Mechanistic Investigations on Reductive Deazaflavin Photocatalysis & the Application of Semiconductor Photocatalysts for Organic Synthesis

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This thesis is dedicated to



Und dann bist du plötzlich an einem Punkt, an dem du sagst:

"Hey, ich bin jetzt 100-mal gefailed, aber jetzt hab ich's gerade hingekriegt

- und es ist besser als Garnichts."

– Simon Krätschmer

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Chapter 1

1 Deazaflavin Reductive Photocatalysis Involves Excited Semiquinone Radicals



1.1 Abstract

Flavin-mediated photocatalytic oxidations are established in synthetic chemistry. In contrast, their use in reductive chemistry is rare. Deazaflavins with a much lower reduction potential are even better suited for reductive chemistry rendering also deazaflavin semiquinones as strong reductants. However, no direct evidence exists for the involvement of these radical species in reductive processes. Here, we synthesize deazaflavins with different substituents at C5 and demonstrate their photocatalytic activity in the dehalogenation of *p*-halogenanisoles with best performance under basic conditions. Mechanistic investigations reveal a consecutive photo-induced electron transfer *via* the semiquinone form of the deazaflavin as part of a triplet-correlated radical pair after electron transfer from a sacrificial electron donor to the triplet state. A second electron transfer from the excited semiquinone to *p*-halogenanisoles triggers the final product formation. This study provides first evidence that the reductive power of excited deazaflavin semiquinones can be used in photocatalytic reductive chemistry.

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Author contributions

R.J.K., R.C., and A.G. wrote the paper with input from all authors. A.G. and T.N. performed the entire synthesis of all used compounds and conducted all photocatalytic dehalogenation reactions. A.G. did the electrochemical and EPR characterization. R.J.K. together with A.G. and T.N. designed the spectroelectrochemistry experiment, which A. G. performed. R.J.K. together with A.G. and T.N. collected the stationary spectroscopic data. R.J.K. performed all time-resolved spectroscopic experiments and conducted the computational studies. Experimental data were analyzed by R.J.K. together with A.G., computational data were analyzed by R.J.K., and results were discussed by all authors. The project was conceived by R.C., R.J.K., and B.K.

1.2 Introduction

Flavins, in the form of flavin mononucleotide (FMN) or flavin adenine dinucleotide (FAD), act as cofactors in various types of enzymes.¹⁻² Some organisms also use deazaflavins (dFls; dF_0 or dF_{420} , Scheme 1-1a) where the N-5 atom of the isoalloxazine ring is replaced by a carbon atom.³⁻⁴ Despite their structural similarity, their roles in biological systems differ substantially.^{3, 5} Flavins (**Fls**) form semiquinones (**Fl**_{sq}) (Scheme 1-1b), which are transiently stable in solution⁶ and more stable in protein environments.⁷⁻⁸ $Fl_{sq}s$ are typically involved in one-electron redox processes.^{1, 9} Fully reduced flavin (Fl_{red}) participates in two-electron reactions or, similarly as \mathbf{Fl}_{sq} , interacts readily with molecular oxygen (O₂), forming reactive oxygen species (ROS) or flavin hydroperoxide (FIOOH).¹⁰⁻¹³ FIOOH is the key agent in oxygenations mediated by flavin dependent monooxygenases.¹⁴⁻¹⁵ In contrast to Fls, dFls serve exclusively as two-electron carriers, thus behaving rather like nicotinamide adenine dinucleotide (phosphate) (NAD(P)H).^{3,5} Fully reduced deazaflavins (dFl_{red}) are considerably stable against oxidation by oxygen, thus avoiding formation of ROS.¹⁰ This is one reason why dFls have been tested as native coenzyme (FAD or FMN) substitutes.¹⁶⁻¹⁸ Both Fls and dFls absorb visible light enabling their involvement in light-dependent processes.¹⁹⁻²² Fl cofactors in their fully reduced form participate in photo-induced electron transfer (PET) reactions in DNA photolyases repairing pyrimidine dimers formed upon exposure to ultraviolet (UV) light.²³⁻²⁴ Fls in their oxidized form are responsible for bacterial bioluminescence²⁵ or perform various functions in photoreceptors.^{8, 26-28} Deazaflavin dF_0 in its oxidized form serves as a lightharvesting antenna in photolyases.²⁹ Inspired by nature, artificial Fl derivatives as well as flavoenzymes have been applied in photoredox catalysis and photobiocatalysis, mainly in oxidative transformations or in energy transfer processes.^{6, 20, 30-44} Photoenzymatic radical polymerization employing highly reducing excited FADH*- known from photolyases is rare and a very recent example of a photoreductive process with Fl.⁴⁵ In the dFl series, dFl_{red} has been found to be generated from dFl by PET from ethylenediaminetetraacetic acid used as sacrificial reductant.⁴⁶ This procedure has been utilized in the NAD(P)H-independent regeneration of FADH₂ from FAD.^{16, 47} dFls belong to the redox cofactors with the lowest redox potential; the first reduction potential of dFl [E(dFl/dFl_{sq})] is even more negative than that of Fls by 0.5 V.³ Therefore, dFls are better suited for reductive chemistry than Fls. The very negative first reduction potential renders the dFl semiquinone (dFl_{sq}) as a strong reducing agent. Despite this fact, there is no precedence of reductive processes involving this radical species. This might result from the very low stability of the dFl_{sa} free in the solution.^{3, 5, 48} Here we demonstrate that the reducing power of excited dFl radicals can be used in the presence of

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two substrates: (i) a sacrificial electron donor, e.g. diisopropyl(ethyl)amine (DIPEA), allowing the photochemical formation of the radical dFl_{sq} and (ii) a substrate for reduction, *p*-halogenanisole, undergoing dehalogenation *via* the excited radical dFl_{sq}^* .



Scheme 1-1: Flavins, deazaflavins, and their redox forms. a: Structures of flavin and deazaflavin cofactors. b: Redox states of flavins and deazaflavins. In contrast to flavins, semiquinone deazaflavins are untypical intermediates in redox chemistry.

1.3 Results and Discussion

1.3.1 Design and Synthesis

A series of 5-dFls 1 - 5 was synthesized with different substituents in position 5 (H-, Me-, *i*Pr-, CF₃-, and Ph-) *via* two different routes depending on the substituent (Scheme 1-2 and section 1.5.2). Derivatives 1 - 4 were obtained following route A starting from 3,4dimethoxyaniline (6). Reductive amination yielded compound 7, which was subsequently coupled with 6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione to give access to the key intermediate 8. Depending on the reaction conditions for the following step, the corresponding products 1 - 4 were obtained. As this synthetic method did not allow the synthesis of the phenyl derivative 5, route B was developed. In this three-component microwave-assisted procedure, adapted from Tu et al.,49 compound 5 was obtained from a reaction of benzaldehyde with N-butyl-3,4-dimethoxyaniline (7) and N-methylbarbituric acid (9). Following this procedure, the phenyl derivative could be isolated in both the oxidized (5_{ox}) and fully reduced form (5_{red}), which reflects the low sensitivity of the dFl_{red} against O_2 .^{3, 50} This observation is further supported by incubation of $\mathbf{5}_{red}$ in darkness for 19 h in non-degassed acetonitrile (ACN) where no considerable formation of 5_{ox} is observed via absorption spectroscopy (see section 1.5.5). However, light excitation of 5_{red} allows to overcome the activation barrier for re-oxidation by O_2 resulting in almost stoichiometric conversion to 5_{ox} .

1.3.2 Photophysical and Electrochemical Characterization

Compounds 1 - 3 have similar UV/visible (Vis) absorption and emission spectra in ACN giving similar electronic transition energies of these dFls with the usual blue-shift of around 40 nm compared to isoalloxazines (Scheme 1-2 and Figure 1-7).⁵¹ In contrast, derivative 4 with the strong electron withdrawing group -CF3 shows a red-shifted electronic transition by 26 nm in ACN compared to isoalloxazines. The compounds 1 - 4 are all highly emitting with fluorescence quantum yields ranging from 67% to 85% in ACN. Their emission lifetimes in ACN range between 6.8 and 11.1 ns (see section 1.5.4). In agreement with literature reports,⁴ cyclo-voltammetry (CV) shows more negative redox potential of the first reduction step of the dFls compared to tetraacetyl riboflavin (TARF) (E(TARF/TARF_{sq}) = -0.79 V)³⁹ by 0.13 -0.52 V (see section 1.5.6). The phenyl derivative 5 shows deviating characteristics compared to the other dFls. While the electronic transition energies are also blue-shifted compared to isoalloxazines and the redox potential of the first reduction step is also more negative compared to TARF, its emission properties are significantly different. The fluorescence quantum yield reaches only 16% and its excited singlet state lifetime is considerably reduced being only 1.7 ns. Furthermore, compound 5 is the only derivative that forms a thermally stable fully reduced form 5_{red} , which is only re-oxidized by light as discussed above.



Scheme 1-2: Synthesis and spectral and electrochemical properties. Electronic transition energies, $E_{0.0}$, and first reduction potentials *vs.* saturated calomel electrode (SCE) are given for all deazaflavins. Full spectra are shown for 5_{ox} and 5_{red} . Data for tetraacetyl riboflavin (TARF) are given for comparison. Further details on synthesis and characterisation are given in section 1.5.2 and 1.5.4, respectively.

1.3.3 Photodehalogenation

Owing to the strong reduction potential of deazaflavin derivatives compared to their flavin analogues, we investigated their use in the reductive photoredox catalysis for the dehalogenation of aryl halides, which is considered as a benchmark reaction because of their very negative redox potentials. For instance, with a one-electron reduction potential of -2.75 V,⁵² *p*-bromoanisole (*p*-BA) is beyond the limits of most organic photoredox catalysts,⁵³⁻⁵⁴ or it requires a combination of electrocatalysis and photocatalysis for dehalogenation.⁵⁵⁻⁵⁶

p-XA	$dFI = 5_{ox} \text{ or } 5_{f}$ $DIPEA (2.0)$ $Cs_2CO_3 (1.0)$ $\lambda_{exc} = 385$	nm, 18 h	H Anisole	
substrate	E _{red} vs. SCE [V]	photocatalyst	product yield [%] ^{[a],[b]}	
X = Br	-2.75	5 _{ox}	79	
X = Br	-2.75	$5_{\rm red}$	80	
$\mathbf{X} = \mathbf{Cl}$	-2.88	$5_{\rm red}$	80	

Table 1-1: Photocatalytic dehalogenation of *p*-halogenanisole by deazaflavin 5_{ox} and 5_{red}.

^[a]Reaction conditions: *p*-XA (75 mM (0.15 mmol)), 5_{ox} or 5_{red} (6 mM (8 mol%)), DIPEA (150 mM (0.3 mmol)), Cs₂CO₃ (75 mM (0.15 mmol)), ACN (2 mL), λ_{exc} = 385 nm, 25 °C, nitrogen atmosphere, 18 h. ^[b]Yields were determined *via* calibrated GC-analysis with 4-methylanisole as internal standard.

We achieved an almost quantitative yield of *p*-BA dehalogenation using the phenyl derivative **5** (6 mM, 8 mol% relative to substrate), when irradiating at 385 nm in the presence of a sacrificial reducing agent, here we used DIPEA, and caesium carbonate (Cs₂CO₃) (**Table 1-1**). The anisole yield is independent of the oxidation state of the photocatalyst, i.e. **5**_{ox} or **5**_{red}, since the reduced deazaflavin **5**_{red} is re-oxidized by O₂ and light as described above (see section 1.5.5). Noteworthy, **5**_{ox} also showed photodehalogenation of p-chloroanisole, whose redox potential is even more negative ($E_{red} = -2.88 \text{ V}$).⁵²

	×	(DIP	dFI (4 mol%) PEA (2.0 equiv. base)	H	
	<i>р-</i> ХА	λ _{ex}	_c = 385 nm, 6	h	Anisole	
base	product yield [%] ^{[a],[b]} using photocatalyst					
	1	2	3	4	5 _{ox}	5_{red}
None	22	12	15	14	24	27
NaHCO ₃	20	-	-	-	22	-
Cs_2CO_3	19	38	67	15	60	64
KO ^t Bu	50	-	-	-	59	-

Table 1-2: Photocatalytic dehalogenation of *p*-bromoanisole by deazaflavin in dependence of the basicity.

^[a]Reaction conditions: *p*-BA (75 mM (0.15 mmol)), dFl (3 mM (4 mol%)), DIPEA (150 mM (0.3 mmol)), base (75 mM (0.15 mmol)), ACN (2 mL), $\lambda_{exc} = 385$ nm, 25 °C, nitrogen atmosphere, 6 h. ^[b]Yields were determined *via* calibrated GC-analysis with 4-methylanisole as internal standard.

We next investigated the influence of the solvent and the excitation wavelength on the total product yield (see section 1.5.7). Interestingly, when dimethylformamide was used as solvent under otherwise identical conditions the product yield decreased by almost 50%. With respect to the excitation wavelength, the best yield, *ca.* 80%, was obtained for wavelengths \leq 400 nm. When using light of 455 nm, only 50% yield could be obtained. As a control, in the absence of photocatalyst, DIPEA, or irradiation, no reaction occurs. Recording the product build-up in case of **5**_{ox} showed that 60% conversion was observed already after 6 h.

Furthermore, we investigated the effect of basicity on the dehalogenation efficiency of p-BA (Table 1-2). Without any base, only yields between 10% and 30% are observed for all photocatalysts. In the presence of Cs₂CO₃, under otherwise identical conditions, the yield was increased to >60% for the **dFls 3** and **5**, while the reactivity of **dFls 1** and **4** remained unchanged or only increased to 38% for the methyl derivative **2**. For the **dFls 1** and **5**, we then tested bases with increasing basicity, i.e. NaHCO₃, Cs₂CO₃, and KO'Bu. While the activity of **5** was significantly enhanced by Cs₂CO₃ or KO'Bu, the reactivity of **1** only increased in presence of KO'Bu. These findings already indicate an important acidobasic equilibrium of a potential intermediate species of the photocatalyst that affects the overall performance. Thus, a deprotonated form of one key intermediate seems to be beneficial (A more detailed discussion can be found in section 1.5.8).

1.3.4 Excited Singlet State Reaction Results in a Loss Channel

The reactivity of the excited states of the compounds 1 and 5_{ox} with the sacrificial substrate DIPEA was investigated by time-resolved absorption and emission spectroscopy in the absence of any additional base, since the main focus was on the understanding of the underlying photocatalytic reaction mechanism (Further studies on the role of specific deprotonation states are currently ongoing in our laboratories and will be presented elsewhere.). In both cases, the excited state quenching was observed without the formation of any additional transient species (Figure 1-1 and section 1.5.9). This indicates the formation of a singlet born radical pair that recombines faster than it is formed owing to spin-allowed radical pair recombination. Such a fast recombination reaction was already observed in the Fl photooxidation of aromatic alcohols and represents a pure loss channel for photocatalytic applications.⁸ In case of the reaction between DIPEA and the excited singlet of the **dFl**, the bi-molecular reactions rates for 1 and 5_{ox} under low substrate concentrations (<200 mM DIPEA) are (1.05±0.01)·10¹⁰ M⁻¹·s⁻¹ and (9.0±0.1)·10⁹ M⁻¹·s⁻¹, respectively (see Stern–Volmer analysis in section 1.5.9). These values are smaller by 56% and 47%, respectively, compared to the theoretical diffusion limited bi-molecular reaction limit, which might indicate a geometrical preference for reactive encounters allowing for necessary interactions, and thus enabling a high probability for the reaction to proceed. In the presence of only the actual substrate *p***-BA** (with a concentration of 100 mM, which is sufficiently high for diffusion controlled encounters with the excited singlet state of the photocatalyst), the transient absorption (TA) data of 1 and 5_{ox} resemble those of the photocatalysts alone demonstrating no reaction between *p*-BA and the corresponding excited states (Figure 1-1c and section 1.5.9). In addition, in case of the stable fully reduced form, 5_{red} , also no reaction between the excited singlet state and the substrate p-**BA** is observed.



Figure 1-1: Excited singlet state dynamics of 5_{ox} . a-c: False colour representation of the time-resolved absorption spectra of 5_{ox} (360 µM) in non-degassed ACN in the absence (a), or presence of either 800 mM DIPEA (b), or 100 mM *p*-BA (c) exciting at $\lambda_{exc} = 450$ nm. d: Species associated spectra (SAS) that contribute to the time-resolved absorption signals in panels a-c with excited singlet state lifetimes as indicated. e: Model used to describe the time-resolved absorption data that results in physically reasonable SAS. On this time window k_{isc} is negligible and since no further species spectrum is detectable the assumption ${}^{1}K'_{beT} \gg {}^{1}K'_{eT}$ [Ssac] is justified. Abbreviations: SE = stimulated emission, rad = radiative, ic = internal conversion, (b)eT = (back) electron transfer, (b)isc = (back) intersystem crossing, S₀ = singlet ground state, S₁ = excited singlet state, T₁ = triplet state, ${}^{1}\text{RP}$ = singlet born radical pair, S_{sac} = sacrificial electron donor, and S = substrate.

1.3.5 Triplet State Reaction Forms Transiently Stable Semiquinone.

TA spectroscopy in the ns to us range was used in order to study the triplet state formation of 5_{ox} (Figure 1-2a, e, as well as further details in section 1.5.4 and 1.5.10). In comparison to isoalloxazines, its yield is low being only ca. 11% (Table 1-3 in section 1.5.4). In the presence of the substrate *p*-BA (50 mM), no reaction is observed with either the excited singlet or triplet state of 5_{ox} (Figure 1-2b, e). In contrast, in the presence of the sacrificial electron donor DIPEA (50 mM) electron transfer (eT) from DIPEA to the triplet state occurs forming the semiquinone 5_{sq} (Figure 1-2c, f), whose spectrum agrees well with the electrochemically generated spectrum (Figure 1-3g and section 1.5.11). The yield for eT can be determined from the corresponding decay rates to $\Phi_{eT} = 1 - k_0 k_q^1 = 87\%$, where k_0 is the total decay rate constant of the triplet in the absence and k_q in the presence of DIPEA. Considering the concentration of DIPEA (50 mM), the corresponding bi-molecular reaction rate with the triplet state is given to $(8.7\pm0.1)\cdot10^8$ M⁻¹ s⁻¹ ($k_{eT} = \Phi_{eT}k_q$ ([DIPEA])⁻¹). However, in the available spectral window of our experiment, we do not observe spectral signatures of the corresponding DIPEA radical cation. The assignment as the semiquinone radical is further proven by recording its electron paramagnetic resonance spectrum under photo-stationary conditions (section 1.5.12). In the presence of both *p*-BA and DIPEA, again, only the triplet reaction with DIPEA is observed, but no indication for a reaction between p-BA and 5_{sq} is found (Figure 1-2d, f). In summary, while the excited singlet state reaction with DIPEA results in a singlet born spin correlated radical pair, ¹[5_{sq}, DIPEA⁺], which recombines faster than it is formed owing to spin allowance, the triplet reaction with DIPEA involves a triplet born radical pair, ³[5_{sq}, DIPEA⁺], which is spin forbidden for recombination, thus allowing its accumulation (Figure 1-2g).



Figure 1-2: Excited singlet and triplet state dynamics of 5_{ox} . a-d: False colour representation of the timeresolved absorption spectra of 5_{ox} (60 µM) in non-degassed ACN in the absence (a), or presence of either 50 mM *p*-BA (b), 50 mM DIPEA (c), or both, 50 mM *p*-BA and 50 mM DIPEA (d) exciting at $\lambda_{exc} = 430$ nm. e: Species associated spectra (SAS) that contribute to the time-resolved absorption signals in panels a-b which were generated by applying the model in g to the decay associated difference spectra (DADS) shown in the inset. f: same as e, but for the data in c-d. Abbreviations: SE = stimulated emission, rad = radiative, ic = internal conversion, (b)eT = (back) electron transfer, (b)isc = (back) intersystem crossing, $^{1/3}$ = singlet or triplet state, RP = spin correlated radical pair containing the 5_{sq} (D = doublet state), S_{sac} = sacrificial electron donor, and S = substrate.

1.3.6 Reactivity of the Excited dFl_{sq}

In the next step, we investigated the reactivity of 5_{sq} in its excited state 5_{sq}^{*} towards the dehalogenation of *p*-BA. For this purpose, we generated the semiquinone form 5_{sq} electrochemically without the need of the light-induced reaction with DIPEA by applying constantly -1.2 V to the sample in ACN and followed its reactivity by UV/Vis absorption over time under the following four conditions: (1) alone in the dark, (2) in the dark and the presence of *p***-BA** (250 mM), (3) alone in the light ($\lambda_{exc} = 385$ nm), and (4) in the light $(\lambda_{exc} = 385 \text{ nm})$ and in the presence of *p***-BA** (250 mM). Alone in the dark, initially the concentration of 5_{ox} depletes completely and 5_{sq} is formed simultaneously (Figure 1-3a). On longer delays, the concentration of 5_{sq} reduces by *ca*. 18% with the simultaneous formation of $\mathbf{5}_{red}$ indicating partial disproportionation of two $\mathbf{5}_{sq}$ molecules into $\mathbf{5}_{ox}$ and $\mathbf{5}_{red}$.¹⁹ The former does not recover considerably because the electrode-driven one electron reduction immediately forms 5_{sq} again. Using the species spectra obtained from the electrochemical experiment (Figure 1-3g and section 1.5.11), the sequence of spectra can be perfectly decomposed in order to obtain the corresponding concentration-time profiles of the contributing species (Figure 1-3c). Repeating this experiment in the dark but now in the presence of **p-BA**, exactly the same behavior is observed within the experimental error (Figure 1-3b, c) demonstrating no reaction between *p***-BA** and either of the **dFl** redox species in their ground states. This additionally confirms the results of the TA spectroscopy. However, in the experiments with simultaneous illumination of the sample, significantly different kinetics are observed compared to the situation in the dark. In the absence of **p-BA** but presence of light, again, a rapid reduction of 5_{ox} is observed (Figure 1-3d). However, under these conditions 5_{sq} does not accumulate to the same extent (here only to 75% in the transient maximum) as in the case without illumination. Instead, a significantly enhanced formation of 5red up to 70% in the transient maximum is observed, indicating a light-induced second eT from the electrode to the excited 5_{sq}^* . Again, these data can be decomposed well with the known species spectra of the three redox states of 5 (Figure 1-3f). In the final experiment with light and p-BA, again, different kinetics are observed compared to the three experiments described before. In this case, 5_{ox} is only converted to *ca.* 75%. This is accompanied by a significantly reduced accumulation of 5_{sq} and 5_{red} (Figure 1-3e), thus indicating a reaction between *p*-BA and 5_{sq} in its excited state reforming 5_{ox} . Using only the known species-associated spectra (SAS) of the dFl intermediates, this time, the decomposition of the data shows significant deviations. Closer inspection of the arising absorption band at 300 nm reveals an asymmetric shape compared to the expected absorption band of 5_{red} indicating some underlying spectral contributions of a

different species than those already known from the dFls. After subtraction of a fitted linear combination of the known spectral features of dFl, an absorption spectrum with a single absorption band peaking at 330 nm remains (magenta spectrum in Figure 1-3g). Considering a potential radical anion of *p*-BA as an intermediate arising after eT from excited 5_{sq}^{*} to *p*-BA, we calculated the absorption spectrum of *p***-BA**^{•-} quantum chemically using a high level of theory, i.e. state-averaged XMCQDPT-CASSCF(12,12), considering also the solvent environment by the polarizable continuum model (PCM) for ACN (see section 1.5.13). As seen in Figure 1-3g and Figure 1-18a, the calculated spectrum matches the measured spectrum accurately, so that we assign this spectrum to p-BA^{•-}. Considering the p-BA^{•-} spectrum together with the already determined species spectra for all dFl intermediates now results in a good fit with deviation within the experimental error. Since the fit does not depend on the scaling of the *p*-BA^{•-} spectrum, we scaled the spectrum arbitrarily so that the resulting concentration-time profile stays below all Fl contributions. Furthermore, the quantum chemical calculation revealed a significantly longer bond length between the bromine and the adjacent carbon atom in p-BA^{•-} (2.86 Å) than in p-BA (1.92 Å) as well as a significantly reduced dissociation energy being close to thermal energy fluctuations (Figure 1-18b), which explains well the observed final dissociation of the bromine during the dehalogenation, which is triggered by a single electron reduction step as summarized in Figure 1-3h (Further details are given in section 1.5.13.). Analogous experiments were conducted with the non-substituted dFl 1. However, in contrast to the experiments with 5, the semi-reduced form could not be observed on the time scale of the measurements. The failure of detecting the semi-reduced form $\mathbf{1}_{sq}$ indicates that its lifetime is significantly shorter compared to that of $\mathbf{5}_{sq}$. This agrees with the observation of a significantly lower yield in the dehalogenation using 1 compared to 5, since less 1_{sq} may be accumulated.



Figure 1-3: Reactivity of electrochemically formed semiquinone 5_{sq} . a, b, d, e: Sequences of UV/Vis absorption spectra after application of -1.2 V to the sample at conditions as indicated. c and f: Concentrationtime profiles from fitting the species spectra shown in g to the data as indicated. The grey vertical lines in g correspond to the quantum chemically calculated stick spectrum of p-BA^{•-} as described in the text. h: Summary of all observed processes. The stick and ball structure of p-BA and p-BA^{•-} are the result of quantum chemical calculations as described in section 1.5.13. The significantly reduced Br⁻ dissociation energy in p-BA^{•-} demonstrates the final bromine dissociation upon one electron reduction.

1.3.7 Photocatalytic Reaction Mechanism Based on Consecutive Photo-Induced

Electron Transfer (conPET)

In summary, our results can be compiled to the photocatalytic reaction mechanism depicted in Figure 1-4. With respect to the redox potential neither $\mathbf{5}_{red}$ (E($\mathbf{5}_{sq}/\mathbf{5}_{red}$) = -1.60 V) nor $\mathbf{5}_{sq}$ $(E(\mathbf{5}_{ox}/\mathbf{5}_{sq}) = -1.41 \text{ V})$ can reduce *p***-BA** ($E_{red} = -2.75 \text{ V}$) in their ground states. The participation of the excited fully reduced form 5_{red}^* is not observed most likely due to very efficient intrinsic deactivation of the excitation energy as seen in fast deactivation kinetics on a ps time scale (see section 1.5.9). In the presence of the sacrificial electron donor DIPEA, we observe different reactivities for either the excited singlet or triplet state of 5_{ox} . In the excited singlet state reaction, a singlet born spin correlated radical pair, ¹[5_{sq}, DIPEA⁺], is formed, which recombines faster than it is formed. Accordingly, this reaction represents a pure loss channel. In contrast, eT to the triplet state results in a triplet born radical pair, ³[5_{sq}, DIPEA⁺], that is spin forbidden for recombination, thus allowing the accumulation of the considerably stable $\mathbf{5}_{sq}$. As a consequence, $\mathbf{5}_{sq}$ can be excited by a second photon ($E^*(\mathbf{5}_{ox}/\mathbf{5}_{sq}) = -3.3$ V), which enables a conPET⁵⁷ from 5_{sq}^* to the substrate, *p*-BA, regenerating 5_{ox} in its ground state and closing the photocatalytic cycle. The dissociation energy for the bond between the bromine and the adjacent carbon in p-BA^{•-} is significantly reduced leading to thermally driven dissociation into Br⁻ and the aryl radical. Finally, anisole is formed via hydrogen abstraction from either a DIPEA radical cation or a solvent molecule.⁵⁷ Owing to the lack of the observation of any protonated $\mathbf{5}_{sq}$ form (see section 1.5.8), the radical anion of $\mathbf{5}_{sq}$ is the active species.



Figure 1-4: Photocatalytic reaction mechanism. A sacrificial electron donor, *e.g.* DIPEA, reacts either with the excited singlet or triplet state of the deazaflavin. In the excited singlet state reaction, a singlet born spin correlated radical pair, ${}^{1}[\mathbf{5}_{sq}, \mathbf{S}_{sac}^{\bullet+}]$, is formed after eT. This radical pair recombines faster than it is formed. In contrast, eT to the triplet state results in a triplet born radical pair, ${}^{3}[\mathbf{5}_{sq}, \mathbf{S}_{sac}^{\bullet+}]$, allowing the accumulation of the considerably stable $\mathbf{5}_{sq}$. $\mathbf{5}_{sq}$ can be excited by a second photon enabling a consecutive photo-induced electron transfer from $\mathbf{5}_{sq}^{*}$ to the substrate, *p*-BA, regenerating $\mathbf{5}_{ox}$ in its ground state and closing the photocatalytic cycle. Finally, anisole is formed *via* hydrogen abstraction from either a $S_{sac}^{\bullet+}$ or a solvent molecule.

1.4 Conclusion

We have described the detailed photocatalytic mechanism of a reductive dehalogenation of phalogenanisole by **dFls**. The key point is the conPET *via* the anionic semiquinone form of the dFl. In doing so, we have revealed that dFls are valuable photocatalysts for reductive chemistry. In summary, after photoexcitation of dFl followed by intersystem crossing a sacrificial electron donor, at a moderate concentration, will enable a first eT to the triplet state resulting in a considerably stable anionic semiquinone. Additional excitation of the anionic semiquinone provides sufficient energy for a second eT process from the semiquinone to compounds with highly negative redox potentials, such as p-halogenanisoles. Finally, downstream reactions resulting in the product formation occur spontaneously. The action spectrum of the conPET reaction comprises the absorption of two different colored photons by the two key photocatalytic forms of dFl, where one is formed from the other having a distinct lifetime in the ns regime. Therefore, a concrete timed illumination of the photocatalytic system with short and intense pulses at the appropriate excitation wavelengths, which are temporally optimized to the lifetime of the key intermediates, should allow further improvement on the efficiency. This aspect is of general importance for all conPET-type reactions and should be addressed in future work. To our knowledge, this study shows for the first time that the reductive power of excited dFl_{sq} can be used in photocatalytic reductive chemistry. Moreover, because of its very negative potential, this species seems to belong to the most powerful reductants.^{53, 55-56, 58-61} Therefore, this study expands the photocatalytic toolbox for new chemical transformations and should serve as a guide for engineering photocatalysts of the next generation.

1.5 Experimental Part

1.5.1 General Information

Materials. Starting materials and reagents were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, Acros, Fluka, VWR, or Fluorochem) and were used without further purification. Solvents were used as p.a. grade or dried and distilled according to literature known procedures.

Nuclear magnetic resonance (NMR) spectroscopy. NMR spectra were recorded at room temperature using a Bruker Avance 300 (300 MHz for 1H, 75 MHz for ¹³C), a Bruker Avance 400 (400 MHz for ¹H, 101 MHz for ¹³C), an Agilent 400-MR DDR2 (400 MHz for ¹H and 101 MHz for ¹³C), or a Varian Mercury Plus 300 (300 MHz for ¹H, 75 MHz for ¹³C) with internal solvent signal as reference. All chemical shifts are reported in δ -scale as parts per million (multiplicity, coupling constant J, number of protons) relative to the solvent residual peaks as the internal standard (IS). NMR spectra are available in section 1.5.14.

Mass spectrometry. The mass spectrometric measurements were performed at the Central Analytical Laboratory of the University of Regensburg or at the Central Analytical Laboratory of UCT, Prague on a Finnigan MAT 95, ThermoQuest Finnigan TSQ 7000, Finnigan MATSSQ 710A, Agilent Q-TOF 6540 UHD, or an LTQ Orbitrap Velos (Thermo Fisher Scientific).

Gas chromatography (GC). GC measurements were performed on a GC 7890 from Agilent Technologies. Data acquisition and evaluation was done with Agilent ChemStation Rev.C.01.04. A capillary column HP-5MS/30 m \times 0.25 mm/0.25 μ M film and helium as carrier gas (flow rate of 1 mL/min) were used. The injector temperature (split injection: 40:1 split) was 280 °C, detection temperature 300 °C (FID). The GC oven temperature program was adjusted as follows: the initial temperature of 40 °C was kept for 3 min and was increased at a rate of 15 °C/min until the injection temperature of 280 °C was reached. After 5 min, the temperature was further increased at a rate of 25 °C/min until the final temperature of 300 °C was reached and kept for 5 min. Using 4-methylanisole as an IS, we obtained the GC calibration given in Figure 1-5 for the quantitative analysis.



Figure 1-5: Gas chromatography calibration curve. 4-methylanisole was used as internal standard (IS) for quantitative analysis.

Cyclo-voltammetry (CV). CV measurements were performed with the three-electrode potentiostat galvanostat (PGSTAT302N, Metrohm Autolab). The control of the measurement instrument, the acquisition, and processing of the CV data were performed with the software Metrohm Autolab NOVA 1.10.4. Electrochemical studies were carried out under argon atmosphere in ACN containing 0.1 M tetra-*N*-butylammonium hexafluorophosphate using ferrocene/ferrocenium (Fc/Fc⁺) as an internal reference. A glassy carbon electrode (working electrode), platinum wire counter electrode, and Ag quasi-reference electrode were employed.

Spectroelectrochemistry. Measurements were performed in an Ottle Cell (Optically transparent thin-layer electrochemical cell), pathlength = 0.02 cm, working electrode: Pt minigrid, counter electrode: Pt minigrid, pseudo reference electrode: Ag wire. Samples were prepared by degassing a solution of 5_{ox} in ACN (3 mM) via bubbling of Argon for several minutes. The substrate, *p*-BA, was added *via* a Hamilton syringe resulting in a solution of 250 mM. A constant electric field of -1.2 V was applied to the cell, and UV/Vis absorption spectra were recorded every 5 s (using an Agilent 8453 spectrometer). Irradiation was done *via* a handheld LED ($\lambda_{max} = 385$ nm) for a time of *ca*. 2 s in between each spectrum. Spectroelectrochemical data are given in Figure 1-3 and section 1.5.11.

General irradiation conditions. Samples were irradiated at 254 nm (UV handlamp from Herolab GmbH Laborgeräte, 254 nm, 8 W), at 365 nm (UV handlamp from Herolab GmbH Laborgeräte, 365 nm, 8 W), at 370 nm (Opulent Starboard, Luminus SST-10-UV-A130, $\lambda_{max} = 370$ nm, $I_{typ} = 500$ mA, $I_{max} = 1.0$ A, $\Phi_{typ} = 875$ mW), at 385 nm (Opulent Starboard, Luminus SST-10-UV-A130, $\lambda_{max} = 385$ nm, $I_{typ} = 500$ mA, $I_{max} = 1.5$ A, $\Phi_{typ} = 1015$ mW), or at 455 nm (CREE XLamp Me-C LED, $\lambda_{max} = 455$ nm, $I_{max} = 700$ mA). The corresponding

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emission spectra of each LED are given in Figure 1-6 or in the corresponding figures containing sequences of UV/Vis absorption spectra.



Figure 1-6: Emission profiles of all used LEDs for sample irradiation. From left to right: $\lambda_{max} = 254$ nm, $\lambda_{max} = 365$ nm, $\lambda_{max} = 370$ nm, $\lambda_{max} = 385$ nm, and $\lambda_{max} = 455$ nm.

Stationary UV/Vis absorption and emission spectroscopy. UV/Vis absorption (Cary 60 or Cary 100 UV-Vis spectrophotometer; Agilent) and UV/Vis emission spectra (Horiba FluoroMax-4 spectrofluorometer) were recorded at room temperature. Fluorescence quantum yields were determined with a Hamamatsu C9920-02 system equipped with a Spectralon integrating sphere. The quantum yield accuracy is <10% according to the manufacturer.

Stepwise illumination and recording of absorption spectra. Stationary UV/Vis absorption spectra were recorded using an Agilent Cary 50 UV/Vis spectrophotometer in a sample cell of 10×10 mm that can be flanged to the freeze pump and thaw apparatus and closed after degassing. A sample of 5_{red} was illuminated using an UV handlamp (UV handlamp from Herolab GmbH Laborgeräte, 254 nm, 365 nm, 8 W) providing either 254 or 365 nm. Continuous light was delivered onto the sample that was reproducibly positioned in *ca*. 2 cm distance without any further optics allowing for direct comparison of data sets recorded under different sample preparation conditions. After each illumination period, an absorption spectrum was recorded directly afterwards. The sample volume of 3 mL was continuously stirred during the illumination periods providing a homogeneously illuminated sample.

Time-resolved UV/Vis emission spectroscopy. A self-constructed time correlated single photon counting set-up⁶² was used to record emission decay data at single detection wavelength. A quartz cuvette with four optical windows of the dimension 2 mm \times 10 mm was used. The sample was excited along the 2 mm pathlength, and the emission was recorded

orthogonally to this. The optical density of the sample was set to *ca*. 0.1 at the excitation wavelength over 2 mm pathlength.

Ns to ms time-resolved UV/Vis absorption spectroscopy. The streak camera set-up described first in refs. ⁶²⁻⁶³ was adapted as follows. The third harmonic of a Nd:YAG laser (10 Hz, Surelite II, Continuum) pumping an Optical Parametric Oscillator (OPO, Continuum) tuned to 450 nm (10 mJ, *ca.* 10 ns) was used for sample excitation. As a probe light, a pulsed 150 W Xe-flash lamp (Applied Photophysics) was used that was focused three times *via* toric mirror optics: (i) before probe shutter, (ii) into sample, and (iii) into spectrograph. The entire white light probe pulse was analyzed by a combination of a spectrograph (200is, Bruker) and a streak camera (C7700, Hamamatsu Photonics). The use of mechanical shutters enabled the recording of a sequence of three individual data sets: (i) an image (D_{FL}) with both flash lamp and laser, (ii) an image (D₀) without any incoming light, and (iii) an image (D_F) only with the flash lamp. One hundred such sequences were recorded, and corresponding data sets were averaged. Then the TA was calculated as:

$$\Delta \text{OD} = \log \left(\frac{D_{\text{F}} - D_{0}}{D_{\text{FL}} - D_{0}} \right)$$

A 10-mL sample was stepwise cycled by a peristaltic pump (ecoline, ISMATEC) through a flow cell with a pathlength of 2 mm for pump and 10 mm for probe beams (dimensions: 2 mm \times 10 mm \times 30 mm, Starna) ensuring a total replacement of the sample prior to each individual measurement. No photocatalyst degradation was observed under the used conditions.

Sub-ps and sub-ns pump/supercontinuum probe spectroscopy. Ultrafast broadband TA experiments were carried out using UV/Vis pump–supercontinuum probe spectroscopy at 1 kHz repetition frequency. In short, a Ti-sapphire amplifier system (Coherent Libra) was used to generate 800 nm with 1.2 mJ pulses at 1 kHz. The output was split into three parts of which only two were used: (1) *Ca.* 50% of the 800 nm pulses were used to pump a collinear Optical Parametric Amplifier (OPA, TOPAS-800-fs, Light Conversion) tuned to pump pulses centered at *ca.* 450 nm (ca. 100 fs, ca. 400 nJ at the sample position) for sample excitation. (2) *Ca.* 10% were used to pump a non-colinear OPA (in-house build) tuned to pulses centered at *ca.* 530 nm (*ca.* 100 fs, *ca.* 5 μ J at the CaF₂ position) for generation of supercontinuum white light probe pulses by focusing into a moving CaF₂ disc of 1-mm thickness giving a probe spectrum ranging from 310 to 700 nm. Pump pulses were delayed *via* a motorized delay line equipped with an open corner cube mirror up to 2 ns. Two complementary high-speed spectrographs (Entwicklungsbüro EB Stresing) for signal and reference recording were used.

The pump and probe pulses were focused colinearly into the sample to spot sizes of ca. 80 and 60 µm full width at half maximum, respectively. For longer delays reaching out from ns to µs time ranges, a similar spectrometer was used in which the pump laser was electronically delayed relative to the probe laser. A detailed description can be found in ref.⁶⁴ The relative polarizations between the pump and probe were set by a half-wave plate in the pump beam path to magic angle (54.71°) for observations of pure population changes or to either parallel (0°) or orthogonal (90°) for observation of the anisotropy. The averaged pre- t_0 laser scatter signal was subtracted from the data and the ca. 1 ps chirp of the white light was corrected for prior to data analysis using the coherent artefact as an indicator for time zero at each wavelength. Throughout the probe range, the spectral resolution was better than 4 nm and the temporal resolution was better than 150 fs. Ten individual scans with averaging 100 spectra per time point were typically recorded. The time axis – within a total of 500 points – was linear between -1 and 2 ps and logarithmic from 2 ps to the maximum time delay ensuring that the dynamics on every time scale will have equal weighting in the fitting analysis. In the sub-ps TA set-up, 10 mL of the sample were cycled through an in-house build cell with a pathlength of 100 µm for pump and probe beams. In sub-ns TA set-up, 10 mL of the sample were cycled through a flow cell (Starna) with a pathlength of 2 mm for pump and probe beams. In all cases, all scans resulted in reproducible data sets. In addition, the integrity of the sample was checked by recording stationary absorption spectra before and after each measurement. No photocatalyst degradation was observed under the used conditions. The shown data correspond to one representative measurement. No smoothing or filtering procedures were applied to the data.

TA data analysis and modelling. Singular value decomposition (SVD)-based rank analysis and global fitting were performed using an in-house written program described previously.⁶²⁻⁶³ In brief, the linear least squares problem

$$\chi^2 = \|\Delta \mathbf{A} - \mathbf{F}\mathbf{B}\|^2 = \mathrm{Min}$$

is solved, where ΔA is the time-resolved absorption data matrix, **F** is the matrix containing the analytical functions accounting for the temporal changes in the data, i.e. exponential decays (convoluted with the instrument response, typically a Gaussian function), and **B** is the matrix with the to be determined spectra. Further optimization of χ^2 is achieved by optimizing the rate constants in **F** by a nonlinear least squares algorithm. As a result of such fits, the so-called decay-associated difference spectra (in matrix **B**) and their associated optimized rate constants are obtained. These are the unique result of the global fit, and this treatment does not require any model for the kinetics involved in the transient processes. The number of exponentials in the global fit is determined by the SVD-based rank analysis, which is described elsewhere.⁶⁵ The model that relates the actual species kinetics to the elementary function is applied afterwards resulting in SAS. The shape of the SAS in terms of identity with well-known spectra or following physical laws decides about the appropriateness of the model. This step does not change the χ^2 value found in the global fit, and therefore, this procedure has the advantage that all interpretation is performed with the same quality of fit. As an alternative analysis, known species spectra, taken either from literature or recorded in this work, were taken in order to decompose the recorded time-resolved data matrix using the transpose of the data matrix and using the basis spectra instead of analytical functions. The resulting concentration– time profiles inform about the appropriateness of the basis spectra and the physical reasonability, i.e. total sum of species being constant to 1.

Quantum chemical calculations. Quantum chemical calculations on all molecular moieties were performed using either the Firefly QC package,⁶⁶ which is partially based on the GAMESS (US)⁶⁷ source code, or the Orca package.⁶⁸⁻⁶⁹ All ground state structures were optimized on the level of restricted open shell density functional theory (ROHF-DFT) using the B3LYP functional and the aug-cc-pDVZ basis set. Complete active space self-consistency field (CASSCF) theory was used in order to calculate the static correlation energy. The highest 12 contributing π and n electrons were included into the CAS, distributed over 12 molecular orbitals (MO), and energy averaging over 10 states with equal weights, i.e. CASSCF(12,12)10, was performed. In order to calculate the dynamic correlation energy, extended multiconfiguration quasi-degenerate perturbation theory (XMCQDPT) was used on top of the CASSCF optimized MOs.⁷⁰ In all cases, an intruder state avoidance denominator shift of 0.02 was used. The absorption spectrum for 5sq was calculated via unrestricted open shell timedependent DFT (TD-DFT) with the aug-cc-pDVZ basis set. Solvent effects were taken into account with the conductor-like PCM for the TD-DFT calculation and with the PCM for the XMCQDPT-CASSCF calculations. Relaxed potential energy surfaces along the C-Br bond in p-BA and p-BA^{•-} were performed on the DFT (B3LYP) level of theory with the aug-ccpVDZ basis set.

1.5.2 Synthesis of Deazaflavins and Precursors

1.5.2.1 Deazaflavins

Synthesis of 10-Butyl-7,8-dimethoxy-3-methyl-5-deazaisoalloxazine (1). 8 (1.24 g, 3.7 mmol) was dissolved in dry DMF (15 mL) and phosphorus trichloride (0.77 g, 5.6 mmol) was added dropwise. The reaction mixture was heated to 110 °C for 30 min. After cooling down to room temperature, the yellow precipitate was filtered off and recrystallized from a mixture of ethanol/DCM (1:2) to give 1 in a yield of 53%. Melting point 296-298 °C.



¹**H NMR** (400 MHz, CDCl₃) δ [ppm] = 8.76 (Ar-*H*, s, 1H), 7.18 (s, 1H), 6.99 (Ar-*H*, s, 1H), 4.80 (*N*-C*H*₂, bs, 2H), 4.10 (*O*-C*H*₃, s, 3H), 4.01 (*O*-C*H*₃, s, 3H), 3.46 (*N*-C*H*₃, s, 3H), 1.86 (C*H*₂, p, *J* = 7.8 Hz, 2H), 1.56 (C*H*₂, h, *J* = 7.4 Hz, 2H), 1.03 (C*H*₃, t, *J* = 7.3 Hz, 3H). ¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 162.6 (C_q), 157.6 (C_q), 156.8 (C_q), 155.4 (C_q), 147.6 (C_q), 140.8 (+), 137.6 (C_q), 116.4 (C_q), 112.6 (C_q), 110.0 (+), 97.5 (+), 56.7(+), 56.5 (+), 44.9 (-),

29.3 (-), 28.2 (+), 20.3 (-), 14.0 (+).

HRMS (ESI) (m/z): $[M+H]^+$ (C₁₈H₂₂N₃O₄) calc.: 344.1605, exp.: 344.1608.

Synthesis of 10-Butyl-7,8-dimethoxy-3,5-dimethyl-5-deazaisoalloxazine (2). 8 (333 mg, 1 mmol) was dissolved in acetic anhydride (5 mL) and heated to gentle reflux for 3 h. After cooling to room temperature, the reaction mixture was diluted with water and extracted with DCM (2 x 25 mL). The organic phase was dried over magnesium sulphate and evaporated. The crude product was recrystallized from an isopropyl alcohol/dichloroethane mixture (1:1) to give 2 in a yield of 43%. Melting point: 223-226 °C.



¹**H NMR** (400 MHz, CDCl₃) δ [ppm] = 7.43 (Ar-*H*, s, 1H), 6.98 (Ar-*H*, s, 1H), 4.80 (*N*-CH₂, bs, 2H), 4.09 (*O*-CH₃, s, 3H), 4.03 (*O*-CH₃, s, 3H), 3.44 (*N*-CH₃, s, 3H), 3.23 (CH₃, s, 3H), 1.83 (CH₂, t, *J* = 8.2 Hz, 2H), 1.54 (CH₂, p, *J* = 7.4 Hz, 2H), 1.03 (CH₃, t, *J* = 7.3 Hz, 3H).
¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 157.1 (C_q), 156.1 (C_q), 155.3 (C_q), 154.9 (C_q), 147.1 (C_q), 136.1 (C_q), 117.6 (C_q), 110.8 (C_q), 110.1 (C_q), 106.7 (+), 97.6 (+), 56.5 (+), 56.4 (+), 45.2 (-), 29.3 (-), 28.2 (+), 20.3 (-), 17.1 (+), 14.1 (+). **HRMS** (ESI) (m/z): [M+H]⁺ (C₁₉H₂₄N₃O₄) calc.: 358.1761, exp.: 358.1768.

Synthesis of 10-Butyl-7,8-dimethoxy-5-isopropyl-3-methyl-5-deazaisoalloxazine (3). 8 (333 mg, 1 mmol) was dissolved in butyric anhydride (4 mL) and heated to 180 °C for 4 h. After cooling to room temperature, the reaction mixture was diluted with water and extracted with DCM (2 x 25 mL). The organic phase was dried over magnesium sulphate and evaporated. The crude product was recrystallized from isopropyl alcohol to give 3 in a yield of 57%. Melting point: 171-175 °C.



¹**H NMR** (400 MHz, CDCl₃) δ [ppm] = 7.72 (Ar-*H*, s, 1H), 6.98 (Ar-*H*, s, 1H), 5.50 – 5.35 (C*H*, m, 1H), 4.78 (N-C*H*₂, s, 2H), 4.07 (O-C*H*₃ s, 3H), 4.00 (C*H*₃, s, 3H), 3.45 (N-C*H*₃, s, 3H), 1.84 (C*H*₂, d, *J* = 8.5 Hz, 2H), 1.63 (C*H*₃, s, 3H), 1.61 (C*H*₃, s, 3H), 1.55 (C*H*₂, q, *J* = 7.5 Hz, 2H), 1.03 (C*H*₃, t, *J* = 7.3 Hz, 3H).

¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 165.4 (C_q), 156.9 (C_q), 155.5 (C_q), 154.9 (C_q), 145.8 (C_q), 136.8 (C_q), 116.5 (C_q), 111.2 (C_q), 109.0 (+), 97.7 (+), 56.4 (+), 56.4 (+), 45.5 (-), 29.2 (-), 28.4 (+), 28.4 (+), 22.2 (+), 20.3 (-), 14.1 (+).

HRMS (ESI) (m/z): $[M+H]^+$ (C₂₁H₂₈N₃O₄) calc.: 386.2074, exp.: 386.2076.

Synthesis of 10-Butyl-7,8-dimethoxy-3-methyl-5-trifluoromethyl-5-deazaisallox-azine (4). 8 (333 mg, 1 mmol) was dissolved in *N*-methyl-2-pyrrolidone (3 mL) and trifluoroacetic anhydride (630 mg, 3 mmol) was added. The reaction mixture was heated to 150 °C for 2 h. After cooling to room temperature, the reaction mixture was diluted with water and extracted with DCM (2 x 25 mL). The organic phase was dried over magnesium sulphate and evaporated. The crude product was recrystallized from isopropyl alcohol to give 4 in a yield of 63%. Melting point: 256-261 °C.



¹**H NMR** (400 MHz, CDCl₃) δ [ppm] = 7.48 (Ar-*H*, q, *J* = 1.8 Hz, 1H), 7.00 (Ar-*H*, s, 1H), 4.80 (*N*-C*H*₂, bs, 2H), 4.10 (*O*-C*H*₃, s, 3H), 4.00 (*O*-C*H*₃, s, 3H), 3.44 (*N*-C*H*₃, s, 3H), 1.94 – 1.82 (C*H*₂, m, 2H), 1.56 (C*H*₂, h, *J* = 7.4 Hz, 2H), 1.04 (C*H*₃, t, *J* = 7.4 Hz, 3H). ¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 160.7 (C_q), 156.8 (C_q), 156.7 (C_q), 154.1 (C_q), 147.6 (C_q), 139.2 (q, *J* = 33.1 Hz), 137.8 (C_q), 122.6 (q, *J* = 279.3 Hz), 114.0 (C_q), 113.3 (C_q), 107.1 (q, *J* = 5.9 Hz), 97.4 (+), 56.7(+), 56.4 (+), 46.2 (-), 29.0 (-), 28.6 (+), 20.3 (-), 14.0 (+). **19F NMR** (282 MHz, CDCl₃) δ [ppm] = -53.72 (d, *J* = 1.9 Hz). **HRMS** (ESI) (m/z): [M+H]⁺ (C₁₉H₂₁N₃O₄F₃) calc.: 412.1479, exp.: 412.1483.

Synthesis of 10-butyl-7,8-dimethoxy-3-methyl-5-phenyl-5-deazaisoalloxazine (5_{ox}), 10-butyl-7,8-dimethoxy-3-methyl-5-phenyl-5,10-dihydropyrimido[4,5-b] quinoli-ne-2,4 (1H,3H)-dione (5_{red}). The procedure has been adapted from the synthesis of similar structures described by Shi *et al.*⁴⁹ A microwave vessel was charged with *N*-butyl-3,4-dimethoxyaniline (7, 2.1 g, 10 mmol, 1.0 equiv.), *N*-methylbarbituric acid (9, 1.42 g, 10 mmol, 1.0 equiv.), and benzaldehyde (10 mL, 10 mmol, 1.0 equiv.). Without addition of a solvent the mixture was heated in a microwave to 140 °C for 30 min. Subsequently, the solid reaction mixture was dissolved in DCM and extracted with H₂O. The oxidized and reduced forms were purified and separated by column chromatography, followed by recrystallization from ethyl acetate (5_{ox}) and from toluene (5_{red}), respectively. The products were obtained in a combined yield of 20%.



 $(\mathbf{5}_{ox}) = {}^{1}\mathbf{H} \mathbf{NMR}$ (400 MHz, CDCl₃) δ [ppm] = 7.60 – 7.50 (Ar-*H*, m, 3H), 7.24 – 7.17 (Ar-*H*, m, 2H), 7.02 (Ar-*H*, s, 1H), 6.63 (Ar-*H*, s, 1H), 4.89 (CH₂, s, 2H), 4.09 (O-CH₃, s, 3H), 3.62

 $(O-CH_3, s, 3H), 3.30 (N-CH_3, s, 3H), 1.92 (CH_2, m, 2H), 1.60 (CH_2, m, 2H), 1.07 (CH_3, t, J = 7.3 Hz, 3H).$

¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 162.0 (C_q), 157.2 (C_q), 156.3 (C_q), 155.5 (C_q), 155.1 (C_q), 146.8 (C_q), 136.9 (C_q), 136.8 (C_q), 128.4 (+), 128.3 (+), 127.0 (+), 117.9 (C_q), 109.7 (C_q), 109.4 (+), 97.1 (+), 56.5 (+), 55.9 (+), 45.3 (-), 29.1 (-), 28.0 (+), 20.3(-), 14.0 (+). **HRMS** (ESI) (m/z): [M+H]⁺ (C₂₄H₂₅N₃O₄) calc.: 420.1918, exp.: 420.1923.



 $(\mathbf{5}_{red}) = {}^{1}\mathbf{H} \ \mathbf{NMR} \ (400 \ \text{MHz}, \text{CDCl}_3) \ \delta \ [\text{ppm}] = 10.69 \ (\text{N}H, \text{s}, 1\text{H}), 7.25 - 7.17 \ (\text{Ar-}H, \text{m}, 4\text{H}), 7.13 \ (\text{Ar-}H, \text{m}, 1\text{H}), 6.64 \ (\text{Ar-}H, \text{d}, J = 1.4 \ \text{Hz}, 2\text{H}), 5.26 \ (\text{C}H, \text{s}, 1\text{H}), 4.02 \ (\text{C}H_2, \text{m}, 2\text{H}), 3.90 \ (\text{O-}\text{C}H_3, \text{s}, 3\text{H}), 3.78 \ (\text{O-}\text{C}H_3, \text{s}, 3\text{H}), 3.31 \ (\text{N-}\text{C}H_3, \text{s}, 3\text{H}), 1.87 - 1.61 \ (\text{C}H_2, \text{m}, 2\text{H}), 1.44 \ (\text{C}H_2 \ \text{m}, 2\text{H}), 0.97 \ (\text{C}H_3 \ \text{t}, J = 7.3 \ \text{Hz}, 3\text{H}).$

¹³**C NMR** (101 MHz, CDCl₃) δ [ppm] = 162.4 (C_q), 152.8 (C_q), 148.3 (C_q), 146.5 (C_q), 146.1 (C_q), 144.9 (C_q), 131.2 (C_q), 128.4 (+), 127.4 (+), 126.5 (+), 119.5 (C_q), 112.9 (+), 99.9 (+), 90.1 (C_q), 56.4 (+), 56.2 (+), 44.1 (-), 40.3 (+), 30.0 (-), 27.3 (+), 20.1 (-), 13.9 (+).

HRMS (ESI) (m/z): $[M+H]^+$ (C₂₄H₂₇N₃O₄) calc.: 422.2074, exp.: 422.2077.

1.5.2.2 Precursors

Synthesis of the flavin precursor *N*-Butyl-3,4-dimethoxyaniline (7). The procedure has been adapted from the synthesis of similar structures described by Abdel-Magid *et al.*⁷¹ 3,4-dimethoxyaniline (1.53 g, 10 mmol, 1.0 equiv.) and butanal (901 μ L, 10 mmol, 1.0 equiv.) were mixed in 35 mL DCE and then treated with sodium triacetoxyborohydride (2.97 g, 14 mmol, 1.4 equiv.). The mixture was stirred at room temperature for 17 h and the reaction progress was observed *via* TLC. After quenching of the reaction mixture with NaHCO₃ (*aq.*), the product was extracted with ethyl acetate and the organic phase was dried over magnesium sulfate. After filtration the ethyl acetate was evaporated and the crude product was purified *via* column chromatography (PE/EE). The product was obtained in a yield of 52%.



¹**H NMR** (300 MHz, CDCl₃) δ [ppm] = 6.72 (Ar-*H*, d, *J* = 8.5 Hz, 1H), 6.22 (Ar-*H*, d, *J* = 2.7 Hz, 1H), 6.12 (Ar-*H*, dd, *J* = 8.5, 2.6 Hz, 1H), 3.80 (O-CH₃, s, 3H), 3.77 (O-CH₃, s, 3H), 3.27 (N*H*, s, 1H), 3.04 (CH₂, t, *J* = 7.1 Hz, 2H), 1.57 (CH₂, m, 2H), 1.42 (CH₂, m, 2H), 0.94 (CH₃, t, *J* = 7.3 Hz, 3H).

¹³**C NMR** (75 MHz, CDCl₃) δ [ppm] = 150.0 (C_q), 143.6 (C_q), 141.3 (C_q), 113.3 (+), 103.4 (+), 98.8 (+), 56.7 (+), 55.7 (+), 44.5 (-), 31.8 (-), 20.3 (+), 14.0 (-).

Synthesis of the flavin precursor 6-(*N*-Butyl(3,4-dimethoxyphenyl)amino)-3methyluracil (8). Aniline 7 (13.1 g, 62.5 mmol), 6-chloro-3-methyl uracil (10.0 g, 62.5 mmol) and *N*,*N*-dimethylaniline (30 mL) were heated to 180 °C for 4 h under inert atmosphere. After cooling to *ca*. 100 °C, the reaction mixture was slowly poured to diethyl ether (350 mL). After several minutes a thick dark oil precipitated. The diethyl ether layer was transferred into a clean flask and kept at 4 °C in a refrigerator for 24 h. The crude product was filtered, washed with diethyl ether and subsequently recrystallized from hot isopropyl alcohol to give **8** as a white crystalline powder in a yield of 55%.



¹**H NMR** (300 MHz, CDCl₃) δ [ppm] = 7.52 (N*H*, s, 1H), 6.89 (Ar-*H*, d, *J* = 8.5 Hz, 1H), 6.74 (Ar-*H*, dd, *J* = 8.5, 2.4 Hz, 1H), 6.63 (Ar-*H*, d, *J* = 2.4 Hz, 1H), 4.95 (C*H*, d, *J* = 2.3 Hz, 1H),

3.90 (O- CH_3 , s, 3H), 3.86 (O- CH_3 , s, 3H), 3.54 – 3.39 (C H_2 , m, 2H), 3.20 (N- CH_3 , s, 3H), 1.59 (C H_2 , m, 2H), 1.29 (C H_2 , m, 2H), 0.89 (C H_3 , t, J = 7.3 Hz, 3H).

¹³**C NMR** (75 MHz, CDCl₃) δ [ppm] = 164.4 (C_q), 151.2 (C_q), 151.0 (C_q), 150.6 (C_q), 149.6 (C_q), 132.3 (C_q), 120.8 (+), 112.0 (+), 111.2 (+), 76.3 (+), 56.3 (+), 52.5 (-), 29.0 (-), 26.8 (+), 20.1 (-), 13.9 (+).

HRMS (ESI) (m/z): [M+H]⁺ (C₁₇H₂₄N₃O₄) calc.: 334.1761, exp.: 334.1769

Synthesis of the flavin precursor *N***-methylbarbituric acid (9).** *N*-methyl urea (11.1 g, 150 mmol, 1.0 equiv.) and malonic acid (15.6 g, 150 mmol, 1.0 equiv.) were dissolved in 40 mL acetic anhydride and heated to 70 °C for 2 h. Subsequently, the acetic acid was evaporated and the residue stored at -40 °C overnight. The precipitate was filtered and washed with cold ethanol. Purification was done by recrystallization from ethanol and the product was obtained as an orange solid with a yield of 45%.



¹**H NMR** (300 MHz, DMSO-d₆) δ [ppm] = 11.33 (N*H*, s, 1H), 3.58 (*CH*₂, s, 2H), 3.05 (*CH*₃, s, 3H).

¹³**C NMR** (75 MHz, DMSO-d₆) δ [ppm] = 166.9 (C_q), 166.4 (C_q), 151.8 (C_q), 39.6 (+), 26.7 (+).

1.5.3 General Procedures

Reduction of TARF to TARFH₂. TARF (109 mg, 0.2 mmol) was dissolved in dimethylformamide (DMF, 10 mL) and placed in a Schlenk tube. Palladium on activated charcoal (10 mg, 10% Pd) was added and the mixture was degassed by the freeze-pump-thaw method, then evacuated and flushed with hydrogen gas. The Schlenk tube was shaken until the fluorescence of **TARF** disappeared. Subsequently, palladium was removed *via* filtration through a syringe filter in a glove box. The final solution of **TARFH₂** was stored inside a glove box until further use.

¹**H NMR** (400 MHz, DMF-*d*₇) δ [ppm] = 10.85 (s, 1H), 10.63 (s, 1H), 6.53 (d, *J* = 8.7 Hz, 2H), 6.14 (s, 1H), 5.44 (ddd, *J* = 9.5, 4.2, 2.7 Hz, 1H), 5.35 (dd, *J* = 6.3, 4.2 Hz, 1H), 5.25 (td, *J* = 6.1, 3.1 Hz, 1H), 4.34 (dd, *J* = 12.3, 3.1 Hz, 1H), 4.24 – 4.10 (m, 2H), 4.01 (dd, *J* = 16.0, 2.7 Hz, 1H), 2.10 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.94 (s, 3H). ¹³**C NMR** (101 MHz, DMF-*d*7) δ [ppm] = 171.2, 170.7, 170.7, 170.6, 158.6, 150.6, 138.9, 133.4, 129.4, 128.7, 120.1, 116.7, 106.5, 71.2, 70.7, 70.5, 62.6, 48.2, 21.1, 21.0, 21.0, 20.9, 19.4, 19.3.

Chemical oxidation of 5_{red}. **5**_{red} (100 mg, 0.24 mmol, 1.0 equiv.) was dissolved in glacial acetic acid. After addition of NaNO₂ (33.6 mg, 0.48 mmol, 2.0 equiv.), the reaction mixture was stirred at room temperature for a few minutes, followed by addition of NaOH (15%) and extraction with dichloromethane (3x). Subsequently, the organic layer was washed with H₂O and dried over MgSO₄. The product was purified by column chromatography (PE/EE) giving a yield of 80%.

General procedure: Photocatalytic reduction of aryl halides. An aryl halide (0.15 mmol, 1.0 equiv.), 1-5 (8 mol%), Cs₂CO₃ (49 mg, 1.0 equiv.), and *N*,*N*-diisopropylethylamine (DIPEA, 52 µL, 2.0 equiv.) were dissolved in the respective solvent (2 mL) and degassed using the freeze-pump-thaw technique (3 x 3 min). The reaction mixture was irradiated at either 365 nm, 385 nm, or 455 nm overnight, while continuously stirring. Analysis was done by calibrated gas chromatography using 4-methylanisole as internal standard.

1.5.4 Photophysical Properties and the Photophysical Model

Stationary absorption and emission spectra in the UV/Vis range were recorded in ACN for all synthesized photocatalysts (Figure 1-7a, c, e, g and i). Additionally, the emission decay was recorded probing at the maximum of the corresponding emission wavelength (Figure 1-7b, d, f, h and j). For all oxidized species the emission decay is mono-exponential indicating clean excited singlet state decays *via* $k_{S_1} = k_{ic} + k_{rad} + k_{isc}$. Thus, measuring the fluorescence quantum yields of the S₁ emission of all oxidized species allowed the determination of k_{rad} *via* $k_{rad} = \Phi_{rad}k_{S_1}$. The triplet formation was recorded *via* transient absorption spectroscopy. Interestingly, only for compound $\mathbf{5}_{ox}$ we observed the formation of its triplet state (Figure 1-2 in section 1.3.5). Its yield can be estimated as follows: For $\mathbf{1} - \mathbf{5}$ alone in solution, we only observe the photophysical processes but no photochemistry. Thus, the rate constants κ_i , which are absolutely obtained from a bi-exponential global fit on the data, represent

$$\kappa_1 = k_{\rm ic} + k_{\rm rad} + k_{\rm isc} \tag{1}$$

$$\kappa_2 = k_{\rm bisc} \tag{2}$$

In this simple model considering the ground state contribution, S_{S_0} , one obtains the following relationship between the SAS, S_i , and the DADS, D_i :

$$S_{S_1} = \frac{(D_1 + D_2)}{c_0} + S_{S_0} \tag{3}$$

$$S_{T_1} = \frac{(\kappa_1 - \kappa_2)D_2}{c_0 \Phi_{T_1} \kappa_1} + S_{S_0}$$
⁽⁴⁾

As can be seen, there are undetermined parameters c_0 and Φ_{T_1} . However, one can at least find upper or lower bounds by the requirement that the resulting SAS must be positive and should not show any of the characteristic bands of the other species. In particular, the negative peaks from the ground state bleach should disappear in the SAS. The best values are summarized in Table 1-3 and the corresponding SAS are shown in Figure 1-1d and Figure 1-2e.



Figure 1-7: Photophysical characterization of deazaflavins. Stationary absorption and emission spectra as well as emission decay curves of the photocatalysts 1 (a-b), 2 (c-d), 3 (e-f), 4 (g-h), and 5 (i-j) in ACN as indicated. In case of 5, also the spectra and decay curves of its fully reduced form 5_{red} were recorded (magenta lines in i). TARF spectra are also presented as reference in grey.

Cat.	k _{S1} [(ns) ⁻¹]	${f \Phi_{{ m fl}}}^{[a]}$	$k_{rad}^{[b]}$ [(ns) ⁻¹]	${f \Phi}_{ m isc}{}^{[c]}$	$k_{\rm isc}{}^{[d]}$ [(ns) ⁻¹]	${\Phi_{ic}}^{[e]}$	$k_{ m ic}{}^{ m [f]}$ $[s^{-1}]$	$k_{T_1}^{O_2[g]}$ [(µs) ⁻¹]
1	0.132±0.002	0.85	0.112	≪1	≈ 0	0.15	0.0198	no
2	0.146 ± 0.002	0.71	0.104	n.d.	n.d.	n.d.	n.d.	n.d.
3	0.141 ± 0.002	0.68	0.096	n.d.	n.d.	n.d.	n.d.	n.d.
4	0.090 ± 0.002	0.67	0.060	n.d.	n.d.	n.d.	n.d.	n.d.
5_{ox}	0.573±0.002	0.16	0.092	0.11	0.063	0.73	0.418	6.45
5_{red}	0.296 ± 0.002	0.03	0.0089	n.d.	n.d.	n.d.	n.d.	n.d.
TARF	0.149 ± 0.002	0.39	0.058	0.45	0.067	0.16	0.024	2.10

Table 1-3: Summary of the photophysical parameters of deazaflavins in ACN.

^[a]The accuracy is <10% according to the manufacturer. ^[b] $k_{rad} = (\tau_{S_1})^{-1} \Phi_{fl}$. ^[c]From spectra modelling. ^[d] $k_{isc} = (\tau_{S_1})^{-1} \Phi_{isc}$. ^[c] $\Phi_{ic} = 1 - \Phi_{fl} - \Phi_{isc}$. ^[f] $k_{ic} = (\tau_{S_1})^{-1} \Phi_{ic}$. ^[g]In non-degassed acetonitrile with expected $c(O_2) = 2.4 \text{ mM}$.⁷² Abbreviations: S₁ = excited singlet state, T₁ = triplet state, fl = fluorescence, rad = radiative, isc = intersystem crossing, ic = internal conversion, no = not observed, nd = not determined.

1.5.5 Stability of 5_{red} Against O₂ and Light

The stability of freshly prepared $\mathbf{5}_{red}$ samples in ACN was tested by recording UV/Vis absorption spectra over time under the following three conditions: 1) in non-degassed ACN in the dark, 2) in non-degassed ACN and excitation of $\mathbf{5}_{red}$, and 3) in degassed ACN and excitation of $\mathbf{5}_{red}$. In the first experiment, spectra were recorded in the dark over a period of 19 h. As shown in Figure 1-8, no significant reduction of $\mathbf{5}_{red}$ and correspondingly no formation of $\mathbf{5}_{ox}$ is observed. Thus, the oxidation rate of the ground state $\mathbf{5}_{red}$ is $\ll 6.1 \ 10^{-3} \ M^{-1} \ s^{-1}$ considering a O₂ concentration of 2.4 mM in ACN⁷² under atmospheric conditions. Correspondingly, the activation energy barrier is $\gg k_{\rm B}T$.



Figure 1-8: Stability of 5_{red} towards molecular oxygen. Sequence of stationary UV/Vis absorption spectra of a freshly prepared sample of 5_{red} in ACN recorded over 19 h incubation in the dark as indicated.

The situation is different when 5_{red} is excited. Excitation of 5_{red} in O₂ saturated ACN at either 254 nm (Figure 1-9 panels a and b) or 365 nm (Figure 1-9 panels c and d) resulted in a clean conversion into its fully oxidized form 5_{ox} . However, the conversion was not complete, since the oxidized form also absorbs substantially in the UV region. In case of excitation at 254 nm, the system reaches the photo-stationary point under the used conditions within 150 s. Under otherwise identical geometrical illumination conditions but with an excitation spectrum peaking at 365 nm, which has much less overlap with the absorption spectrum of 5_{red} and is 500 times as intensive compared to the 254 nm spectrum of the excitation source, the photostationary point is not reached even after 2600 s. However, significant conversion is still observed. Considering the fact that 5_{red} in O₂ saturated ACN is stable for days in the dark (Figure 1-8), this provides proof of a light-induced re-oxidation. The only potential oxidant present in the system is O₂. This should be proofed by a complete inhibition of the re-oxidation or at least a significantly reduced turnover rate when O₂ is removed or reduced in concentration from the system. As can be readily seen in Figure 1-9 panels e and f the turnover

rate of $\mathbf{5}_{red}$ is indeed significantly reduced as the photo-stationary point is reached only after 4000 s compared to 150 s when O₂ is present. Under the used conditions for our freeze-pump-thaw apparatus, we estimate a reduction of the O₂ concentration only down to the μ M range, which explains the observation of almost quantitative conversion under these conditions. To note, under reduced O₂ concentration conditions illumination also leads to decomposition pathways that become available when oxidation by O₂ is significantly reduced. However, we do not want to address these decomposition pathways in this work.



Figure 1-9: Photooxidation of 5_{red} . Sequences of stationary absorption spectra of 5_{red} in non-degassed (a-d) ACN and in degassed (e-f) ACN after stepwise illumination at wavelengths as indicated under identical geometrical illumination conditions. The panels on the left (a, c, and e) show the raw data. The corresponding panels on the right (b, d, and f) show the decomposed species spectra and corresponding concentration–time profiles (insets).

1.5.6 Electrochemical Characterization

Cyclic voltammograms for **TARF**, **1**, **2**, **3**, **4**, and **5** in ACN were recorded against ferrocene (Figure 1-10). The corresponding redox potentials were calculated as follows: potential of sample against electrode minus potential of reference system against electrode plus correction of +0.38 V for conversion to the potential against saturated calomel electrode (SCE). These values are summarized in Table 1-4.

Catalyst	$E_{1/2}$ [V]
TARF	-0.79
1	-1.34
2	-1.44
3	-1.44
4	-0.92
5	-1.41

Table 1-4: Calculated $E_{1/2}$ values for TARF, 1, 2, 3, 4, and 5 in ACN.



Figure 1-10: Cyclic voltammograms. TARF (a), 1 (b), 2 (c), 3 (d), 4 (e), and 5 (f) in ACN vs. ferrocene as indicated.

1.5.7 Screening of Reaction Conditions

Table 1-5 summarizes the results of the investigations on the influence of the solvent and the excitation wavelength on the total product yield.

Table 1-5: Screening of the reaction conditions.^[a] Photocatalytic dehalogenation of *p*-bromoanisole or *p*-chloroanisole by deazaflavin in dependence on the solvent and the excitation wavelength for 5_{ox} in ACN.



entry	c(5) [mM]	<i>t</i> [h]	solvent	Cs ₂ CO ₃ [equiv.]	λ _{exc} [nm]	DIPEA [mM]	Substra te <i>p</i> -XA	product yield ^[b]
1	6	16	DMF	0	365	150	Br	29
2	6	16	ACN	0	365	150	Br	55
3	6	16	DMF	1	365	150	Br	44
4	6	16	ACN	1	365	150	Br	80
5	6	16	ACN	0.1	365	150	Br	58
6	6	18	ACN	1	455	150	Br	50
7	6	18	ACN	1	385	150	Br	80
8	6	18	ACN	1	365	150	Br	78
9	3	18	ACN	1	365	150	Br	60
10	0.75	18	ACN	1	365	150	Br	33
11	0	16	ACN	1	365	150	Br	5
12	6	16	ACN	1	dark	150	Br	trace
13	3	16	ACN	1	385	0	Br	3
14	3	16	ACN	1	385	0	Br	trace
15	6	15	ACN	1	385	150	Cl	80

^[a]Reaction conditions: *p*-XA (75 mM (0.15 mmol)), DIPEA (150 mM (0.3 mmol)), ACN (2 mL), 25 °C, nitrogen atmosphere. ^[b]Yields were determined *via* calibrated GC-analysis with 4-methylanisole as internal standard.

1.5.8 Theoretical Absorption Spectra of All Protonated States of 5_{sq}

The total photocatalytic conversion from *p*-BA to *p*-A (anisole) shows a dependence on the used solvent, the used excitation wavelength, and the basicity. Since the semiquinone form, 5_{sq} , of the photocatalyst is one key intermediate for the successful dehalogenation, we calculated quantum chemically absorption spectra of 5_{sq} and its two potential protonation states, *i.e.* **5**^{C-H}_{sq} and **5**^{N-H}_{sq} in PCM for ACN and DMF (Figure 1-11). As evident, the theoretical and experimental absorption spectra of 5_{sq} in ACN are in excellent agreement (Figure 1-11a and Figure 1-2f, as well as section 1.5.11). Considering the significant deviations of the absorption spectra of both protonated forms (Figure 1-11b and c) from the experimentally recorded transient spectrum (Figure 1-2f and section 1.5.11) in the absence of base, we can already exclude the involvement of these species under neutral conditions and, thus, identify 5_{sq} as the key intermediate of the consecutive photo-induced electron transfer (conPET) reaction. Furthermore, this is in accord with the observation that with excitation wavelength <400 nm the total conversion under otherwise identical reaction conditions increased by a factor of 1.6, since 5_{sq} has its highest absorption probability at around 360 nm. Moreover, the calculation shows that the most intense transitions around 365 nm of the 5_{sq} in DMF shift apart resulting in an expected overall decreased extinction coefficient compared to the situation in ACN (Figure 1-11a). Therefore, this might explain the observed decreased conversion yield by a factor of ca. 2 in DMF (Table 1-5).

In order to get more insights on the impact of the basicity on the reaction mechanism further studies are currently ongoing in our lab. At present, the working hypothesis explaining the observed enhanced yields under basic conditions are given by the following possible scenarios: 1) enhanced triplet yield; 2) longer triplet lifetime; 3) enhanced **dFl**_{sq} yield; or 4) longer lifetime of **dFl**_{sq}. However, an enhancement of the final dehalogenation step after initiation by the second electron transfer can already be excluded since this part of the reaction is identical, thus, independent on the tested deazaflavin.



Figure 1-11: Calculated electronic absorption spectra of 5_{sq} radicals. Electronic transitions (sticks) for all possible protonation states of 5_{sq} (a-c) convoluted with Gaussians (FWHM = 0.2 eV) calculated at the UHF-TD-DFT(B3LYP)-CPCM(ACN,DMF)//aug-cc-pVDZ level of theory. The corresponding optimized structures are on the right.

1.5.9 Excited Singlet State Reactivity

The Smoluchowski theory⁷³⁻⁷⁴ is used in order to quantify, on the one hand, the diffusion limits for a bi-molecular reaction and, on the other hand, its efficiency on encounter of the reacting species. In accordance to the Smoluchowski theory, one would not expect to observe a monoexponential kinetic behavior for bi-molecular reactions under pseudo-first order conditions, but instead an $e^{\sqrt{t}}$ dependence. The diffusion-controlled quenching rate using the sum of molecular radii $R = R_{0,A} + R_{0,B}$ and the sum of diffusion constants $D = D_A + D_B$ of two reacting species A and B is given by

$$k_{\rm diff}(t) = 4 \,\pi\,\mathrm{R}\,\mathrm{D}\,\mathrm{N}_{\mathrm{A}}\,\mathrm{p}\left(1 + \frac{\mathrm{p}\,\mathrm{R}}{\sqrt{\pi\,\mathrm{D}\,t}}\right) \tag{5}$$

Here, p is a factor for the interaction probability upon encounter of the photocatalyst and the substrate. In case p = 1, the reaction is totally diffusion controlled. According to the Stokes-Einstein relation the diffusion coefficient of a molecule can be estimated to:

$$D = \frac{k_{\rm B}T}{6\,\pi\,\eta\,R_{0,\rm molecule}}\tag{6}$$

where R_{0,molecule} might be estimated as the radius of a sphere with the molecular volume. The molecular volume itself might be estimated by the volume enclosed by the solvent-excluded surface (SES). Strategies to determine the SES might be found in.⁷⁵ Table 1-6 summarizes the corresponding parameters for the description of diffusion controlled processes taking ACN as solvent, which has a viscosity of $3.5 \cdot 10^{-5}$ kg·(dm)⁻¹·s⁻¹ at a temperature of T = 293.15 K.⁷⁶ In case of diffusion-controlled quenching of the excited singlet states of 1 and 5_{ox} by DIPEA due to electron transfer from DIPEA to the excited singlet state, the non-linear contribution drops below 25% after 1 ns. Therefore, the emission decay data obtained from TCSPC with an instrument response function (IRF) of ca. 1 ns can sufficiently be analysed by the pseudo-first order approximation. The bi-molecular rate constants for the excited singlet state quenching of either 1 or 5_{ox} by DIPEA was determined by time-resolved emission spectroscopy. As can be seen in Figure 1-12, the excited singlet of both photocatalysts is increasingly quenched in the presence of increasing DIPEA concentration. In both cases, a Stern-Volmer based bimolecular quenching model describes the data well under low DIPEA concentrations (insets in panels b and d of Figure 1-12). The resulting bi-molecular rate constants are $(1.05\pm0.01)\cdot10^{10}$ M⁻¹·s⁻¹ and $(9.0\pm0.1)\cdot10^{9}$ M⁻¹·s⁻¹ for 1 and 5_{ox}, respectively. However, using higher DIPEA concentrations, deviations from the Stern-Volmer analysis are observed. For instance, in the case of 5_{ox} as presented in Figure 1-1b and d in section 1.3.4, a longer lifetime

of 210 ps for 800 mM is observed although a lifetime of 138 ps is theoretically expected. This illustrates that the solvent properties are affected by the high DIPEA concentration (DIPEA as pure solvent is 5.8 mol/L).

Cat /Salt	r _{0,Cat}	r _{0,Sub}	D _{Cat}	$D_{ m Sub}$	$4 \pi r_0 DN_A$	$\frac{r_0}{\sqrt{\pi \ D}}$
Cat/Sub	[dm]	[dm]	[(dm) ² s ⁻¹]	[(dm) ² s ⁻¹]	[M ⁻¹ s ⁻¹]	$\left[\frac{1}{\sqrt{s^{-1}}}\right]$
TARF/DIPEA	4.78·10 ⁻⁹	3.21·10 ⁻⁹	1.28.10-7	1.91·10 ⁻⁷	$1.93 \cdot 10^{10}$	7.99·10 ⁻⁶
1/DIPEA	4.12·10 ⁻⁹	3.21·10 ⁻⁹	1.49·10 ⁻⁷	1.91·10 ⁻⁷	$1.89 \cdot 10^{10}$	7.10.10-6
5 _{0x} /DIPEA	4.45·10 ⁻⁹	3.21·10 ⁻⁹	1.38.10-7	1.91·10 ⁻⁷	$1.91 \cdot 10^{10}$	7.54·10 ⁻⁶
$\mathbf{TARF}/\mathrm{O}_2$	4.78·10 ⁻⁹	1.59·10 ⁻⁹	1.28.10-7	3.86·10 ⁻⁷	$2.48 \cdot 10^{10}$	5.01·10 ⁻⁶
$1/O_2$	4.12·10 ⁻⁹	1.59·10 ⁻⁹	1.49·10 ⁻⁷	3.86·10 ⁻⁷	$2.31 \cdot 10^{10}$	4.41 •10 ⁻⁶
$5_{ox}/O_2$	4.45·10 ⁻⁹	1.59·10 ⁻⁹	1.38·10 ⁻⁷	3.86·10 ⁻⁷	$2.40 \cdot 10^{10}$	4.71·10 ⁻⁶

Table 1-6: Parameter for the Smoluchowski model. The diffusion coefficients are in ACN at 293.15 K.



Figure 1-12: Excited singlet state quenching of 1 and 5_{ox} . Quenching of the excited singlet state of 1 (a-b) and 5_{ox} (c-d) by DIPEA in O₂ saturated ACN. a and c: Stationary absorption and emission spectra in dependence on the DIPEA concentration as indicated. b and d: Time-resolved emission after excitation at $\lambda_{exc} = 443$ nm and detection at $\lambda_{det} = 490$ nm ($\lambda_{IRF} < 1$ ns) in dependence on the DIPEA concentration as indicated. The red lines represent exponential fits. The inset shows the Stern-Volmer analysis.

Comparison of these rates with the theoretical totally diffusion controlled bi-molecular rate constants estimated by the Smoluchowski theory (Table 1-6), shows a preference on encounter in both cases so that only 56% and 47% of all encounters lead to a reaction, respectively. As already discussed in section 1.3.4, the excited singlet state reaction of **1** with DIPEA results in a pure loss channel as also observed for 5_{ox} . In the presence of *p*-BA, also no reaction with the excited singlet state of **1** is observed. Figure 1-13 shows the corresponding transient absorption data for compound **1** in ACN. In case of the stable fully reduced form 5_{red} no reaction between the excited singlet state and the substrate *p*-BA is observed, even at substrate concentrations up to 400 mM (Figure 1-14).



Figure 1-13: Excited singlet state dynamics of 1. a-c: False color representation of the time-resolved absorption spectra of 1 (1 mM) in non-degassed ACN in the absence (a), or presence of either 800 mM DIPEA (b), or 100 mM *p*-BA (c) excited at $\lambda_{exc} = 450$ nm. d: Species associated spectra (SAS) that contribute to the time-resolved absorption signals in panels a-c with excited singlet state lifetimes as indicated. e: Model used to describe the time-resolved absorption data that results in physically reasonable SAS. On this time window k_{isc} is negligible and since no further species spectrum is detectable the assumption ${}^{1}K'_{beT} \gg {}^{1}K'_{eT}[S_{sac}]$ is justified. Abbreviations: SE = stimulated emission, rad = radiative, ic = internal conversion, (b)eT = (back) electron transfer, (b)isc = (back) intersystem crossing, S_0 = singlet ground state, S_1 = excited singlet state, T_1 = triplet state, {}^{1}RP = singlet born radical pair, S_{sac} = sacrificial electron donor, and S = substrate.

As can be seen, the excited state dynamics of 5_{red} do not only show a single spectral component with some minor spectral shifts due to internal conversion and vibrational relaxation that might be attributed to the excited singlet state alone, but, interestingly, show more transient intermediates. However, since the presence of *p*-BA does not change these dynamics, we do not address this point any further in this work. A more detailed elucidation of these dynamics is currently in progress in our labs and will be presented in a separate article.



Figure 1-14: Excited singlet state dynamics of 5_{red} . False color representation of the time-resolved absorption spectra of 5_{red} (500 µM) in O₂ saturated DMF exciting at $\lambda_{exc} = 340$ nm with (**b-d** and **f-h**) or without (**a** and **e**) p-bromoanisole (*p*-BA); **b** and **f**: 100 mM; **c** and **g**: 200 mM; **d** and **h**: 400 mM. The lower panels **e-f** show the decay associated difference spectra (DADS) from a global tri-exponential fit.

1.5.10 Triplet State Reactivity and Photochemical Model

In the presence of the sacrificial electron donor DIPEA we observe, additionally to the unproductive excited singlet state reaction, a reaction with the triplet state of 5_{ox} as seen by a reduced triplet state lifetime and the semiquinone 5_{sq} (Figure 1-2 in section 1.3.5). Thus, in the kinetic model an additional rate constant enters. The global tri-exponential fit absolutely determines the three rate constants, which represent

$$\kappa_1 = k_{\rm ic} + k_{\rm rad} + k_{\rm isc} + {}^1k_{\rm eT} \tag{7}$$

$$\kappa_2 = k_{\rm bisc} + {}^3k_{\rm eT} \tag{8}$$

$$\kappa_3 = {}^3k_{\rm beT} \tag{9}$$

The model shown in Figure 1-2g leads to the following relationship between the SAS and the DADS:

$$S_{S_1} = \frac{(D_1 + D_2 + D_3)}{c_0} + S_{S_0}$$
(10)

$$S_{T_1} = \frac{(\kappa_1 - \kappa_2)D_2 + (\kappa_1 - \kappa_3)D_3}{c_0 \Phi_{T_1} \kappa_1} + S_{S_0}$$
(11)

$$S_{D_0} = \frac{(\kappa_2 - \kappa_3)(\kappa_1 - \kappa_3)D_3}{c_0 \Phi_{T_1} \kappa_1 \Phi_{D_0} \kappa_2} + S_{S_0}$$
(12)

Here, c_0 is the contribution of the ground state spectrum and the Φ_i are the yields for the conversion from state *i* to the subsequent state i + 1. As can be seen, there are undetermined parameters c_0 , Φ_{T_1} , and Φ_{D_0} . However, one can at least find upper or lower bounds by the requirement that the resulting SAS must be positive and should not show any of the characteristic bands of the other species. In particular, the negative peaks from the ground state bleach should disappear in the SAS. In case of Φ_{T_1} one knows from data sets with and without DIPEA that the yield of the unproductive excited singlet state reaction is given by $\Phi_{1_{\rm RP}} = 1 - k_{1,0}k_1^{-1}$, where $k_{1,0}$ is the excited singlet decay rate without DIPEA and k_1 is the excited singlet decay rate in the presence of DIPEA, respectively. Thus, for 50 mM DIPEA the loss yield *via* the excited singlet reaction is 29%. Consequently, the triplet yield reaches only 7.6% under these conditions. Analogously, $\Phi_{D_0} = 1 - k_{2,0}k_2^{-1}$ is valid, where $k_{2,0}$ is the triplet decay rate without DIPEA and k_2 is the triplet decay rate in the presence of DIPEA, respectively. Thus, for 50 mM DIPEA, respectively. Thus, for 50 mM DIPEA the vield of $\mathbf{5}_{sq}$ is 87%.

1.5.11 Spectroelectrochemistry

Photocatalyst **5** in either its fully oxidized or its fully reduced form was electrochemically converted by application of either increasingly negative (Figure 1-15) or positive (Figure 1-16) potentials, respectively, and recording the UV/Vis absorption spectrum at the corresponding potential. Starting from 5_{ox} and applying increasingly negative potentials, one observes initially on the expense of 5_{ox} a build-up of a spectrum, that is similar to the pure species spectrum of 5_{red} (black to red in Figure 1-15a). However, a comparison with the pure species spectrum of 5_{red} (Figure 1-15b and d) reveals significant differences. Furthermore, the first step does not show the formation of a spectrum known for semiquinones. Thus, it is tempting to speculate that in the initial conversion phase the main fraction of semiquinone molecules disproportionate faster than they are formed. Due to the lack of matching shape to the spectrum of 5_{red} , this conversion is accompanied by partial degradation. Interestingly, decreasing the potential further results in a clean build-up of the semiquinone form on the expense of 5_{ox} as seen in clear isosbestic points (red to blue in Figure 1-15a).



Figure 1-15 Electrochemical reduction of 5_{ox} in degassed ACN. a and c: Sequence of UV/Vis absorption spectra after stepwise application of increasingly negative voltage to the sample in 0.05 V increments as indicated. The inset in c shows the corresponding cyclic voltammogram. b and d: Species spectra contributing to corresponding data in a and c. The grey vertical lines in b correspond to the quantum chemically calculated stick spectrum of 5_{sq} as described in the methods.

Finally, going down to -2.0 V, 5_{sq} converts to 5_{red} (blue to pink in Figure 1-15c) by taking up a second electron. This step, again, occurs with clear isosbestic points indicating a clean conversion. Thus, the electrochemical reduction of 5_{ox} in degassed ACN solution shows the transient formation of 5_{sq} , which indicates a higher stability compared to isoalloxazine semiquinones under similar conditions.⁷⁷

In the next step, it was started from $\mathbf{5}_{red}$ and applied increasingly positive potentials. Initially, only small spectral changes in the UV region below 300 nm are observed (black to red in Figure 1-16a). These might be attributed to small impurities in the sample that degrade. Subsequently, between 0.65 V and 1.25 V a clean conversion from $\mathbf{5}_{red}$ to $\mathbf{5}_{ox}$ with clear isosbestic points is observed (red to blue in Figure 1-16a). Further increase of the potential results in complete degradation of the sample (blue to pink in Figure 1-16c). Interestingly, no formation of $\mathbf{5}_{sq}$ is detected following this electrochemical route.



Figure 1-16 Electrochemical oxidation of 5_{red} in ACN. a and c: Sequence of UV/Vis absorption spectra after stepwise application of increasingly positive voltage to the sample in 0.05 V increments. b and d: Species spectra contributing to corresponding data in a and c.

1.5.12 Electron Paramagnetic Resonance (EPR)

 5_{ox} in degassed ACN in the presence of DIPEA was irradiated at 455 nm forming the semiquinone form (5_{sq}) to a considerable amount which allowed the recording of its EPR spectrum (MiniScope MS400, Magnettech, 9.45 MHz, Figure 1-17). Additionally, the structure of 5_{sq} was calculated quantum chemically with the programme package Orca⁶⁸⁻⁶⁹ using DFT/B3LYP level of theory with EPR-II basis set in order to obtain the spin densities and the isotropic *g* value. A model including only hyperfine couplings between three nuclei, for instance representing ¹H-43, ¹H-44, and ¹N-14, and the electron was used to fit the data *via* the EasySpin toolbox⁷⁸ (Figure 1-17).



Figure 1-17: Electron paramagnetic resonance spectrum of 5_{sq} in ACN. Data plus fit (blue line) (a) and quantum chemically calculated structure (b). The nuclei used in the fitting model are ¹N-14 (Spin = 1, $A_{iso} = 42.37 \text{ mHz}$), ¹H-43 (Spin = ¹/₂, $A_{iso} = 11.35 \text{ mHz}$), and ¹H-44 (Spin = ¹/₂, $A_{iso} = 12.38 \text{ mHz}$).

1.5.13 Potential Reaction Intermediates of *p-BA*

On the conversion from p-BA to p-A (anisole) two reaction intermediates should be theoretically observed. These are the radical anion, p-BA^{•-}, and the neutral radical, p-A[•]. In our experimental data we observed at least one intermediate arising from the conversion of p-BA, which shows a prominent absorption band peaking at 330 nm that is shown in Figure 1-3g in section 1.3.6.



Figure 1-18 Quantum chemical investigation on potential intermediates. Quantum chemical calculations of all species potentially involved in the conversion from *p*-BA to *p*-A (anisole). a: Electronic transitions (sticks) for the substrate, *p*-BA (black), and the final product, *p*-A (grey), as well as the two potential reaction intermediates *p*-BA^{•-} (blue) and *p*-A[•] (red) convoluted with Gaussians (FWHM = 0.2 eV) calculated at the state-averaged XMCQDPT-CASSCF(12,12)-PCM(ACN)//aug-cc-pVDZ level of theory. **b**: Relaxed potential energy surface along the C-Br bond for *p*-BA and *p*-BA^{•-} using DFT(B3LYP) level of theory with the aug-cc-pVDZ basis set. The indicated thermal energy *k*_BT is plotted for 300 K. **c**: The corresponding optimized structures on the DFT(B3LYP) level of theory with aug-cc-pVDZ basis set.

In order to make a structural assignment to this transiently observed absorption spectrum, we calculated the absorption spectra of the substrate, *p*-BA, and the final product, *p*-A, as well as the potential two reaction intermediates *p*-BA^{•-} and *p*-A[•] in the PCM(ACN) on the XMCQDPT-CASSCF level of theory using the aug-cc-pVDZ basis set. As evident from the calculations (Figure 1-18a), the absorption spectrum of *p*-BA^{•-} is in very good agreement with the experimentally observed transient spectrum. This proofs electron transfer from the excited deazaflavin radical anion to the substrate *p*-BA forming the *p*-BA^{•-}. Furthermore, calculation of the relaxed potential energy surface along the C-Br bond for *p*-BA and *p*-BA^{•-} (Figure *1-18*b) shows that on the one hand the bond length is considerably enlarged from 1.92 to 2.86 Å and on the other hand the dissociation energy is significantly reduced from 4.3 to 0.09 eV, respectively. Although the C-Br bond is clearly weakened in *p*-BA^{•-}, its dissociation energy is still within the thermal energy range allowing its transient observation which is in excellent agreement with our experimental data (Figure 1-3g in section 1.3.6).

1.5.14 NMR Spectra

NMR Spectra of TARF-H₂.





NMR spectra of 10-Butyl-7,8-dimethoxy-3-methyl-5-deazaisoalloxazine (1).



NMR spectra of 10-Butyl-7,8-dimethoxy-3,5-dimethyl-5-deazaisoalloxazine (2).



90 80 f1 (ppm)

0 -:

NMR spectra of 10-Butyl-7,8-dimethoxy-5-isopropyl-3-methyl-5-deazaisoalloxazine (3).









NMR spectra of 10-butyl-7,8-dimethoxy-3-methyl-5-phenyl-5-deazaisoalloxazine (5_{ox}).

NMR spectra of 10-butyl-7,8-dimethoxy-3-methyl-5-phenyl-5,10-dihydropyrimido[4,5-b]quinoline-2,4(1H,3H)-dione (**5**_{red}).





NMR spectra of *N*-butyl-3,4-dimethoxyaniline (7).



NMR spectra of 6-(N-Butyl(3,4-dimethoxyphenyl)amino)-3-methyluracil (8).


NMR spectra of 1-methylpyrimidine-2,4,6(1H,3H,5H)-trione (9).

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2 Photocatalytic Generation of Redox Equivalents for the Formal Anti-Markovnikov Water Addition to Styrenes



2.1 Abstract

We report an efficient method for the formal *anti*-Markovnikov addition of water to styrenes through photocatalytic generation of redox equivalents using a gold-doped titanium dioxide (Au/TiO_2) semiconductor as photocatalyst. Under irradiation with UV-A light the photocatalytic activity of Au/TiO₂ generates *in situ* under aerobic conditions hydrogen peroxide (H_2O_2) and under anaerobic conditions dihydrogen (H_2) . In presence of oxygen and a Ru-catalyst, the epoxidation of different styrene derivatives is achieved. Subsequently regioselective reductive Pd-catalyzed epoxide opening in absence of oxygen gives the corresponding 2-phenylethanol derivative.

2.2 Introduction

TiO2-based semiconductor materials are used in photocatalytic processes, especially in applications for wastewater treatment and air purification.¹⁻⁴ In most cases, hydrogen peroxide and hydroxyl radicals are produced by irradiation of TiO₂ with light under aerobic conditions. Among others, these species are mainly responsible for the oxidative degradation of pollutants. Besides that, TiO₂ has attracted a lot of attention in photocatalytic energy production. It is considered one of the most promising materials for hydrogen generation from oxidation of water under inert conditions.⁵⁻⁶ In contrast, the use of TiO₂ as photocatalyst for organic synthesis remains less explored with considerably fewer reports.⁷⁻¹¹ Herein, we report a specific application of TiO₂ in the synthesis of 2-phenylethanol derivatives from the corresponding styrenes via epoxidation and subsequent reductive ring opening. In particular, we are using a heterogeneous Au-doped TiO₂ photocatalyst for the *in situ* production of H₂O₂ under oxygen atmosphere as well as H₂ under an inert atmosphere in THF, in combination with a rutheniumbased catalyst for the epoxidation and a palladium-based catalyst for the epoxide opening. Scheme 2-1 summarizes the overall process. The deposition of gold nanoparticles on TiO₂ is beneficial for the overall photocatalytic performance.¹²⁻¹³ Due to the semiconductors intrinsic band gap of 3.2 eV for anatase and 3.0 eV for rutile, even non-doped TiO₂ is capable of absorbing light in the ultraviolet region.¹⁴ This causes excitation of electrons into the conduction band, which can be used for reductive processes and holes in the valence band, which can be used for oxidative processes. Deposition of metal nanoparticles results in better spatial charge separation (metal NP act as electron traps) and less prominent charge recombination, thus enhancing the photocatalytic performance of the material.¹⁵⁻¹⁶



Scheme 2-1: Schematic depiction of the synthesis of 2-phenylethanol from styrene in two steps. Left: Photocatalytic generation of H_2O_2 under oxygen atmosphere and ruthenium-catalyzed epoxidation step. Right: Photocatalytic generation of H_2 under inert atmosphere and palladium-catalyzed regioselective epoxide opening.

In this work, we show a photocatalytic alternative to classic synthetic strategies for 2phenylethanol derivatives, which include Grignard reactions, Friedel-Crafts-type reactions, or biochemical approaches.¹⁷⁻²⁰ In contrast to those, our strategy is based on a two-step photocatalytic approach, with no need for stoichiometric amounts of metal reagents, due to the use of cheap and abundant organic solvents as terminal reductants. Additionally, our method is very safe, due to the *in situ* generation of H_2O_2 and H_2 . Thus, handling of the commonly used hazardous 30% aqueous H_2O_2 for the epoxidations and inflammable H_2 -gas under great pressure or in large reservoirs for the reduction is avoided. Alteration between H_2O_2 - and H_2 -production can easily be achieved by switching between aerobic and anaerobic conditions in the reaction vial. A convenient sample preparation strategy was developed, without the need for isolation of the intermediate epoxide. Both individual steps were optimized using the two most used modifications of TiO₂ (P25 and rutile) and we compare the catalytic activity of both materials.

2.3 Results and Discussion

2.3.1 Photocatalytic Generation of Redox Equivalents Using Au/TiO2

Previous work has shown that Au/TiO₂ is suitable for the photocatalytic generation of H_2O_2 as well as H_2 from water or organic solvents.²¹ For both reactions, gold-doping was necessary to achieve sufficient amounts of H_2O_2 or H_2 in order to be applicable to organic reactions. Here we used two distinct Au/TiO₂-catalysts differing in the respective modification of the TiO₂ support material. In the following the two catalysts are referred to as Au/TiO₂ (rutile), where the supporting material was TiO₂ in the rutile modification, and Au/TiO₂ (P25), where the supporting material was TiO₂ in the P25 modification, which in itself is a mixture of 75%-85% anatase, 15% rutile and a small amount of amorphous phase.

Previous detailed investigations²¹ showed that no significant difference for H₂O₂ production between both modifications is observed. The H₂ production for both materials under various reaction conditions was quantified by measurement of the amount of H₂ in the gas phase of a reaction vial using headspace-GC (HS-GC) after 1 hour of irradiation with light. To calculate the actual amount of hydrogen a calibration curve derived from the HS-GC-response for defined amounts of H₂ in the reaction vial was used assuming ideal gas behavior. The measurements showed linear behavior for at least up to 82 µmol (2 mL) of hydrogen. For a detailed description of the HS-GC set-up and the calibration procedure see experimental part (Figure 2-3). Figure 2-1 shows the H₂ evolution activity under varying reaction conditions. In i) the amount of H₂ produced from 2 mg of either Au/TiO₂ (rutile) or Au/TiO₂ (P25) under 385 nm irradiation for 1 hour in different solvents is compared. In contrast to the similar performance of both materials for the H2O2-production, in this case the P25-modification clearly outperformed the rutile-modification in all solvents. This effect can be attributed to the high anatase content in the P25 support material, which has been reported by Murdoch et al. to exhibit a higher H₂-evolution activity compared to a purely rutile-based support material.²² Furthermore, the data shows that hydrogen evolution from pure THF is very inefficient. However, hydrogen production can be enhanced using a mixture of THF and water (10 µL per hour) or even more by using ethanol (59 µL per hour) or methanol (67 µL per hour). With all solvents, hydrogen generation is realized by reduction of protons that are derived from the oxidation of the corresponding solvent. Hydrogen evolution from sacrificial reductants (like alcohols) is well reported in literature.²³⁻²⁴ The use of THF as sacrificial reductant has been reported by Kisch et al. in 1984.²⁵ The adaptation of this process with our AuTiO₂ system has been the topic of previous work.²¹ Further optimization was done by adjustment of the

irradiation wavelength and the catalyst loading (see ii)). The photocatalytic H₂-production using Au/TiO₂ is known to be driven by UV-light.²⁶ As expected, utilizing shorter wavelengths significantly increased the amount of hydrogen produced from a THF/H₂O mixture (3/1), with only traces being detected at 400 nm, 10 μ mol at 385 nm, and 41 μ mol at 365 nm. Higher catalyst loadings correlate to an increase in hydrogen production. With 10 mg of Au/TiO₂ (P25), which was the highest amount that was tested, 122 μ mol of hydrogen were generated after 1 h of irradiation at 365 nm.



Figure 2-1: Influence of TiO_2 modification, amount of catalyst, solvent and irradiation wavelength on the amount of H_2 produced after 1 hour of irradiation. i) Comparison of Au/TiO₂ (rutile) and Au/TiO₂ (P25) in different solvents (2 mL). ii) Comparison of irradiation wavelength and amount of Au/TiO₂ (P25).

2.3.2 Synthetic Application of Photocatalytically Generated Redox Equivalents for

the Synthesis of 2-Phenylethanol Derivatives

Based on these results, our aim was now to utilize the photocatalytic hydrogen peroxide and the hydrogen production by Au/TiO_2 in an organic synthesis sequence. The synthesis of 2phenylethanol from styrene *via* the corresponding epoxide requires hydrogen peroxide for the first step and dihydrogen for the second step. In combination with suitable catalysts, aerobic conditions can be applied for H_2O_2 production and the synthesis of styrene oxide and subsequently inert conditions for H_2 production and the regioselective epoxide opening. The main challenge was to find catalyst systems that not only work for the individual reactions, but also allow for an efficient sequential coupling of both reaction steps.

2.3.3 Epoxidation of Styrenes Using Au/TiO₂ as H₂O₂-Source

After a quick screening of different epoxidation catalysts we optimized our reaction conditions with a catalytic system consisting of a combination of $RuCl_3xH_2O$ and dipicolinic acid, which was reported earlier by Beller *et al.*²⁷ To be compatible with the photocatalytic *in situ* generation of H_2O_2 from THF the catalytic epoxidation system must tolerate THF as solvent, the use of H_2O_2 as oxidant (instead of frequently used peroxoacids), and show photostability under the irradiation conditions. Another aspect in favor of the $RuCl_3xH_2O$ /dipicolinic acid system is the use of only three equivalents of H_2O_2 and the continuous addition under the reported conditions, which is mimicked by the continuous *in situ* generation in the photocatalytic approach.

The result of different reaction parameters under the photocatalytic conditions at the example of the epoxidation of para-fluorostyrene is given in Table 2-1. All reactions were carried out with 0.3 mmol of para-fluorostyrene in 1.5 mL of THF. Preliminary experiments have shown that the photocatalytic system is producing H₂O₂ in a steady state concentration resulting from the equilibrium between its generation and decomposition. This equilibrium turned out to be influenced by the Au/TiO₂-loading, with the catalyst in excess having a negative effect on the H₂O₂ concentration.²¹ Therefore, the epoxide-yield using different amounts of Au/TiO₂ varies with high catalyst loadings resulting in low epoxide yields (entry 1, 2 and 4). While after 16 h, comparable yields of 37% and 42% were achieved with 1.5 mg and 2.5 mg, using 5 mg a yield of only 35% was achieved even after significantly prolonged reaction time. From our experiments, 2 mg were concluded to be the ideal catalyst loading for the given reaction volume. For the RuCl₃xH₂O and dipicolinic acid loadings, very similar results as described by Beller et al. were obtained.²⁷ Only minor deviations in the yield were observed for different RuCl₃xH₂O loadings with the best results for 0.1 mg (<0.1 mol% calculated for RuCl₃•5H₂O and 0.3 mmol substrate; entries 3 - 6). A bigger effect was observed varying the amount of dipicolinic acid, where the product yield could be increased by using up to 8 mol% of the ligand. The use of higher amounts of dipicolinic acid did not enhance the yield any further (entries 7 - 9). Prolongation of the reaction time to 24 h led to full conversion and a yield of 65% of the epoxide-product (entry 10).

	Au/TiO ₂ RuCl ₃ xH ₂ O Dipicolinic acid	
F	THF 1.5 mL, O ₂ -atmosphere λ, 25 °C	F

Entry	Au/TiO2 [mg]	RuCl ₃ xH ₂ O [mg]	Dip. ac. [mol%]	λ [nm]	t [h]	Conv. [%] ^[a]	Yield [%] ^[a]
1	2.5	0.1	7	385	14.5	85	42
2	1.5	0.1	7	385	14.5	81	37
3	5	0.05	7	385	22	78	29
4	5	0.1	7	385	22	77	35
5	5	0.2	7	385	22	76	29
6	5	0.4	7	385	22	78	28
7	2	0.1	6	400	20	85	50
8	2	0.1	8	400	20	92	58
9	2	0.1	10	400	20	92	59
10	2	0.1	8	400	24	100	65
11	2	0.1	4	365	16	100	41
12	2	0.1	4	385	16	90	46
13	2	0.1	4	400	16	85	47
14	2	0.1	4	455	24	43	25
15 ^[b]	2	0.1	8	400	20	95	58
16 ^[c]	2	0.1	4	385	24	82	44
17	2	0	8	400	24	25	0
18	2	0.1	0	400	24	65	3

^[a]Conversion and yield were determined by quantitative NMR analysis using para-fluorotoluene as internal standard. ^[b]Au/TiO₂ (P25) was used instead of Au/TiO₂ (rutile). ^[c]Addition of the substrate as a solution in THF via syringe pump (0.15 mM, 2.0 mL, flowrate: 200 μ L/h). While H₂O₂-prodction is enhanced by shorter irradiation wavelengths, the product yield was highest for 400 nm under otherwise equal conditions (entries 11 - 14). The low yields using 455 nm can be attributed to the significantly lower H₂O₂ production under blue-light irradiation. In contrast, shorter wavelengths lead to an increase in side-reactions, as can be seen by the higher substrate conversion at lower overall product yields. Besides low amounts of (para-fluorophenyl)acetaldehyde (<10%), which is also reported by Beller et al.²⁷ to be a side product, the photocatalytic conditions apparently lead to further side product formation. Unfortunately, we could not identify the nature of the side-products, but we assume that the irradiation is causing polymerization reactions of the fluorostyrene-monomers. The use of 400 nm constitutes the best compromise between efficient H_2O_2 production and suppression of side reactions (entry 13). Performing the reaction under our optimized conditions, but with Au/TiO₂ (P25) instead of Au/TiO₂ (rutile) showed that both catalyst modifications lead to the same product yield (compare entry 15 and 8). Noteworthy to mention here is that upon deviation from the optimized conditions usually the rutile modification showed a slightly better performance. This may be due to minor differences in the effectivity in H_2O_2 production. Therefore, the scope of the reaction was explored using only the rutile modification. Continuous addition of the substrate via syringe pump did not reduce the amount of side reactions (entry 16). Finally, control reactions without RuCl₃xH₂O or dipicolinic acid showed the necessity of both for the epoxide formation (entry 17 and 18). Interestingly, the presence of only dipicolinic acid still leads to substrate consumption, however with a low conversion of 25%. In contrast to that, in presence of only RuCl₃xH₂O, 65% of the substrate were consumed, but only trace amounts of the desired product were observed.

2.3.4 Reductive Epoxide Opening Using Au/TiO2 as H2-Source

In the same way as for the epoxidation catalyst, hydrogenation catalysts were screened. As a result, two palladium catalysts turned out to be promising candidates for the epoxide opening reaction, $Pd(OAc)_2$ and Pd(0)EnCat (encapsulated palladium nanoparticles). With both catalysts, regioselective ring opening to the *anti*-Markovnikov product was achieved in trial reactions and no significant deviation in the performance between both catalysts could be observed. The scope was investigated using $Pd(OAc)_2$ as catalyst, due to the simplicity of the set-up and a lower overall Pd-loading. Consequently, in the following only the optimization using $Pd(OAc)_2$ is shown (Table 2-2). A comparison to the Pd(0)EnCat system can be found in the experimental part (section 2.5.4, Table 2-5).

Table 2-2: Evaluation of Pd(OAc)₂ as ring opening catalyst.



Entry	H ₂ source and reaction conditions	Solvent	Product formation
1	H ₂ -balloon	THF	yes
2	H ₂ -balloon or Au/TiO_2 + irrad.	MeOH or EtOH	no
3	$Au/TiO_2 + irrad.$	THF	no
4	$Au/TiO_2 + irrad.$	$\mathrm{THF}/\mathrm{H_2O}\;3/1$	yes
5	$Au/TiO_2 + irrad. + RuCl_3xH_2O + acid$	$\mathrm{THF}/\mathrm{H_2O}\;3/1$	no
6	Au/TiO_2 + irrad. + after epoxidation	$\mathrm{THF}/\mathrm{H_2O}\;3/1$	no

At first it was tested whether $Pd(OAc)_2$ can be used in THF as catalyst for the regioselective ring opening of styrene oxides under standard conditions using an H₂-balloon (entry 1). As expected, this was possible with the desired alcohol as the main product and ethylbenzene as the only side product detected *via* GC. In contrast to that, running the reaction in methanol or ethanol (entry 2), which would provide larger amounts of H₂ (see Figure 2-1), led to the formation of alcohol adducts as the main product *via* a nucleophilic attack of the alcohol during the ring opening reaction (analyzed *via* GC-MS). *In situ* generation of H₂ with Au/TiO₂ and irradiation did not lead to significant substrate conversion in pure THF (entry 3). However, due to the synergistic effect of a mixture of water and THF generating higher amounts of H₂, product formation could be observed under irradiation with 365 nm (entry 4). In order to use

similar conditions to the previous epoxidation reaction RuCl₃xH₂O and dipicolinic acid were added in entry 5, under otherwise identical conditions as in entry 4. Unfortunately, this led to the formation of an unidentified side product. In a similar way, sequential epoxidation and ring opening (entry 6) suffered from low epoxide conversions and side product formation. Thus, the ideal scenario of a direct coupling by simple switching from oxidative to reductive conditions by exchanging the atmosphere is not possible, due to the incompatibility of the catalytic systems for epoxidation and epoxide opening. At the same time, complete isolation of the epoxides between the reactions is not desirable due to low chemical stability and relatively high volatility of some of the styrene oxide derivatives. Therefore, a quick and simple washing protocol was developed. A visualization of the protocol is given in Scheme 2-2.



Scheme 2-2. Depiction of the work-up protocol.

In order to separate RuCl₃xH₂O and dipicolinic acid from the solution, the reaction mixture is extracted with 2 mL of a 1M NaOH-solution and 3x1 mL of diethylether (DEE). Both are directly added to the reaction vial *via* syringe. Due to the miscibility gap between THF and water under basic conditions, the organic phase can easily be separated and transferred into a new glass-vial. In this step, the heterogeneous Au/TiO₂ remains in the aqueous phase. Subsequently the organic phase is washed with 1 mL of H₂O in order to remove excess NaOH from the organic phase. Too basic conditions should be avoided for the reduction step as the photocatalytic H₂-generation is hampered in basic medium. In a last washing step, the aqueous phase is extracted with 1.5 mL of DEE to minimize loss of organic material. Afterwards the organic solution is concentrated under reduced pressure to around 0.5 mL and can then be used for the epoxide opening reaction. For the detailed procedure, see the general procedure in the experimental part.

After the work-up process the epoxide opening was performed, using $Pd(OAc)_2$ or Pd(0)EnCat. In both cases regioselective ring opening to the *anti*-Markovnikov product was observed, with the only side product being small amounts of 4-fluoro-ethylbenzene. The reaction conditions were optimized with regard to the time required for full conversion of the epoxide. The optimization of the reaction conditions for $Pd(OAc)_2$ is depicted in Table 2-3. The comparison to Pd(0)EnCat can be found in the experimental part (section 2.5.4, Table 2-6).

Table 2-3: Optimization	of the reaction	conditions fo	or the epoxide	opening	using Pd	(OAc) _{2.}
1			1	1 0		· /-·

	Au-TiO ₂ Pd(OAc) ₂	\wedge	ОН
F	THF/H ₂ O (3/1) 2 mL N ₂ -atmosphere λ, 25 °C	F	
	Conditions		t (full conv.) [h]
5 mg Au/TiO ₂ (P25), 1.2 mol% Pd(OAc))2, 365 nm	> 24

5		()[]
1	5 mg Au/TiO ₂ (P25), 1.2 mol% Pd(OAc) ₂ , 365 nm	> 24
2	10 mg Au/TiO ₂ (P25), 2.2 mol% Pd(OAc) ₂ , 385 nm	> 18
3	10 mg Au/TiO_2 (P25), 2.2 mol% Pd(OAc) ₂ , 365 nm	18
4	5 mg Au/TiO ₂ (P25), 1.8 mol% Pd(OAc) ₂ , 365 nm	15
5	10 mg Au/TiO_2 (rutile), 2.2 mol% Pd(OAc) ₂ , 365 nm	> 24
6 ^[a]	10 mg Au/TiO ₂ (P25), 2.2 mol% Pd(OAc) ₂ , 365 nm	n.d.

^[a]Successive epoxidation and epoxide opening without work-up protocol.

Entry

All reactions were performed after the epoxidation reaction using 0.3 mmol para-fluorostyrene and the work-up procedure (unless otherwise stated). The results are in accordance with the results from the screening for the highest H₂-generation activity. Analogously as higher AuTiO₂ loadings and irradiation with a shorter wavelength led to a higher H₂-evolution, it also allowed to shorten the reaction time for full substrate conversion (entries 1 - 3). Adjusting the amount of Pd(OAc)₂ showed, that using 1.8 mol% was sufficient for full conversion after 15 h (entry 4). While lower amounts of Pd(OAc)₂ caused slower substrate conversion, larger amounts also slowed down the reaction by increased light absorption, due to darkening of the reaction mixture. Catalytic activity is also observed using AuTiO₂ (rutile), but product formation is significantly slower, which can be attributed to the lower H₂-evolution from the rutile modification. Finally, entry 6 shows the attempt of direct epoxidation and epoxide opening without intermediate work-up process. In this case, no detectable epoxide consumption was observed after 24 h.

2.3.5 Scope and Limitations of the Two-Step Process

With the optimized conditions for both reaction steps and a work-up procedure in hand, we investigated the scope of the reaction. Yields for the epoxidation were determined by NMRanalysis using trichloroethylene (TCE) as internal standard (values in blue and in brackets in Table 2-4). The overall yield after both steps was determined by isolation of the products (values in pink). Most substrates gave moderate epoxide yields between 42% and 71%. The yields for the epoxide opening can be determined indirectly from the epoxidation yields and the yields of the isolated products. In general, the performance of the ring opening reaction was better than that of the epoxidation, with the corresponding yields ranging between 60%and 85% (not directly given in the Table). Para-fluorostyrene gave an overall yield of 50% of the corresponding primary alcohol **3a**, with the yields for the individual steps being 65% for the epoxidation and 77% for the ring opening. Very similar yields were obtained with unsubstituted styrene (3b), as well as a trimethylsilyl group in para position (3e), with each giving the product in a yield of 49% after both steps. Compound **3c** with a methyl group in para position was obtained in an overall yield of 48%, but the epoxidation step was less efficient with only 57%. A phenyl substituent in the para position (3d) caused the overall yield to drop to 35%, while the epoxidation step went equally well with 58%. Furthermore, an electron pushing acetoxy group gave the final product in a yield of only 28% with a corresponding epoxide yield of 48%. Substitution at the double bond is tolerated. The best results in the epoxidation step were achieved for cis- and trans- β -methylstyrene with 71% (2g) and 66% (2h). After ring opening 3g was obtained with a yield of 67% and 3h with 42%. At the same time, α -methylstyrene (3i) gave slightly lower yields with 56% and 37%, respectively. Substitution of the methyl group with a more sterically hindered phenyl group resulted in yields of 42% and 28% (3j). Limitations for this reaction system can be seen in the bottom row of Table 2-4. In the case of 2k the epoxide yield after 24 h of irradiation was only 20% with around 65% of substrate remaining. This can be rationalized by the electron withdrawing effect of the CF_3 group, deactivating the double bond for the reaction with H_2O_2 . In the case of 21, full substrate conversion was observed, while no epoxide formation could be detected. Most likely, the electron donation from the methoxy substituent is activating the double bond for unwanted side reactions. Compounds 2m and 2n are examples of substrates with reasonable yields of the corresponding epoxides, while not being suited for the epoxide opening. In both cases, the reactants decomposed and the corresponding primary alcohols could not be isolated.

Table 2-4: Scope of the reaction. The yields in pink correspond to the final products after both reaction steps, the yields in blue and in brackets correspond to the yield of the epoxide intermediate.



2.3.6 Reactor Design for Heterogeneous Phocatalytic Reactions

A new photo reactor setup was designed for running several heterogeneous reactions simultaneously under reproducible conditions. In contrast to homogeneous systems, reproducible stirring conditions are of importance in heterogeneous systems. Unlike homogeneous catalysts, even distribution of heterogeneous material has to be achieved by thorough stirring. Thereby, insufficient stirring can cause the heterogeneous material to precipitate, decreasing interaction between catalyst and reagents and causing a non-transparent layer at the bottom of the vial. By blocking off most of the light, this is inhibiting the photocatalytic reaction. On the other hand, violent stirring can cause splashing of the reaction mixture, distributing the heterogenous material over the lid and the sides of the glass vial, ultimately removing it from the reaction medium. Our setup consists of a multi-spot magnetic stirrer with 15 individual stirring centres and a tailor-made LED plate with a cooling element on top. A reproducible stirring quality is ensured as the reaction vials and the stirring centres are concentric. Temperature control is achieved by water cooling, through a metal cooling block that is placed directly on top of the LEDs holding the reaction vials. Irradiation of the samples is done from the plain bottom side of the glass vials. Alteration of the irradiation wavelength is possible by exchange of the LED base plate

Figure 2-2. Reactor design for heterogeneous reactions. Left: Design drawing of the LED plate and cooling element of the 15-spot reactor. Right: Picture of the reactor including magnetic stirrer, LED plate and cooling system.

2.4 Conclusion

In conclusion, a series of 2-phenylethanol derivatives has been synthesized *via* epoxidation of the corresponding styrenes and subsequent reductive ring opening. In both reaction steps, the corresponding redox equivalents in the form of H_2O_2 and H_2 were generated *in situ* using Au/TiO₂ as photoredox catalyst. Alteration between hydrogen peroxide and hydrogen production is achieved by the application of aerobic or anaerobic conditions. Operating under oxidative and reductive reaction conditions shows the versatility of the gold-doped TiO₂ catalyst. While a one-pot reaction could not be achieved, both individual steps were optimized to give satisfactory yields and a procedure for sequential epoxidation and epoxide opening has been developed. However, further simplification of the process can be envisaged using more compatible homogeneous catalytic systems or using a heterogeneous epoxidation catalyst and filter techniques.

2.5 Experimental Part

2.5.1 General Information

Materials. Starting materials and reagents were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, Acros, Fluka, VWR, or Fluorochem) and were used without further purification. Solvents were used as p.a. grade or dried and distilled according to literature known procedures.

Nuclear magnetic resonance (NMR) spectroscopy. NMR spectra were recorded at room temperature using a Bruker Avance 300 (300 MHz for 1H, 75 MHz for 13C), a Bruker Avance 400 (400 MHz for ¹H, 101 MHz for ¹³C, 377 MHz for ¹⁹F), an Agilent 400-MR DDR2 (400 MHz for ¹H and 101 MHz for ¹³C, 377 MHz for ¹⁹F), or a Varian Mercury Plus 300 (300 MHz for ¹H, 75 MHz for ¹³C) with internal solvent signal as reference. All chemical shifts are reported in δ -scale as parts per million (multiplicity, coupling constant J, number of protons) relative to the solvent residual peaks as the internal standard (IS). In ¹⁹F-NMR parafluorotoluene was used as internal standard. In ¹H-NMR trichloroethylene (TCE) was used as internal standard.

Mass spectrometry. The mass spectrometric measurements were performed at the Central Analytical Laboratory of the University of Regensburg or at the Central Analytical Laboratory of UCT, Prague on a Finnigan MAT 95, ThermoQuest Finnigan TSQ 7000, Finnigan MATSSQ 710A, Agilent Q-TOF 6540 UHD, or a LTQ Orbitrap Velos (Thermo Fisher Scientific).

Gas chromatography (GC). GC measurements were performed on a GC 7890 from Agilent Technologies. Data acquisition and evaluation was done with Agilent ChemStation Rev.C.01.04. A capillary column HP-5MS/30 m \times 0.25 mm/0.25 μ M film and helium as carrier gas (flow rate of 1 mL/min) were used. The injector temperature (split injection: 40:1 split) was 280 °C, detection temperature 300 °C (FID). The GC oven temperature program was adjusted as follows: the initial temperature of 40 °C was kept for 3 min and was increased at a rate of 15 °C/min until the injection temperature of 280 °C was reached. After 5 min, the temperature was further increased at a rate of 25 °C/min until the final temperature of 300 °C was reached and kept for 5 min.

Headspace-GC (HS-GC). Measurements were performed on INFICON 3000 Micro GC equipped with MS-5A column and thermal conductivity detector using argon as a carrier gas.

General irradiation conditions. Samples were irradiated at 365 nm (Soeul VIOSYS, SSC VIOSYS CUN66A1B, $\lambda_{max} = 365$ nm, $I_{max} = 700$ mA), at 385 nm (Opulent Starboard, Luminus SST-10-UV-A130, $\lambda_{max} = 385$ nm, $I_{typ} = 500$ mA, $I_{max} = 1.5$ A, $\Phi_{typ} = 1015$ mW), at 400 nm (Edison, EDEV-SLC1-03, $\lambda_{max} = 400$ nm, $I_{max} = 700$ mA), or at 455 nm (CREE XLamp Me-C LED, $\lambda_{max} = 455$ nm, $I_{max} = 700$ mA).

2.5.2 General Procedures

General procedure: Epoxidation

A 5 mL crimp cap vial equipped with Au/TiO₂, dipicolinic acid and a stirring bar was capped and the atmosphere was exchanged 3 times with oxygen. After addition of 1.5 mL of a solution of RuCl₃xH₂O in oxygen saturated THF, the corresponding styrene (0.3 mmol, 1.0 equiv.) was added with the help of a Hamilton syringe. Subsequently, the reaction mixture was ultrasonicated for 5 minutes. An oxygen balloon was connected to the vial *via* a thick needle through the septum of the crimp cap. Finally, the reaction mixture was stirred at 400 rpm and irradiated with 400 nm LEDs for 24 h.

General procedure: Work-up

After the epoxidation reaction, 2 mL of a 2M NaOH solution were directly added to the vial through the septum of the crimp cap. The mixture was extracted with DEE (3x1 mL) and the combined organic phases were transferred to another crimp cap vial. Residues of the sodium hydroxide solution were washed with 1 mL of a 3/1 mixture of water and brine, followed by a final washing step of the water phase with 1.5 mL of DEE. The combined organic phases were evaporated *via* a thick needle through the septum of the crimp cap and the mixture was concentrated to an overall volume of around 0.5 mL following a standardized procedure (40 °C, 5 min at 750 mbar, then 3 min at 300 mbar).

General procedure: Epoxide opening

Reaction with $Pd(OAc)_2$: After the work-up, 2 mL of a solution of $Pd(OAc)_2$ in THF/water (3/1) was added to the remainder. After addition of Au/TiO₂ and a stirring bar the vial was closed again and the atmosphere was exchanged for N₂ 9 times (15 s at 300 mbar, then 5 s N₂). After ultrasonication for 5 min, the samples were irradiated for 15 h using 365 nm LEDs.

Reaction with Pd(0)EnCat: After the work-up, Pd(0)EnCat and 2 mL of ethanol were added to the remainder. After addition of Au/TiO₂ and a stirring bar the vial was closed again and the atmosphere was exchanged for N₂ 9 times (15 s at 300 mbar, then 5 s N₂). After ultrasonication for 5 min, the samples were irradiated for 15 h using 365 nm LEDs.

After the reaction was stopped the reaction mixture was transferred to a sintered glass funnel (lower vacuum assembly) containing a layer of a few millimetres of MgSO₄ and the reaction vial was washed with *ca.* 25 mL of THF. After stirring of the mixture for a few minutes, the filtrate was directly collected in a connected round bottom flask. After evaporation of the solvent, the crude product was purified *via* automated flash column chromatography.

2.5.3 Preparation and Characterization of Products

All products were synthesized following the general procedures under the optimized conditions. Consequently, epoxidations were performed using 2 mg Au/TiO₂ (rutile), 1.5 mL of a solution of RuCl₃xH₂O (0.1 mg, <0.1 mol% calculated for RuCl₃•5H₂O) and dipicolinic acid (4 mg, 8.0 mol%) in THF and 0.3 mmol (1.0 equiv.) of the corresponding styrene. Epoxide openings were performed after the work-up step using Pd(OAc)₂ as a solution in 2 ml of THF/H₂O (3/1) (1.2 mg, 0.005 mmol, c= 2.7mM) and 7 mg of Au/TiO₂ (P25).

2-(4-fluorophenyl)ethan-1-ol (3a)²⁸

3a

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.23 – 7.12 (Ar-*H*, m, 2H), 7.03 – 6.95 (Ar-*H*, m, 2H), 3.82 (CH₂, t, *J* = 6.6 Hz, 2H), 2.83 (CH₂, t, *J* = 6.5 Hz, 2H), 1.84 (O-*H*, s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 163.3 (C_q), 160.1 (C_q), 134.2 (C_q), 134.2 (C_q), 130.4 (+), 130.3 (+), 115.5 (+), 115.2 (+), 63.6 (-), 63.6 (-), 38.3 (-). HRMS (EI+) (m/z): [M]⁺⁺ (C₈H₉OF) calc.: 140.0632, exp.: 140.0628.

2-phenylethan-1-ol (3b)²⁹

3b

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.41 – 7.18 (Ar-*H*, m, 5H), 3.86 (C*H*₂ t, *J* = 6.6 Hz, 2H), 2.87 (C*H*₂ t, *J* = 6.6 Hz, 2H), 1.67 (O-*H*, s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 138.5 (C_q), 129.1 (+), 128.6 (+), 126.5 (+), 63.7 (-), 39.2 (-). HRMS (EI+) (m/z): [M]⁺⁺ (C₈H₁₀O) calc.: 122.0726, exp.: 122.0731.

2-(*p*-tolyl)ethan-1-ol (3c)²⁹

3c

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.08 (Ar-*H*, s, 4H), 3.75 (C*H*₂, t, *J* = 6.7 Hz, 2H), 2.77 (C*H*₂, t, *J* = 6.7 Hz, 2H), 2.29 (C*H*₃, s, 3H), 2.08 (O-*H*, s, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 135.9 (C_q), 135.5 (C_q), 129.3 (+), 128.9 (+), 63.7 (-), 38.8 (-), 21.1 (+).

HRMS (EI+) (m/z): $[M]^{+}$ (C₉H₁₂O) calc.: 136.0883, exp.: 136.0880.

2-([1,1'-biphenyl]-4-yl)ethan-1-ol (3d)²⁸

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.64 – 7.52 (Ar-*H*, m, 4H), 7.45 (Ar-*H*, m, 2H), 7.41 – 7.27 (Ar-*H*, m, 3H), 3.91 (CH₂, t, *J* = 6.6 Hz, 2H), 2.93 (CH₂, t, *J* = 6.5 Hz, 2H), 1.71 (O-*H*, s, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 141.0 (C_q), 139.6 (C_q), 137.7 (C_q), 129.6 (+), 128.9 (+), 127.4 (+), 127.3 (+), 127.1 (+), 63.7 (-), 38.9 (-).

HRMS (EI+) (m/z): [M]^{•+} (C₁₄H₁₄O) calc.: 198.1039, exp.: 198.1039.

2-(4-(trimethylsilyl)phenyl)ethan-1-ol (3e)

3e

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.50 – 7.44 (Ar-*H*, m, 2H), 7.25 – 7.17 (Ar-*H*, m, 2H), 3.80 (CH₂, t, *J* = 6.7 Hz, 2H), 2.82 (CH₂, t, *J* = 6.7 Hz, 2H), 2.18 (O-*H*, s, 1H), 0.26 (Si-(CH₃)₃, s, 9H).

¹³C NMR (75 MHz, CDCl₃) δ 140.2 (C_q), 139.2 (C_q), 134.7 (+), 129.6 (+), 64.6(-), 40.2 (-), 0.0 (+)

HRMS (EI+) (m/z): [M]^{•+} (C₁₁H₁₈OSi) calc.: 194.1121, exp.: 194.1112.

4-(2-hydroxyethyl)phenyl acetate (3f)³⁰

3f

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.23 (Ar-*H*, d, *J* = 8.4 Hz, 2H), 7.02 (Ar-*H*, d, *J* = 8.5 Hz, 2H), 3.83 (CH₂, t, *J* = 6.6 Hz, 2H), 2.84 (CH₂, t, *J* = 6.6 Hz, 2H), 2.29 (CH₃, s, 3H), 1.70 (O-*H*, s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 169.8 (C_q), 149.4 (C_q), 136.3 (C_q), 130.1 (+), 121.7(+), 63.6 (-),

38.7 (-), 21.2 (+).

HRMS (EI+) (m/z): [M]^{•+} (C₁₀H₁₂O₃) calc.: 180.0781, exp.: 180.0783.

1-phenylpropan-2-ol (3g/h)³¹

3g/h

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.40 – 7.18 (Ar-H, m, 5H), 4.08 – 3.94 (CH, m, 1H), 2.88 – 2.60 (CH₂, m, 2H), 1.90 (O-H, s, 1H), 1.24 (CH₃, d, *J* = 6.2 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 138.6 (C_q), 129.4 (+), 128.6 (+), 126.5 (+), 68.9 (+), 45.8 (-), 22.8 (+).

HRMS (EI+) (m/z): [M]^{•+} (C₉H₁₂O) calc.: 136.0883, exp.: 136.0873

2-phenylpropan-1-ol (3i)²⁸

3i

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.38 – 7.30 (Ar-*H*, m, 2H), 7.27 – 7.22 (Ar-*H*, m, 3H), 3.70 (CH₂, d, *J* = 6.9 Hz, 2H), 2.95 (C*H*, h, *J* = 7.0 Hz, 1H), 1.57 (O-*H*, s, 1H), 1.29 (CH₃, d, *J* = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 143.8 (C_q), 128.7 (+), 127.6 (+), 126.8 (+), 68.8 (-), 42.6 (-), 17.7 (+).

HRMS (EI+) (m/z): $[M]^{+}$ (C₉H₁₂O) calc.: 136.0883, exp.: 136.0882.

2,2-diphenylethan-1-ol (3j)²⁸

3j

¹H NMR (300 MHz, CDCl₃) δ [ppm] = 7.24 – 7.09 (Ar-*H*, m, 10H), 4.15 – 3.96 (C*H*₂-C*H*, m, 3H), 1.78 (O-*H*, s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 141.5 (C_q), 128.7 (+), 128.4 (+), 126.8 (+), 66.1 (-), 53.7 (-). HRMS (EI+) (m/z): [M]⁺⁺ (C₁₄H₁₄O) calc.: 198.1039, exp.: 198.1038.

2.5.4 Epoxide Opening Using Pd(0)EnCat

	$R \xrightarrow{ }{ } \qquad \qquad$		
Entry	H ₂ source and reaction condition	Solvent	Product formation
1	H ₂ -balloon	EtOH	yes
2	$Au/TiO_2 + irrad.$	EtOH	yes
3	$Au/TiO_2 + irrad.$	MeOH or THF/H ₂ O 3/1	no
4	$Au/TiO_2 + irrad.$	THF/EtOH 1/3	yes
5	Au/TiO ₂ + irrad. + RuCl ₃ xH ₂ O + dipicolinic acid	THF/EtOH 1/3	no
6	Au/TiO_2 + irrad. + after epoxidation	THF/EtOH 1/3	no

Table 2-5: Evaluation of Pd(0)EnCat as ring opening catalyst.

Pd(0)EnCat was investigated in a very similar way as Pd(OAc)₂ for the possibility of using it as the catalyst for the epoxide opening. The advantage of this catalyst is that it is reported to work in ethanol as the solvent,³² which would be desirable for our reaction set-up as H₂-generation from ethanol showed a much higher efficiency than from THF. Again, as a first step the reaction was performed using a hydrogen balloon as hydrogen source and ethanol as a reference, giving the desired primary alcohol as the main product (entry 1). The reaction still worked when the hydrogen balloon was exchanged for the *in situ* generation using Au/TiO₂, however, exclusively if ethanol was used as the solvent (entry 2 and 3), due to side product formation with other solvents (as reported by Beller *et al.*).²⁷ A mixture of THF and ethanol (1/3) was tolerated (entry 4), which is an important result as there would always be some THF present in the final two-step-process as the epoxidation reaction can only be performed in THF. Unfortunately, again in presence of RuCl₃xH₂O and dipicolinic acid significant side product formation was observed (entry 5) and also a direct one-pot-experiment (entry 6) failed like in case of Pd(OAc)₂ as catalyst. Consequently, also with Pd(0)EnCat a simple work up in between epoxidation and epoxide opening is indispensable.

	Au/TiO ₂ Pd(0)EnCat	ОН
F	THF/EtOH (1/3) 4 mL N ₂ -atmosphere λ, 25 °C	F

Table 2-6: Optimization	of the reaction	conditions for	the epoxide	opening	using Pd(0)EnCat.
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Entry	Conditions	t (full conv.) [h]
1	5 mg Au/TiO ₂ (P25), 5.3 mol% Pd(0)EnCat, 385 nm	n.d.
2	10 mg Au/TiO ₂ (P25), 5.3 mol% Pd(0)EnCat, 385 nm	>24
3	5 mg Au/TiO ₂ (P25), 10.6 mol% Pd(0)EnCat 385 nm	>18
4	10 mg Au/TiO ₂ (P25), 10.6 mol% Pd(0)EnCat, 385 nm	18
5	5 mg Au/TiO ₂ (P25), 8.0 mol% Pd(0)EnCat, 365 nm	15
6	5 mg Au/TiO ₂ (rutile), 10.6 mol% Pd(0)EnCat, 385 nm	>24

The reaction conditions for the epoxide opening after work-up were optimized for Pd(0)EnCat in the same way as for Pd(OAc)₂ by analyzing the time for full substrate conversion. Again, higher Au/TiO₂ loadings led to shorter times for full conversion (compare entry 1 + 2 and 3 + 4 in Table 2-6). Using only 5 mg of Au/TiO₂ at an irradiation with 385 nm, the time for full conversion could not be estimated as only trace amounts of the product could be detected after 24 h. Increasing the amount of Pd(0)EnCat from 5.3 mol% to 10.6 mol% decreased the reaction time. Due, to the more efficient H₂-evolution from ethanol compared to THF/water that was used with Pd(OAc)₂ the reaction was at first carried out under 385 nm irradiation. However, changing to 365 nm light enhanced the reactivity so much that the use of only 5 mg of Au/TiO₂ and 8.0 mol% of Pd(0)EnCat were sufficient for full conversion after 15 h (entry 5). Again, the comparison with Au/TiO₂ (rutile) showed the inferiority of the rutile support material for the hydrogenation reaction (entry 6).

2.5.5 Headspace-GC Setup and Calibration Curve for the H₂ Detection

For quantification of the amount of hydrogen produced from Au/TiO₂ a calibration curve was set up, measuring the HS-GC-response for defined amounts of hydrogen in the reaction vials (Figure 2-3). The transfer of hydrogen to the vials was realized by gastight Hamilton syringes. To ensure correctness of the collected data the following tests were conducted: Firstly, the reproducibility of the hydrogen transfer via Hamilton syringe was investigated. For this purpose, three crimp cap vials were filled with nitrogen (several exchanges of atmosphere with nitrogen) and 250 µL of hydrogen were transferred to each of them via Hamilton syringe from a fourth vial filled with H_2 (several exchanges of atmosphere with H_2 from a balloon). Subsequently, individual measurements for each vial were performed showing good reproducibility with a relative standard deviation of less than 1%. Furthermore, the reproducibility of each individual measurement from the same vial was investigated by repeated measurements from a vial filled with 100 µL or 200 µL of H₂ respectively. Again, the results were well reproducible with a relative standard deviation of around 1%. Finally, the calibration curve was prepared measuring samples between 100 µL and 2000 µL. The corresponding amounts in nmol were calculated assuming ideal gas behavior and standard conditions. Linear dependency was observed for at least up to 80 µmol of H₂.

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Figure 2-3: Reproducibility tests for HS-GC setup and calibration curve for the H_2 detection. i) Reproducibility of the H_2 -transfer, ii) reproducibility of individual measurements, iii) calibration curve.

2.5.6 NMR Spectra

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40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 fl (ppm)

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NMR spectra of 2-phenylethan-1-ol $(\mathbf{3b})$



NMR spectra of 2-(*p*-tolyl)ethan-1-ol (**3c**)



NMR spectra of 2-([1,1'-biphenyl]-4-yl)ethan-1-ol (3d)



NMR spectra of 2-(4-(trimethylsilyl)phenyl)ethan-1-ol (3e)

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NMR spectra of 1-phenylpropan-2-ol (3g/h)



NMR spectra of 2-phenylpropan-1-ol (3i)

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NMR spectra of 2,2-diphenylethan-1-ol (3j)

2.6 References

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Chapter 2

3 Enhancement of Reaction Kinetics for Anthraquinone-Dye

Catalyzed Reactions by Carbon Nitride Materials



3.1 Abstract

Through the addition of carbon nitride materials, an acceleration in reaction speed could be observed for C - C couplings catalyzed by 1,8-dihydroxy-9,10-anthraquinone. While the observation is assumed to originate from non-covalent interactions between photocatalyst and carbon nitride, no direct proof for this hypothesis could be found. The effect was analyzed thoroughly for the model reaction but could not be applied to other reactions. A more indepth mechanistic investigation is necessary to interpret the observation, but this requires advanced analytical tools.

3.2 Introduction

Aggregation between two or more molecules can have a significant effect on their chemical properties. One explanation of such a non-covalent interaction, was given by Robert Mulliken in 1952 with his theory about charge transfer complexes, which are significantly changing the spectroscopic properties of the complex compared to the individual molecules.¹ Since then, a lot of effort has been made for the investigation and synthetic use of such complexes.²⁻⁴ Especially, in the field of photochemistry, donor-acceptor complexes have become a topic of major interest, enabling many chemical transformation under mild conditions by the use of visible light.⁵⁻⁹ Another prominent example are non-covalent interactions between aromatic compounds with large π -systems (often referred to as π - π interactions or π -stacking). Even though the concept is known for a long time, the exact mode of action is still under debate.¹⁰⁻ ¹³ The motivation for this project was to study the influence of non-covalent interactions between different types of molecules on the reactivity of photocatalytic reactions. A starting point was the observation of the apparent acceleration of the C – C coupling reaction between methyl 3-bromobenzoate and N-methylpyrrole catalyzed by 1,8-dihydroxy-9,10anthraquinone in the presence of carbon nitride. Compared to the reaction under reported conditions¹⁴ (without carbon nitride as additive), the reaction rate as well as overall yield could be increased. Due to its large flat surface and aromatic character a non-covalent aggregation effect between carbon nitride and anthraquinone is possible. Recently, examples for π - π interactions of organic molecules and carbon nitrides and the implications for the catalytic activity have been reported.¹⁵⁻¹⁶ Carbon nitrides could constitute ideal additives for this purpose due to their cheap and easy synthesis, chemical and thermal stability and last but not least their heterogeneous character, enabling simple material recovery and multiple use.¹⁷ In the course of this project, the acceleration effect was evaluated and different photocatalyst and additive combinations were tested with the aforementioned photocatalytic C - C coupling. Unfortunately, the mode of action could not be determined and the application seems to be limited to the combination of some carbon nitrides with 1,8-dihydroxy-9,10-anthraquinone. Due to the limitations in the application and a lack of tools for further mechanistic evaluations the project was not pursued further.

3.3 Results and Discussion

3.3.1 Initial Observation

In preliminary experiments, the addition of C_3N_4 -materials to various established photocatalytic reactions was investigated and analyzed for changes in reactivity. Among these, an increase in product yield could be observed for photocatalytic C – C couplings with 1,8dihydroxy-9,10-anthrachinone (Aq-OH) as reported by König *et al.*¹⁴ In order to evaluate the results, a series of control reactions was performed using methyl 3-bromobenzoate as model substrate in a coupling reaction with *N*-methylpyrrole. The key results are given in Table 3-1.

Table 3-1: Preliminary experiments with the Aq-OH system and control experiments.

Br	0 +		Aq-OH + PHIK DIPEA (2.0 equiv.) DMSO 2 mL 455 nm, 17h	N	
Entry ^[a]	РС	Additive	DIPEA	Conv. [%] ^[b]	Yield [%] ^[b]
1	Aq-OH	-	2.0	56	45
2	-	PHIK	2.0	2	1
3	Aq-OH	PHIK	2.0	80	67
4	Aq-OH	-	-	0	0
5	Aq-OH	PHIK	-	2	1
6 ^[c]	Aq-OH	-	2.0	3	3
7 ^[c]	Aq-OH	PHIK	2.0	3	3

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 10 mol% Aq-OH and/or 10 mg PHIK. ^[b]Yields were determined by GC-analysis comparing the areas of products and substrate. ^[c]4-Bromoanisol was used as starting material.

After 17 h of irradiation under the reported conditions, the coupling product between methyl 3-bromobenzoate and N-methylpyrrole was obtained in a yield of 45% at a conversion of methyl 3-bromobenzoate of 56% (entry 1). Additionally, methyl benzoate could be found as minor side-product, which is typical for these kinds of transformations and was also observed in the aforementioned report. At the same time, substitution of Aq-OH with potassium poly heptazine imide (PHIK) shut down the reaction almost completely, with only trace amounts of both products detectable (entry 2). In contrast to that, a combination of Aq-OH and PHIK enhanced the product yield to 67% at a substrate conversion of 80% (entry 3). The beneficial effect of the carbon nitride becomes even more evident when this result is compared to the published result, where a yield of 56% (at 90% conversion) is reported only after 62 h of

Enhancement of Reaction Kinetics for Anthraquinone-Dye Catalyzed Reactions by Carbon Nitride Materials

irradiation. The fact that PHIK alone is not catalyzing the reaction, while the combination with Aq-OH does, shows that the increased yield is not a consequence of two parallel reaction pathways but rather a sign for an increased reactivity of Aq-OH in presence of the carbon nitride. Next, control reactions under omission of DIPEA as sacrificial electron donor were undertaken, once using only Aq-OH (entry 4) and once in presence of Aq-OH and PHIK. In both cases not more than trace amounts of the product could be observed, which excludes the possibility of PHIK substituting DIPEA in its role as a sacrificial electron donor. Finally, experiments using 4-bromoanisol were conducted. This substrate was reported to react only extremely slow in this reaction, due to its very negative redox potential.¹⁴ Entry 6 shows that only very low amounts of product were formed after 17 h. The fact that the same result was achieved with additional PHIK in the reaction mixture (entry 7), suggests that the carbon nitride might affect the reaction kinetics rather than the redox potential of catalyst or substrate. Closer investigations on this effect were undertaken by monitoring the reaction progress over the course of 24 h for both cases. A graphical representation of the results is given in Figure 3-1.



Figure 3-1: Concentration – time profile for the C - C coupling reaction. Substrate consumption is given in red, coupling product formation in green and reduction product formation in blue. Data from the standard reaction using only Aq-OH is represented as • and the reaction with Aq-OH and PHIK as •.

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The concentration – time profiles exhibit the same shape under both reaction conditions, with both reactions practically stopping after 24 h. A major difference can be seen in the absolute values which clearly showcase the higher reactivity when PHIK is added to the reaction mixture. In presence of the carbon nitride material, after 24 h a yield of 72% is achieved, compared to only 50% under the standard conditions. In presence of PHIK the same yield is already achieved after around 9 h. In a similar way, the amount of reduced substrate that is detected increases by a small amount in presence of PHIK. Overall, the reaction progress is accelerated, effectively also leading to a higher overall yield.

3.3.2 Optimization

With a quick screening, the influence of the amounts of DIPEA and PHIK were investigated. The results are listed in Table 3-2.

Table 3-2: Screening of reaction parameters.

Br	+	Aq-OH F D DMS 45	(10 mol%) PHIK MPEA 50 2 mL, 55 nm		
Entry ^[a]	DIPEA [equiv.]	PHIK [mg]	t [h]	Conv. [%] ^[b]	Yield [%] ^[b]
1	1.5	5	17	60	50
2	2.0	5	17	70	58
3	3.0	5	17	83	62
4	2 0	5	16	64	53
4	2.0	5	10	04	55
4	2.0	10	16	78	65

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 10 mol% Aq-OH. ^[b]Yields were determined by GCanalysis comparing the areas of products and substrate.

As already seen before, the presence of DIPEA in the reaction mixture is indispensable, due to its role as sacrificial electron donor. Furthermore, as entries 1 - 3 show, an increased amount of DIPEA results in higher conversion as well as product formation. However, while going from 1.5 equiv. and 2.0 equiv., conversion and yield increase in a similar way, the use of more than 2.0 equiv. mainly promotes the formation of the reduction product. This matches the typical observations for these types of photocatalytic systems. Control reactions without PHIK (not depicted in the table) showed identical behavior. When it comes to the amount of PHIK, higher product yields could be obtained using higher carbon nitride loadings (entries 4 - 6). However, the use of more than 10 mg of carbon nitride did not further enhance the yield in a significant way.

3.3.3 Scope of Photocatalysts

In order to broaden the scope of reactions where this effect can be exploited, a series of other commonly used organic photocatalysts was investigated for similar findings. However, no other photocatalyst than 1,8-dihydroxy-9,10-anthraquinone showed a similar behavior in combination with PHIK. In order to resemble most closely the structural motive of this particular photocatalyst, anthraquinone dyes with different substituents in the positions 1 and 8 were tested. A list of the corresponding dyes is given in Scheme 3-1.



Scheme 3-1: List of anthraquinone-based dyes which were tested in combination with PHIK.

In order to evaluate their individual performance, two reactions were conducted in parallel, one with only the dye and one with the dye and PHIK as additive. The results are depicted in Table 3-3.

Br O Br O C C C C C C C C C C C C C					
Entry ^[a]	PC	Additive	Conv. [%] ^[b]	Yield [%] ^[b]	
1	Aq-OH	-	50	40	
2	Aq-OH	PHIK	78	62	
3	Aq-H	-	0	0	
4	Aq-H	PHIK	0	0	
5	Aq-SO ₃	-	17	16	
6	Aq-SO ₃	PHIK	1	trace	
7	Aq-Cl	-	1	trace	
8	Aq-Cl	PHIK	25	20	
9	Aq-OMe	-	45	40	
10	Aq-OMe	PHIK	59	52	

Table 3-3: Screening of various anthraquinone derivatives as photoredox catalysts.

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 2.0 equiv. DIPEA, 10 mg PHIK and/or 10 mol% PC. ^[b]Yields were determined by GC-analysis comparing the areas of products and substrate.

Enhancement of Reaction Kinetics for Anthraquinone-Dye Catalyzed Reactions by Carbon Nitride Materials

As a reference entry 1 and 2 give the results for the Aq-OH catalyzed reactions with and without PHIK. In contrast to that, unsubstituted anthraquinone (entry 3 and 4) did not promote the reaction at all, independent of whether PHIK was present or not. In case of sulfate substituents (entry 5 and 6) the reactivity of the dye alone was already very low, but even dropped to zero by the addition of the carbon nitride. Surprisingly, the opposite was true for Cl-substituents (entry 7 and 8) where the addition of PHIK led to 20% of the coupling product although Aq-Cl alone did not promote the reaction at all. Still, the overall performance was low compared to Aq-OH. In contrast to the other dyes, methoxy-substitued anthraquinone showed similar activity as Aq-OH with no additives (entry 9). Moreover, upon addition of PHIK (entry 10) an acceleration of the reaction could be observed, however the effect was less pronounced as in case of Aq-OH. Unfortunately, the scope of organic dyes showing enhanced activity in combination with carbon nitrides could not be extended. Even among the structurally similar anthraquinone derivatives, a strong effect could only be observed for Aq-OH.

3.3.4 Scope of Additives

Besides different organic dyes, also other additives might show similar effects. Among possible candidates are other carbon nitride materials, as well as flat soluble organic molecules. After a preselection, candidates of both species were investigated.

3.3.4.1 Carbon Nitrides

The carbon nitride materials that were used can be divided in two groups, depending on their structural motives. The main difference is the connection of the individual monomers. Linear polymers of heptazines units in form of metal salts are called poly heptazine imides (PHI), while the more densely interconnected covalent structures are called meso-porous graphitic carbon nitride (mpg- C_3N_4). A list of all used derivatives is given in Scheme 3-2.



Scheme 3-2: List of carbon nitride materials that were tested.

Br +	/ + N	Aq-OH (10 mol%) additive (10 mg) DIPEA (2.0 equiv.)	N O	
		DMSO 2 mL 455 nm, 16h		

Entry ^[a]	Additive	Conv. [%] ^[b]	Yield [%] ^[b]
1	$no^{[c]}$	50	40
2	PHIK	78	62
3	PHINa	75	62
4	PHIK-CN	58	44
5	PHIK-Urea	55	43
6	mpg-C ₃ N ₄	76	60
7	PHIK (recovered)	81	64
8	mpg-C ₃ N ₄ (recovered)	78	61

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 2.0 equiv. DIPEA, 10 mg C_3N_4 and/or 10 mol% Aq-OH. ^[b]Yields were determined by GC-analysis comparing the areas of products and substrate. ^[c]Average of several experiments under same conditions; deviation +/- 2%.

The results using different materials are depicted in Table 3-4. Entry 1 and 2 show the results for the combination of Aq-OH and PHIK, matching previous observations and serving as reverence for the other reactions. Entry 3 shows that using the sodium salt instead of the potassium salt of the poly heptazine imide preserves the acceleration effect giving almost identical results. This is different for substitutions at the free amino group. In case of an CN-group (entry 4) and a urea-group (entry 5) no significant deviation in the product yields compared to the reference reaction without carbon nitride could be observed. Furthermore, the structurally different mpg-C₃N₄ again showed the acceleration effect, with almost the same yield as PHIK and PHINa (entry 6). Finally, two additional experiments with already used PHIK as well as mpg-C₃N₄ were conducted. In both cases the heterogeneous material could easily be recovered from the reaction mixture by centrifugation. After washing and drying under high vacuum, the material could be reused, showing no loss in activity (entry 7 and 8). The recovery procedure can be found in the experimental part.

3.3.4.2 Use of Other Support Materials

One hypothesis about the origin of the observed acceleration-effect is an interaction between the photocatalyst and the heterogeneous material. A possible explanation would be π interactions between Aq-OH and the flat heterogeneous carbon nitride material. Therefore, also flat soluble aromatic compounds are possible candidates for such interactions. In preliminary experiments two promising candidates could be found that showed higher product yields than the standard reaction using only Aq-OH. The results, including control reactions, are depicted in Table 3-5.

Table 3-5: Screening of soluble flat organic additives.

Br	0 +	Aq-OH (10 n additive (10 n DIPEA (2.0 e DMSO 2 n 455 nm, 1	nol%) mol%) equiv.) mL 9h	
Entry ^[a]	РС	Additive	Conv. [%] ^[b]	Yield [%] ^[b]
1	Aq-OH	pyrene	72	60
2	-	pyrene	70	56
3	Aq-OH	phenanthrene	76	65
4	-	phenanthrene	12	9
4	-	phenanumene	12	9

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 2.0 equiv. DIPEA, 10 mol% Aq-OH and/or 10 mol% additive. ^[b]Yields were determined by GC-analysis comparing the areas of products and substrate.

From the initial experiments using a combination of Aq-OH with either pyrene (entry 1) or phenanthrene (entry 3), similar yields as for the combination of Aq-OH and PHIK were obtained. With 60% and 65% respectively, the reactions clearly performed better than in absence of the corresponding additive. However, unlike for PHIK, here in both cases, control reactions without Aq-OH showed significant background reactions, catalyzed by the additives alone. In case of pyrene almost the same yield is obtained from pyrene alone, compared to the reaction in presence of pyrene and Aq-OH (entry 2). In case of phenanthrene, at least a minor background reaction from the additive can be seen with 9% product yield (entry 4). Therefore, it is not possible to clearly distinguish whether the higher yield is derived from a cooperative effect or a simultaneous background reaction.

3.3.5 Miscellaneous Observations

In the course of our experiments strong color changes of the reaction mixtures could be observed, depending on the corresponding reaction conditions. An example is given in Figure 3-2a. In contrast to the dark green color of the reaction mixture under the literature reported conditions (left), the color changes to red upon addition of PHIK (right). When only PHIK is mixed with DIPEA in DMSO, there is no color change observable (middle). The brownish appearance stems from floating particles of the heterogeneous material. The solution is clear and colorless again when the sample is filtered.



Figure 3-2: Visual appearance of Aq-OH solutions and corresponding UV-Vis spectra. a) Left: Solution of Aq-OH and DIPEA in DMSO; Middle: PHIK suspension in a solution of DIPEA in DMSO; Right: Suspension of PHIK in a solution of Aq-OH and DIPEA in DMSO (all in reaction concentrations). b) Left: Solution of Aq-OH in DMSO (c=50 μ M); Right: Mixture of PHIK and Aq-OH in DMSO (c=50 μ M) (filtered). c) UV-Vis titration spectrum of a solution of Aq-OH in DMSO and a mixture of PHIK and the same solution of Aq-OH in DMSO (filtered), both titrated with DIPEA.

In Figure 3-2b solutions of Aq-OH in DMSO can be seen. On the left with no further additives, on the right the Aq-OH solution was stirred for 30 min with 1 mg of PHIK and then filtered. Interestingly, even after filtration the solution is red and not yellow. For a more detailed investigation UV-Vis spectra of both samples were recorded and both samples were additionally titrated with DIPEA. The spectra are shown in Figure 3-2c. In dark green the expected spectrum of Aq-OH with a maximum at around 430 nm can be seen. Upon titration with DIPEA, the spectrum is gradually changing (green to light blue), with a decrease in absorption at 430 nm and a new broad band with a maximum around 570 nm arising and clear isosbestic points. In contrast to that, the sample that was stirred with PHIK and filtered gives a completely different spectrum with a maximum at 300 nm and a broader band around 550 nm. This time upon titration with DIPEA, no changes in the spectra are visible. With these results in mind some further experiments were conducted that can be seen in Table 3-6.

Chapter 3

Aq-OH + PHIK

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Br		+ (N)	Aq-OH + PHIK DIPEA (2.0 equiv.) DMSO 2 mL 455 nm, 19.5 h	N Y	
Entry ^[a]	РС	Additive	Condition	Conv. [%] ^[b]	Yield [%] ^[b]
1	Aq-OH	-	Control reaction	49	41
2	Aq-OH	PHIK	Control reaction	83	70
3	Aq-OH	PHIK	Filtered solution	59	50
4	Aq-OH	PHIK	Centrifuged solution	59	50
5	-	PHIK	Washed CN	1	1
6	Aq-OH	PHIK	535 nm irradiation	11	8
7	Aq-OH	PHIK	630 nm irradiation	0	0

Table 3-6: Additional experiments under various reaction conditions.

^[a]Standard conditions: 0.2 mmol methyl 3-bromobenzoate, 2.0 equiv. DIPEA, 10 mol% Aq-OH and/or 10 mg PHIK. [b]Yields were determined by GC-analysis comparing the areas of products and substrate.

 $Cs_2CO_3 + DIPEA$

Entry 1 and 2 are control reactions, showing the already observed behavior of Aq-OH and PHIK. Due to the persistent color change even after filtration the reaction was performed with a filtered and a centrifuged solution of Aq-OH and PHIK. Surprisingly, the results were neither comparable to entry 1 nor entry 2. With 50%, the product yield is higher than under standard conditions, however also significantly lower than in presence of the heterogeneous material. Furthermore, the reaction was performed with the recovered PHIK from entry 4, after washing and drying of the material without new addition of Aq-OH. In this case only trace amounts of the product could be found. As the red reaction mixture with PHIK and Aq-OH shows a minimum in the absorbance spectrum close to the excitation wavelength but a new maximum at higher wavelengths, the reaction was also run with green LEDs (535 nm, entry 6) and red LEDs (630 nm, entry 7). While with green light the reaction still works, although with drastically lowered yield, using red light leads to a complete stop of the reaction. Another idea was that not the surface properties of PHIK influenced the reaction but the basic character of the negatively charged semiconductor. Thus, Cs₂CO₃ was added instead of PHIK, but the yield dropped to only 17% of the coupling product. During these experiments it became clear that Aq-OH is very sensitive to any kind of additive in terms of its color. A dependency between color and reactivity could not be proven and was not furthermore considered a relevant indicator.

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Aq-OH

3.4 Conclusion

Within this work it could be shown that carbon nitrides, though not catalyzing the tested reactions themselves, have a beneficial effect on the C - C coupling reactions catalyzed by Aq-OH. In particular the presence of carbon nitrides seems to enhance the reaction kinetics leading to a significant decrease in reaction times. While the presence of this effect could be observed very clearly and for different carbon nitride structures, the mode of action of this effect could not be found. A better understanding of the actual role of the carbon nitrides could give ideas for a rational design of additives with even higher efficiency. Besides carbon nitride materials, flat soluble organic molecules were also investigated, but no such effect could be observed in any of the tested compounds. Moreover, also on the photocatalyst side, no other examples but Aq-OH could be found, where a significant acceleration of the reaction was observed. Overall, the applicability of the method seems limited. Due to the lack of examples and available techniques for a deeper investigation of the interaction between Aq-OH and carbon nitrides, no further experiments were conducted on this topic at this stage.

3.5 Experimental Part

3.5.1 General Information

Materials. Starting materials and reagents were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, Acros, Fluka, VWR, or Fluorochem) and were used without further purification. Solvents were used as p.a. grade or dried and distilled according to literature known procedures.

Gas chromatography (GC). GC measurements were performed on a GC 7890 from Agilent Technologies. Data acquisition and evaluation was done with Agilent ChemStation Rev.C.01.04. A capillary column HP-5MS/30 m \times 0.25 mm/0.25 μ M film and helium as carrier gas (flow rate of 1 mL/min) were used. The injector temperature (split injection: 40:1 split) was 280 °C, detection temperature 300 °C (FID). The GC oven temperature program was adjusted as follows: the initial temperature of 40 °C was kept for 3 min and was increased at a rate of 15 °C/min until the injection temperature of 280 °C was reached. After 5 min, the temperature was further increased at a rate of 25 °C/min until the final temperature of 300 °C was reached and kept for 5 min.

General irradiation conditions. Samples were irradiated at 455 nm (CREE XLamp Me-C LED, $\lambda_{max} = 455$ nm, $I_{max} = 700$ mA) or at 535 nm (CREE XLamp Me-C LED, $\lambda_{max} = 535$ nm, $I_{max} = 700$ mA) or at 630 nm (CREE XLamp Me-C LED, $\lambda_{max} = 630$ nm, $I_{max} = 700$ mA).

UV-Vis spectroscopy. Absorption spectra were recorded at room temperature on a Cary 60 or Cary 100 UV-Vis spectrophotometer; Agilent.

3.5.2 General Procedures

General procedure: C – C coupling reaction

A 5 mL crimp cap vial is charged with all solid reactants, including the halogenated aromatic substrate (0.2 mmol, 1.0 equiv.). Depending on the respective reaction the PC (0.02 mmol, 10 mol%) and/or the respective carbon nitride (10 mg) were added (in case of an organic additive: 0.02 mmol, 10 mol%). After addition of a stirring bar the vial was closed and DMSO (2 mL) as well as DIPEA (0.4 mmol, 2.0 equiv.) and *N*-methylpyrrole (4.0 mmol, 20 equiv.) were added through the septum. The reaction mixture was then degassed using the freeze-pump-thaw technique (3x3 min) and then irradiated. Analysis was done via GC.

General procedure: Carbon nitride recovery

After the photoreaction, the reaction mixture was transferred into a centrifuge tube and the reaction vial was washed several times with acetone. Subsequently, the mixture was centrifuged at 4400 rpm for a defined amount of time (15 min for PHIK, 5 min for mpg- C_3N_4 , due to quicker precipitation of mpg- C_3N_4). After decantation of the supernatant, the residue was washed two more times with a few millilitres of acetone and centrifuged again until the supernatant is colorless. After drying for two hours under high vacuum, the recovered carbon nitride is ready to use again.

- 3.6 References
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4 Summary

This theses can be divided in two conceptionally distinct sections. While **Chapter 1** is focused on elucidating the mechanistic details of photocatalysis using deazaflavins as a new class of highly reductive photocatalysts, **Chapter 2** and **Chapter 3** are dealing with new strategies for the application of heterogeneous semiconductors in photocatalytic transformations.

In **Chapter 1** various C5-substituted deazaflavin derivatives were synthesized and characterized. Their application as highly reductive photoredox catalysts was demonstrated for the photocatalytic reduction of *p*-halogenanisoles, which exhibit highly negative redox potentials. In-depth mechanistic investigations were undertaken with a phenyl-substituted deazaflavin derivative. With the help of a combination of various techniques, such as electrochemistry, spectroelectrochemistry, transient absorption spectroscopy and electron paramagnetic resonance spectroscopy, the involvement of a deazaflavin radical species in the photocatalytic cycle could be proven. Based on this, the mechanism was described as a consecutive photo-induced electron transfer process *via* the semiquinone form of the deazaflavin in the triplet state. This work provides unprecedented evidence, that the reductive power of excited deazaflavin semiquinones can be used in photocatalytic reductive chemistry.

Chapter 2 was dealing with the photocatalytic generation of redox equivalents and their implementation in organic synthesis. Under aerobic conditions and irradiation with UV-A light, Au/TiO₂ is capable of generating H_2O_2 through the reduction of oxygen. Under inert conditions the catalytic activity switches to the generation of H_2 from proton reduction. For both reactions the catalytic cycle is closed by quenching the photogenerated holes in the valence band of the semiconductor, by a sacrificial reductant. In this work, we used Au/TiO₂ as photocatalyst for the two-step synthesis of 2-phenylethanol derivatives from the corresponding styrenes, with THF functioning simultaneously as the solvent as well as the sacrificial reductant. In step one, the photocatalytic H_2O_2 -production is combined with a ruthenium-catalyzed epoxidation reaction to give the corresponding epoxides as intermediates. In step two, the photocatalytically produced H_2 is used in combination with a palladiumcatalyst, for the regioselective epoxide opening to the anti-Markovnikov product. Due, to the incompatibility of the catalytic systems for both steps, a workup protocol was developed, for the sequential coupling of both reactions, without isolation of the intermediates. After optimization of both individual reaction steps the scope and limitations of this method were investigated. Additionally, a new type of reactor specifically for working with heterogeneous materials was designed and built in the course of this project.

Summary

In **Chapter 3** non-covalent interactions between heterogeneous semiconductors and organic dyes in photocatalytic transformations were studied. In particular, the enhancement of the reaction kinetics in photocatalytic C - C coupling reactions was observed for combinations of carbon nitrides with an anthraquinone-based photocatalyst. While the effect could be observed for several different carbon nitride materials, extension of the scope of organic photocatalysts was not possible. Due to the physical and electronic properties of the carbon nitrides, non-covalent aggregation effects between photocatalyst and carbon nitride were assumed to be the origin of the observed effect. However, due to a lack of analytic tools for further investigations, the mechanistic fundamentals behind this observation could ultimately not be determined.

5 Zusammenfassung

Diese Arbeit teilt sich in zwei konzeptionell unterschiedliche Bereiche. Während sich **Kapitel 1** auf die mechanistische Betrachtung von Deazaflavinen als neue Klasse von Photokatalysatoren konzentriert, beschäftigen sich **Kapitel 2** und **Kapitel 3** mit neuen Strategien für die Verwendung von heterogenen Halbleitermaterialien in photokatalytischen Prozessen.

In **Kapitel 1** wurden diverse C5-substituierte Deazaflavinderivate synthetisiert und charakterisiert. Ihre Anwendung als stark reduzierende Photokatalysatoren wurde durch Reduktion von *p*-Halogenanisolen, welche stark negative Redoxpotentiale aufweisen, gezeigt. Der Reaktionsmechanismus wurde für ein phenyl-substituiertes Deazaflavin im Detail untersucht. Mit Hilfe verschiedener Analysetechniken wie der Elektrochemie, Spektroelektrochemie, der transienten Absorptions-spektroskopie, sowie Elektronenspin-resonanz Spektroskopie, konnte die Beteiligung einer Radikalspezies des Deazaflavins im Katalysezyklus nachgewiesen werden. Auf Basis dieser Resultate wird ein konsekutiver photoinduzierter Elektronentransfer durch die Semichinon-Form des Deazaflavins im Triplett-Zustand als Mechanismus vorgeschlagen. Die Arbeit beschreibt erstmals die Nutzung von angeregten Deazaflavin-Semichinonen in der reduktiven Photokatalyse.

Kapitel 2 behandelte die photocatalytische Erzeugung von Redox-Äquivalenten und ihre Nutzung in der organischen Synthese. Bei der Belichtung von Au/TiO2 mit UV-Licht kann durch die Reduktion von Sauerstoff H2O2 erzeugt werden. Unter Luftausschluss wiederum, werden Protonen zu H2 reduziert. In beiden Fällen wird der Katalysekreislauf durch Übertragung von Elektronen von einem Reduktionsmittel auf das Valenzband des Halbleiters geschlossen. In dieser Arbeit wurde Au/TiO2 als Katalysator für die Zwei-Stufen-Synthese von 2-Phenylethanolen aus den entsprechenden Styrolen verwendet. THF diente dabei sowohl als Lösemittel, als auch als Reduktionsmittel. Im ersten Schritt wurde die photokatalytische H2O2-Produktion mit einem Ruthenium-Katalysator kombiniert um die jeweiligen Epoxide als Zwischenprodukte zu erhalten. Im zweiten Schritt wurde photokatalytisch H2 erzeugt und in Kombination mit einem Palladium-Katalysator für die regioselektive Epoxid-Öffnung zum anti-Markovnikov Produkt genutzt. Da beide Schritte nicht im gleichen Reaktionsgemisch ablaufen, wurde ein Aufarbeitungs-Protokoll erarbeitet, um die sequenzielle Verknüpfung der Einzelschritte zu gewährleisten, ohne die Zwischenprodukte isolieren zu müssen. Ein neuer Photoreaktor wurde im Rahmen dieses Projekts gebaut, der speziell für die Arbeit mit heterogenen Materialien entworfen wurde.

In **Kapitel 3** wurden nicht-kovalente Effekte zwischen heterogenen Halbleitermaterialien und organischen Farbstoffen in photokatalytischen Prozessen untersucht. Insbesondere wurde bei einer C – C Kupplungsreaktion durch die Kombination von Kohlenstoffnitriden und einem Anthrachinon-basierten Photokatalysator eine Reaktionsbeschleunigung festgestellt. Während der Effekt für mehrere Kohlenstoffnitride nachweisbar war, konnte das Konzept nicht auf andere organische Photokatalysatoren übertragen werden. Aufgrund der physikalischen und elektronischen Eigenschaften der Kohlenstoffnitride wurde nicht-kovalente Aggregation zwischen Photokatalysator und Kohlenstoffnitrid als Ursprung des Effekts vermutet. Eine mechanistische Grundlage für die Beobachtung konnte in Ermangelung geeigneter Analysemethoden aber letztendlich nicht bestimmt werden.

6 List of Abbreviations

°C	degree Celsius
(b)eT	(back) electron transfer
(b)isc	(back) inter system crossing
Å	Ångström
ACN	acetonitrile
aq.	aqueous
Aq-OH	1,8-dihydroxy-9,10-anthraquinone
C_3N_4	carbon nitride
calc.	calculated
Cat	catalyst
CF ₃	trifluoromethyl
conPET	consecutive photo-induced electron transfer
conv.	conversion
CV	cyclic voltammetry
d	deci
DADS	decay associated difference spectrum
DCE	dichloroethane
DCM	dichloromethane
DEE	diethylether
dFl	deazaflavin
dip. ac.	dipicolinic acid
DIPEA	diisopropyl(ethyl)amine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
EE	ethyl acetate
EI	electron ionization
EPR	electron paramagnetic resonance
equiv.	equivalents
ESI	electrospray ionization
EtOH	ethanol
eV	electron volt

exc.	excited
exp.	experimental
f	femto
FAD	Flavin adenine dinucleotide
Fc	ferrocene
FID	flame ionization detector
Fl	flavin
FlOOH	flavin hydroperoxide
FMN	flavin mononucleotide
g	gram
GC	gas chromatography
h	hour
HRMS	high resolution mass spectrometry
HS-GC	headspace gas chromatography
Hz	hertz
ic	internal conversion
<i>i</i> Pr	isopropyl
IRF	instrument response function
irrad.	irradiation
IS	internal standard
iso	isotropic
J	joule
k	kilo
L	litre
LED	light emitting diode
Μ	molar
m	milli
Me	methyl
MeOH	methanol
min	minutes
MO	molecular orbital
mpg-C ₃ N ₄	mesoporous graphitic carbon nitride
MS	mass spectrometry
n	nano
NAD(P)H	nicotinamide adenine dinucleotide (phosphate)
----------------	---
n.d.	not determined
nd:YAG	neodymium-doped yttrium aluminum garnet
NMR	nuclear magnetic resonance
NP	nano particle
OPA	optical parametric amplifier
OPO	optical parametric oscillator
ottle cell	optical transparent thin-layer electrochemical cell
OX	oxidized
р	pico
p-A	anisole
p-BA	para-bromoanisole
PC	photo catalyst
PCM	polarizable continuum model
PE	petrol ether
PET	photo-induced electron transfer
Ph	phenyl
РНІ	poly heptazine imide
ppm	parts per million
rad	radiative
rctn.	reaction
red	reduced
RF	riboflavin
ROS	reactive oxygen species
RP	radical pair
S ₁	singlet state
sac	sacrificial
SAS	species associated spectra
SCE	standard calomel electrode
SE	stimulated emission
SES	solvent-excluded surface
SVD	singular value decomposition
sq	semiquinone
sub	substrate

List of Abbreviations

Т	temperature
t	time
T_1	triplet state
ТА	transient absorption
TARF	tetraacetyl riboflavin
TCE	trichloroethane
TD-DFT	time dependent density functional theory
THF	tetrahydrofuran
UV	ultraviolet
V	volt
Vis	visible
W	watt
μ	micro

7 Curriculum Vitae

Name	Andreas Josef Graml
Date of birth	21.11.1991
Place of birth	Passau
Nationality	German
Education	
11/2016 - 10/2020	Ph.D. in Chemistry (Dr. rer. nat.)
	Institute of Organic Chemistry, University of Regensburg
	Mechanistic Investigations on Reductive Deazaflavin Photocatalysis & the
	Application of Semiconductor Photocatalysts for Organic Synthesis.
	Supervisor: Prof. Dr. Burkhard König
10/2014 - 09/2016	Master of Science in Chemistry
	Institute of Organic Chemistry, University of Regensburg
	Synthesis of Arylated Nucleobases by Visible Light Photoredox Catalysis
	Supervisor: Prof. Dr. Burkhard König
10/2011 - 09/2014	Bachelor of Science in Chemistry
	Institute of Organic Chemistry, University of Regensburg
	Photokatalysierte Oxidation von Sekundären Alkoholen unter Einsatz von
	Nitrat Radikalen als Mediatoren
	Supervisor: Prof. Dr. Burkhard König
09/2002 - 05/2011	Allgemeine Hochschulreife
	Wilhelm-Diess-Gymnasium Pocking
	Majors: Mathematics and Chemistry

International Experience

05/2018 – 06/2018 Research stay with Prof. Xinchen Wang at the College of Chemistry, Fuzhou University, China.

Scientific Publications

03/2017	Synthesis of Arylated Nucleobases by Visible Light Photoredox Catalysis
	Graml, A., Ghosh, I., and König, B., J. Org. Chem., 2017, 82, 3552-
	3560
06/2020	Deazaflavin Reductive Photocatalysis Involves Excited Semiquinone
	Radicals
	Graml, A., Neveselý, T., Kutta, R. J., Cibulka, R., and König, B.,
	Nat. Commun., 2020, 11, 3174.

Conference Contributions

10/2016	27th GRK Seminar Days, Regensburg, Germany
	oral contribution
03/2017	29th GRK Seminar Days, Regensburg, Germany
	oral contribution
03/2018	32 nd GRK Seminar Days, Regensburg, Germany
	oral contribution
06/2018	EuCheMS Conference on Organic Free Radicals, Marseille,
	France
	poster presentation
09/2018	26 th Lecture Conference on Photochemistry,
	Garching/Munich, Germany
	poster presentation
03/2019	35th GRK Seminar Days, Regensburg, Germany
	oral contribution

Memberships

11/2016 - 03/2019	Associate member of the DFG Research Training Group GRK
	1626 "Chemical Photocatalysis"
11/2016 – present	Member of the GDCh (Gesellschaft Deutscher Chemiker e.V.)

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