however, only came with the successful synthesis of fatigue resistant photoswitches, which were capable of reversible conversion between their two forms over many cycles. These include spirooxazines/spiropyrans (Figure 4) and dithienylethenes (Figure 5).

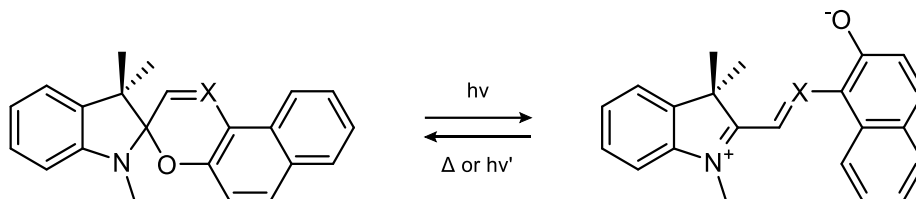


Figure 4. Photoswitching of spiro-oxazines (X=N) and spiropyrans (X=C)¹³.

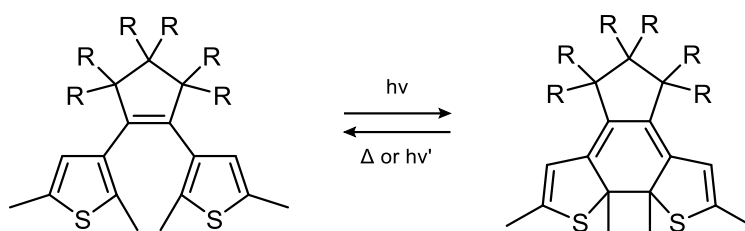


Figure 5. Photoswitching of dithienylethenes ($R=H, F$)¹⁵.

2.2 Photoswitch properties

In the past decades researchers studied the above mentioned photoswitch families and aimed to tune their properties, such as the wavelength at which the isomerization occurs, the quantum efficiency, the relative amount of the two isomers in the equilibrium state, and the stability of the photogenerated form⁶. Based on the latter, photoswitches can be categorized into two families; there are P-type photoswitches, that require light at a different wavelength to go back to their initial form, and T-type photoswitches, which revert to their original state thermally¹³ (mostly even at room temperature). Thermal stability is essential for some applications, for example in data storage, where it is crucial to prevent data leakage¹⁶. However, in imaging for example, T-type switches can be useful¹⁷, because they can regenerate in the dark without external stimulus, so they become capable of functioning again (e.g. as photosensitive materials).

2.3 Dithienylethenes

Recent studies mainly focus on P-type photoswitches, and the most successful family in this group are the dithienylethenes¹⁰. Since their first discovery, a lot of their properties were successfully altered with different substituents, resulting in thermally stable, fatigue resistant photoswitches, that may even work with visible light instead of UV¹⁸. Another huge advantage of this family over others (e.g. azobenzenes) is that most of them work in solid state too because of the small conformational change that occurs during the photoreaction.

2.3.1 Conformation of dithienylethenes and its effect on photoswitching

To understand the photoswitching of dithienylethenes, we first have to take a look at the 3 main conformers which can be found in their solution (Figure 6):

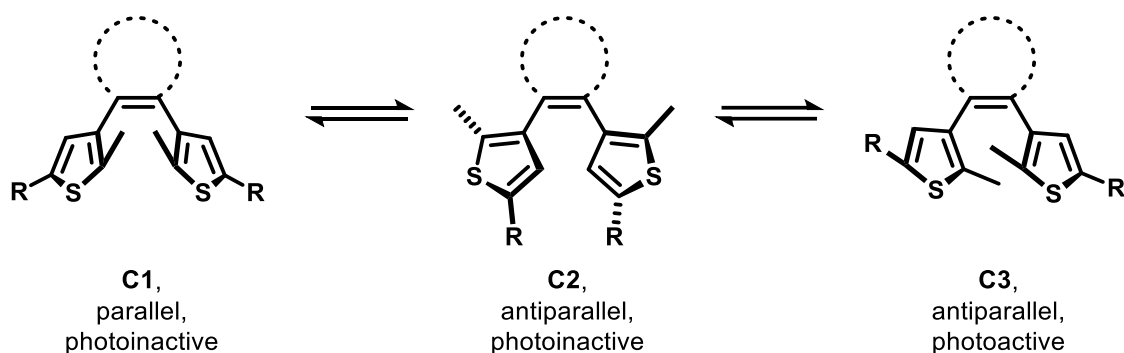


Figure 6. The equilibrium state conformers of dithienylethenes.

In the C1 conformation the two methyl groups are parallel, which means that the light activated ring closure would go in a disrotatory/suprafacial way. That is forbidden by the Woodward-Hoffman rules¹⁹, so this conformer is not photoactive. In the C2 conformer the electrocyclization can go in a conrotatory way, but by rotating the two methyl groups toward each other for the ring closure, we end up in C3, which is the conformation where the photoreaction can really happen. While in solution the interconversion of the conformers is possible²⁰, in rigid solid systems it is not the case²¹. Kobatake et al. found 4.2 Å as the maximum distance between the reactive carbon atoms where photoreaction can occur even in solid state²², so in case of a bigger distance (which is defined in this paper as C2 conformer) the molecule will be photoinactive just like the parallel C1 conformation.

Therefore, we can say, that only C3 is photoactive out of these conformers, where only a small rotation is needed for the ring closure. In solution this is not a problem, because the conformers can convert into each other with a low activation barrier, and luckily, dithienylethenes tend to crystallize in this C3 form in most of the cases, with only a few exceptions in the literature^{21,23}.

2.4 Dithienylbenzenes

Based on the advantages of dithienylethenes, similar T-type photoswitches would be of great importance. For this, dithienylbenzene photoswitches are promising alternatives, as they undergo a ring closure reaction similar to that of dithienylethenes, but the ethene moiety is part of an aromatic ring (Figure 7) and therefore these molecules are capable of an extremely rapid, spontaneous ring opening even at room temperature¹⁰.

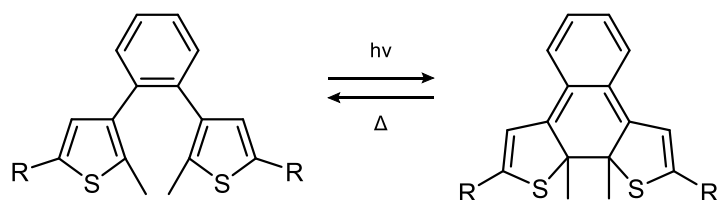


Figure 7. Photoswitching of dithienylbenzenes.

2.4.1 Conformation of dithienylbenzenes in the literature

For dithienylbenzenes the same 3 conformation exists (Figure 8) as for the dithienylethenes (Figure 6).

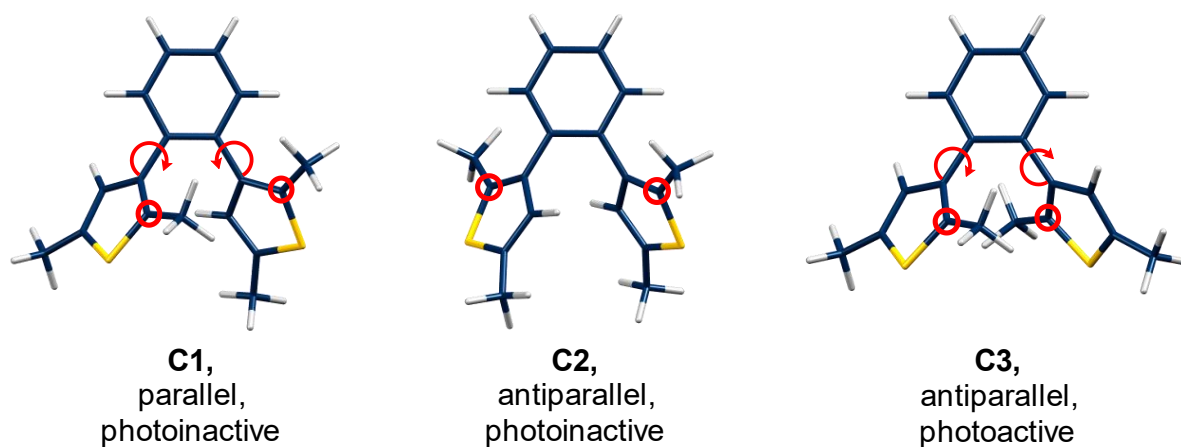


Figure 8. Conformation of dithienylbenzenes. The ring closure can happen through the circled carbon atoms, with a rotation indicated by the arrows.

As mentioned earlier, this conformational variety causes no problem in the case of dithienylethenes, as they tend to crystallize in the C3 form. However, this is not the case for dithienylbenzenes and other dithienylethene type structures, where the ethene moiety is part of a six-membered ring. During my literature search, for which I used spectroscopic (CSD) and literature databases (Reaxys and Scifinder), I found 32 of these molecules that were synthesized and crystallized until now^{10,24–44} (Figure 9, Figure 10, Figure 11, Figure 12).

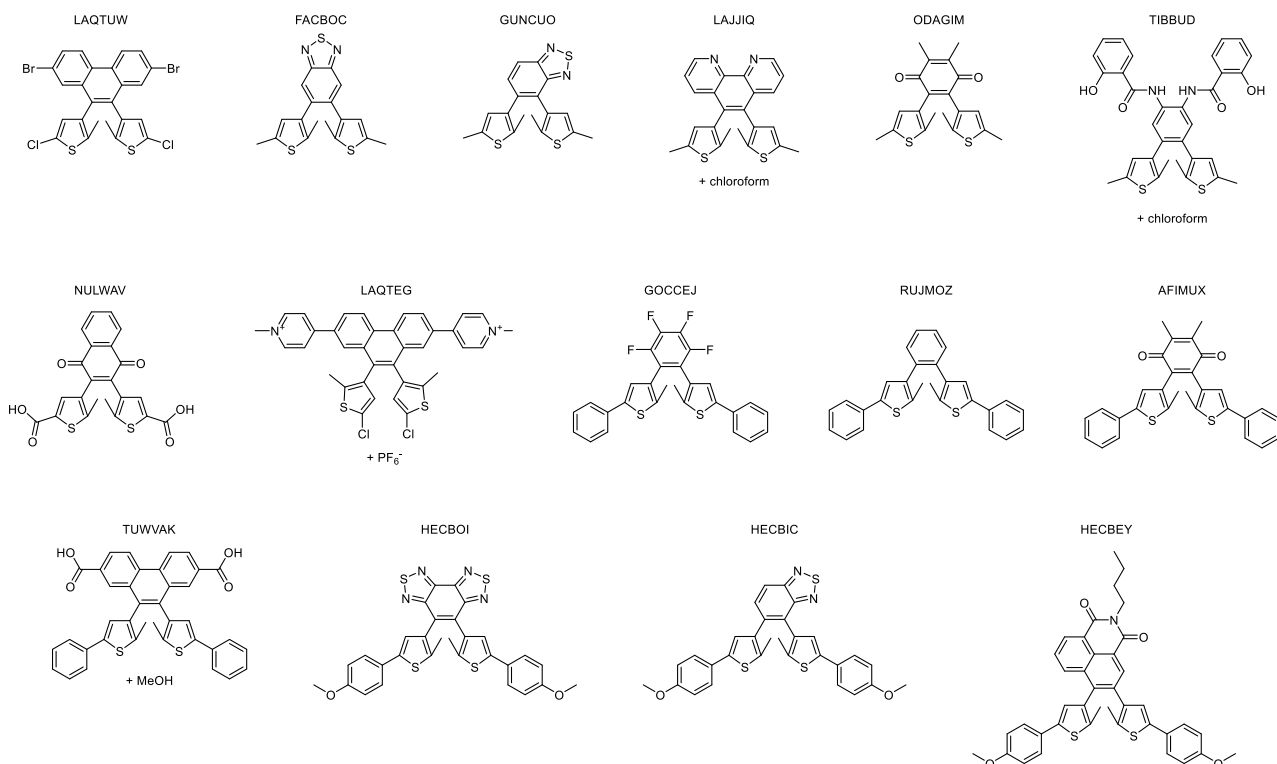


Figure 9. Molecules with C1 type parallel crystal structures, with the corresponding CCDC database identifiers written above^{10,24–36}.

As can be seen, 15 derivatives crystallized in the parallel form. Out of these, NULWAV (Figure 9) crystallized together with NUMBIJ³² (Figure 12), which is the same molecule but in a photoswitchable antiparallel form. Another important note is that while GOCCEJ¹⁰ (Figure 9) is photoinactive in its crystal form, when it was implemented in a polymer gel, that provides some conformational freedom for the molecules, photoswitching could be observed. TUWVAK³⁶ (Figure 9) was also modified to be photoactive by integrating it into a MOF structure, where the photoswitch happened to crystallize in the active antiparallel form.

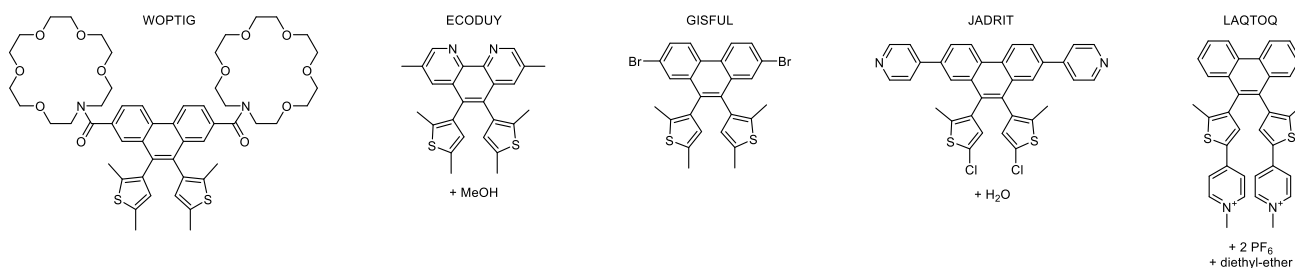


Figure 10. Molecules with C2 type antiparallel crystal structures, with the corresponding CCDC database identifiers written above^{24,37–40}.

In the literature C2 type crystal structures can also be found, that are usually photoinactive. However, JADRIT⁴⁰ (Figure 10) is photoactive in the crystal form, despite the larger than 4.2 Å bond distance, making it the only known exception in this category.

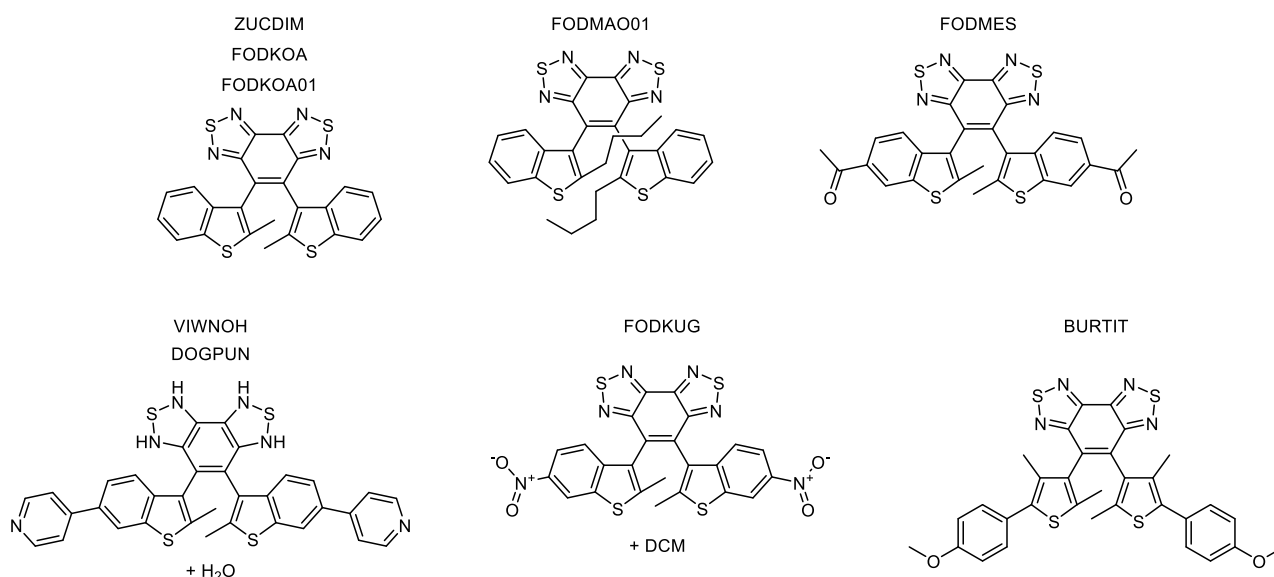


Figure 11. Molecules with C3 type antiparallel crystal structures with sterically hindered rotation, with the corresponding CCDC database identifiers written above^{26,27,29,41}.

Above (Figure 11) I collected those structures that were specifically designed to overcome the conformational challenges, by making the rotation of the thienyl groups sterically hindered. These attempts were successful, the molecules crystallized in a C3 type antiparallel structure, however the rotation was so limited in these cases, that the ring closure could not proceed as expected. Therefore only 6 structures remained, that are photoactive in their pure crystal forms (Figure 12).

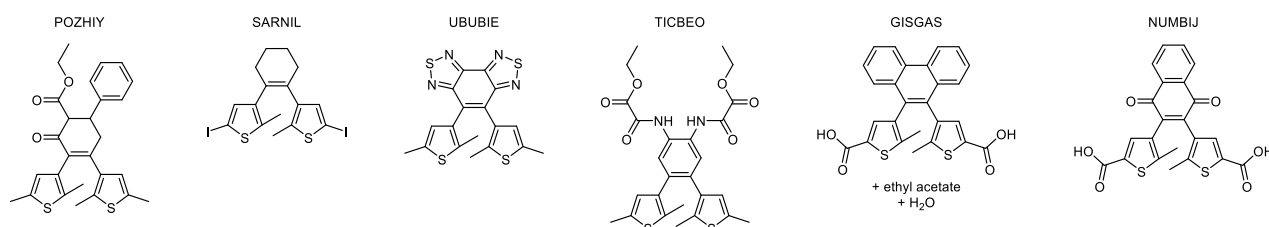


Figure 12. Molecules with C3 type photoactive antiparallel crystal structures, with the corresponding CCDC database identifiers written above^{32,35,39,42–44}.

2.5 Virtual screening of potential photoswitches with conformational analysis

There is no study until now that could give an answer to the conformational differences between dithienylethenes and dithienylbenzenes and there is no visible correlation between the substituents on these photoswitches and their crystal structure⁴⁵. Therefore more and more dithienylbenzenes are synthesized only to be found ineffective as solid-state photoswitches. To prevent such cases, I tried to develop a theoretical method during my BSc studies⁴⁶, and searched for photoswitches, that are more likely to crystallize in the photoactive form when synthesized.

For this virtual screening, I performed calculations on molecule **1** and its substituted derivatives (Figure 13). An important property of these photoswitches, that they contain a pyridine linker group, so if they are synthesized and they turn out to be in the wrong conformation in solid state, they can still be integrated into various solid-state structures (such as MOFs), and that may alter their structure and therefore their switching properties.

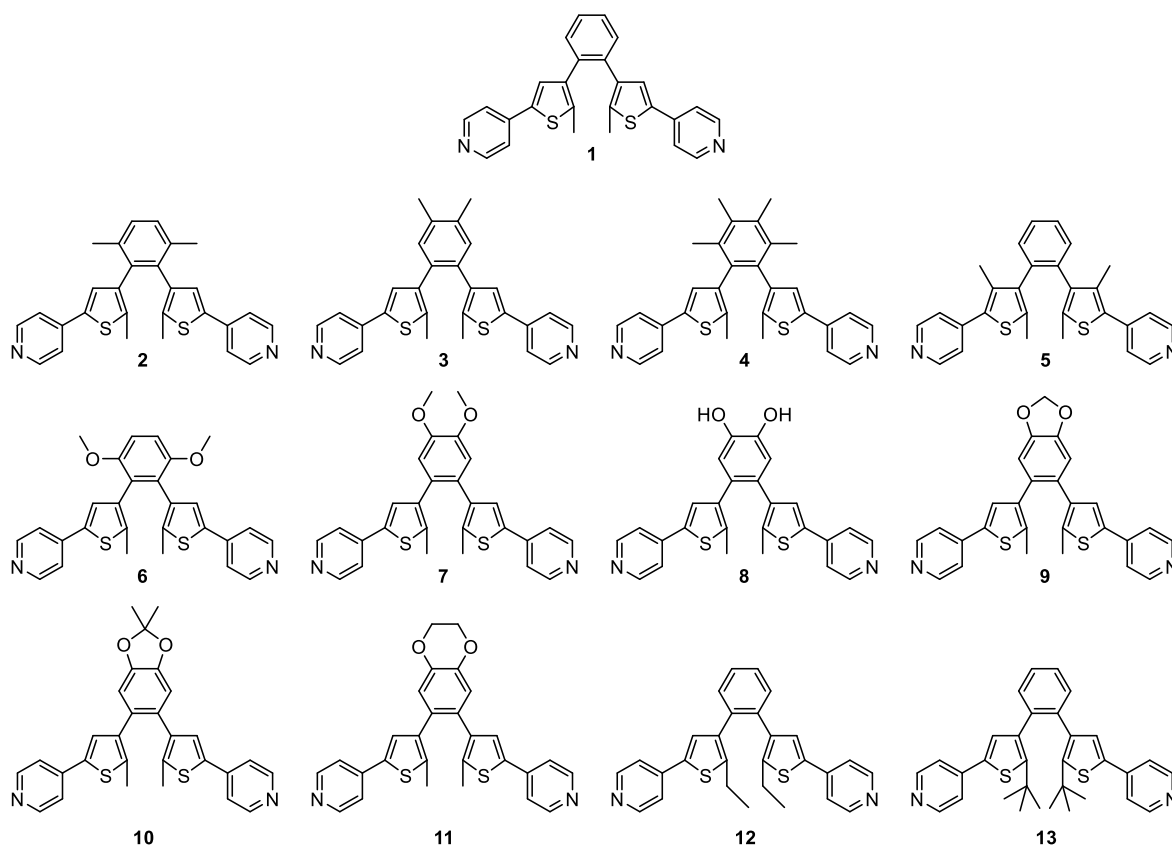


Figure 13. Substituted derivatives of the photoswitch **1** for the virtual screening.

The three main conformers (Figure 14) of these molecules were drawn in 3D with Avogadro. After that, I optimized the geometries with the GFN2-xTB⁴⁷ method, then at DFT level with ORCA and the B97-3c⁴⁸ method using the cpcm solvent model (and DCM or DMF as solvents).

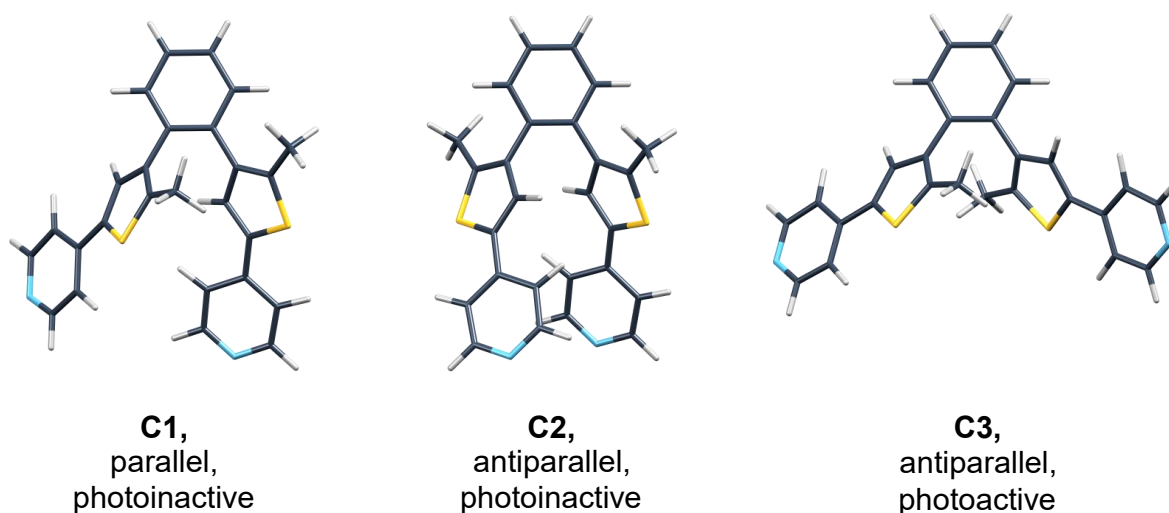


Figure 14. The geometry optimized conformations of photoswitch **1** (B97-3c method and DCM solvent model were used).

The acquired data contained Gibbs free energy values, that can be decomposed into the following terms with the use of equations E1-E3:

$$\mathbf{E1: } G = H - TS$$

$$\mathbf{E2: } H = U_e + U_v + U_r + U_t + RT$$

$$\mathbf{E3: } S = S_e + S_v + S_r + S_t + R$$

From the optimized structures the electronic energy ($\sim U_e$, E2) was recalculated using a higher level method, B97M-V/def2-TZVPP⁴⁹, and I acquired more accurate Gibbs free energy values for the conformers this way.

From these, I determined the ΔG values relative to the lowest energy conformer, then I estimated the ratio of the conformers with the use of the Boltzmann-distribution (E4):

$$\mathbf{E4: } p_i = \frac{e^{-\Delta G_{Ci} / kT}}{\sum_{i=1}^n e^{-\Delta G_{Ci} / kT}}$$

In the formula, p_i is the conformer ratio, ΔG_{Ci} is the Gibbs free energy difference between the C_i ($i = 1, 2$ or 3) conformer (Figure 14) and the lowest energy conformer, k is the Boltzmann constant, T is the temperature (298.15 K in the calculations) and n is the number of conformers. In reality, the

latter can be more than 3, but to build up a qualitative picture of the conformers present in solution, I took only the optimized structures of the three main conformations.

The calculations showed that the energy differences between the conformers are not significant, as in the vast majority of cases 0-1 kcal/mol ΔG values were obtained (Table 1-2), and this is likely to be outweighed by other forces during crystallization and is also within the margin of error of the method. The data also shows that the effect of solvent exchange is not significant in this case of virtual screening.

Molecule number	ΔG_{C1} (kcal/mol)	ΔG_{C2} (kcal/mol)	ΔG_{C3} (kcal/mol)	Molecule number	ΔG_{C1} (kcal/mol)	ΔG_{C2} (kcal/mol)	ΔG_{C3} (kcal/mol)
1	0	0.5	0.2	8	0	0.5	0.1
2	0.7	0	1.1	9	0.1	0.3	0
3	0	0.4	0.2	10	0.4	1	0
4	0.7	0.3	0	11	0	0.5	0.2
5	0.3	0	0.7	12	0.6	0.9	0
6	0.6	0	1	13	2.2	0.3	0
7	0	0.3	0.1				

Table 1. ΔG_{Ci} values of the substituted derivatives of **1** in DCM.

Molecule number	ΔG_{C1} (kcal/mol)	ΔG_{C2} (kcal/mol)	ΔG_{C3} (kcal/mol)	Molecule number	ΔG_{C1} (kcal/mol)	ΔG_{C2} (kcal/mol)	ΔG_{C3} (kcal/mol)
1	0	0.5	0.2	8	0.2	0	0.5
2	0.3	0	1	9	0	0.1	0.3
3	0	0.4	0.2	10	0	0.3	0.9
4	0.7	0.3	0	11	0.3	0	0.5
5	0.3	0	0.6	12	0	0.6	0.8
6	3.2	0	0.8	13	0	2.1	0.3
7	0	0.3	0				

Table 2. ΔG_{Ci} values of the substituted derivatives of **1** in DMF.

Seeing these results, I made a second round of virtual screening, where I was interested in the effect of substituents, that may have a bigger steric or electronic effect (Figure 15), and therefore result in bigger energy differences between the conformers.

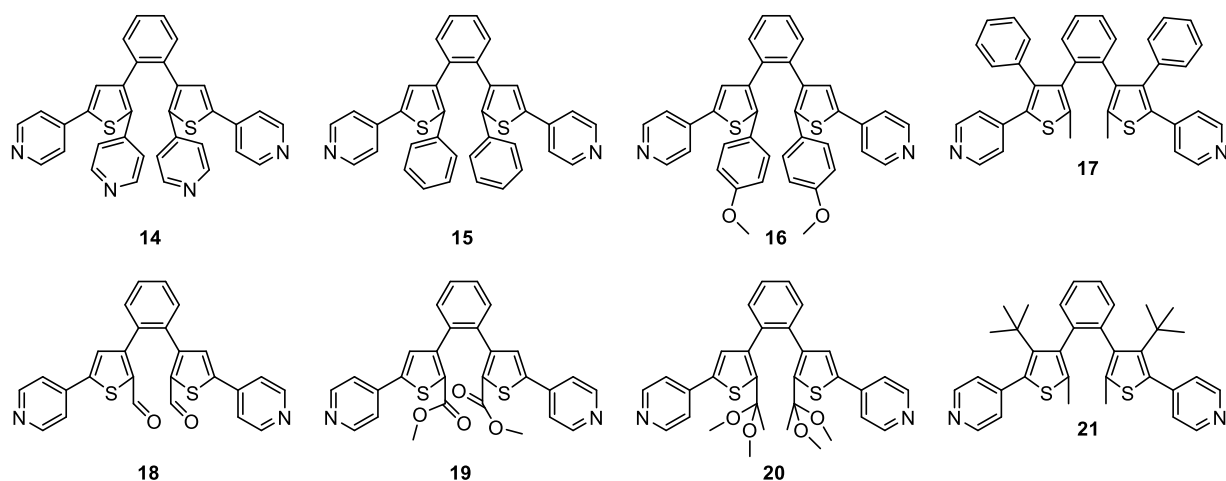


Figure 15. Substituted derivatives of photoswitch **1** in the second round of the virtual screening.

In this case, the acquired data is presented in Table 3:

Molecule number	ΔG_{C1} (kcal/mol)	ΔG_{C2} (kcal/mol)	ΔG_{C3} (kcal/mol)	P_{C1}	P_{C2}	P_{C3}
14	3,9	5,5	0	0%	0%	100%
15	3,9	5,7	0	0%	0%	100%
16	5,2	7,6	0	0%	0%	100%
17	1,7	0	4,6	5%	95%	0%
18	2,2	0,3	0	2%	36%	62%
19	2,9	2,2	0	1%	2%	97%
20	3,8	0	4,1	0%	100%	0%
21	2,4	0	3,8	2%	98%	0%

Table 3. ΔG_{Ci} values and the conformer ratios of the substituted derivatives of **1** in DCM from the second round of virtual screening.

As can be seen, molecules number **14**, **15**, **16** and **19** gave promising results. Apparently, by incorporating aromatic or strong electron withdrawing substituents to the reactive carbon atom, big energy differences can be obtained between the photoinactive and photoactive conformers, and therefore there may be a bigger chance to obtain crystals that are photoswitchable. However, the effect of the proposed, substantial structural modifications on the photoswitching properties are unknown (there are no such molecules in the literature, that have an aromatic substituent on the reactive carbon atom). Therefore in my lab work, I rather attempted to obtain photoswitches that are relatively easy to synthesize, and tried to tune their conformational properties by integrating them into various solid-state structures.

3. Goals

The aim of my research was to get a better understanding on the photoswitching properties of dithienylbenzenes and find such structures, that are capable of an ultrafast photoreaction even in solid-state.

For this, I wanted to study differently substituted dithienylbenzene photoswitches that contain pyridine, so they have the potential to be methylated or integrated into MOFs and other solid-state structures. The photoreaction occurs, if these molecules are irradiated with UV light, as they form a ring through an electrocyclization reaction (Figure 16).

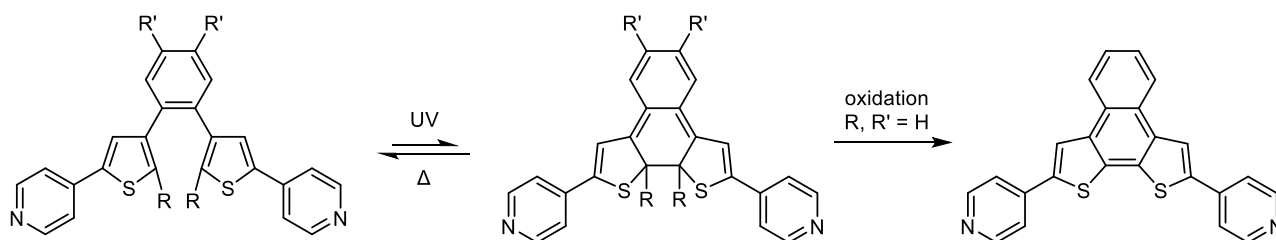


Figure 16. Reactivity of the photoswitches to be synthesized.

The first two photoswitch to be synthesized contains H at the R' position, and depending on the substituent on the reactive carbon atoms, the transformation is reversible ($R=CH_3$) or irreversible ($R=H$). I wanted to investigate both, as the former is more important for applications, but for the latter it is easier to detect the photoreaction. Other than that, I planned to synthesize a substituted derivative of the reversible photoswitch as well (where $R = CH_3$ and $R' = OMe$) and investigate the effect of the substituent on the photoswitching and conformation.

Besides these, I also planned to integrate the molecules into various solid phases and get information of their structure, and therefore the photoswitching.

4. Results and discussion

4.1 Synthesis of the photoswitches

The total synthesis of the photoswitches below have not yet been reported in the literature, but the preparation of dithienylethene photoswitches containing a pyridine linker have been described⁵⁰. The four-step synthesis design was partly based on this and on the experience in my research group for synthesizing similar molecules. Some of the molecules and synthetic steps here were mentioned in my BSc work⁴⁶ as well, but I resynthesized these molecules multiple times since then and made some modifications, therefore I show here my latest results.

4.1.1 Synthesis of the reversible photoswitch (1)

The synthetic steps for 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene are shown in Figure 17:

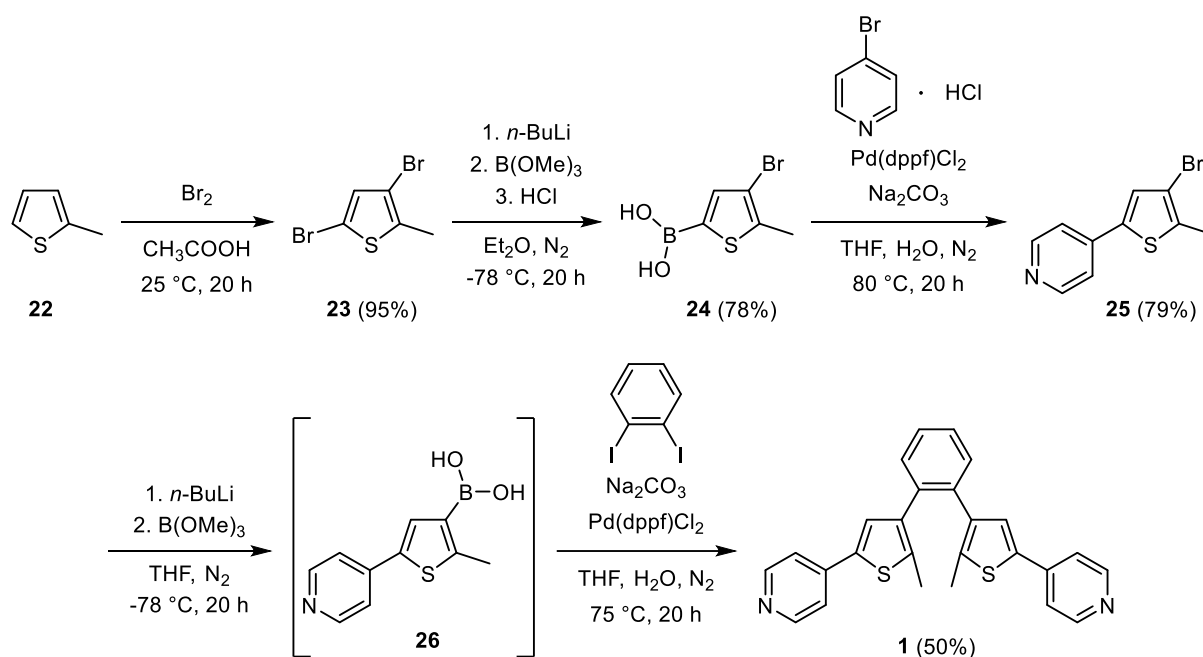


Figure 17. Synthesis of the reversible photoswitch (1).

As can be seen, I started the synthesis with 2-methylthiophene (**22**), which I dissolved in glacial acetic acid, then brominated with elemental bromine. The resulting hydrogen bromide, which is a highly toxic and corrosive gas, was introduced into a NaOH-filled degassing flask using a nitrogen stream. After 3 hours, the reaction progress was monitored by GC-MS, but as the percentage of the monosubstituted product was still high, the reaction was stirred overnight. Afterwards, the GC-MS measurement showed that I had only a negligible amount of the monosubstituted species left. After extraction I got the product (**23**) with an excellent yield of 95 %.

In the next step, I aimed to make a boronic acid (**24**), which is required for the following Suzuki cross-coupling reaction. The preparation of **24** was carried out under anhydrous conditions in freshly distilled ether under nitrogen atmosphere, cooling the flask with dry ice-acetone mixture. The bromine on the fifth carbon of the dibromo derivative (**23**) was first replaced by Li using n-BuLi, which then reacted with trimethyl borate to give the boronic acid ester. Hydrochloric acid was added to the reaction mixture to hydrolyze the boronic acid ester and the resulting boronic acid was separated from the other organic byproducts by an extraction with base. The precipitate was filtered off from the aqueous phase by lowering the pH to give the pure product (**24**) with a yield of 78%.

The Suzuki cross-coupling reaction between **24** and 4-bromopyridine hydrochloride was carried out using Pd(dppf)Cl₂ as catalyst and Na₂CO₃ as base. For the reaction I used abs. THF and the reaction mixture was refluxed under inert conditions to give the desired product (**25**), which was separated from the byproducts (e.g. dehalogenated and homocoupled derivatives) on a chromatographic column.

The photoswitch (**1**) was then prepared from compound **25** by using a one-pot procedure. A Vigreux column was placed on the flask, the system was flushed with N₂, and the solution of the starting material (**25**) was cooled to -78 °C. First n-BuLi, then 30 minutes later trimethyl borate were added dropwise and the reaction mixture was stirred overnight at room temperature. The reagents required for Suzuki coupling (1,2-diiodobenzene, Pd(dppf)Cl₂, Na₂CO₃) were then added to the mixture and it was stirred at 75 °C for 24 hours. After workup, purification was carried out by gradient elution with DCM/methanol, but the product still contained impurities, so I also used a reverse phase column with acetonitrile/water eluent to give the pure product (**1**) in 50% yield. The structure of the product was determined by NMR (Figure 18, Figure 19) and HRMS (Figure 20) measurements.

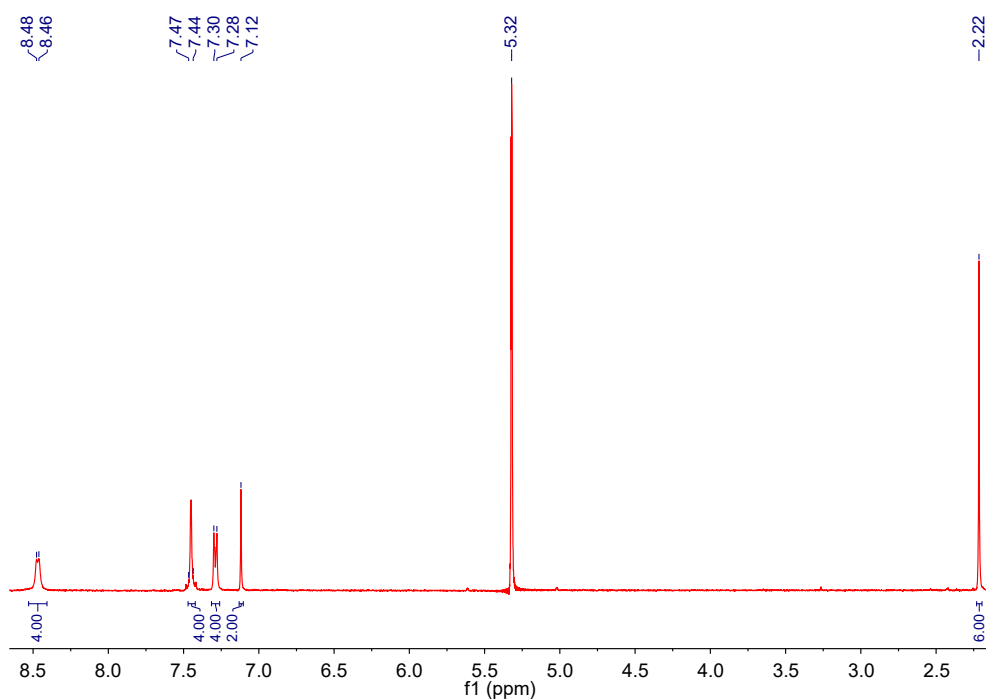


Figure 18. The ^1H NMR (300 MHz, CD_2Cl_2) spectrum of the reversible photoswitch (**1**).

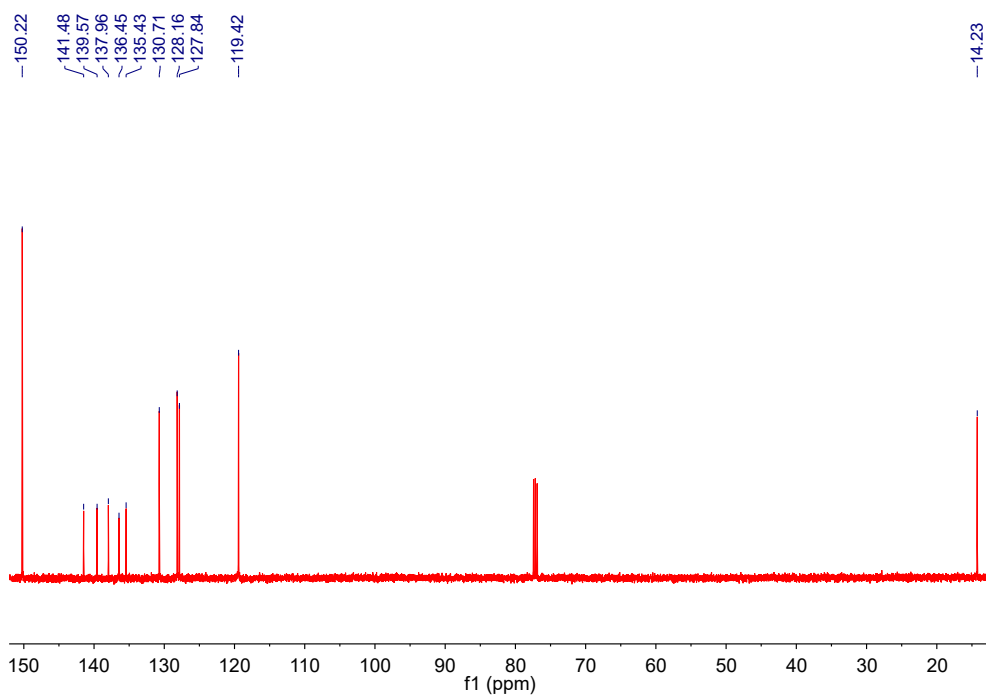


Figure 19. The ^{13}C NMR (126 MHz, CDCl_3) spectrum of the reversible photoswitch (**1**).

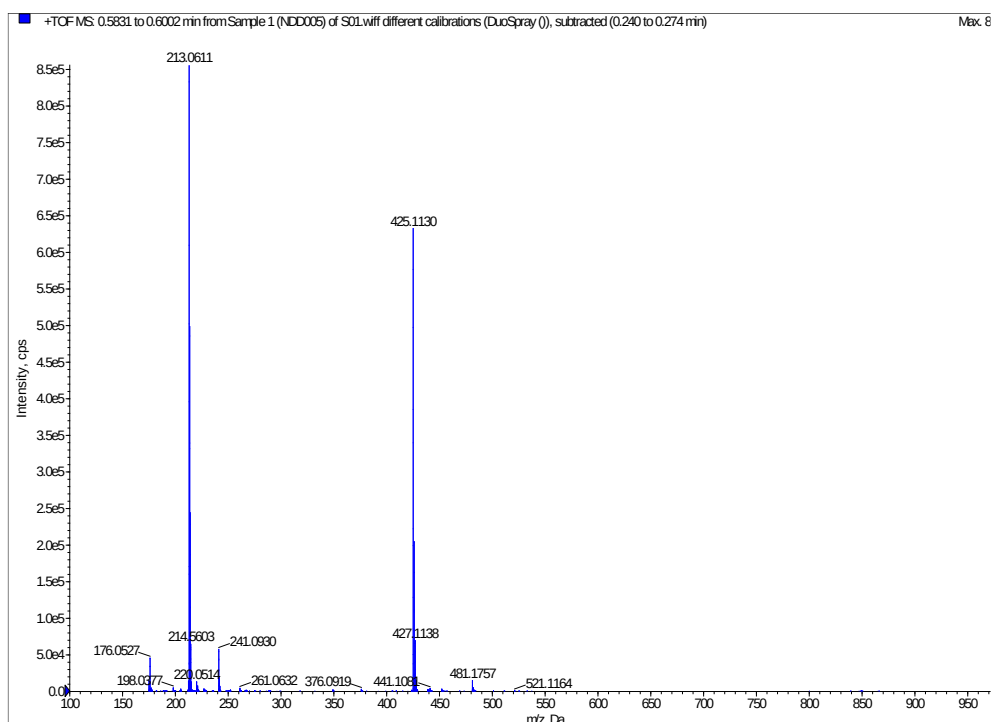


Figure 20. The HRMS spectrum of the reversible photoswitch (**1**).

4.1.2 Synthesis of the irreversible photoswitch (**31**)

The irreversible photoswitch can be produced as described above (Figure 17) with small modifications (Figure 21, Figure 22).

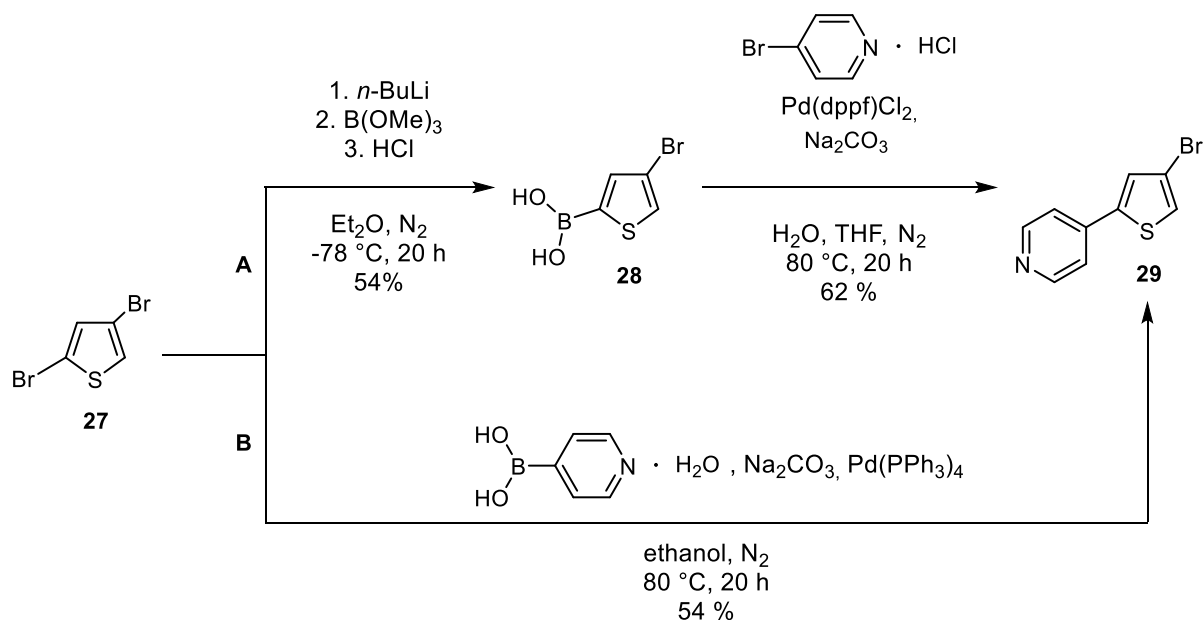


Figure 21. Synthetic approaches to 4-(4-bromothiophen-2-yl)pyridine (**29**).

I did not attempt the preparation of 2,4-dibromothiophene (**27**), as the syntheses found in the literature were much more complicated than for 3,5-dibromo-2-methylthiophene (**23**), because bromination of thiophene leads to the formation of byproducts (2,3-dibromothiophene⁵¹, 3,4-dibromothiophene⁵², 2,3,5-tribromothiophene⁵³). Fortunately, 2,4-dibromothiophene was commercially available, so I used it as starting material. The preparation of 4-(4-bromothiophen-2-yl)-pyridine (**29**) was first carried out in two steps (Figure 21, route **A**), similar to the synthesis of molecule **25** (Figure 17). The reactions in the synthesis of **29** also gave the expected product, but the yields were lower (54% for **28**, 62% for **29**) compared to the analog syntheses of compound **24** (78%) and **25** (79%). Our main goal in the lab work was not to optimize the individual steps, but to get to the product as fast as possible, but here I tried an alternative one-step synthesis, where I mixed 2,4-dibromothiophene (**27**) with 4-pyridinylboronic acid and optimized the conditions by testing different bases (K_2CO_3 , Na_2CO_3 , Cs_2CO_3) as well as two solvents (THF and ethanol). In the end I achieved a yield of 54 % in the one-step procedure by using the combination of Na_2CO_3 and ethanol (Figure 21, route **B**).

The final product **31** was prepared by a two step process (Figure 22), as the one-pot procedure what was used for the reversible photoswitch (**1**) resulted in even lower yield in this case.

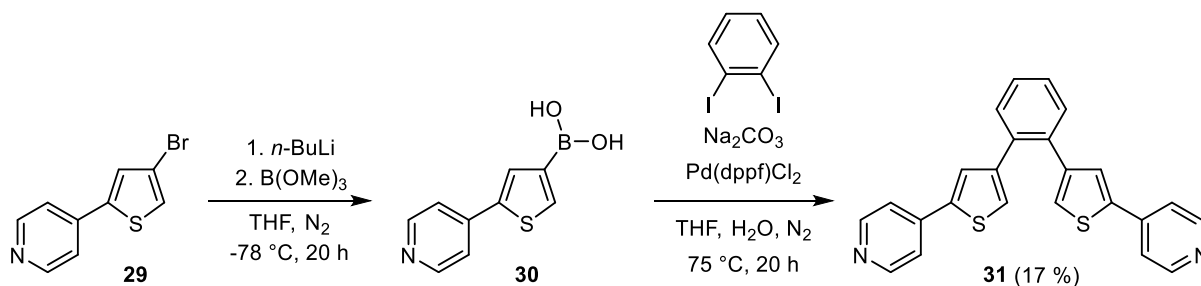


Figure 22. Last steps in the synthesis of the irreversible photoswitch (**31**).

The structure of **31** was confirmed by NMR (Figure 23, Figure 24) and HRMS (Figure 25) measurements.

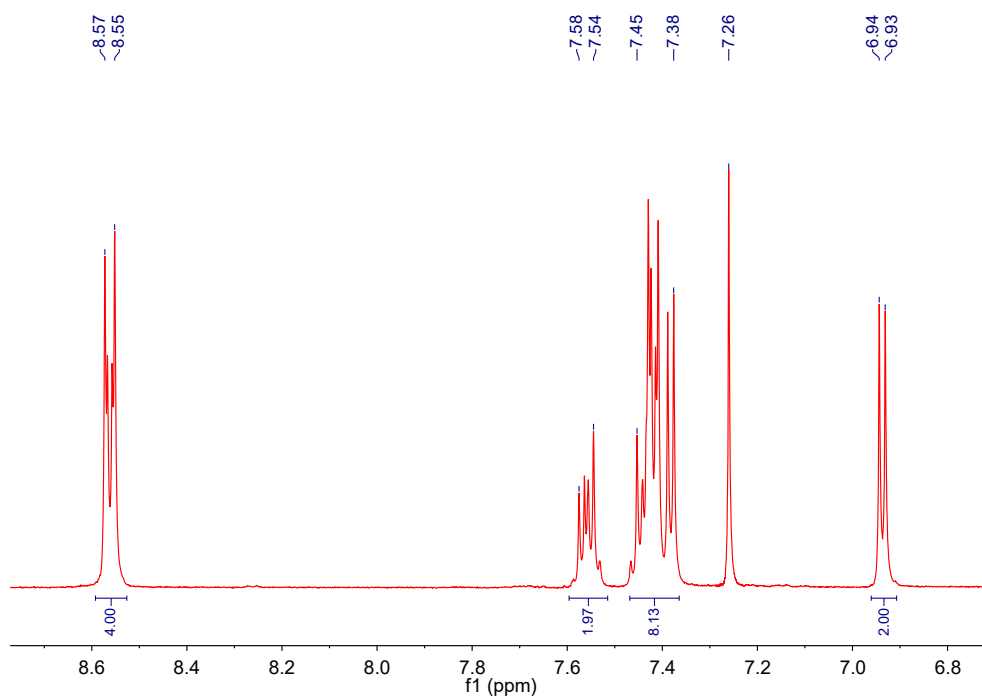


Figure 23. The ¹H NMR (300 MHz, CD₂Cl₂) spectrum of the irreversible photoswitch (**31**).

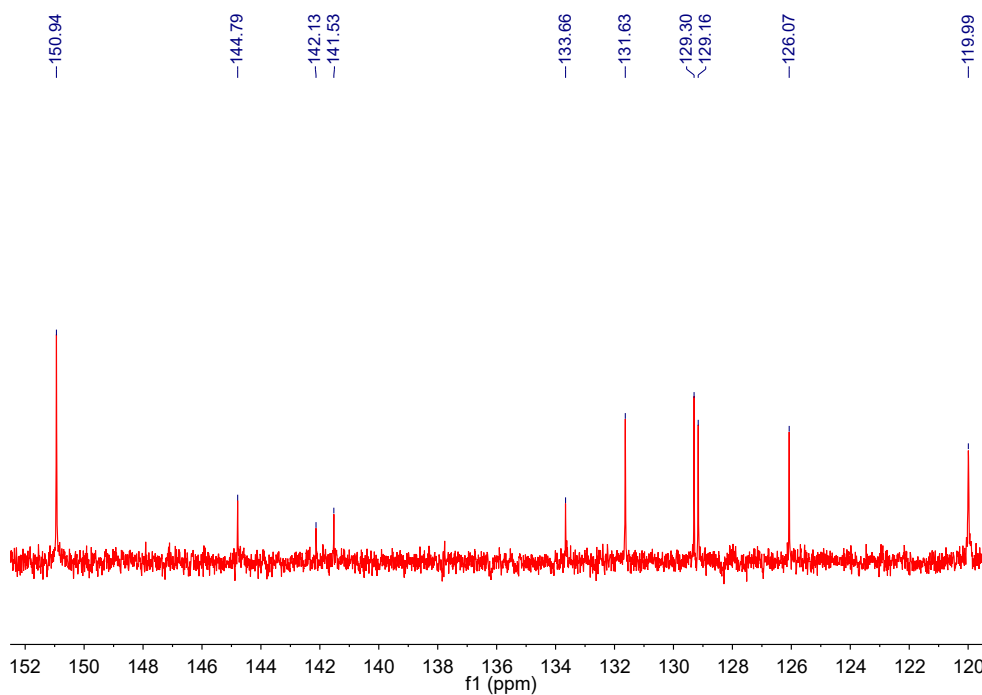


Figure 24. The ¹³C NMR (126 MHz, CDCl₃) spectrum of the irreversible photoswitch (**31**).

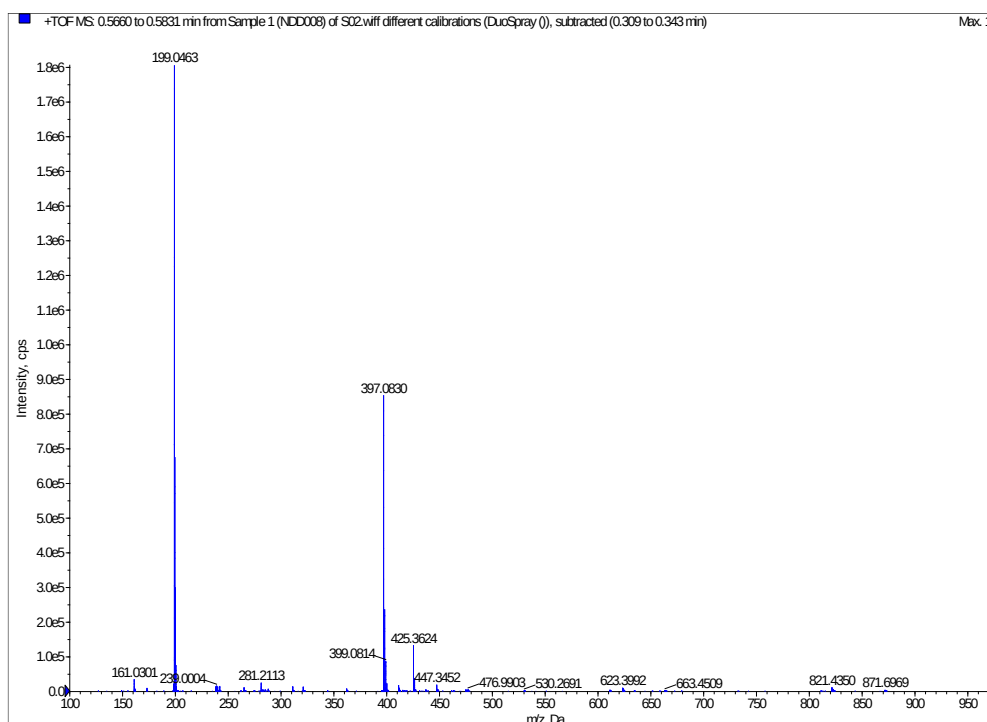


Figure 25. The HRMS spectrum of the irreversible photoswitch (**31**).

4.1.3 Synthesis of the modified reversible photoswitch (**7**)

To investigate the effect of a substituent, I synthesized **7** (Figure 26) using the key intermediate **25** from the synthesis of the reversible photoswitch **1** (Figure 17):

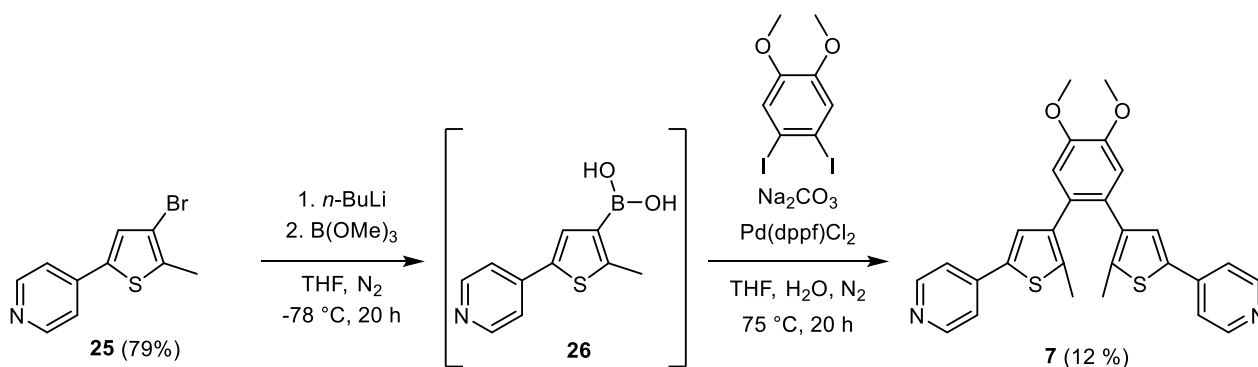


Figure 26. Last steps in the synthesis of the modified reversible photoswitch (**7**).

The crude product was purified by gradient elution with hexane (+ 0.5% TEA) / EtOAc (+ 0.5 % TEA), and the pure product was acquired in 12 % yield. The structure of **7** was confirmed by NMR (Figure 27, Figure 28) and HRMS (Figure 29) measurements.

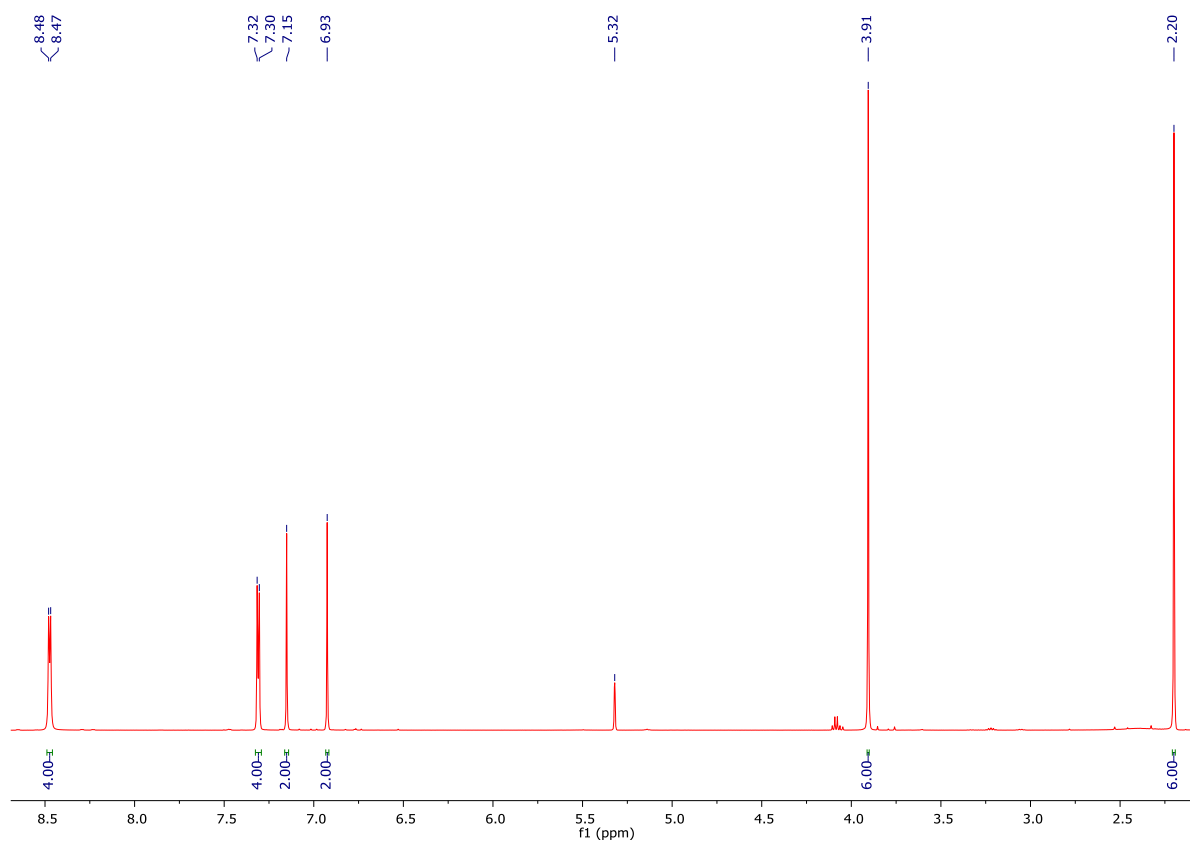


Figure 27. The ¹H NMR (500 MHz, CD₂Cl₂) spectrum of the modified reversible photoswitch (7).

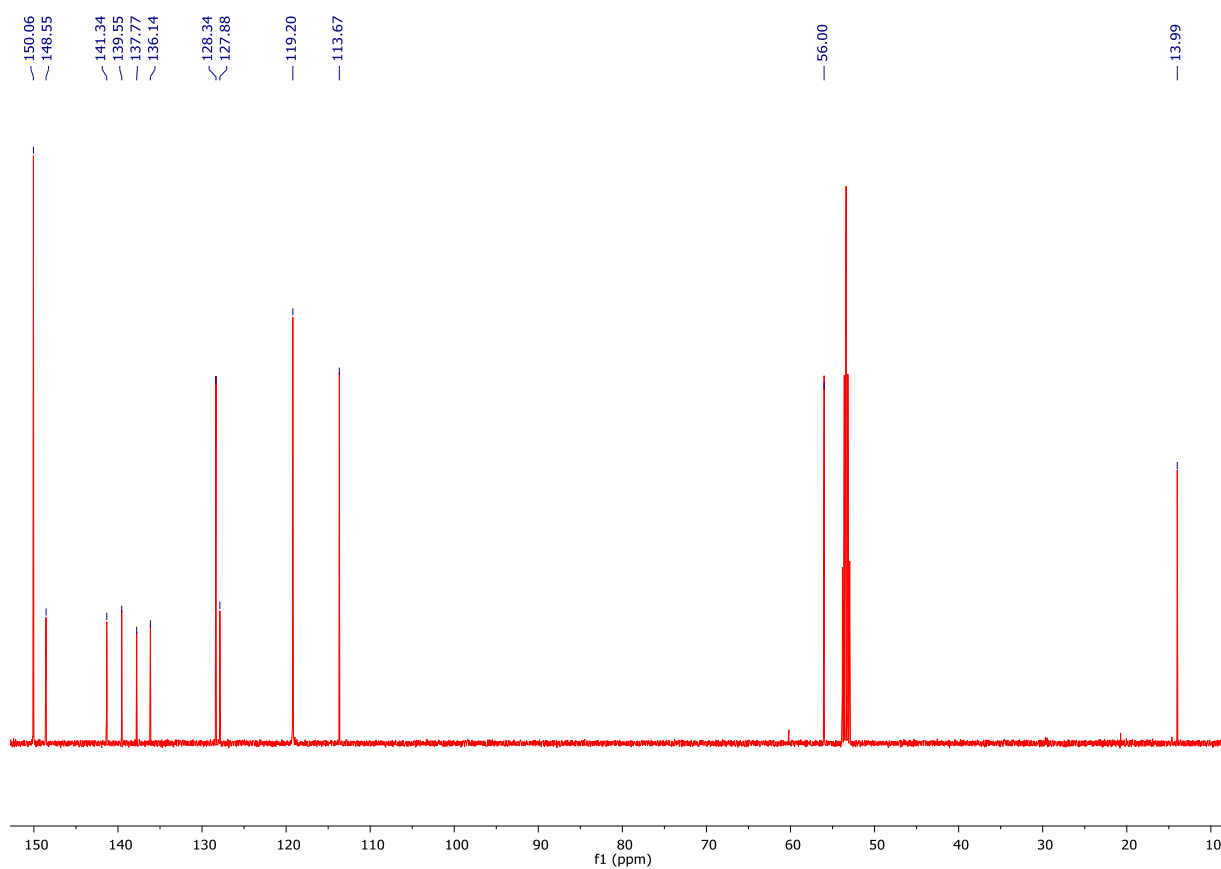


Figure 28. The ¹³C NMR (500 MHz, CD₂Cl₂) spectrum of the modified reversible photoswitch (7).

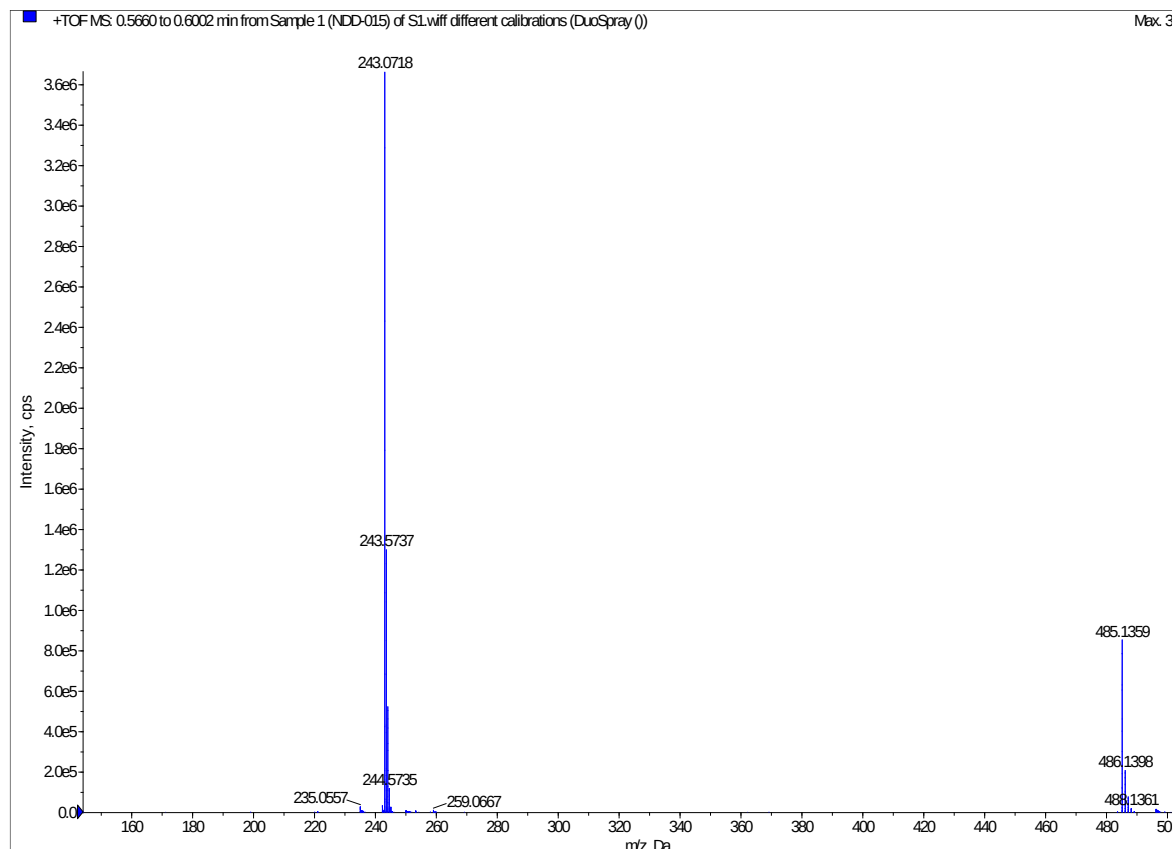


Figure 29. The HRMS spectrum of the modified reversible photoswitch (7).

4.2 Photochemical measurements

The photoswitching properties of the prepared molecules were investigated by UV-Vis spectrophotometry. The pure products were dissolved in a spectroscopic grade solvent and diluted until a solution of $\sim 10^{-5}$ M was obtained. The solutions were loaded into quartz cuvettes and purged with argon before measurement. For the irradiations I used the biggest wavelength, where there is still significant absorption of the open form, as this way the possible photodegradation can be minimized, while a sufficient photoswitching can still take place.

4.2.1 Photoswitching of the reversible photoswitch (1) in solution

The spectrum of the reversible photoswitch (1) and its change upon light irradiation in room temperature is shown in Figure 30:

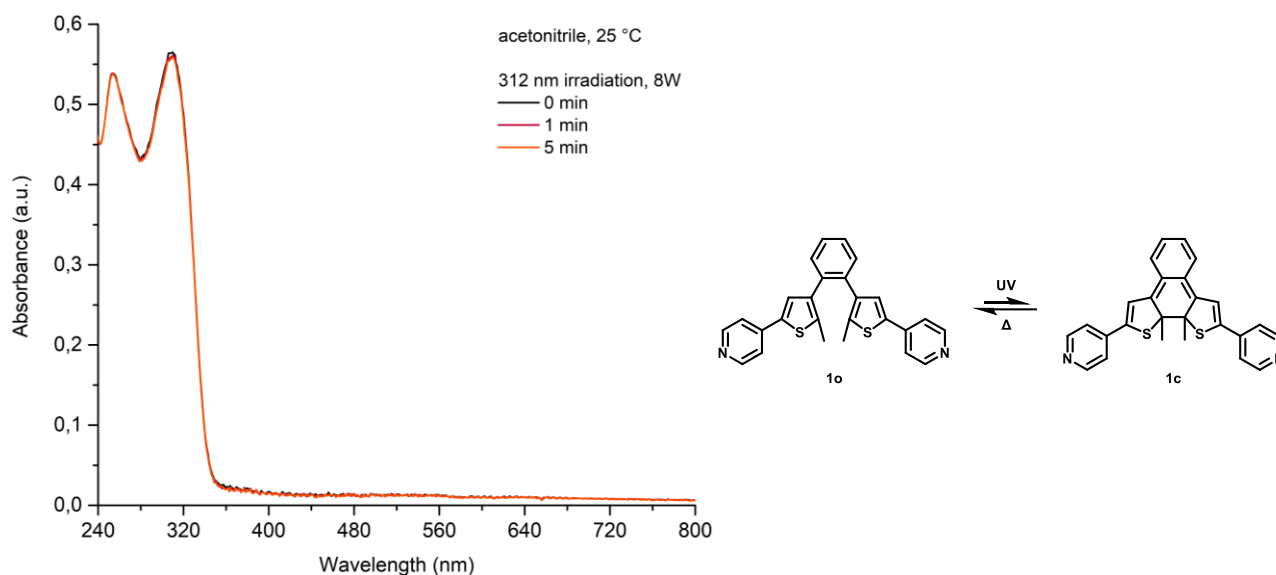


Figure 30. Changes in UV-Vis absorption spectrum of the reversible photoswitch (**1**) upon irradiation at 25 °C. At this temperature, there is no change in the spectrum, presumably due to the ultrafast cycloreversion of **1c** to **1o**.

From the results, we could not conclude that this molecule is a photoswitch, as we don't see a change in the spectrum even after 5 minutes of irradiation. However, if we cool down the solution to -60 °C, we can see that new absorption bands appear (Figure 31), that indicate a structural change upon irradiation.

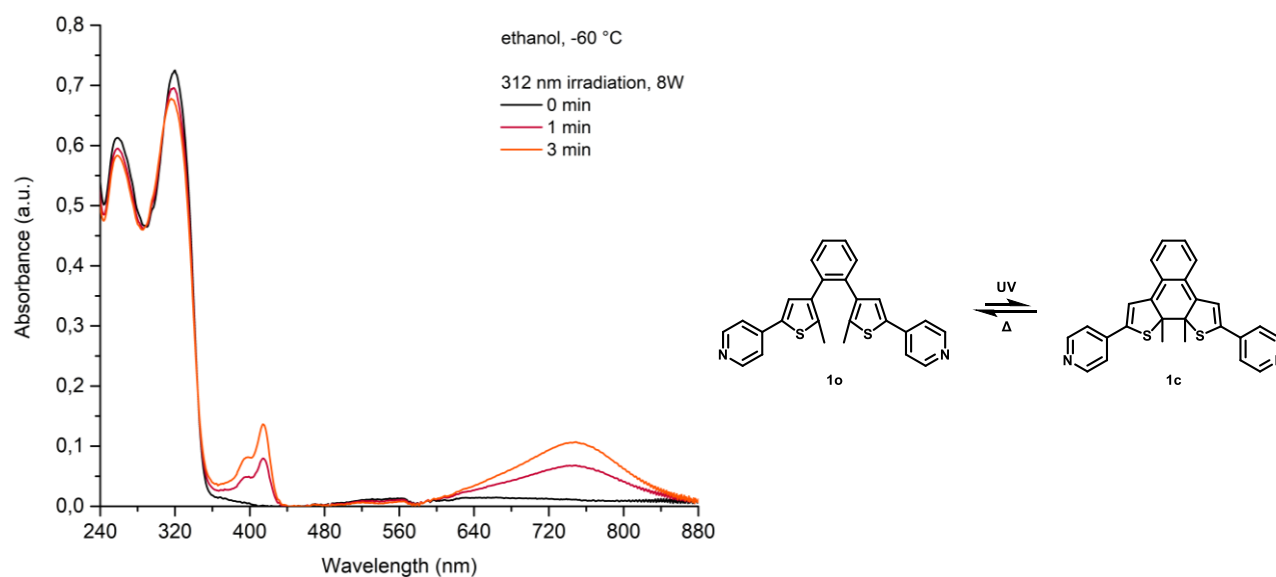


Figure 31. Changes in UV-Vis absorption spectrum of the reversible photoswitch (**1**) upon irradiation at -60 °C. At this temperature, we can see new absorption bands appear, because of the electrocyclic of **1o** to **1c**.

Based on this it is suggested that photoswitching occurs at room temperature as well, but the rate of the thermal ring-opening does not allow the detection of the closed form in solution under the measurement conditions. I also made measurements at -80 and -100 °C, where the closed form can

be generated as well, but it is so stable, that it doesn't convert back to the open form even after 10 minutes of waiting.

4.2.2 Photoswitching of the irreversible photoswitch (31) in solution

The spectrum of the irreversible photoswitch (**31**) and its change upon light irradiation is shown in Figure 32:

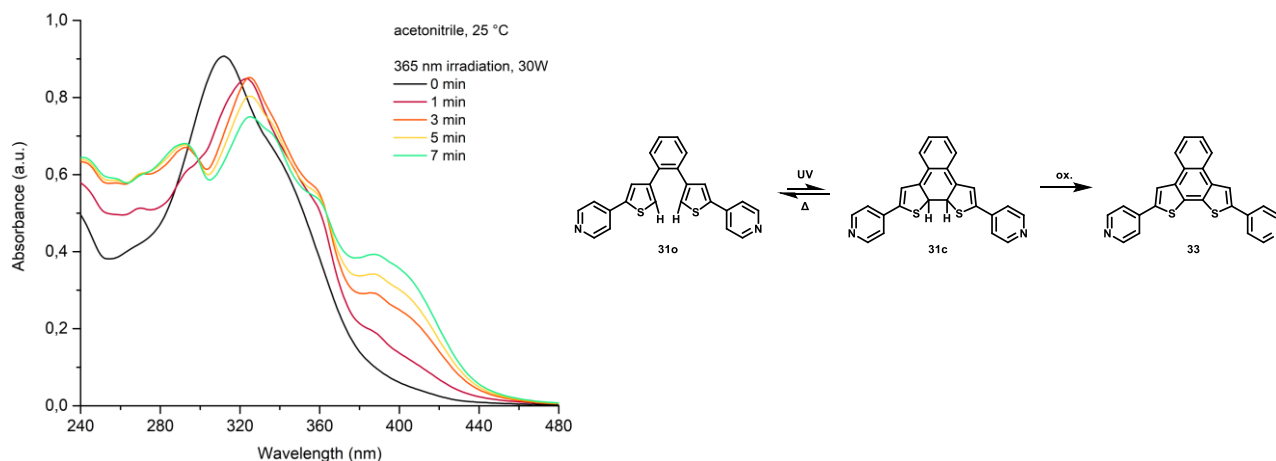


Figure 32. Changes in the UV-Vis spectrum of the irreversible photoswitch (**31**) upon irradiation. The new absorption bands are presumably due to the presence of **33**, because the photoswitching was irreversible in this case.

The results show that after only 1 minute of exposure to 365 nm light, new absorption bands appeared in the spectrum in both the UV and visible regions. After irradiating the solution for a longer period, the intensity of the new bands increased even further, but this process could not be reversed by stopping the irradiation or with visible light. The results of the measurements therefore suggest that the molecule is capable of photochemical transformation, but that this process is irreversible, presumably due to the oxidation of the closed form to a stable, non-photoactive product⁹ (Figure 16).

4.2.3 Photoswitching of the modified reversible photoswitch (7) in solution

The spectrum of the modified reversible photoswitch (**7**) and its change upon light irradiation is shown in Figure 33:

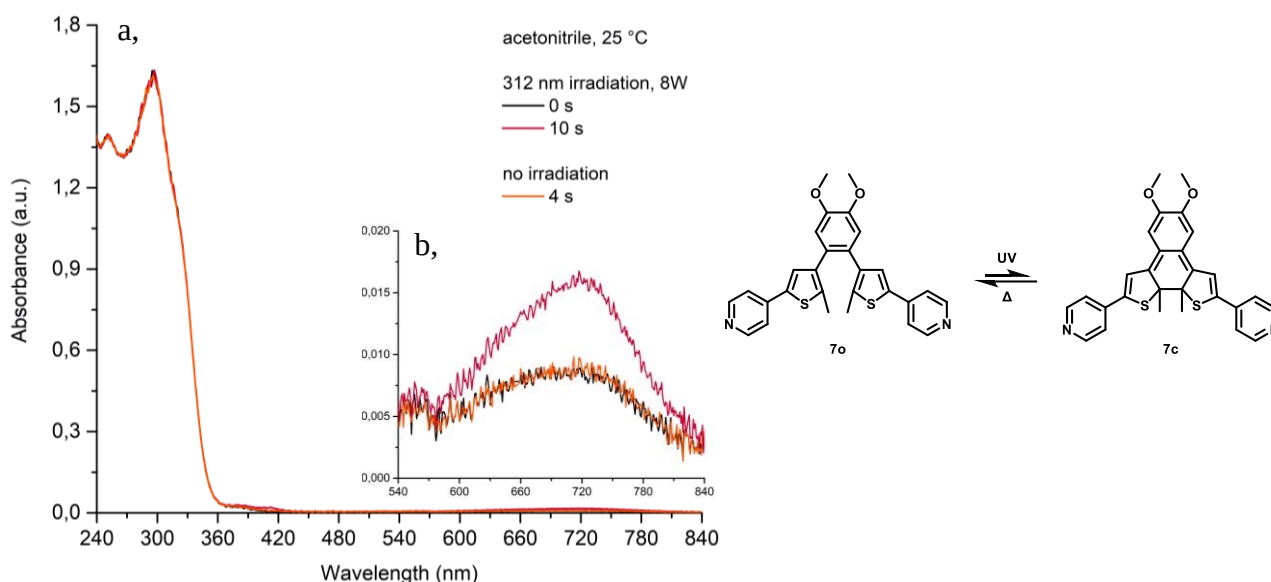


Figure 33. Changes in the UV-Vis spectrum of the modified reversible photoswitch (7) upon irradiation. a, shows the whole spectrum while b, is zoomed into where the new absorption band appeared then disappeared due to reversible photoswitching between **7o** and **7c**.

At first glance, it is hard to see the new absorption band in the total spectrum, but taking a closer look reveals that the reversible photoswitching occurred even at room temperature in this case. I could observe this change with my eyes as well, as the solution turned green (Figure 34) when irradiated with UV light and became transparent again after the irradiation stopped.



Figure 34. Color change of the modified reversible photoswitch (7) upon irradiation with 312 nm light.

4.3 Single crystal structure of the reversible photoswitch (1)

For the investigation of the solid state structure and properties, the reversible photoswitch was crystallized from its solution by the slow evaporation of ethyl acetate. The crystal obtained was measured with X-ray crystallography and the structure can be seen in Figure 35.

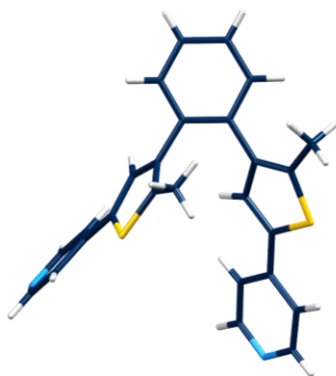


Figure 35. X-ray crystal structure of the reversible photoswitch (**1**).

As can be seen, the photoswitch crystallized in a parallel configuration (C1 in Figure 14). In this form, the photoswitching cannot occur, it is forbidden by the Woodward-Hoffman rules¹⁹. To get photoactive solid materials, I tried different modification approaches.

4.4 Synthetic modification of the reversible photoswitch (**1**)

4.4.1 Methylation

The easiest way to modify the reversible photoswitch (**1**) is its methylation at the pyridine nitrogen. Beyond synthetic ease, it provides an ionic species, which might have an affect on solid-state structure compared to the neutral species. The reaction was carried out by using MeI as methylating agent and acetonitrile as a solvent, and the mixture was stirred and heated to 80 °C overnight. The product was isolated as a brown oily material with quantitative yield.

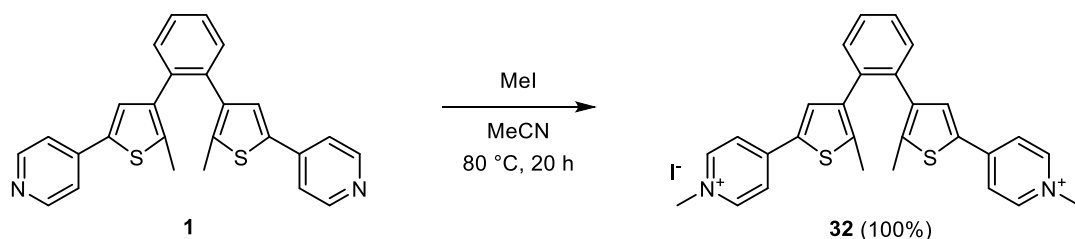


Figure 36. Synthesis of the methylated reversible photoswitch (**32**).

The ¹H NMR spectrum of **32** showed that the product does not require purification, as it only has solvent traces in it (Figure 37):

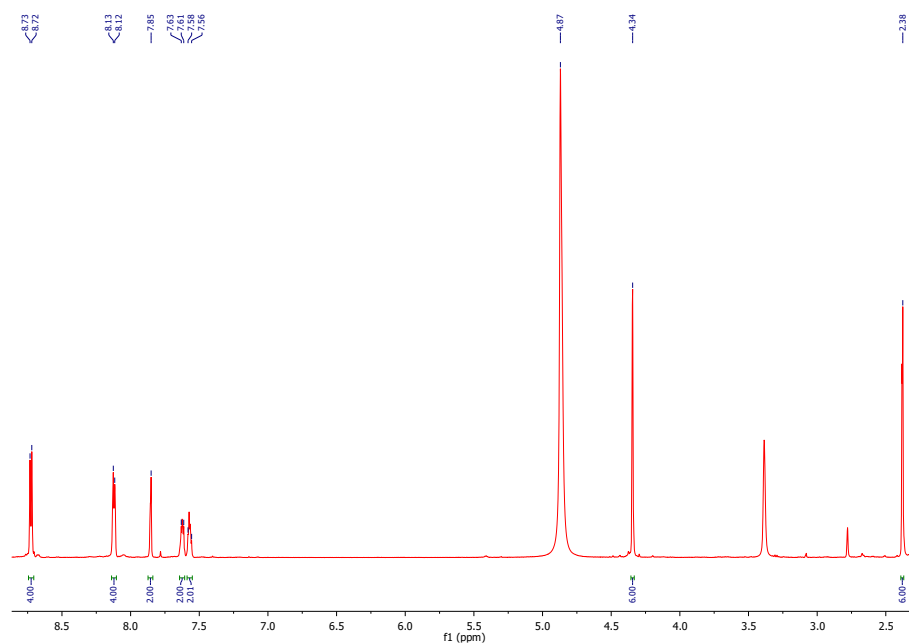


Figure 37. The ^1H NMR (500 MHz, MeOD) spectrum of the methylated reversible photoswitch (**32**).

The UV/Vis spectra (Figure 38) tells, that photodegradation occurs, when the sample is irradiated with UV light:

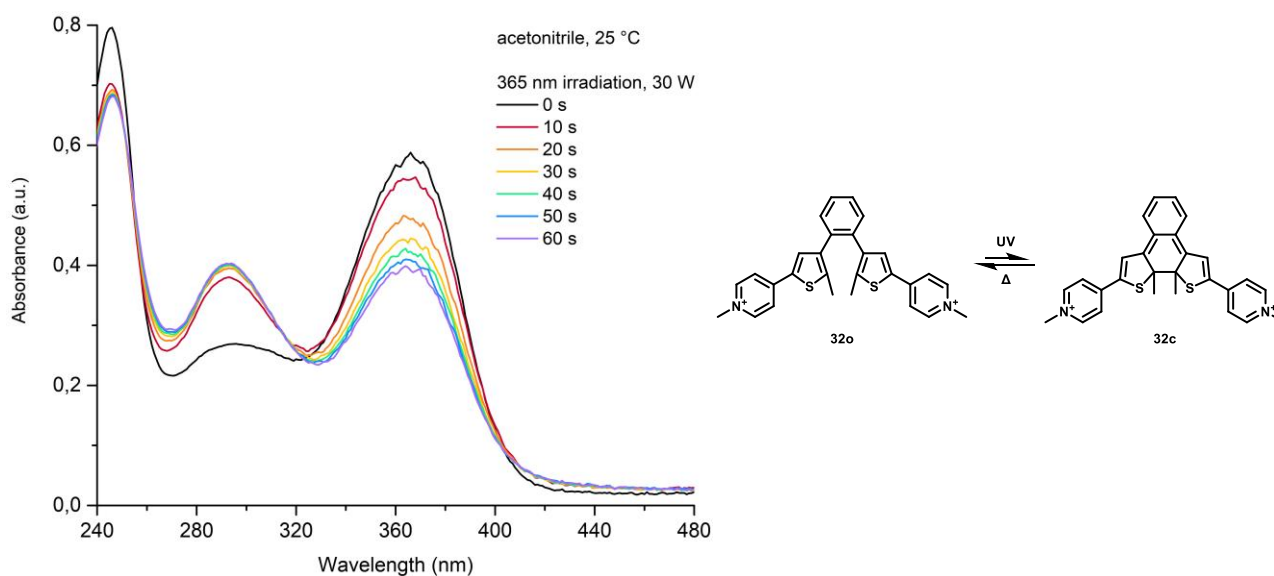


Figure 38. Changes in the UV-Vis absorption spectrum of the methylated reversible photoswitch (**32**) upon irradiation.

Single crystals suitable for X-ray diffraction measurements could not be obtained until submitting this paper, but it will be interesting to see whether the presence of the pyridinium ions affect the solid-state conformation compared to the neutral species.

4.4.2 Metal-organic frameworks

Another possible way to alter the structure of the reversible photoswitch (**1**) in solid state is to integrate it into a metal organic framework. This method requires metal ions to which organic molecules coordinate through an electron donating linker atom. The structure of the crystals formed is a large three-dimensional rigid structure (Figure 39).

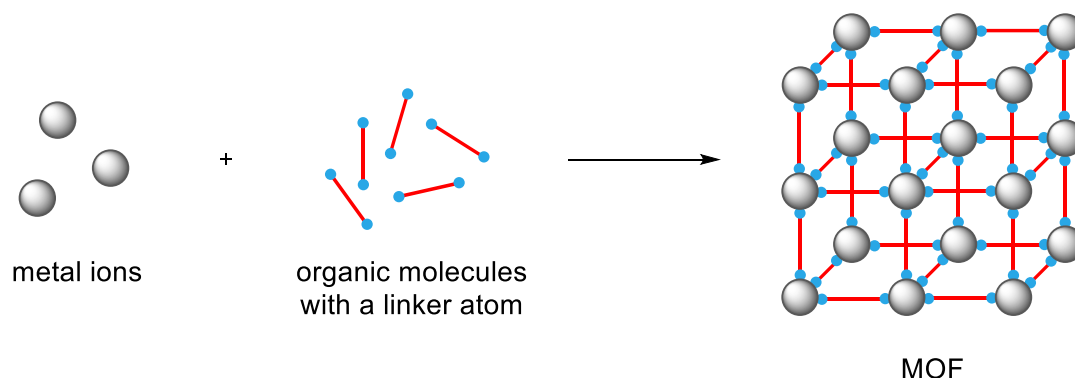


Figure 39. Schematic synthesis of MOFs.

In my case, the photoswitch (**1**), zinc nitrate and [1,1'-biphenyl]-4,4'-dicarboxylic acid was put into a vial, and DMF was added. At room temperature a yellowish, cloudy mixture was obtained, which cleared upon heating to 110 °C. The vial was then allowed to cool slowly to room temperature, where orange crystals were obtained in about 24 h. To reveal the structure, single crystal X-ray diffraction measurements were carried out, the results of which are reported in Figure 40.

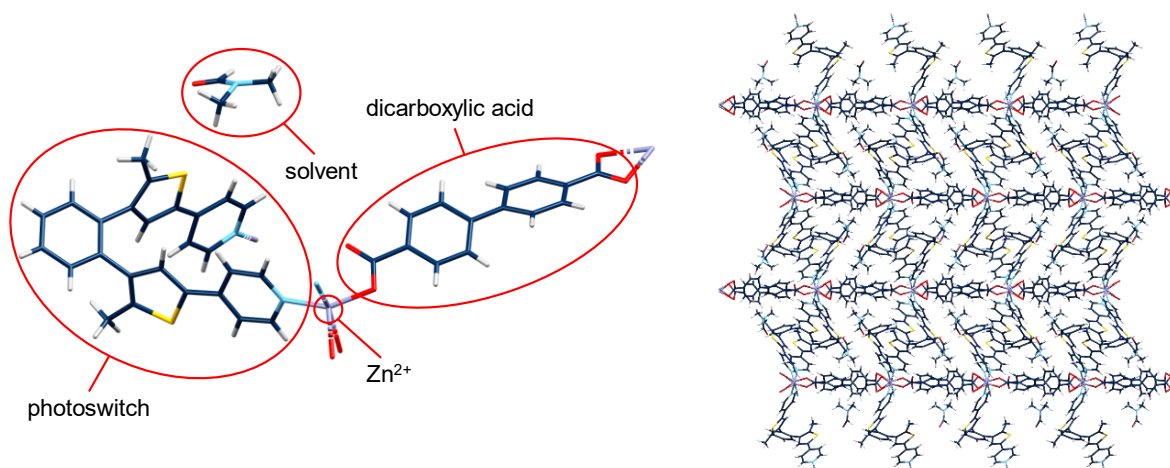


Figure 40. X-ray crystal structure of the synthesized MOF involving compound **1**.

Unfortunately, the photoswitch is in a photoinactive antiparallel configuration (marked as C2 in Figure 8) in this case. Another downside of this method is that it is difficult to obtain the material in

a form of single crystals, as the MOF is precipitated as an amorphous powder most of the times, which complicates structural characterization.

4.4.3 Organometallic complexes

There are reports in the literature that substituted dithienylethenes can form different organopalladium species with well-defined structures^{54–56}, where the photoswitches coordinate to only 2-3 metal ions (Figure 41), so we decided to make such organometallic complexes as the next step.

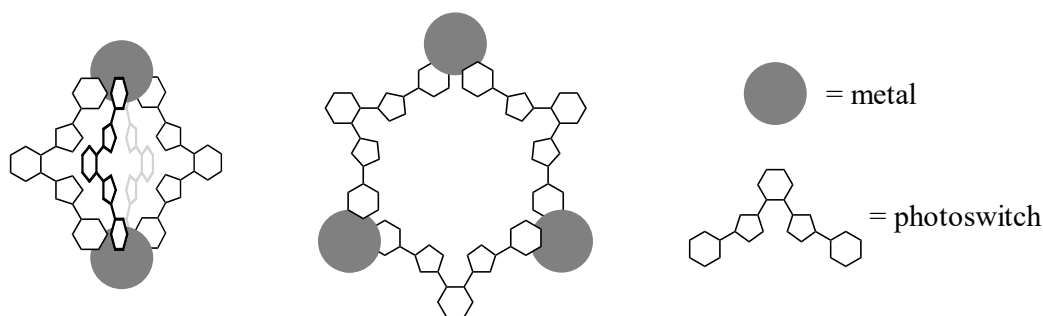


Figure 41. Some possible structures of organometallic complexes from **1**.

These complexes are soluble in room temperature, but can be crystallized, and various conditions can be generated by changing the metal, ligand, temperature or the solvent, with which we may tune the solid-state structure of the molecules.

During my research, I tried to synthesize an organometallic complex using the reversible photoswitch (**1**) as the ligand. For this, I used a synthesis from the literature⁵⁷; I dissolved the photoswitch and $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in acetonitrile and heated the vial under inert atmosphere for 1 hour. The exact structural determination of the product is not done yet, as the crystallization is not finished at the time of writing this paper. However the ^1H NMR spectrum (Figure 42) shows that the hydrogens of pyridine (H_a , H_b) which are the closest to the proposed Pd-N coordination bond, are shifted toward higher chemical shifts, which implicates that the reaction took place. When I tried the synthesis again, I got the same spectrum for the product, which shows that the complex can be reproducibly acquired.

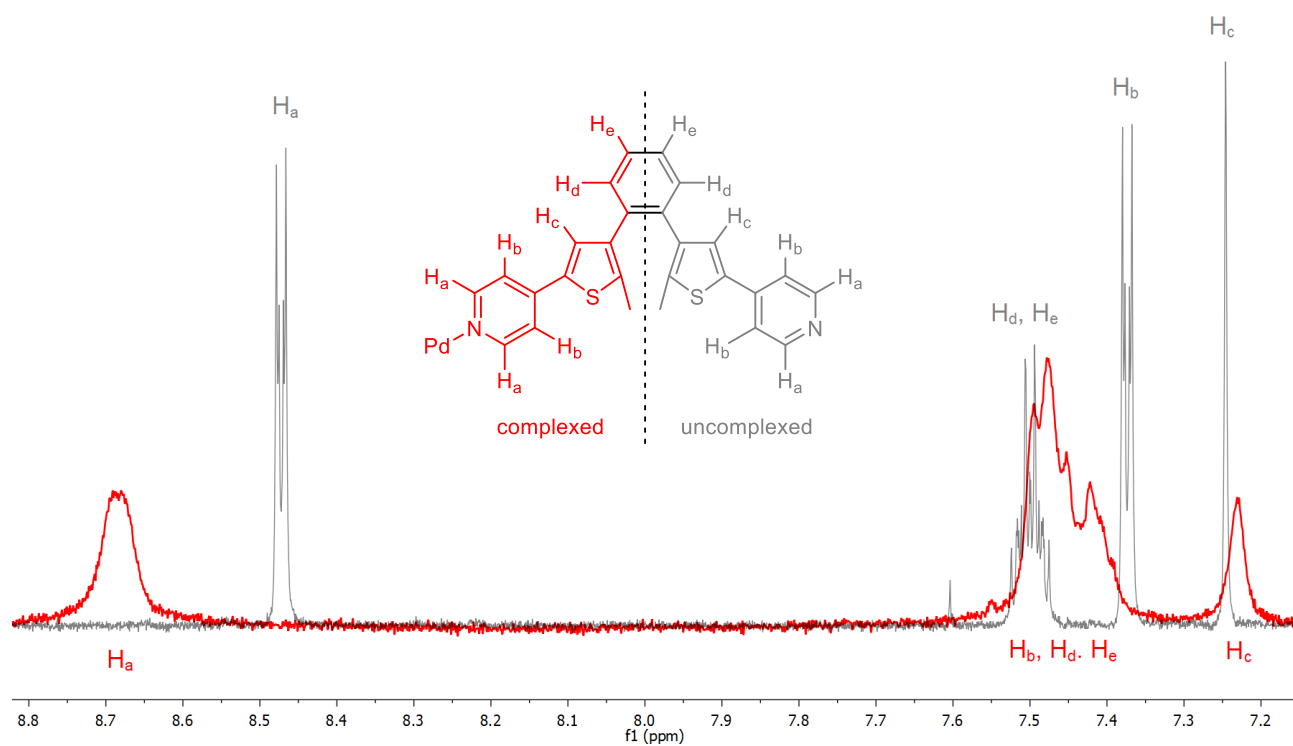


Figure 42. The ^1H NMR spectrum of the photoswitch complex (red, 300 MHz, CD_3CN) differs from the spectrum of the reversible photoswitch **1** (grey, 500 MHz, CD_3CN).

5. Summary of the results

In my research, my aim was to get a better understanding on the photoswitching properties of dithienylbenzenes and to synthesize such structures that are capable of an ultrafast photoreaction even in solid-state.

I successfully synthesized and purified three new photoswitches during my work. I investigated their switching properties in solution with UV-Vis spectroscopy. For photoswitch **1** we cannot prove the photoswitching in solution at room temperature, but at -60 °C we could observe the closed form as well as the cycloreversion. For photoswitch **32** we could also see a stable closed form, but even at room temperature, and this is because of its stabilization by oxidation due to the H substituents in the reactive carbon atoms. For photoswitch **7** we got the most interesting results, as we saw that it is capable of a reversible photoswitching even at room temperature with a cycloreversion as fast as a few seconds.

As we are interested in the solid-state photoswitching, I investigated photoswitch **1** from this aspect as well. First I crystallized it in its pure form, but the X-ray measurements revealed, that it is in a photoinactive parallel form in this case. I also integrated the photoswitch into a MOF and made measurements on the crystal structure, which revealed that although the conformation of the photoswitch was successfully altered to become antiparallel, it is still photoinactive as the reactive carbon atoms are too far away from each other for the solid-state photoswitching. To solve this issue, I tried two alternative methods; I methylated the pyridine and I synthesized an organometallic complex. At the time of writing this paper, these new compounds are not yet crystallized, but I hope that in the near future I will be able to get photoactive solid-state structures, and provide a method, which can give options for the solid-state conformational tuning of other dithienylbenzenes as well.

6. Experimental section

6.1 Materials and equipment

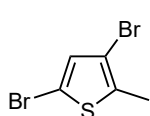
Starting materials, reagents and solvents were bought from Fluorochem, VWR and Sigma-Aldrich (Merck). Technical grade organic solvents were used during the extractions, and were removed at 40 °C using a rotary evaporator. Automated column chromatographic purifications were performed on a Teledyne Isco CombiFlash Rf+ automatic flash chromatography system, using Redisep Rf GOLD silica column and Redisep GOLD C18 reverse phase columns, with technical grade solvents.

NMR spectra were recorded on a Varian Vx 300 and Varian AS 500 spectrometer. For evaluation, I used the non-deuterated solvent signals as internal references ($\delta_{\text{CDCl}_3}({}^1\text{H}) = 7.26$ ppm; $\delta_{\text{DMSO}}({}^1\text{H}) = 2.50$ ppm; $\delta_{\text{CD}_2\text{Cl}_2}({}^1\text{H}) = 5.32$ ppm; $\delta_{\text{MeOD}}({}^1\text{H}) = 4.87$ ppm). When presenting the ${}^1\text{H}$ NMR spectra, I considered chemical shifts (δ) in ppm units relative to tetramethylsilane ($\delta_{\text{TMS}} = 0$ ppm). Additionally, I indicated multiplicity (singlet (s), doublet (d), multiplet (m)), coupling constants (J in Hz), and proton counts.

The UV-Vis spectra were recorded on a PerkinElmer Lambda 465 instrument using spectroscopic grade solvents.

6.2 Synthesis of 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene (1)

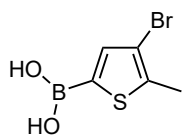
6.2.1 3,5-dibromo-2-methylthiophene (23)



In a 250 mL round bottom flask, 5 g (50.94 mmol) 2-methylthiophene (**22**) was dissolved in 100 mL acetic acid. In a vial 16,28 g (101,87 mmol; 5,25 ml) bromine was measured under the fume hood. The bromine was added dropwise into the flask, and the mixture was stirred overnight using a nitrogen stream and a gas neutralizer with concentrated NaOH solution. The reaction mixture was poured onto ice and extracted three times with diethyl ether. The combined organic phase was washed with water, Na_2CO_3 solution, NaHSO_3 solution, then water again, dried over MgSO_4 and filtered. The solvent was removed under reduced pressure. The product was a dark brown liquid (12.4214 g; 95%); NMR integrals showed only trace amounts of impurities, which can be removed by chromatographic purification to give a pale yellow liquid.

${}^1\text{H}$ NMR (300 MHz, CDCl_3) δ = 6.85 (s, 1H); 2.34 (s, 3H) ppm.

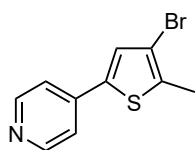
6.2.2 (4-bromo-5-methylthiophen-2-yl)boronic acid (24)



In a 100 mL two-neck round bottom flask under nitrogen atmosphere 3 g (11.72 mmol) 3,5-dibromo-2-methylthiophene (**23**) was dissolved in 50 mL freshly distilled ether. The mixture was then cooled to -78 °C and 4.69 mL 2.5 M n-BuLi (11.72 mmol) was added dropwise. Half an hour later 1.96 mL (17.58 mmol) trimethyl borate was added to the flask and the reaction mixture was stirred overnight. After that, 45 mL 1M HCl solution was added to the mixture while cooling with ice-water bath and stirring for another 3 hour. The ether phase was separated, the aqueous phase was extracted with ether and the combined organic phase was extracted three times with 1 M NaOH solution. Concentrated hydrochloric acid was added to the combined aqueous phase until pH 1 was reached. The flask was then cooled in an ice-water bath and the precipitate was filtered out, washed with water and dried on a rotary vacuum evaporator. The product is a beige solid material (2,0249 g; 78 %).

¹H NMR (300 MHz, DMSO) δ = 8.29 (s, 2H); 7.50 (s, 1H); 2.37 (s, 3H) ppm.

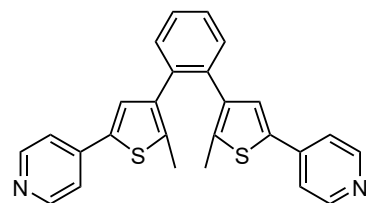
6.2.3 4-(4-bromo-5-methylthiophen-2-yl)pyridine (25)



In a 30 mL vial under nitrogen atmosphere, 480.0 mg (2.17 mmol) 4-(4-bromo-5-methylthiophen-2-yl)boronic acid (**24**); 676.1 mg (3.48 mmol) 4-bromopyridine hydrochloride and 111.3 mg (0.15 mmol) Pd(dppf)Cl₂ were dissolved in 5 mL THF, 5 mL 20% Na₂CO₃ solution was added, and the reaction mixture was stirred at 80 °C overnight. After that it was poured into a separatory funnel, 1 M NaHCO₃ solution was added and the mixture was extracted three times with DCM. The combined organic phase was washed with water and saturated NaCl solution, dried over MgSO₄, filtered, and the solvent was removed under reduced pressure. The crude product was purified on a chromatographic column (SiO₂; n-hexane → n-hexane/EtOAc 30%) to give a dark orange solid (435.6 mg; 79 %).

¹H NMR (300 MHz, CDCl₃) δ = 8.59-8.57 (m, 2H); 7.38-7.36 (m, 2H); 7.31 (s, 1H); 2.45 (s, 3H) ppm.

6.2.4 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene (1)



In a 50 mL two-neck round bottom flask under nitrogen atmosphere and with Vigreux column on top of it, 800.0 mg (3.15 mmol) 4-(4-bromo-5-methylthiophen-2-yl)pyridine (**25**) was dissolved in 17 mL freshly distilled THF. After cooling to -78 °C, 1.76 mL 2.5 M n-BuLi (4.41 mmol) was added dropwise, half an hour later 0.56 mL (5.04 mmol) trimethyl borate, and the reaction mixture was stirred overnight. After 346.2 mg (1.05 mmol) 1,2-diiodobenzene, 115.2 mg

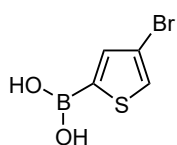
(0.16 mmol) Pd(dppf)Cl₂ and 2.67 ml 20% Na₂CO₃ solution was added. The system was inerted again with nitrogen and the reaction mixture was stirred at 75 °C for another day. The reaction mixture was then transferred to a separating funnel, 1 M NaHCO₃ solution was added and extracted three times with DCM. The combined organic phase was dried, filtered, and the solvent was removed under reduced pressure. The crude product was purified on a reverse phase chromatography column (C18; A → A/B 30%, where eluent A is 95:5 water:acetonitrile + 1% TFA, eluent B is acetonitrile + 1% TFA). The final product is a beige solid material (222.6 mg; 50%).

¹H NMR (300 MHz, CD₂Cl₂) δ = 8.48-8.46 (m, 4H); 7.47-7.44 (m, 4H); 7.30-7.28 (m, 4H); 7.12 (s, 2H); 2.22 (s, 6H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 150.22; 141.48; 139.57; 137.96; 136.45; 135.43; 130.71; 128.16; 127.84; 119.42; 14.23 ppm.

6.3 Synthesis of 1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene (31)

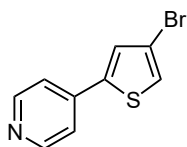
6.3.1 (4-bromothiophen-2-yl)boronic acid (28)



In a 100 mL two-neck round bottom flask under nitrogen atmosphere, 1 g (4.13 mmol) 2,4-dibromothiophene (**27**) was dissolved in 20 mL freshly distilled diethyl ether. The mixture was then cooled to -78 °C, 1.65 mL of 2.5 M n-BuLi (4.13 mmol) and 0.69 mL (6.20 mmol) trimethyl borate was added to the flask and the reaction mixture was stirred overnight. After that, 45 mL 1M HCl solution was added to the mixture while cooling with ice-water bath and stirring for another 3 hour. The ether phase was separated, the aqueous phase was extracted with ether and the combined organic phase was extracted three times with 1 M NaOH solution. Concentrated hydrochloric acid was added to the combined aqueous phase until pH 1 was reached. The flask was then cooled in an ice-water bath but as the amount of precipitate seemed very low, I extracted three times with DCM rather than filtration. The combined organic phase was dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The product is a beige solid material (0.4674 g; 54 %).

¹H NMR (300 MHz, DMSO) δ = 8.40 (s, 2H); 7.84 (d, 1H, J = 1.2 Hz); δ = 7.59 (d, 1H, J = 1.2 Hz) ppm.

6.3.2 4-(4-bromothiophen-2-yl)pyridine (29)

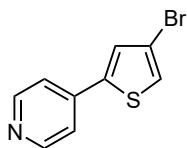


In a 100 mL two-neck round bottom flask under nitrogen atmosphere and with Vigreux column on top of it, 400.0 mg (1.93 mmol) (4-bromothiophen-2-yl)boronic acid (**28**); 601.7 mg (3.09 mmol) 4-bromopyridine hydrochloride and 56.6 mg (0.08 mmol) Pd(dppf)Cl₂ were dissolved in 4.6 mL THF, 4.6 mL 20% Na₂CO₃ solution was added, and the reaction mixture was stirred at 80 °C overnight. After that it was poured into a separatory funnel, 1 M NaHCO₃ solution was added and the mixture was extracted three times with DCM. The combined organic phase was washed with water and saturated NaCl solution, dried over MgSO₄, filtered, and the solvent was removed under reduced pressure. The crude product was purified on a chromatographic column (SiO₂; n-hexane → n-hexane/EtOAc 30%) to give a pale yellow solid material (289.8 mg; 62 %).

¹H NMR (300 MHz, DMSO) δ = 8.61-8.59 (m, 2H); δ = 7.89-7.87 (m, 2H); δ = 7.68-7.66 (m, 2H) ppm.

¹³C NMR (75 MHz, CDCl₃) δ = 150.48; 142.01; 139.92; 127.76; 124.17; 119.46; 111.15 ppm.

6.3.3 Alternative synthesis of 4-(4-bromothiophen-2-yl)pyridine (29)

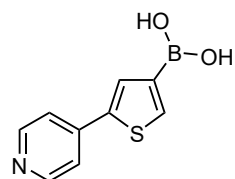


In a 100 mL two-neck round bottom flask under nitrogen atmosphere and with Vigreux column on top of it, 1 g (4.13 mmol) of 2,4-dibromothiophene (**27**), 582.5 mg (4.13 mmol) pyridine-4-ylboronic acid monohydrate, and 143.3 mg (0.12 mmol) Pd(PPh₃)₄ were dissolved in 30 ml ethanol, 876.2 mg (8.27 mmol) Na₂CO₃ was dissolved in 3 ml water and added to the reaction mixture, and stirred at 80 °C overnight. After that, the ethanol was removed under reduced pressure, then water was added and the mixture was extracted two times with ethyl acetate, the combined organic phase was washed with saturated NaCl solution, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was purified on a chromatographic column (SiO₂; n-hexane → n-hexane/EtOAc 30%) to give a pale yellow solid material (534.1 mg; 54 %).

¹H NMR (300 MHz, DMSO) δ = 8.61-8.59 (m, 2H); 7.89-7.87 (m, 2H); 7.68-7.66 (m, 2H) ppm.

¹³C NMR (75 MHz, CDCl₃) δ = 150.48; 142.01; 139.92; 127.76; 124.17; 119.46; 111.15 ppm.

6.3.4 (5-(pyridin-4-yl)thiophen-3-yl)boronic acid (30)

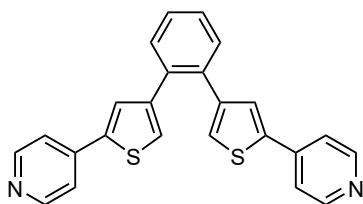


In a 30 mL vial under nitrogen atmosphere, 464.4 mg (1.93 mmol) 4-(4-bromothiophen-2-yl)pyridine (**29**) was dissolved in 1 mL abs. THF. The mixture was then cooled to -78 °C and 1.45 mL 1.6 M n-BuLi (2.32 mmol) was added dropwise. An hour later 0.32 mL (2.90 mmol) trimethyl borate was added to the flask and the

reaction mixture was stirred overnight. After that, the THF was removed under reduced pressure, DCM was added and the mixture was extracted with 1 M NaOH solution. Concentrated hydrochloric acid was added to the combined aqueous phase until precipitate appeared (pH = 5.36). The mixture then was extracted with ethyl-acetate, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The product is a blood orange color solid material (201 mg; 51 %).

¹H NMR (300 MHz, MeOD) δ = 8.52 – 8.50 (m, 2H), 7.74 – 7.70 (m, 3H), 7.63 (d, J = 3.5 Hz, 1H) ppm.

6.3.5 1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene (31)

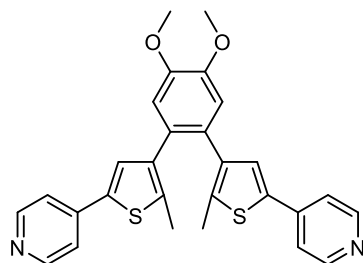


In a 60 ml vial under nitrogen atmosphere, 200 mg (0.98 mmol) (5-(pyridin-4-yl)thiophen-3-yl)boronic acid (**30**), 129 mg (0.39 mmol) 1,2-diiodobenzene and 21.4 mg (0.03 mmol) Pd(dppf)Cl₂ was dissolved in 10 ml THF, 248 mg (2.34 mmol) Na₂CO₃ was dissolved in 2 ml water and added to the reaction mixture, and stirred at 75 °C overnight. After that the reaction mixture was filtered under vacuum using diatomite over glass filter and ethyl acetate, then the solvent was removed under reduced pressure. The crude product was purified on a chromatographic column (SiO₂ ; DCM → DCM/methanol 5 %) to give a pale brown solid material (27 mg; 17 %).

¹H NMR (300 MHz, CDCl₃) δ = 8.56 (dd, J = 6.2 Hz, 4H); 7.58-7.38 (m, 10H); 6.94 (d, 2H, J = 3.8 Hz) ppm.

¹³C NMR (75 MHz, CD₂Cl₂) δ = 150.94; 144.79; 142.13; 141.53; 133.66; 131.63; 129.30; 129.16; 126.07; 119.99 ppm.

6.4 4,4'-((4,5-dimethoxy-1,2-phenylene)bi(5-methylthiophene-4,2-diyl))dipyridine (7)



In a 30 mL vial under nitrogen atmosphere, 200.0 mg (0.79 mmol) 4-(4-bromo-5-methylthiophen-2-yl)pyridine (**4**) was dissolved in 5 mL freshly distilled THF. After cooling to -78 °C, 0.69 mL 1.6 M n-BuLi (1.1 mmol) was added dropwise, then half an hour later 0.14 mL (1.26 mmol) trimethyl borate, and the reaction mixture was stirred overnight. After 102 mg (0.26 mmol) 1,2-diiodo-4,5-dimethoxybenzene, 28.8 mg (0.04 mmol) Pd(dppf)Cl₂, 195 mg (1.84 mmol) Na₂CO₃ and 1 ml water was added. The system was inerted again with nitrogen and the reaction mixture was stirred at 75 °C for another day. The mixture was then filtered with celite and glass filter and washed with DCM. The solvent was removed under reduced pressure. The

crude product was purified on a chromatographic column (SiO₂; n-hexane (+5 % TEA) → n-hexane (+5 % TEA):EtOAc (+5 % TEA) 90%). The final product is a beige solid material (14.9 mg; 12 %).

¹H NMR (500 MHz, CD₂Cl₂) δ = 8.47 (d, *J* = 5.7 Hz, 4H); 7.31 (d, *J* = 6.1 Hz, 4H); 7.15 (s, 2H); 6.93 (s, 2H); 3.91 (s, 6H); 2.20 (s, 6H) ppm.

¹³C NMR (126 MHz, CD₂Cl₂) δ = 150.06; 148.55; 141.34; 139.55; 137.77; 136.14; 128.34; 127.88; 119.20; 113.67; 56.00; 13.99 ppm.

6.5 Synthesis of the methylated reversible photoswitch (32)

In a 20 mL vial 10 mg (0.024 mmol) 1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene and 44 μ l (0.71 mmol) MeI was dissolved in 5 ml abs. MeCN and was stirred at 80 °C overnight. The solvent was then evaporated and the product was achieved in a quantitative yield as a brown solid material.

¹H NMR (500 MHz, MeOD) δ = 8.73 (d, *J* = 6.3 Hz, 4H); 8.12 (d, *J* = 5.2 Hz, 4H); 7.85 (s, 2H); 7.63-7.61 (m, 2H); 7.58-7.56 (m, 2H); 4.34 (s, 6H); 2.38 (s, 6H) ppm.

6.6 Synthesis of MOF

In a 40 mL vial, 50 mg (0.12 mmol) 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)benzene, 35 mg (0.12 mmol) Zn(NO₃)₂ · 6 H₂O, 28.5 mg (0.12 mmol) of [1,1'-biphenyl]4,4'-dicarboxylic acid and 10 mL DMF were added. After sonication, the reaction mixture was heated to 110 °C until a clear solution was obtained, then the mixture was left to cool at room temperature. The product is given as orange crystals.

6.7 Synthesis of the organometallic complex

In a 4 mL vial, 2 mg (0.005 mmol) 1,2-bis(5-(pyridin-4-yl)thiophen-3-yl)benzene and 1.1 mg (0.0025 mmol) [Pd(CH₃CN)₄](BF₄)₂ was dissolved in 1 mL CD₃CN, inerted, and heated for 1 hour.

Summary

Tuning the Conformational Properties of Dithienylbenzene Photoswitches for Solid-State Applications

Dávid Dorián Németh, Chemistry MSc, ELTE TTK and HUN-REN TTK

Supervisor: **Gábor London**, senior research fellow, HUN-REN TTK, Institute of Organic Chemistry

Co-supervisor: **Attila Kunfi**, research fellow, HUN-REN TTK, Institute of Organic Chemistry

Dithienylbenzenes are promising candidates for applications in molecular electronics¹⁷, however they often crystallize in a photoinactive conformation, therefore they cannot be used as solid-state photoswitches. To prevent such cases, I investigated the effect of the substituents on a photoswitch and also studied different synthetic methods for the tuning of the conformation at solid-state.

At the beginning, I made calculations for differently substituted dithienylbenzenes, that have a pyridine linker group in them, so they can be integrated into solid-state structures as well. The virtual screening showed, that for most of the derivatives the energy differences between the photoactive and inactive forms are negligible, but substantial structural modifications alter the conformational space in a way that may be beneficial. However the effect of these modifications on the photoswitching properties are unknown, therefore in my lab work, I rather focused on obtaining the photoswitches, investigating their properties in solution and then try to tune their conformational properties by integrating them into various solid-state structures.

During my research I synthesized three photoswitches (molecule **1**, **2** and **3**), that form a ring through an electrocyclization reaction if irradiated with UV light (Figure 43).

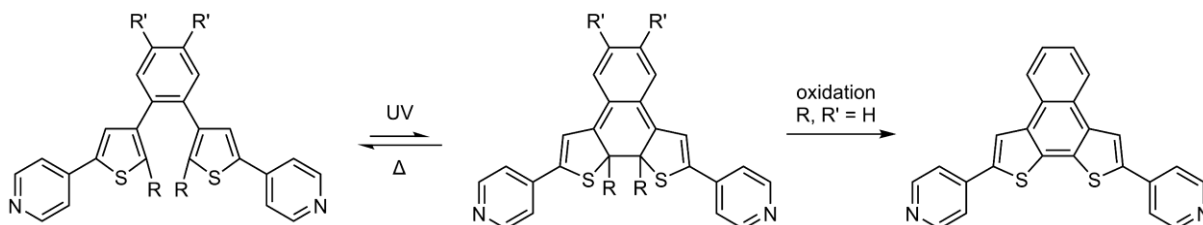


Figure 43. Reactivity of the photoswitches to be synthesized. During my research I studied molecule **1** (R=CH₃, R'=H), **2** (R,R'=H), and **3** (R=CH₃, R'=OMe).

I investigated the photoswitching properties in solution with UV-Vis spectroscopy. I found that for **1**, the reversible photoreaction can be measured at lower temperatures (-60 °C), but at room temperature the thermal cycloreversion is too fast to see the closed-ring form. For **2**, the photoswitching can be measured at room temperature, but it is irreversible due to the oxidation of the closed form. However **3** is capable of a reversible photoreaction even at room temperature with a cycloreversion as fast as a few seconds.

I studied **1** in solid-state as well. First, I crystallized it in its pure form, but the X-ray measurements revealed, that it is in a photoinactive parallel form in this case. I also integrated **1** into a MOF, but although the conformation of the photoswitch was successfully altered to become antiparallel, it is still photoinactive as the reactive carbon atoms are too far away for the solid-state photoswitching. Other than these I made a methylated derivative and synthesized an organometallic complex as well, but these new compounds are not yet crystallized. I hope that from these, I will be able to get photoactive solid-state structures, and provide a method, that can give options for the solid-state conformational tuning of other dithienylbenzenes as well.

Ditienil-arén fotokapcsolók konformációs viszonyainak hangolása szilárd fázisú alkalmazásukhoz

Németh Dávid Dorián, Chemistry MSc, ELTE TTK és HUN-REN TTK

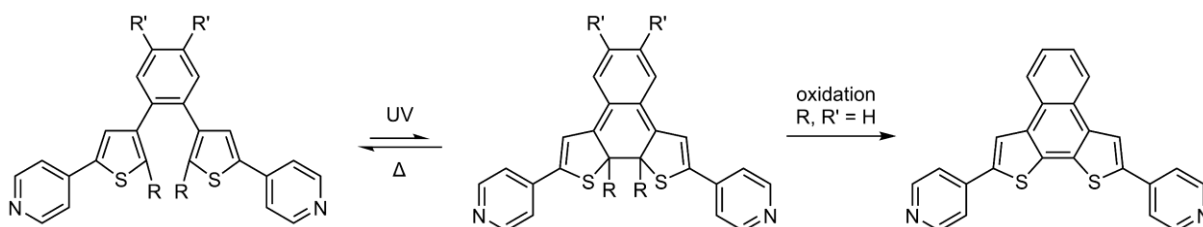
Témavezető: **London Gábor**, tudományos főmunkatárs, HUN-REN TTK, Szerves Kémiai Intézet

Társtémavezető: **Kunfi Attila**, tudományos munkatárs, HUN-REN TTK, Szerves Kémiai Intézet

A ditienil-arének ígéretes alkalmazási lehetőségekkel kecsegtetnek a molekuláris elektronikában¹⁷, azonban gyakran fotoinaktív konformációban kristályosodnak, amely miatt nem használhatóak szilárd fázisú fotokapcsolóként. Ennek megelőzésére a szubsztituensek hatását vizsgáltam egy fotokapcsolón, illetve szintetikus eljárásokat teszteltem a szilárd fázisú konformáció hangolására.

Kezdetekben olyan ditienil-arénekre végeztem számításokat, amelyek piridin linkert tartalmaznak, így később különböző szilárd fázisokba integrálhatóak. A virtuális szűrés azt mutatta, hogy a legtöbb szubsztituált származék esetén a fotoaktív és inaktív formák közti energiakülönbség elhanyagolható, azonban egyes szélsőséges esetekben a konformációs viszonyok eltolhatóak a fotoaktív forma felé. Ezen drasztikus változtatások hatása a fotokapcsolásra azonban ismeretlen, ezért labormunkám során inkább a fotokapcsolók szintézisére, oldatfázisbeli tulajdonságaik feltárására helyeztem a hangsúlyt, és próbáltam a szerkezetüket hangolni szilárd rendszerekbe történő integrálással.

Kutatómunkám során három fotokapcsolót szintetizáltam (fotokapcsoló **1**, **2** és **3**), amelyek elektrociklizációs reakción keresztül gyűrűt zárnak UV besugárzás hatására (44. ábra).



44. ábra. A szintetizált fotokapcsolók reaktivitása. A kutatómunkám során vizsgált molekulák az **1** ($R=CH_3$, $R'=H$), **2** ($R,R'=H$), és **3** ($R=CH_3$, $R'=OMe$).

A kapcsolási tulajdonságokat oldatban UV-Vis spektroszkópiával vizsgáltam. Az **1**-es molekula esetén reverzibilis fotokapcsolást tapasztaltam alacsony hőmérsékleten ($-60\text{ }^{\circ}\text{C}$), azonban szobahőmérsékleten a termális visszaalakulás túl gyorsnak bizonyult ahhoz, hogy a gyűrűzárt formát megfigyelhessem. A **2**-es molekula esetén a fotokapcsolás mérhető volt szobahőmérsékleten, de ez az átalakulás irreverzibilis a zárt forma oxidációja miatt. Azonban a **3**-as származék képes reverzibilis átalakulásra szobahőmérsékleten is, pár másodperces gyűrűnyílási gyorsasággal.

Az **1**-es fotokapcsolót szilárd fázisban is vizsgáltam. Először egymagában kristályosítottam, azonban a röntgendiffrakciós mérések azt mutatták, hogy a kapcsoló fotoinaktív parallel formában van a kristályban. Ezután MOF-ba építettem a fotokapcsolót, amely hatására antiparallel konformációt láttam, azonban ez esetben a reaktív szénatomok túl távol vannak egymástól a szilárd-fázisú fotokapcsoláshoz. Előállítottam továbbá a metilezett származékot, illetve fémorganikus komplexet is szintetizáltam, azonban ezek eddig még nem kristályosodtak. Remélem, hogy ezekből sikerül majd fotoaktív szilárd rendszerekhez jutnom, és ez alapján olyan módszert dolgozhatok ki, amely más ditienil-arének szilárd-fázisú konformációs hangolására is lehetőséget biztosít.

References

1. Desborough, M. J. R. & Keeling, D. M. The aspirin story – from willow to wonder drug. *Br. J. Haematol.* **177**, 674–683 (2017).
2. Roach, P., Shirtcliffe, N. J. & Newton, M. I. Progress in superhydrophobic surface development. *Soft Matter* **4**, 224–240 (2008).
3. Kassem, S. *et al.* Artificial molecular motors. *Chem. Soc. Rev.* **46**, 2592–2621 (2017).
4. Schoenlein, R. W., Peteanu, L. A., Mathies, R. A. & Shank, C. V. The First Step in Vision: Femtosecond Isomerization of Rhodopsin. *Science* **254**, 412–415 (1991).
5. Eighth Edition Acknowledgments and History. in *Basic Neurochemistry* xxi (Elsevier, 2012). doi:10.1016/B978-0-12-374947-5.00067-5.
6. Crespi, S., Simeth, N. A. & König, B. Heteroaryl azo dyes as molecular photoswitches. *Nat. Rev. Chem.* **3**, 133–146 (2019).
7. Beharry, A. A. & Woolley, G. A. Photoswitch Design. in *Photosensitive Molecules for Controlling Biological Function* (eds. Chambers, J. J. & Kramer, R. H.) vol. 55 171–184 (Humana Press, Totowa, NJ, 2011).
8. Chan, J. C.-H., Lam, W. H. & Yam, V. W.-W. A Highly Efficient Silole-Containing Dithienylethene with Excellent Thermal Stability and Fatigue Resistance: A Promising Candidate for Optical Memory Storage Materials. *J. Am. Chem. Soc.* **136**, 16994–16997 (2014).
9. Oruganti, B., Pál Kalapos, P., Bhargav, V., London, G. & Durbeej, B. Photoinduced Changes in Aromaticity Facilitate Electrocyclization of Dithienylbenzene Switches. *J. Am. Chem. Soc.* **142**, 13941–13953 (2020).
10. Kitagawa, D., Nakahama, T., Nakai, Y. & Kobatake, S. 1,2-Diarylbenzene as fast T-type photochromic switch. *J. Mater. Chem. C* **7**, 2865–2870 (2019).
11. Sun, C., Wang, C. & Boulatov, R. Applications of Photoswitches in the Storage of Solar Energy. *ChemPhotoChem* **3**, 268–283 (2019).
12. Bouas-Laurent, H. & Dürr, H. Organic photochromism (IUPAC Technical Report). *Pure Appl. Chem.* **73**, 639–665 (2001).
13. *Photochromism: Molecules and Systems*. (Elsevier, Amsterdam, 2003).
14. Ribeiro Da Cunha, B., Fonseca, L. P. & Calado, C. R. C. Antibiotic Discovery: Where Have We Come from, Where Do We Go? *Antibiotics* **8**, 45 (2019).
15. Irie, M. Diarylethene Molecular Photoswitches.
16. Vela, S., Scheidegger, A., Fabregat, R. & Corminboeuf, C. Tuning the Thermal Stability and Photoisomerization of Azoheteroarenes through Macrocyclic Strain**. *Chem. – Eur. J.* **27**, 419–426 (2021).
17. Kang, M. *et al.* A Molecular-Switch-Embedded Organic Photodiode for Capturing Images against Strong Backlight. *Adv. Mater.* **34**, 2200526 (2022).
18. Xi, H. *et al.* All-Visible-Light-Activated Dithienylethenes Induced by Intramolecular Proton Transfer. *J. Am. Chem. Soc.* **141**, 18467–18474 (2019).
19. Woodward, R. B. & Hoffmann, R. Stereochemistry of Electrocyclic Reactions. *J. Am. Chem. Soc.* **87**, 395–397 (1965).
20. Milić, J. V. *et al.* Light-Responsive Pyrazine-Based Systems: Probing Aromatic Diarylethene Photocyclization. *J. Phys. Chem. C* **122**, 19100–19109 (2018).
21. Tan, W., Zhang, Q., Zhang, J. & Tian, H. Near-Infrared Photochromic Diarylethene Iridium (III) Complex. *Org. Lett.* **11**, 161–164 (2009).
22. Kobatake, S., Uchida, K., Tsuchida, E. & Irie, M. Single-crystalline photochromism of diarylethenes: reactivity–structure relationship. *Chem Commun* 2804–2805 (2002) doi:10.1039/B208419H.
23. Li, X., Ma, Y., Wang, B. & Li, G. “Lock and Key Control” of Photochromic Reactivity by Controlling the Oxidation/Reduction State. *Org. Lett.* **10**, 3639–3642 (2008).

24. Chatir, E. *et al.* Synthesis of Redox-Active Photochromic Phenanthrene Derivatives. *Chem. – Eur. J.* **28**, e202103755 (2022).
25. Deng, X. & Liebeskind, L. S. A Contribution to the Design of Molecular Switches: Novel Acid-Mediated Ring-Closing–Photochemical Ring-Opening of 2,3-Bis(heteroaryl)quinones (Heteroaryl = Thienyl, Furanyl, Pyrrolyl). *J. Am. Chem. Soc.* **123**, 7703–7704 (2001).
26. Li, W. *et al.* Sterically hindered diarylethenes with a benzobis(thiadiazole) bridge: photochemical and kinetic studies. *J. Mater. Chem. C* **3**, 8665–8674 (2015).
27. Li, M. *et al.* Conformer-dependent self-assembled metallacycles with photo-reversible response. *Chem. Sci.* **10**, 4896–4904 (2019).
28. Zhu, W. *et al.* Bisthienylethenes Containing a Benzothiadiazole Unit as a Bridge: Photochromic Performance Dependence on Substitution Position. *Chem. – Eur. J.* **16**, 899–906 (2010).
29. Li, W. *et al.* Separation of Photoactive Conformers Based on Hindered Diarylethenes: Efficient Modulation in Photocyclization Quantum Yields. *Angew. Chem. Int. Ed.* **53**, 4603–4607 (2014).
30. Yang, Y. *et al.* Aromaticity-Controlled Thermal Stability of Photochromic Systems Based on a Six-Membered Ring as Ethene Bridges: Photochemical and Kinetic Studies. *Chem. – Eur. J.* **18**, 11685–11694 (2012).
31. Yam, V. W.-W., Ko, C.-C. & Zhu, N. Photochromic and Luminescence Switching Properties of a Versatile Diarylethene-Containing 1,10-Phenanthroline Ligand and Its Rhenium(I) Complex. *J. Am. Chem. Soc.* **126**, 12734–12735 (2004).
32. Patel, D. G., Mitchell, T. B., Myers, S. D., Carter, D. A. & Novak, F. A. A Suzuki Approach to Quinone-Based Diarylethene Photochromes. *J. Org. Chem.* **85**, 2646–2653 (2020).
33. Saito, E., Ako, T., Kobori, Y. & Tsuda, A. Switching of the π -electronic conjugations in the reduction of a dithienylethene-fused p-benzoquinone. *RSC Adv.* **7**, 2403–2406 (2017).
34. Miao, W.-J., Li, L.-H., Lu, S., Liu, G. & Fan, C.-B. 1,2-Bis(2-methyl-5-phenyl-3-thienyl)benzene. *Acta Crystallogr. Sect. E Struct. Rep. Online* **65**, o3003–o3003 (2009).
35. Milek, M., Witt, A., Streb, C., Heinemann, F. W. & Khusniyarov, M. M. Tetraanionic N2O2-coordinating ligands as potential building blocks for supramolecular magnetic networks. *Dalton Trans.* **42**, 5237 (2013).
36. Walton, I. M. *et al.* The role of atropisomers on the photo-reactivity and fatigue of diarylethene-based metal–organic frameworks. *New J. Chem.* **40**, 101–106 (2016).
37. He, J., He, J., Wang, T. & Zeng, H. Ion-induced cycle opening of a diarylethene and its application on visual detection of Cu^{2+} and Hg^{2+} and keypad lock. *J Mater Chem C* **2**, 7531–7540 (2014).
38. Mörtel, M. *et al.* Synthesis, Characterization, and Properties of Iron(II) Spin-Crossover Molecular Photoswitches Functioning at Room Temperature. *Inorg. Chem.* **56**, 13174–13186 (2017).
39. Patel, D. G. (Dan) *et al.* Photoresponsive porous materials: the design and synthesis of photochromic diarylethene-based linkers and a metal–organic framework. *Chem Commun* **50**, 2653–2656 (2014).
40. Jin, G.-X., Wang, T., Sun, Y., Li, Y.-L. & Ma, J.-P. Photochromic Rhenium-Based Molecular Rectangles: Syntheses, Structures, Photophysical Properties, and Electrochemistry. *Inorg. Chem.* **59**, 15019–15027 (2020).
41. Li, W. *et al.* Enantiospecific photoresponse of sterically hindered diarylethenes for chiroptical switches and photomemories. *Sci. Rep.* **5**, 9186 (2015).
42. Zhu, W. *et al.* Unprecedented Stability of a Photochromic Bisthienylethene Based on Benzobisthiadiazole as an Ethene Bridge. *Angew. Chem. Int. Ed.* **50**, 10986–10990 (2011).
43. Lvov, A. G. *et al.* Reversible Shifting of a Chemical Equilibrium by Light: The Case of Keto–Enol Tautomerism of a β -Ketoester. *Org. Lett.* **22**, 604–609 (2020).
44. Steenbock, T., Escribano, A., Heck, J. & Herrmann, C. Photoswitching Behavior of a Cyclohexene-Bridged versus a Cyclopentene-Bridged Dithienylethene System. *ChemPhysChem* **16**, 1491–1501 (2015).

45. Qiu, S., Frawley, A. T., Leslie, K. G. & Anderson, H. L. How do donor and acceptor substituents change the photophysical and photochemical behavior of dithienylethenes? The search for a water-soluble visible-light photoswitch. *Chem. Sci.* **14**, 9123–9135 (2023).
46. Németh, D. D. Ditiénil-arén fotokapcsolók virtuális szűrése, szintézise és beépítése fémorganikus térhálóba. in *BSc Szakdolgozat* (Budapest, 2023).
47. Bannwarth, C., Ehlert, S. & Grimme, S. GFN2-xTB—An Accurate and Broadly Parametrized Self-Consistent Tight-Binding Quantum Chemical Method with Multipole Electrostatics and Density-Dependent Dispersion Contributions. *J. Chem. Theory Comput.* **15**, 1652–1671 (2019).
48. Brandenburg, J. G., Bannwarth, C., Hansen, A. & Grimme, S. B97-3c: A revised low-cost variant of the B97-D density functional method. *J. Chem. Phys.* **148**, 064104 (2018).
49. Mardirossian, N. & Head-Gordon, M. Mapping the genome of meta-generalized gradient approximation density functionals: The search for B97M-V. *J. Chem. Phys.* **142**, 074111 (2015).
50. Dolgoplova, E. A. *et al.* Connecting Wires: Photoinduced Electronic Structure Modulation in Metal–Organic Frameworks. *J. Am. Chem. Soc.* **141**, 5350–5358 (2019).
51. Gronowitz, S., Zhang, Y. & Hörnfeldt, A. B. Pyridine-Substituted Hydroxythiophenes. I. Preparation of o-(2-, 3- and 4-pyridyl)-3-hydroxythiophenes. *Acta Chem. Scand.* **46**, 654–660 (1992).
52. Nielsen, C. B. & Bjørnholm, T. New Regiosymmetrical Dioxopyrrolo- and Dihydropyrrolo-Functionalized Polythiophenes. *Org. Lett.* **6**, 3381–3384 (2004).
53. Gabrieli, S. *et al.* BITHIENOLS: Promising C₂-Symmetric Biheteroaromatic Diols for Organic Transformation. *Eur. J. Org. Chem.* **2017**, 861–870 (2017).
54. Benchimol, E., Tessarolo, J. & Clever, G. H. Photoswitchable coordination cages. *Nat. Chem.* **16**, 13–21 (2024).
55. Guo, S. *et al.* Light-regulating chirality of metallacages featuring dithienylethene switches. *Chem. Sci.* **14**, 6237–6243 (2023).
56. Han, M. *et al.* Light-Triggered Guest Uptake and Release by a Photochromic Coordination Cage. *Angew. Chem. Int. Ed.* **52**, 1319–1323 (2013).
57. Han, M. *et al.* Light-Controlled Interconversion between a Self-Assembled Triangle and a Rhombicuboctahedral Sphere. *Angew. Chem. Int. Ed.* **55**, 445–449 (2016).