

NEWSLETTER

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CONTENTS

EPA EXECUTIVE COMMITTEE	7
EDITORIAL	9
President's Letter	9
AWARDS	10
PHOTOCHEMICAL & PHOTOBIOLOGICAL SCIENCES	11
PUBLICATIONS	12
Large scale visible light photochemical transformations	12
The application of Pulse Radiolysis to elucidate the degradation mechanism of aromatic hydrocarbon-based proton exchange fuel cell membranes	15
Imine Photochemistry: Photoinduced Radical Reactions of Imines (IMPHOCHEM)	19
ABSTRACTS OF THESIS ON PHOTOCHEMISTRY	24
Intermolecular [2+2]-Photocycloaddition Reactions of complex Acceptor-Donor Systems and Development of an Enantioselective Photocatalyzed Hydroformylation Reaction.....	24
BODIPY compounds: fluorescent markers for biomacromolecules and phototherapeutics	27
Exciton coupling and energy transfer in perylene-based systems.	31

Molecular Properties in an Optical Microcavity: From Ensembles to Single Molecules	35
Synthesis and characterization of new chromophores with two photon absorption properties and study of their application in bioimaging	39
CONFERENCE ANNOUNCEMENTS	44
Central European Conference on Photochemistry (CECP 2022)..	44
28th PhotoIUPAC (2022).....	45
EPA IS ON FACEBOOK AND TWITTER.....	46
MEMBERSHIP APPLICATION FORM	47

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EDITORIAL

President's Letter

Dear EPA Members,

We are finishing another year, where unfortunately the realization of presential scientific meetings has been a very rare occasion. This has had also severe impact on the activities of EPA, being one of our goals the promotion of photochemistry by supporting broad scientific exchange. Online events may be a temporary alternative, but surely we all look forward to meet again in person. Let's hope that this will be possible in 2022. In fact, two major events are announced in this Newsletter: the Central European Conference on Photochemistry (CECP 2022; Bad Hofgastein) and the 28th IUPAC Symposium on Photochemistry (PhotoIUPAC 2022; Amsterdam).

During the International Conference on Photochemistry, held as online event last summer, EPA organized an Awards Ceremony. On this occasion several members of our community received recognition for their scientific achievements: **Dr. Bogdan Dereka** (EPA PhD Prize 2020), **Prof. Dr. Bo Albinsson** (EPA PPS Prize 2020), **Dr. Haining Tian** (EPA Young Investigator Award 2021), and **Prof. Dr. Silvia Braslavsky** (European Ambassador of Photochemistry Award 2021). I wish to express my sincerest congratulations to all awardees. In 2022 we will award the **PhD Prize** and **nominations can be made until the end of February 2022** (see call text in this Newsletter). Do not miss the opportunity to participate!

I hope to count on your continued support, especially by sending your contributions to our society journal *Photochemical and Photobiological Sciences*, which finishes now its first year in partnership with Springer-Nature. If you meanwhile wish to announce any conferences or meetings of broader interest, please get in touch to use our diverse channels to publicize the event.

Finally, I wish you and your families all the best for the coming 2022.

Yours sincerely,
Uwe Pischel

AWARDS

The EPA Prize for the best PhD thesis in Photochemistry will be awarded during the IUPAC Symposium on Photochemistry in Amsterdam in July 2022 (<https://photoiupac2022.amsterdam>).

The prize is 1000 €, plus travel costs to Amsterdam (within the limit of 500 €) **AND** three free years of EPA membership.

The candidate must have defended their PhD thesis between 2019-2021 and be nominated by an EPA member.

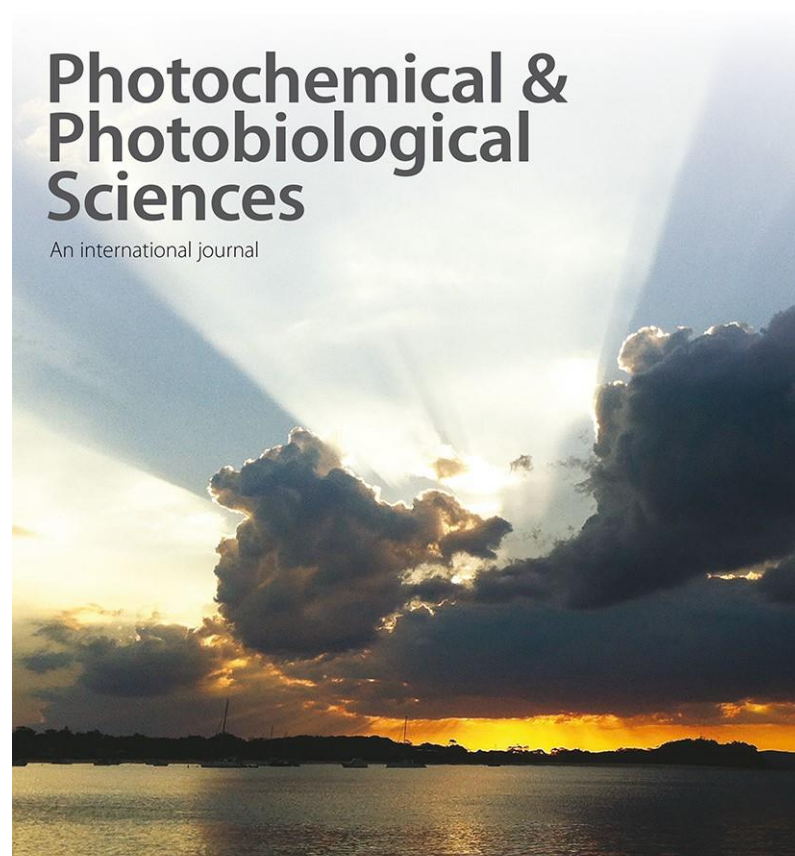
Nominations for this prize are now open and all nominations should be sent directly to w.nau@jacobs-university.de. The nomination package (electronic version only) should include:

- *Curriculum vitae* of the candidate
- Copy of the thesis
- An abstract of the thesis in English of no more than five pages in length
- A publication list, with publications that arose from the thesis underlined
- A letter of support

The closing date for the receipt of nominations: 28th February 2022

PHOTOCHEMICAL & PHOTOBIOLOGICAL SCIENCES

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An international journal



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PUBLICATIONS

Large scale visible light photochemical transformations

Pierre Zimmerlin, Maxime Lancel, Zacharias Amara
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The year 2021 has been marked by significant achievements in industrial photochemistry. Two successful productions of small molecules from Merck and Syngenta using visible light have been reported in the literature. These articles provide valuable insights into the way photochemistry can be efficiently scaled up. The first example is a photochemical bromination using continuous flow photochemistry, a key

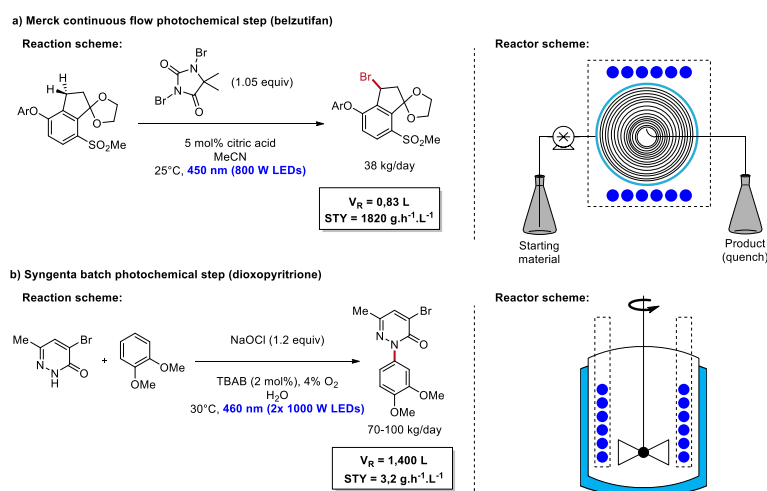


Figure 1. a) Flow production of belzutifan (Merck process) involving a photoinitiated radical bromination. b) Batch production of dioxopyrtrione (Syngenta process) involving an oxidative C-N coupling.

step in the manufacturing of belzutifan, an anticancer drug from Merck (Figure 1a).¹ The second is an oxidative C-N coupling operated in a large batch vessel at Syngenta, to produce an herbicide candidate dioxopyrithione (Figure 1b).²

The scale-up of the photochemical benzylic bromination was accomplished by transposing batch conditions in a continuous plug flow reactor (PFR) where the use of transparent perfluorinated tubes enables better exposure to light. The improved control of the residence time enabled to minimize the amount of impurities formed in the reaction. The reaction was scaled up to 50 kg scale using a coiled tubular reactor (0.83 L, 7.1 mm internal diameter) irradiated by a bank of high-intensity LEDs (800 W) emitting at 450 nm. A productivity of 38 kg/day was finally obtained with an assay yield of 93 % for a residence time of 1.5 minutes. Numbering up by connecting these reactors in series (“train reactor”) subsequently allowed to achieve over 100 kg/day productivity (residence time of 3 min, assay yield of 94 %). Finally, this development led to a ton scale production campaign.

Syngenta scientists, in partnership with the University of Fribourg, adopted an alternative option, by optimizing and transposing to large scale using a batch approach. The task was particularly challenging given the heterogeneity of the reaction (solid/liquid/liquid/gas). Optimization led to very good conversion and isolated yield in only 4.5 hours in a 20 L batch reactor (>99%, 85%). The process was eventually modified to fulfill all the conditions for a scale-up in 1,4 m³ reactor using two immersed-well LED banks with a total input power of 2 kW, leading to a production of 71 kg of the coupled intermediates (3.2 kg/hour) per batch with an average purity of 98.7%. This work enabled a production campaign reaching 853 kg.

Although these processes involve different reactions and are not directly comparable, it is interesting to see how choices have been oriented towards the use of a batch or flow reactor. Although flow chemistry enables high Space Time Yield (STY), it is not an easily applied option when handling solids and complex multiphasic conditions. In this case, a batch or continuous stirred tank reactor is often preferred³ and the overall difficulty to efficiently irradiate the reaction medium is compensated by the use of high power light sources. In both cases, the concept of “photon equivalents” has been a useful parameter to enable linear transposition from lab to large scale.

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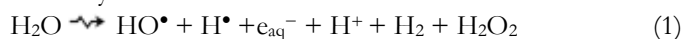
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The application of Pulse Radiolysis to elucidate the degradation mechanism of aromatic hydrocarbon-based proton exchange fuel cell membranes

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Although both photochemistry and radiochemistry have played a substantial role in establishing our understanding of (complex) chemical mechanisms, there are several key differences.¹ Photochemistry deals with the interaction of matter and low energy photons resulting in electronic excited states and follow-up reactions. Radiation chemistry, on the other hand, involves the interactions of ionising radiation with matter. In photochemistry, the energy is deposited directly on the chromophore; efficiency of a given photochemical process is described by its quantum yield and, according to the definition of the IUPAC Gold Book, applies strictly for monochromatic excitation.² Competing reactions coupled with unproductive energy losses incur difficulty to ascertain full mass balance. In radiolysis, ionisation of matter is mass proportional. In the cases of dilute solutions, the energy is quantitatively deposited on the solvent, which is then ionized; i.e. pulse irradiation of water generates primary species with known yields, according to scheme (1). Overall reactivities are determined by both the solvent and solute.



While photochemistry has become one of the most widely spread disciplines in chemistry and biology, interest concerning radiolysis seems to have declined.

It is our intention to show here that pulse radiolysis can be used to elucidate the deleterious processes of aromatic hydrocarbon-based fuel cell membranes and support the development of novel materials.

Renewable energy sources in combination with electrochemical devices for energy storage have partially been able to mitigate the problems of climate change and anthropogenic air pollution, especially those associated

with vehicular transportation. It is conceivable to replace traditional combustion engines with environmentally friendly fuel cell-based systems (FCs).³

Oxidative degradation is the most deleterious lifetime-shortening factor of sulfonated proton exchange membranes (PEMs).⁴ During the operation of FCs oxidising species are formed in the presence of humidified gases, H_2 / O_2 , and the noble metal catalyst. In FCs HO^\bullet is the degradation initiating electrophile with the highest reactivity. It incurs damage at close to diffusion controlled rates. Understanding the exact reaction mechanism enables specific optimization, such as the use of radical scavengers or polymer repair agents, and aids the design of inherently more stable PEMs. Direct spectroscopic study on the effects of oxidative damage of PEMs is challenging due to the comparatively small changes in the bulk membrane material, however oligomers and monomer analogous compounds are applicable models of PEMs.

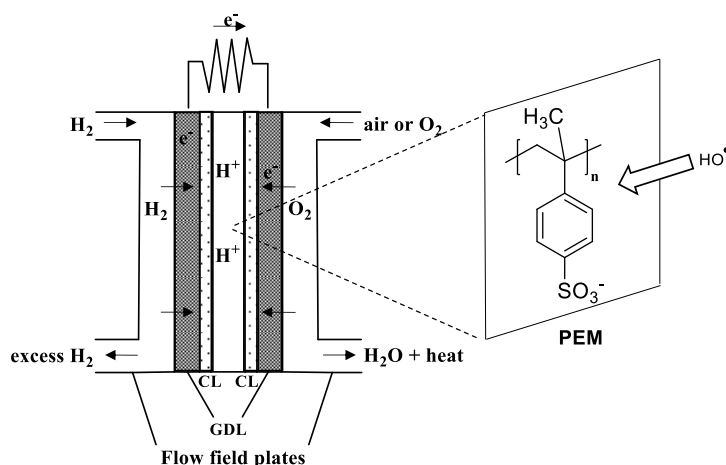
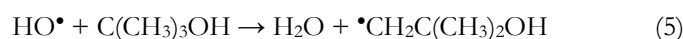
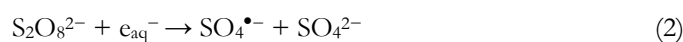


Figure 1. The membrane electrode assembly (MEA) is the heart of a PEM fuel cell, consisting of an ionomer membrane, catalyst layers (CL) and gas diffusion layers (GDL), sandwiched between two flow field plates. α -methylstyrene sulfonate (PAMSS) is a typical constituent of irradiation grafted aromatic hydrocarbon-based membranes. During operation of an FC the formed highly oxidising HO^\bullet attack the membrane.

The nature of the intermediates, the kinetics of their formation and reactivity strongly depend on the environment.⁵

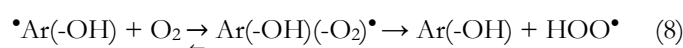
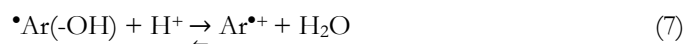
The primary products of water radiolysis may be transformed *via* secondary reactions,⁵ for example reactions (2)–(5), dependent on the experimental conditions. Reaction (2) provides highly oxidising tetraoxidosulfate radical anions. Dependent on the pH, hydrated electrons may react with protons, reaction (3), the yield of hydroxyl radicals can be increased by N₂O-saturation, reaction (4), or they can be quenched in reaction (5); the respective rates are known.⁵



These competing reactions, dependent on the applied conditions, allow control of the formation of the desired species. This enables the study of the involved reactions and reaction cascades.

In our studies, we used oligomers of α -methylstyrene sulfonate and monomer analogous compounds as typical representatives of aromatic hydrocarbon-based PEMs, Fig. 1, and studied their reactivity in an oxidising environment mimicking that of a proton exchange membrane fuel cell (PEMFC).⁶⁻⁸

Electrophilic attack of HO \bullet on aromatics results in the formation of HO \bullet -adducts, reaction (6).⁶⁻⁸ At low pH, present in a typical PEMFC, this intermediate is in a protolysis equilibrium with cation radicals, reaction (7).⁶⁻⁸ Oxygen reacts with the hydroxyl radical adducts to form peroxy radicals, reaction (8).^{6,7} Cation radicals can be formed directly via SO₄ \bullet -induced electron transfer, reaction (9).⁶⁻⁸



These general reactions are the main routes of degradation for a typical aromatic hydrocarbon-based PEM. Possible competing reactions are at least one order of magnitude slower.

Our results indicate that reaction rates depend both on the electron density of the aromatic core and on the chain length of oligomers.⁶⁻⁸ This knowledge may be indispensable for the development of more durable PEMFCs.

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Imine Photochemistry: Photoinduced Radical Reactions of Imines (IMPHOCHEM)

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Context

Photochemical reactions are an important tool of organic synthesis. Electronic excitation by light absorption considerably changes the chemical reactivity of chemical compounds.¹ Thus, new compounds or compound families becomes available which are hardly or not obtained by more classical methods of organic synthesis. Especially, in the field biologically active compounds, photochemical reactions have now become highly interesting.² Research activities in synthetic organic photochemistry have been intensified in both the academic and industrial domain. It should be pointed out that the application of photochemical reaction to organic synthesis is part of sustainable (green) chemistry. Photons can be thus used by chemists as "traceless" reagent.³⁻⁵

Heterocyclic compounds play a key role in the pharmaceutical as well as well as the agrochemical domain and photochemical reactions for the preparation of such compounds are very attractive.⁶⁻⁸ In this context, imine photochemistry became particularly interesting.⁹ The organic photochemistry of imines combines aspects of photochemistry of carbonyl compounds and alkenes.¹⁰ Typical photochemical reactions such E/Z-isomerization, cycloaddition, photoreductions and related reactions

or rearrangements are also observed with imines. In the context of the IMPHOCHEM project, we are particularly interested in photochemically induced hydrogen atom transfer (HAT) and its application to organic synthesis.

Continuous-flow microstructured technologies, which involve channels or tubes from tens of micrometres to a few millimetres in diameter are now recognized as alternatives to batch processing. Their benefits for organic photochemistry have been highlighted recently.¹¹⁻¹⁴ While reducing irradiation time, higher conversions and selectivities can be achieved because of (i) extensive penetration of light, even for concentrated chromophore solutions, (ii) minimization of side reactions or decompositions by flow-operation, (iii) easy control of the irradiation time and (iv) safer conditions (for example when involving heat-sensitive oxygenated intermediates). The integration of LEDs (Light-Emitting Diodes) as light sources in these technologies provides also additional opportunities. They present high electrical yields, long lifetimes, and spatial compactness, with the possibility of selecting the emission spectral domain and modulating the emitted radiant power.

Implementing flow photochemistry emerges thus as a relevant strategy to study imine photochemistry in terms of reaction pathways but also for rapid reaction screening and optimization

The project

IMPHOCHEM (<https://youtu.be/O4XrOmJeBsI>) is a comprehensive research project on photochemical reactions of imines (Figure 1). The project is funded by the French Research Agency (ANR-18-CE07-0026). Theoretical and physicochemical aspects, stereoselectivity and scope of the reaction will be investigated as important parameters for organic synthesis. For that, in addition to conventional batch reactors, LED-driven microreactors will be implemented, in an original way and from the beginning of the study, as a tool (i) to perfectly control the operating parameters (irradiation, temperature) that could influence selectivity and yield, (ii) to understand and model their influence of the reaction's output, and (iii) to access the feasibility of the transfer into meso-scale continuous flow-equipment.

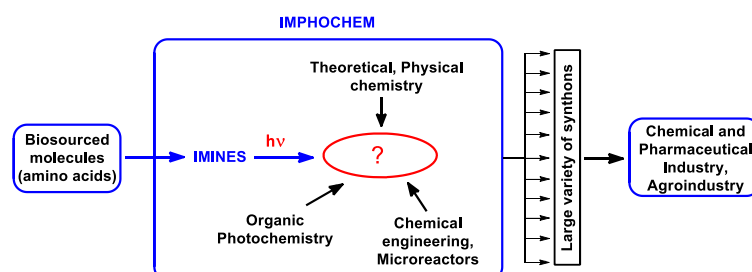





Figure 1. IMPHOCHEM as a comprehensive and multidisciplinary research project.

The consortium

The consortium is composed of three partners from France and Japan.

	<p>N. Hoffmann, M. Latrache Institut de Chimie Moléculaire de Reims (ICMR, UMR7312, Reims) https://www.univ-reims.fr/minisite_68/</p>
	<p>K. Loubière, M. Schmitt, J.-F. Blanco Laboratoire de Génie Chimique (LGC, UMR 5503, Toulouse) https://lgc.cnrs.fr/</p>
	<p>M. Abe Hiroshima University, Department of Chemistry, (Hiroshima, Japan) https://www.hiu-roc.com/</p>

The **scientific objectives** are to

- Acquire profound knowledge of the basic photochemistry of cyclic imines.
- Control the selectivity of the reaction.
- Identify scope and limitations
- Implement continuous-flow chemistry all along the stages of the proposal

These objectives will be achieved by the following tasks:

Task 1 will take over the comprehensive study of the photochemical reaction of imines and the optimisation of the operating conditions for a large substrate scope.

Task 2 will take over the computational calculations for the characterisation of diradical species involved in the reaction to identify the key structural parameters that influence selectivity.

Task 3 will develop the reaction under flow conditions in microreactors irradiated by a purpose-built UV-LED array. This process allowed accurate control of irradiation (emission spectrum and intensity), temperature and reaction time. A modelling approach will be also implemented.

Impact and benefits of the project

IMPHOCHEM deals with a comprehensive study of the **photochemical transformation of imines**. The global objective is to have access to a large structural variety of molecules useful as synthons, mainly **nitrogen containing heterocycles**, for chemical and pharmaceutical companies, from bio sourced substrates. The methodology is based on an original combination of **organic photochemistry, theoretical physical chemistry, chemical engineering and flow photochemistry** expertises. The use of LED-driven microreactors from the first steps will offer undeniable advantages for understanding how operating conditions control selectivity, but also for acquiring information (kinetic data) to transpose these photochemical routes to an **industrial scale using continuous-flow technologies**. Thus, this proposal will contribute to the development of **continuous, integrated processes for a safe and sustainable production of fine chemicals and pharmaceuticals**.

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ABSTRACTS OF THESIS ON PHOTOCHEMISTRY

Intermolecular [2+2]-Photocycloaddition Reactions of complex Acceptor-Donor Systems and Development of an Enantioselective Photocatalyzed Hydroformylation Reaction

Jens Lefarth

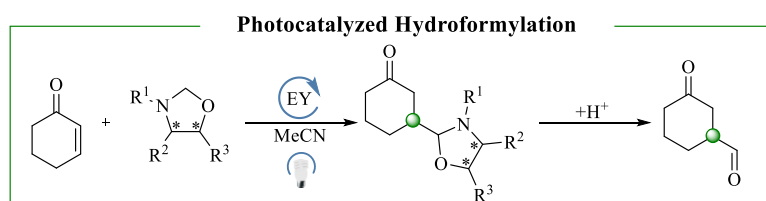
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In modern synthetic organic chemistry, photochemistry depicts a powerful method to achieve thermally challenging chemical transformation. Especially the field of photo(redox)catalysis has gained a tremendous growth over the last two decades.^[1-3] Therein, highly energetic excited state photocatalysts could enable a wide array of open-shell reactions under mild conditions.^[4] In consideration of the actual severe problems of global warming and the replacement of fossil fuels, photocatalysis allows the use of visible light, resulting in milder and more environmentally friendly methodologies for chemical transformations.

In this Ph.D. thesis, such photocatalyzed processes were investigated in more detail in case of two different reactions: the introduction of C₁-building blocks in small organic molecules by a (formally) photocatalyzed hydroformylation and intermolecular photocatalyzed [2+2]-cycloadditions of acceptor-donor systems.^[5]

The hydroformylation has, since the discovery by Otto Roelen in 1938, become one of the largest homogenous industrial processes.^[6] However, current processes are still in need of rare transition metal catalysts and require a high energy consumption. Hence, a visible light mediated approach by organic dyes, such as Eosin Y, were anticipated to achieve a benign, environmentally friendly and mild approach for a photocatalyzed hydroformylation reaction. For this, the industrially used syngas (CO/H₂) was replaced by formyl equivalents such as 1,3-dioxolane. In addition, the overall goal was to achieve an asymmetric approach by the use of chiral

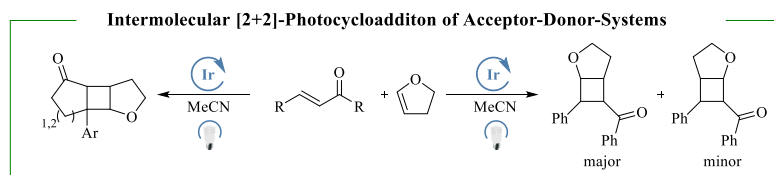
formyl equivalents based on easily accessible amino acids (Scheme 1). A sustainable methodology for achiral oxazolidines could be established under mild conditions and with high chemical yields (>80%). A general proof-of-concept could then be achieved for chiral formyl equivalents, while further optimization of the chemical yield is still required.



Scheme 1. Visible light mediated hydroformylation by Eosin Y (EY) as the photocatalyst.

The second topic of this thesis was concerned with mechanistic aspects of [2+2]-photocycloaddition reactions and the behaviour of acceptor-donor systems in regard to the product chemo-, regio- and diastereoselectivity (Scheme 2). An extensive study was performed for the two model substrates of chalcone and 2,3-dihydrofuran due to their unique photophysical and electrochemical properties. Therein, a complex product mixture of four diastereo- and regioisomers as well as four other products that consisted of chalcone dimerization and reduction products were obtained. While the product distribution could be optimized based on several experimental parameters (photocatalyst, concentration, stoichiometry, additives, solvent) that also resulted in details about mechanistic insights, the regioselectivity and product diversity could be analyzed further by electrochemical analysis and DFT calculations.

Furthermore, the scope of several cyclic enones and different alkenes was performed that resulted in an increased diastereo- and regioselectivity for more constrained systems.^[7]



Scheme 2. Visible light mediated [2+2]-photocycloaddition of acceptor-donor systems.

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BODIPY compounds: fluorescent markers for biomacromolecules and phototherapeutics

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This PhD thesis features a new approach of cancer phototreatment, as well as a design of new photoreactive fluorescent markers for biomolecules.^{1,2} Expected antiproliferative activity of investigated molecules relies on photochemical generation of quinone methides (QMs) that can react with biomacromolecules causing cytotoxicity.³ This approach has a major advantage compared to the classical photodynamic therapy since it does not require oxygen for biological activity, as tumour tissues are often hypoxic.⁴ Moreover, it was expected that investigated molecules would covalently bind to biomolecules and could be used as fluorescent markers.

Thesis describes synthesis of four classes of new fluorescent BODIPY dyes that were substituted by photochemically reactive substituents (Figure 1). Molecules **1-11** as photoreactive group have *N,N*-dimethylaminomethyl substituents for which it was expected to react in photodeamination reaction generating reactive QM (Scheme 1).⁵ On the other hand, for molecules **12-15** it was expected that QM would be formed by a cleavage of the substituent at the *meso*-position of the BODIPY core in a photoheterolysis reaction,⁶ whereupon an elimination of the acetyl group would give rise to QMs (Scheme 1).

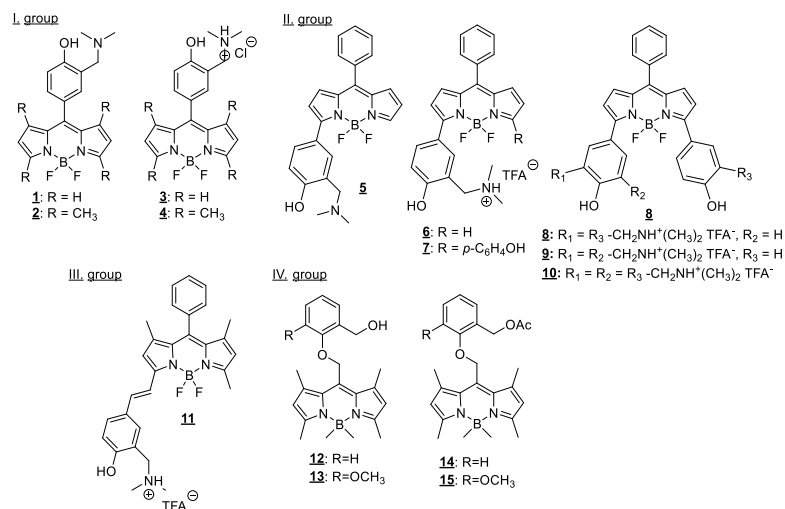
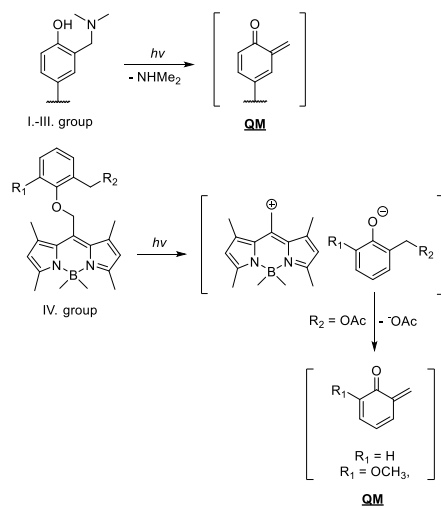


Figure 1. Structures of investigated BODIPY quinone methide (QM) precursors.



Scheme 1. Photochemical deamination reactivity of I-III groups of BODIPY compounds and anticipated photochemical reactivity of IV. group.

Photochemical reactivity and photophysical properties of the prepared QM precursors were investigated by photosolvolyses and spectroscopic techniques – UV-vis and fluorescence spectroscopy and laser flash photolysis (LFP). Binding to a model protein bovine serum albumin (BSA) was tested after irradiation of the dye-protein complexes using gel electrophoresis, and antiproliferative activity of the dyes was investigated on human cancer cells by MTT test.

Methanolysis products for molecules **1-11** indicated formation of QMs, which were detected by laser flash photolysis. Furthermore, for molecule **4** we have shown that photogenerated QMs react with BSA and induce covalent attachment to the protein. One of our major discoveries is that the photodeamination of molecules takes place only upon excitation to higher singlet excited states, whereas S_1 states deactivate by fluorescence. This unusual anti-Kasha photochemical reactivity was fully elucidated by computations at the TD-DFT level of theory. This concept to use one wavelength of light to photoactivate the dye and attach it to a protein, and other wavelength to read the fluorescence is highly applicable in the development of fluorescent sensors (Figure 2).¹

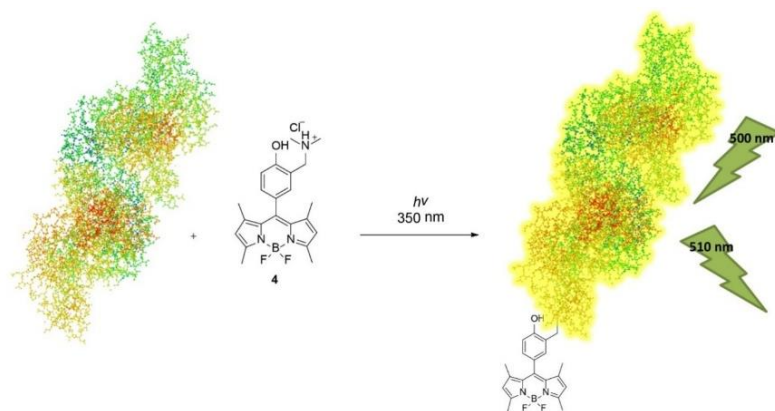


Figure 2. Covalent binding of compound **4** to a protein by irradiation with a wavelength of 350 nm and visualization of the labelled protein with visible light by emission detection at 510 nm

Fourth class of molecules also showed unexpected photochemical reactivity, since anticipated photoproducts of methanolysis were not detected. Isolated product suggest that reaction is occurring at the boron

atom of the BODIPY core. Upon treatment of cells with the dyes and irradiation with visible light ($\lambda > 500$ nm), molecules **12-14** showed significant enhanced activity, which makes them potential leads in the development of cancer phototherapeutics. However, for the ultimate application, all details of the photochemical reaction mechanism have to be unravelled.

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Exciton coupling and energy transfer in perylene-based systems.

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Understanding the nature of photoinduced processes in organic molecules is essential for the design and synthesis of compounds with desired photochemical properties. Molecules that are able to transfer the excitation energy between the states of different multiplicity are of particular interest both fundamentally, but also for the design and production of systems with precise function. For instance, triplet harvesting is of practical importance in the field of organic light-emitting diodes (OLEDs) where electrically excited molecules undergo a charge recombination process.¹ Due to the slow emission from the excited triplet states, a significant efficiency roll-off is observed in OLEDs, thus making new triplet harvesting strategies important.

The Förster resonance energy transfer (FRET) formalism does not include the spin component in the energy transfer mechanism, instead it relies on the strength of dipole-dipole coupling between the donor and the acceptor.² This theoretically allows for spin-forbidden triplet-to-singlet (TtoS) energy transfer. Indeed, FRET-mediated triplet-to-singlet energy transfer has been observed using freely diffusing donors and acceptors as early as in the 1960s,³ but the connection between measured FRET efficiencies and theoretically derived values based on photophysical parameters and the distance and angles between transition dipole moments in a molecular dyad has been missing.

In this thesis the possibility of FRET between a triplet and a singlet state was explored using an iridium-based triplet donor and a perylene-based singlet acceptor. To be able to verify the TtoS energy transfer in a controlled manner, two covalently linked isomeric donor-bridge-acceptor (peri-DBA and ortho-DBA) systems (Fig. 1) were used. The molecules were synthesized in convergent synthetic pathways in 14 steps (peri) and 13 steps (ortho).^{4,5} The target systems were designed with an intention to favour the excitation energy transfer from the excited triplet state of the donor to the excited singlet state of the acceptor. Performing

intramolecular TtoS in covalently linked DBA systems with experimentally determined donor-acceptor distances and known orientation factors of the oscillating dipoles allowed for a detailed comparison between the theory and experiment. In both dyads the triplet-to-singlet energy transfer was fully explained using the theory of Förster-type resonance energy transfer, making this study the first example where TtoS is experimentally verified and aligned with the theory. The TtoS energy transfer was 36 times faster than the rate of donor phosphorescence. This allowed to harvest the triplet excitation energy in the deep-blue region of the electromagnetic spectrum where the making of efficient OLEDs is particularly challenging.

In parallel to Förster-type TtoS, Dexter-type triple-triplet energy transfer (TET) was observed in both systems. It was noted that, when attaching the acceptor chromophore in the ortho position, the rate of Dexter-type TET increased but the rate of triplet-to-singlet FRET decreased. This interplay demonstrates the sensitivity of both Förster and Dexter types of energy transfer towards molecular alignment. Furthermore, it shows that it is possible to increase the rate of one energy transfer pathway, while simultaneously decreasing the other one.

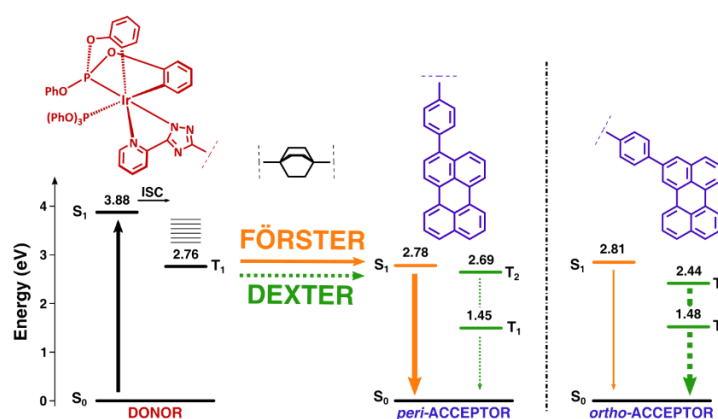


Figure 1. Jablonski diagram showing Förster-type triplet-to-singlet energy transfer and Dexter-type triplet-triplet energy transfer in isomeric donor-bridge-acceptor systems.

Another research direction that was explored in this thesis, was the making of efficient light-emitting molecules in the near-infrared (NIR) region of the electromagnetic spectrum. The current progress in this area is limited by the framework of the energy gap law. The absorption and the

emission in the NIR regime are associated with photons of low energy, meaning that the energy gap between the excited state and non-excited (ground) state is small. Consequentially, this results in an exponentially increased probability for the molecule to return to the ground state without photon emission. Developing strategies for overcoming the energy gap law is therefore essential for being able to achieve high emission quantum yields in the NIR region of the electromagnetic spectrum.⁶

Limited solubility represents another challenge in synthesis of NIR chromophores. Bay-alkylation of perylene allowed us to synthesize soluble dihexylquaterrylene scaffold and measure its photophysical properties in such inert solvent as toluene (Fig.2).

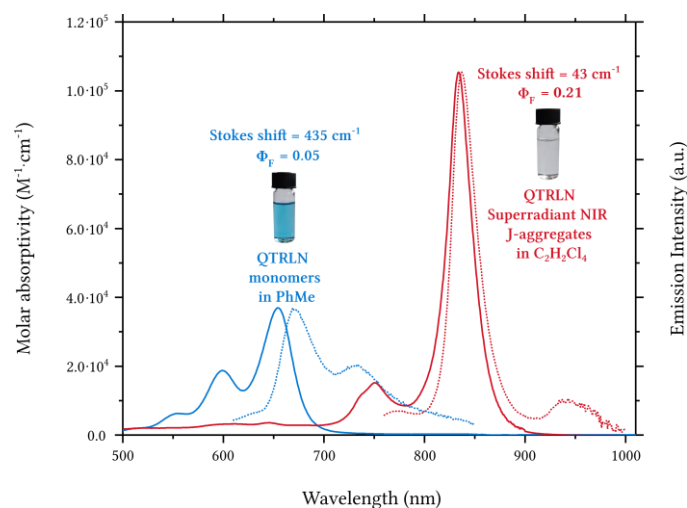


Figure 2. Absorption and emission spectra of dihexylquaterrylene recorded in toluene and in $C_2H_2Cl_4$ scaled according to their molar absorption coefficients. Dihexylquaterrylene is present in its monomeric form in toluene, while in $C_2H_2Cl_4$ it forms superradiant J-aggregates.

Unexpectedly, dissolving dihexylquaterrylene in $C_2H_2Cl_4$ resulted in discoloration, indicating formation of a new species. Spectroscopical investigations of this phenomenon concluded that the newly formed species were dihexylquaterrylene J-aggregates (Fig. 2). The increased radiative rate (k_r) and decreased non-radiative rate (k_{nr}) resulted in a 4-fold increase of the emission quantum yield in the J-aggregates when compared to the monomers. The increase of k_r was attributed to the superradiance

effect, which is a common phenomenon in J-aggregates. However, the decrease of k_{nr} was unexpected and indicated that the J-aggregates can successfully overcome the limitations set by the energy gap law. The deviations from the exponential increase were previously shown using platinum-based complexes,⁶ however the decrease of k_{nr} had not been observed previously. The decrease in k_{nr} was achieved because of the reduced reorganization energy due to the delocalized nature of the excited state in J-aggregates.⁷ This emphasizes the importance of controlled aggregation strategies that could potentially open up a new approach towards highly emissive NIR dyes.

These results contribute to the understanding of the fundamental photophysics behind such processes as: multiplicity conversion, directional energy funnelling, switching between energy transfer pathways and aggregation-induced enhanced emission.

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Molecular Properties in an Optical Microcavity: From Ensembles to Single Molecules

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The resonance interaction between a confined optical mode within a microcavity and a molecular transition results in either enhancement of spontaneous emission rate in the weak coupling light-matter regime (the so-called Purcell effect)¹ or alteration of energy levels of molecules through the formation of polaritonic states in the strong coupling regime.² Due to these effects, light-matter interaction phenomena inside a microcavity can be used as a “physical” method to control the physical and chemical properties of molecules.³ In this work, the spectral and photophysical properties, as well as excited state reactivity of molecules, were modulated using the vacuum electromagnetic field of an optical microcavity.

A voltage-tunable open IR-microcavity was prepared and characterized in order to study the influence of the confined field of the microcavity on the IR absorption properties of molecules in a liquid phase (Fig 1a).⁴ This cavity is a versatile tool to hybridize essentially any vibrational transition in the mid-IR regime with a cavity mode. Multimode vibrational strong coupling was demonstrated in methyl salicylate using this cavity. A coupled damped harmonic oscillator model was employed as a theoretical tool to describe the multimode vibrational strong coupling. The theoretical results revealed that absorption of uncoupled molecules and spectrally close off-resonance molecular vibrations, in addition to the resonance vibrations, must be simultaneously considered to describe the behaviour of the multimode vibrational strong coupling adequately (Fig.

1b-d).⁴ The same cavity was used to investigate the effect of vibrational strong coupling on the Raman scattering properties of selected systems. Our results confirmed that even though the system is in the vibrational strong coupling regime, changes in the Raman spectra do not necessarily result from the strong coupling, but are caused by the surface enhancement effects.⁵

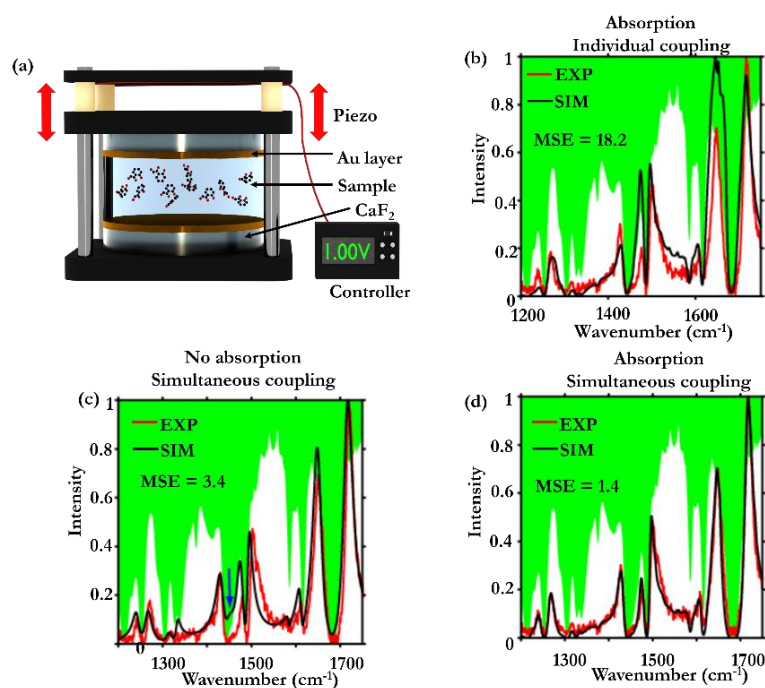


Fig. 1. (a) Schematic of the open microcavity structure employed to couple liquid phase samples. (b-d) Experimental (red line) and calculated (black line) cavity transmission spectra for a 25% v/v solution of methyl salicylate (MS) inside an on-resonant cavity. The green area shows the transmission spectrum of MS in free space. The mean square error (MSE) indicates the fit quality. In panel (a), only absorption is considered, while in (b), we take into account both absorption and individual coupling - the interaction of the vibrations that are only resonant with the respective cavity mode. Panel (c) demonstrates the case of multimode coupling - simultaneous coupling of the resonant and the closest two off-resonant molecular vibrations to the same cavity mode, and in this scenario, the

absorption was excluded. The simulated spectrum shown in panel (d) was obtained by including both absorption and simultaneous coupling of the nearest MS vibrations to a single cavity mode. Modified from ref. 4. Copyright (2020) American Chemical Society.

The photophysical properties of individual phthalocyanine (PcS_4) molecules embedded in PVA film were studied under the Purcell effect, using $\lambda/2$ -microcavity, confocal laser scanning microscopy, and time-resolved fluorescence techniques. Molecules on resonance with the microcavity mode have a shorter fluorescence lifetime, and the excited singlet state is depopulated faster; as a consequence, the transition rate to the triplet state is reduced.⁶ As a result, we observed that the molecules in a resonant cavity stay locked in a specific tautomeric form for a longer time, since the lowest triplet state is less frequently populated (Fig. 2).⁶ This suggests that in our single-molecule method, we probe tautomerization reactions in the lowest triplet state. Interestingly, these findings show that the weak light-matter coupling phenomenon can be used to steer photophysical and photochemical processes that occur in the triplet states to the desired direction.

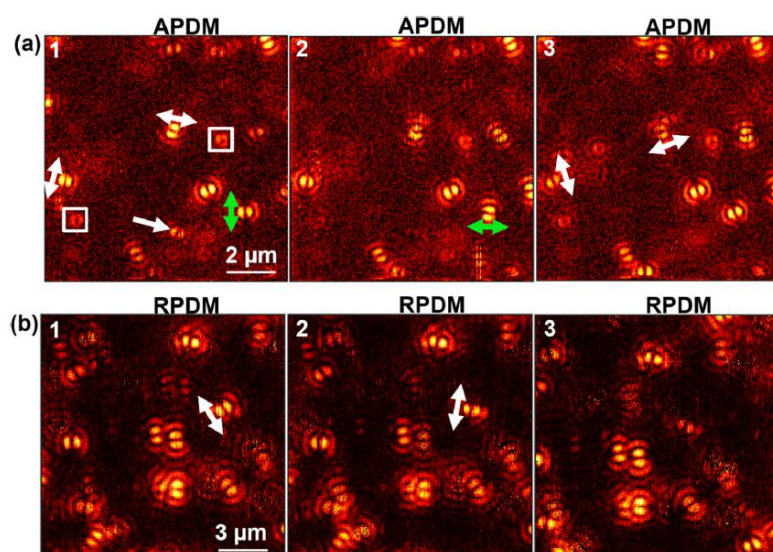


Fig. 2. Impact of the Purcell effect on the tautomerization of individual PcS_4 molecules. Series of confocal fluorescence images of single PcS_4 molecules.

molecules embedded in PVA acquired with azimuthal (APDM) and radial (RPDM) polarizations in free space (a) and in a $\lambda/2$ microcavity (b). Molecules that show double-lobe patterns and a reorientation of the transition dipole moment are marked with double-headed arrows, whereas white rectangles mark those that show ring-like patterns. For the molecule marked by the green double arrow, the orientation of the transition dipole moment rotates by 90° upon tautomerization. Copied from ref. 6. Copyright (2021) American Chemical Society.

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Synthesis and characterization of new chromophores with two photon absorption properties and study of their application in bioimaging

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As consequence of the non-invasive nature of the light, fluorescence-based methods have become essential to understand biological processes, these including, for instances, the monitoring of cellular events or the identification of subcellular organelles. In addition, two-photon microscopy has attracted recently elevated interest in this field, mainly because of the use of lower energy excitation wavelengths as well as the three-dimensional control of the excitation process.¹ Thus, the design and development of new molecular tools for two-photon (2P) microscopy bioimaging is an interesting research challenge, being this the central topic of my thesis: “*Synthesis and characterization of new chromophores with two photon absorption properties and study of their application in bioimaging*”.

During the past four years, my research has been focused mainly on the development of new indolenines and indoliniums derivatives conceived to be employed in 2P microscopy (see the general structures in **Figure 1a**). These molecular architectures are characterized for outstanding synthetic flexibility and adequate photophysical properties for 2P microscopy bioimaging. Indeed, their versatility allows readily implementation of these dyes in diverse applications *via* straightforward and efficient structural modifications. One of such example is displayed in **Figure 1b-d**.² The reduction of the fluorescent form, so-called “on”, leads to a non-fluorescent stage referred as “off”.

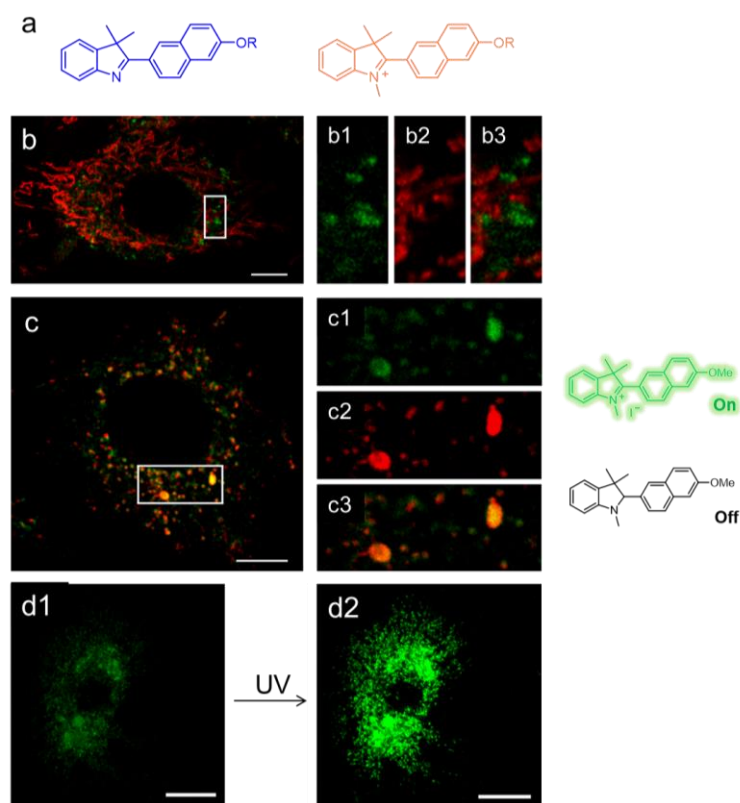


Figure 1. (a) General structures of indolenines (blue) and indoliniums (orange) scaffolds. From (b) to (d), it is shown the performance of the system represented at the right, which was conceived for the detection of lysosomal hydroxyl radical. In all of these images, cells were treated with a solution of the "off" compound ($0.025 \mu\text{M}$, $\lambda_{\text{exc},2\text{P}} = 740 \text{ nm}$, $\lambda_{\text{em}} = 500\text{-}550 \text{ nm}$, represented in green), and the hydroxyl-radical-induced fluorescence was examined in the presence of (b) mitochondrial (Mitotracker Red, $\lambda_{\text{exc},1\text{P}} = 561 \text{ nm}$, $\lambda_{\text{em}} = 600\text{-}640 \text{ nm}$, represented in red) and (c) lysosomal commercial trackers (Lysotracker Deep Red, $\lambda_{\text{exc},1\text{P}} = 633 \text{ nm}$, $\lambda_{\text{em}} = 645\text{-}740 \text{ nm}$, represented in red) Selected areas in (b) and (c) are enlarged in b1-3 and c1-3, respectively. In (d), it is illustrated the response of the system towards the production of endogenous ROS generation upon UV irradiation. d1 and d2 are the images recorded from living MEFs before and after a 10 s exposure to UV light, correspondingly.

This last one selective accumulates in lysosomes due to the presence of a tertiary amine in its structure, where the later action of hydroxyl radical together with the acid environment in these organelles are responsible for the recovery of the emissive state (“on”). This is illustrated when comparing **Figure 1b** vs. **c**, in which it can be observed that the overlap between the emission outcoming from our compound (represented in green) and the ones of the diverse commercial trackers (shown in red) is only appreciable within lysosomes (see **Figure 1c**). This process is further enhanced when inducing oxidative stress (see **Figure 1d**). That is, by using this system is possible to measure the endogenous production of lysosomal hydroxyl radical as well as the stimulated generation of this species by other agents affecting cellular oxidative stress.

Noteworthy, it should be noted that this is not the only application that this type of molecules finds. For example, tuning the indolenine scaffold conducts to different derivatives with ability for detecting pH changes in cellular environments. More concretely, the performance of these indolenine-based analogues for measuring changes in the internal pH as well as selectively staining lysosomes has been thoroughly examined.³ In addition, certain decorations over indolinium backbone enable simultaneous and dual-color labeling of lysosomes and mitochondria, that is, we have also devised dyes that exhibit organelle-specific photophysical properties and can be monitored by combination of confocal and 2P microscopy. By and large, these new class of compounds are pointed as promising candidates to gain insights into biological contexts by means of 2P microscopy.

On the other hand, other objective of this thesis work that has been fulfilled is the development of a new strategy that allow to overcome one of the drawbacks of 2P microscopy: the 3D-resolution. Considering that the 3D-resolution is better as long as more photons are concurrently involved in the excitation process, a new dyad system consisting in the combination of a fluorenyl derivative and a diarylethene photoswitch was designed (see **Figure 2a**). This system is operated by two 2P-mediated processes: FRET sensitized by 2P-excitation, and 2P-excited fluorescence. The performance of this system under ideal conditions would lead to a quartic dependence of the emission intensity on the excitation energy, typically observed in compounds capable of absorbing four photons. Thus, this system based on conventional two-photon absorber dyes would proportionate an improved 3D resolution when applied into 2P microscopy. It is worth noting that the experimental performance is in line

with the theoretical-experimental models, and the proof-of-principle is nicely demonstrated (see **Figure 2b**). This strategy, that can be applied to any pair of 2P-dye and a FRET-efficient photochromic system, could suppose a redynamization of the 2P absorption process in many diverse fields.⁴

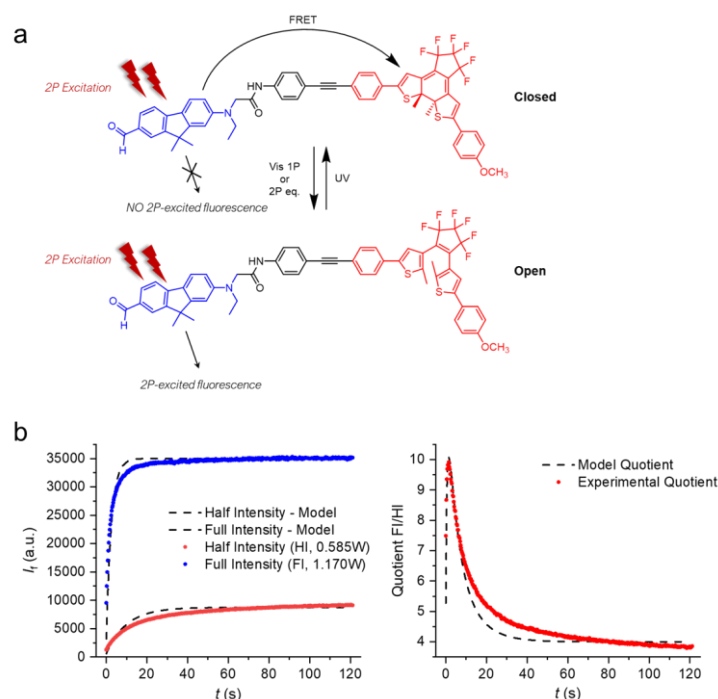


Figure 2. (a) Working principle of a photochromic dyad having a DTE appended to a 2PA dye. The FRET acceptor, FRET donor and the used bridge are distinguished in red, blue, and black, respectively. (b) At the left, it is shown the kinetics of fluorescence build-up on irradiation of the dyad (10 μ M in aerated methanol) with 820 nm laser light at full intensity (FI, blue points) and at half intensity (HI, red points). Modeling of these conditions, introducing the initial 6% of the open isomer, are included as dashed black lines. At the right, it is represented the ratio of time-dependent fluorescence intensities shown at the left, these including the theoretical curves

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4. Benitez-Martin, C.; Li, S.; Dominguez-Alfaro, A.; Najera, F.; Pérez-Inestrosa, E.; Pischel, U.; Andréasson, J. Toward Two-Photon Absorbing Dyes with Unusually Potentiated Nonlinear Fluorescence Response. *J. Am. Chem. Soc.* **2020**, *142* (35), 14854–14858. <https://doi.org/10.1021/JACS.0C07377>.

CONFERENCE ANNOUNCEMENTS

Central European Conference on Photochemistry (CECP 2022)



[HTTP://WWW.CECP.AT/INDEX.PHP/HOME](http://www.cecp.at/index.php/home)

Upcoming Photochemistry Meeting:

CECP 2022 "Central European Conference on Photochemistry"

organized by EPA Austria

Sunday, February 13 to Thursday, February 17, 2022, Bad Hofgastein

Lectures

short talks

poster sessions

industrial exhibition



Bad Hofgastein in winter



Congress center

Let us meet again!

www.cecp.at

28th PhotoIUPAC (2022)



<https://photoiupac2022.amsterdam/>

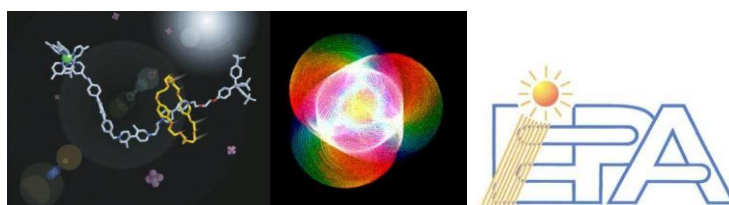
After the unfortunate cancellation in 2020 due to the COVID-19 pandemic, we hope to welcome the photochemistry community in Amsterdam in July 2022.

The 28th IUPAC Symposium on Photochemistry continues a long tradition of conferences where experts in photochemistry in a broad sense exchange the latest results, and where scientists and engineers who use light in their research or application can pick up new ideas and strengthen their knowledge of the specifics of the interaction of light and matter.

The scientific topics to be covered in the Symposium include areas of unparalleled impact in the world today. These include renewable energy sources, green chemistry, atmospheric photochemistry, single molecule microscopy and super resolution imaging. The latter are key for biosciences and trace analysis of proteins, nucleic acids, and small bioregulators. With more efficient light sources and means to collect solar energy, there is an on-going resurgence in the development of photochemical reactions using flow process, which are beginning to make an impact in an industrial context. This will be an excellent opportunity to engage scientists from pharmaceutical, materials, and other industries. The symposium will also cover advanced spectroscopic methods with increased time and space resolution and methods for analyzing complex samples.

- **Opening of registration:** 15th December 2021
- **Call for abstracts:** 15th December 2021
- **Deadline for submission of oral abstracts:** 15th February 2022
- **End of Early Bird registration:** 20th April 2022
- **Deadline for submission of poster abstracts:** 20th May 2022
- **Symposium dates:** 17th-22nd July 2022

EPA IS ON FACEBOOK AND TWITTER



European Photochemistry Association



MEMBERSHIP APPLICATION FORM



EUROPEAN PHOTOCHEMISTRY ASSOCIATION 2021 MEMBERSHIP RENEWAL/APPLICATION FORM

Please complete the form and send it to the Treasurer by mail
(do not use e-mail for security reasons!):

Dr. Alexandre Fürstenberg
Department of Physical Chemistry and
Department of Inorganic and Analytical Chemistry
University of Geneva
1211 Genève 4, Switzerland

I wish to renew/apply for membership of the European Photochemistry Association (EPA)

Family name: _____ **First name:** _____ **Middle initial(s):** _____
Date of birth (dd/mm/yyyy): _____

If you are applying for a new membership or if your contact details have changed, please fill in the following section:

Address: (Please use your institutional address)

Tel: _____ **Fax:** _____ **Email:** _____

Membership fees for 2022 in EUR (please check one box)

The membership fee includes electronic subscription to the EPA official journal
Photochemical & Photobiological Sciences, the EPA Newsletter and reduced conference fees.

	1 year	3 years	5 years
regular	<input type="checkbox"/> 35 EUR	<input type="checkbox"/> 100 EUR	<input type="checkbox"/> 150 EUR
student*	<input type="checkbox"/> 15 EUR * please supply attestation	<input type="checkbox"/> 30 EUR * please supply attestation	

*For non-EU countries with economic difficulties, a reduced fee can
exceptionally be applied on request (only upon written approval by the Treasurer).*

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For questions contact Dr. Alexandre Fürstenberg (e-mail:
alexandre.fuerstenberg@unige.ch or treasurer@photochemistry.eu)
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