Tuning Deazaflavins Towards Highly Potent Reducing Photocatalysts Guided by Mechanistic Understanding – Enhancement of the Key Step by the Internal Heavy Atom Effect

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Abstract: Deazaflavins are well suited for reductive chemistry acting via a consecutive photo-induced electron transfer, in which their triplet state and semiquinone – the latter is formed from the former after electron transfer from a sacrificial electron donor – are key intermediates. Guided by mechanistic investigations aiming to increase intersystem crossing by the internal heavy atom effect and optimising the concentration conditions to avoid unproductive excited singlet reactions, we synthesised 5-aryldazaflavins with Br or Cl substituents on different structural positions via a three-component reaction. Bromination of the deazaisoalloxazine core leads to almost 100% triplet yield but causes photostability and enhances unproductive side reactions. Bromine on the 5-phenyl group in ortho position does not affect the photostability, increases the triplet yield, and allows its efficient usage in the photocatalytic dehalogenation of bromo- and chloroarenes with electron-donating methoxy and alkyl groups even under aerobic conditions. Reductive powers comparable to lithium are achieved.

Introduction

Recent developments in photoredox catalysis have substantially affected synthetic chemistry by providing photocatalytic counterparts to traditional methods that even significantly overcome their limitations.[1–2] In photoredox catalysis, an excited photocatalyst – usually an organic dye or transition-metal complex – initiates a single electron transfer (SET) from/to the substrate, forming a radical species, which undergoes a desired transformation.[3] Simultaneously, the additional energy of light absorbed by a photocatalyst allows redox chemical processes, which are inaccessible in the dark. In reductive photocatalysis, the generation of aryl radicals represents one of the most important achievements. Such radical species can be trapped with a suitable reagent to form C–C and C-heteroatom bonds.[4] Originally, activated compounds like aryl diazonium or iodo- nium salts, but not the commercially available halides, were used as aryl radical sources in photocatalysis. Although there is a particular success in photoreduction of aryl iodides, some aryl bromides, and aryl chlorides, that are activated by an electron-withdrawing group,[5] the reduction of non-activated aryl halides remains challenging.

The redox potentials, $E^*$, of the strongest reducing photocatalysts in an excited state range between $−2\text{ V}$ and $−2.2\text{ V}$ vs. SCE (saturated calomel electrode) even after structure optimisations,[6,7–8] which are insufficient for challenging substrates like 4-bromoanisole and 4-chloroanisole with $E_{\text{red}}^* = −2.75\text{ V}$ and $−2.88\text{ V}$ (values from ref.[6e]), respectively (see Figure 1a). Recently, reduction of non-activated and deactivated aryl bromides or chlorides was achieved by either consecutive photo-induced electron transfer (conPET) or photo-electrochemistry (Figure 1b).[9] In these transformations the reducing power of the excited state of either radical anions or neutral radicals is used. The radical species are formed either by PET from a sacrificial electron donor ($S_{\text{don}}$) to the excited photocatalyst,[10–13] or without light by reduction of the photocatalyst on an electrode.[14–15] However, so far, naphthalene imide 4,[16] dicyanoanthracene 5,[17] acridinium salt...
and benzo[ghi]perylene monoimide (BPI) derivatives\(^\text{[16]}\) are the only photocatalysts that allow the reduction of substrates with \(E_{\text{red}} \approx 3 \) V via an excited state radical. To note, excited tetrakis(dimethylamino)ethylene (TDAE) is also capable to reduce substrates with \(E_{\text{red}} < 3 \) V, but the reported dehalogenation is not catalytic.\(^\text{[17]}\) Hence, the development of novel photocatalysts with high reductive power for mild and efficient aryl radical generation of the wide range of aryl halides is of high interest.

Within the last decades, flavins (FI), derivatives of flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD), or riboflavin, have been recognised as beneficial photocatalysts for oxidations.\(^\text{[18–19]}\) However, only rare examples of flavin-based photocatalytic reductive processes are reported.\(^\text{[20–21]}\) The structurally similar 5-deazaflavins (dFI), where the N-5 of the flavin isalloxazine moiety is replaced by a methine group (Figure 1c, position 5 is highlighted), are better suited for reductive chemistry due to their more negative reduction potential (ca. \(-1.3 \) V vs. SCE). However, dFIs are usually involved in two-electron reductions, both, in natural and artificial systems, owing to the low stability of the semiquinone (dFI\(^-\)).

Formed by a one-electron reduction.\(^\text{[22]}\) Direct evidence for the involvement of deazaflavin semiquinone radicals in a reductive process was missing until recently. We proved the formation of the deazaflavin semiquinone by PET from the electron donor \(N, N\)-diisopropylethylamine (DIPEA) to the triplet state of the dFl, while the reaction with the excited singlet state results in a spin-correlated radical pair which is spin-allowed for recombination and, thus, represents a complete loss channel of the excitation energy. The radical can be excited by a second photon to form an extremely strong reducing species allowing the reduction of 4-bromoanisole and even 4-chloroanisole.\(^\text{[23]}\)

Here, we present a comprehensive investigation of the 5-aryldeazaflavin reactivity in model dehalogenation reactions with the special focus on non-activated and deactivated substrates with very negative reduction potentials. Since the first crucial intermediate in the productive reaction mechanism is the triplet state of dFI, we aimed to enhance the intersystem crossing (ISC) by increasing the spin-orbit coupling (SOC) via – at least in principle – introduction of a heavy atom into the dFl manifold. Hence, we designed and prepared a series of 5-aryldeazaflavin derivatives 10 via three-component reactions in

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**Figure 1.** Overview of the strongest species in the excited state and schemes of their generation. Selected examples of reductants are shown for less powerful systems (\(E^* > -3 \) V). Values \(E(M^+/M)\) for sodium and lithium are taken from ref.\(^\text{[24]}\). Abbreviations: SET – single electron transfer; EDG – Electron Donating Group; PC – photocatalyst; S – substrate; S\(_{\text{sac}}\) – sacrificial electron donor; Ar – Aryl; ppy – 4-(1-pyrrolidinyl)pyridine; NacNac – \(\beta\)-diketiminato ligands; TDAE – tetrakis(dimethylamino)ethylene; NpMI – naphthlene-based analogue; PDI – perylene diimide; BPI – benzo[ghi]perylene monoimide.
which a bromine is located at different structural positions. In order to elucidate the heavy atom effect on the photophysics and photocatalytic reactivity, the results were compared with those of the corresponding chlorinated dFl derivatives. Furthermore, as the diffusion-controlled reaction with the sacrificial electron donor can occur either with the excited singlet or triplet state of dFl forming spin-correlated radical pairs, we optimised the concentration conditions for maximal avoidance of the unproductive reaction via the excited singlet state. This allowed us to elucidate a structure vs. conditions vs. catalytic activity relationship and to develop extremely strong reducing agents comparable to sodium and lithium.

Results and Discussion

Design and synthesis of the 5-aryldезazaflavins. In our previous study,[23] we have shown that the 5-aryl and 7,8-methoxy groups have a positive effect on the photocatalytic activity/reduction potential of deazaflavins. Thus, this was considered in the design of the new photocatalysts with either a chlorine or a bromine located either on the deazaalloxazine core or on the phenyl ring. Several methods can be applied for the synthesis of the 5-deazaflavins, which include the condensations of ananthral aldehydes with barbituric acid or 6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione with aryl aldehydes.[25] However, these approaches are not suitable for the involvement of the aryl substituent in position 5 of the deazaalloxazine core. Our previously developed microwave-assisted three-component reaction between benzaldehyde, N-butyl-3,4-dimethoxyaniline, and N-methylbarbituric acid without additional solvent, yielded 5-aryldeazaflavin derivatives. Further modification does not influence the photocatalyst activity, aromatic aldehydes 12, and N-methylbarbituric acid (13) in AcOH/PPA (polyphosphoric acid) resulting in 5-aryldезazaflavins 10a–f and 10red in overall moderate to high yields (Scheme 1 and Figure S1; see Supporting Information for details). To note, the amount of the reduced forms of compounds 10a (–H), 10c (p-Br), and 10f (iso-Br) was lower than 10%, so that only the oxidised 5-deazaflavins were isolated. However, in the absence of PPA and under inert atmosphere, the reduced forms 10ared, 10bred (p-Cl), 10cred, and 10fred were formed as major products and were obtained in pure form by recrystallisation from propan-2-ol.

General photocatalytic performance of dFl 10 in the dehalogenation. Based on our previous study, the acid-base equilibrium of the deazaflavin semiquinone impacts on the overall performance of the dehalogenation, since the deproto-nated form seems to be beneficial potentially due to: 1) an enhanced triplet yield; 2) a longer triplet lifetime; 3) an enhanced dFl° yield; or 4) longer lifetime of dFl°.[23] Detailed studies on the impact of the basicity on the reaction mechanism are currently ongoing in our lab. However, here we focus on enhancing the ISC by an internal heavy atom effect (IHAE) and, thus, we performed all photocatalytic experiments under the most efficient conditions as previously described, i.e. in the presence of caesium carbonate (Cs₂CO₃) as a base and at 6 mM (8 mol%) dFl 10.[23] Similar to our previous results, a lower concentration of the novel dFls results in a lower product yield (see Scheme S4 in the Supporting Information).

Initially, the performance of the synthesised 5-aryldезazaflavins 10 in the dehalogenation of 4-bromoanisole (14) and 4-chloroanisole (15) (Table 1) was explored. Most of the 5-aryldезazaflavin derivatives were capable of debrominations and declorinations with high to quantitative yields. Interestingly, derivatives 10e (iso-Cl) and 10f (iso-Br) with halogen atoms on the deazaalloxazine core performed less efficient compared to the other dFl 10 particularly in terms of the declorination of 15. In the absence of the photocatalyst no formation of the respective anisole 22 was observed.

Importantly, the dFls 10a–d even allowed the conversion of bromo- and chloroaenres 16–21 whose reduction is highly deactivated owing to electron-donating methoxy and alkyl groups (Table 2). The best performance was observed for the debromination of 1-bromo-2,4-dimethoxybenzene (16) using...
the photocatalysts 10a-d and for 1-bromo-2,4,6-trimethoxybenzene (18) using the photocatalysts 10a and d. In these cases, the conversion was almost quantitative. Furthermore, the novel dFl 10 catalysed the dehalogenation of aryl chlorides such as 1-chloro-2,4,6-trimethoxybenzene (19) and 3,5-di-tert-butyl-1-chloroanisole (21) ($E_{red} = 3.4$ V) as well as its bromo analogue 20 albeit in moderate yields. However, defluorination of 1-fluoro-4-methoxybenzene (26) could not be achieved by dFl 10. To the best of our knowledge, no photocatalytic system capable to defluorinate 26 is reported so far. Anyhow, we observed the defluorination of 1,2-difluorobenzene (28) in the presence of either 10a (-H) or 10d (o-Br) (Scheme 2a). Furthermore, the dFl 10 can also be used in coupling reactions as is exemplarily shown on the reaction of 14 with N-methylpyrrole (Scheme 2b, see Supporting Information for details).

Moreover, in order to avoid undesired reactions between the radical intermediates and molecular oxygen, reductive chemistry using photoelectrocatalysis is usually performed under strictly inert conditions. Interestingly, the reductive photodehalogenation catalysed by 10 can also be performed under aerobic conditions resulting in only slightly reduced yields in comparison to inert conditions after 24 h of illumination (Table 2). However, it should be noted that after 1 h of illumination, the photodehalogenation reaction under aerobic conditions is only half as efficient as compared to

### Table 1. Dehalogenation of 4-bromo-(14) and 4-chloroanisoles (15) catalysed by dFl 10.[a]

| Catalyst | Yields [%] | 14 | 15 |
|----------|------------|----|----|
| 10a (-H) | 98         | 82 |
| 10b (p-Cl) | 89        | 90 |
| 10c (p-Br) | 93        | 70 |
| 10d (o-Br) | 98        | 99 |
| 10e (iso-Cl) | 95      | 31 |
| 10f (iso-Br) | 37       | 6  |
| 10g (iso-H) | 64       | n.d. |
| –         | < 1        | 0  |

[a] Reaction conditions: 14 or 15 (0.038 mmol, ca. 73 mM), 10 (0.003 mmol, ca. 6 mM), DIPEA (0.072 mmol; ca. 140 mM), ACN (0.5 mL), Cs$_2$CO$_3$ (0.038 mmol, ca. 73 mM), $T = 25$ °C, argon atmosphere, $\lambda_{exc} = 400$ nm, $t_{rea} = 24$ h. n.d. = not determined.

### Table 2. Dehalogenation reactions with selected electron-rich aromatic halides.[b]

| Substrate | Product | Yields [%] |
|-----------|---------|------------|
| Br, OMe | 16 | 99 |
| Cl, OMe | 17 | 59 |
| Br, OMe | 18 | 92 (60)[c] |
| Cl, OMe | 19 | 59 |
| Br, OMe | 20 | 55 |
| Cl, OMe | 21 | 51 |

| Catalyst | Yields [%] | 10 | 11 | 12 | 13 | 14 |
|----------|------------|----|----|----|----|----|
| 10a (-H) | 74 (68)[c] | 31 |
| 10b (p-Cl) | 50 | 52 |
| 10c (p-Br) | 65 | 47 |
| 10d (o-Br) | 67 (62)[c] | 24 |

[a] Reaction conditions: substrate (0.038 mmol, ca. 73 mM), 10 (0.003 mmol, ca. 6 mM), DIPEA (0.072 mmol; ca. 140 mM), ACN (0.5 mL), Cs$_2$CO$_3$ (0.038 mmol, ca. 73 mM), $T = 25$ °C, argon atmosphere, $\lambda_{exc} = 400$ nm, $t_{rea} = 24$ h. [b] Yields determined via HPLC for 23 and via $^1$H NMR for 24 and 25. [c] Data in parenthesis are from experiments under aerobic conditions.
the inert conditions (see Scheme S2). Since under the used photocatalytic conditions, the DIPEA concentration is significantly higher than the O₂ concentration, i.e. [O₂] = 2.4 mM⁰₉ vs. [DIPEA] > 140 mM, the diffusion-controlled eT by DIPEA is outcompeting any O₂ quenching of the triplet state in the beginning of the reaction and, thus, the drop in the initial catalytic efficiency under aerobic conditions results from the reaction of O₂ with the dFl semiquinone form, re-oxidising the dFl⁺. Hence, the used reaction conditions allow for efficient photocatalytic transformation of the substrate at least partially outcompeting potential undesired reactions with molecular oxygen.

The aerobic conditions can also be used for efficient dehalogenation on a preparative scale. For example, good dehalogenation product yields could be obtained after photo-reduction of 18 and 20 by 10a (-H) or 10d (o-Br) regardless on the molecular oxygen concentration (Table 3).

### Influence of the bromine position on the photophysics of dFl 10

The energy for the first electronic transition, $E_{0-0}$, of all dFls have a higher energy gap by 0.2–0.35 eV between the ground and first excited singlet state compared to tetraacetylriboflavin (TARF, see Figure S17 in the Supporting Information). The variants with two MeO groups in the deazaisoalloxazine core, i.e., 10a (-H), 10c (p-Br), and 10d (o-Br), have all a $E_{0-0}$ around 2.7 eV, thus, indicating that the bromination in the phenyl-side group does not have any influence on the transition energy.

However, among the dFls with two MeO groups, 10d with the bromine in ortho position of the phenyl ring shows significantly altered photophysics in terms of a 50% higher fluorescence quantum yield (see Figure S17 in the Supporting Information), a 30% higher triplet yield (see Figure 2), and a five times longer excited singlet state lifetime compared to 10a (-H) and 10c (p-Br) (see Figure S17, Table S2, and further details in the Supporting Information). Quantum-mechanical calculations reveal that the significantly enhanced ISC in 10d compared to 10a and 10c is explained by: i) a more favoured molecular orbital situation participating in the electronic transitions and ii) a beneficial steric situation in ortho position altering the torsion phenyl motion (for further details see Supporting Information and Figures S4–S6, S10–S12, and S16).

Substitution of one of the MeO groups by either H, Cl, or Br results in an increased transition energy $E_{0-0}$ by ca. 0.1 eV (see Figures S17 and S18 in the Supporting Information). Comparing all dFls the S₁ decay is shortest for 10f (iso-Br) caused entirely by triplet state formation (see Figure 2). While the S₁ of 10g (iso-H, debromination product of 10f, Scheme 3) decays with a lifetime of ca. 1 ns similarly to 10a (-H) and 10c (p-Br) – those without a bulky substituent in ortho position of the phenyl ring, the S₁ lifetime of 10e (iso-Cl) is by a factor of 2 longer. Considering also the triplet and fluorescence quantum yields for the iso substituted dFls, an IHAE becomes evident. While the S₁ of 10a (-H) mainly deactivates back to the ground state via internal conversion, the intersystem crossing becomes increasingly dominant from 10a (-H) to 10f (iso-Br) (see Figures 2 and S19 in the Supporting Information). In non-degassed ACN the triplet lifetimes for all dFls are very similar (see Figure S20 in the Supporting Information) and are mainly caused by bimolecular diffusion-controlled quenching by molecular oxygen as evident from the theoretically expected values (Table S3 in the Supporting Information). Table S2 in the Supporting Information summarises the photophysical parameters of all investigated dFls. In the absence of molecular oxygen (see Figure S21 in the Supporting Information), the dFls with two methoxy groups, i.e., 10a (-H), 10c (p-Br), and 10d (o-Br), show a significantly enhanced triplet lifetime resembling the intrinsic triplet decay for these compounds. The lifetime of 10a – the compound without heavy atom – is with 508 μs significantly longer than those observed for the two compounds with a bromine on the phenyl ring. Thus, for back ISC the bromine provides efficient SOC even if the bromine is located on the phenyl ring. Since the triplet yield of the dFls with only one methoxy group is much higher compared to the other dFls, a significantly higher transient triplet concentration may be reached in the absence of molecular oxygen under comparable excitation conditions. Accordingly, for 10g (iso-H) and 10e (iso-Cl) the formation of additional long-lived products via a triplet-triplet reaction is observed, which most likely corresponds to the radical ion pair as a result of electron transfer that recombines with a lifetime of ca. 500 μs in both cases. For 10f (iso-Br) no further species are detected arising from the triplet decay because of the much more efficient SOC so that the intrinsic back ISC is completed with a lifetime of 55 μs outcompeting a potential reactive triplet-triplet encounter under these experimental conditions.

### Ability to avoid the loss channel reaction via enhanced ISC

In the first step of the conPET reaction, spin-correlation of...
the initially formed radical pair plays a major role for the productive outcome. Thus, the concentration of the sacrificial electron donor DIPEA represents a crucial factor. As evident from Figure 3, at 500 mM DIPEA the dFls 10a (-H), 10c (p-Br), and 10d (o-Br) undergo efficient and complete diffusion-controlled electron transfer forming the singlet-born radical pair that recombines faster than it is formed (see also Figures S23–S24 and further details in the Supporting Information).
plus stimulated emission (SE) giving a negative signal). Consequently, under this condition the systems follow the unproductive pathway via the excited singlet reaction and, thus, no dehalogenation is observed. The situation is different in case of $^{10}$f (iso-Br). Here, the ISC is so enhanced that even at 500 mM DIPEA a significant quantity of triplet is formed (blue spectrum in Figure 3k, T$_{1}$−T$_{3}$). Subsequently, the triplet reacts with DIPEA forming the triplet-born radical pair that is now detectable due to its spin-forbiddness for recombination. To note, the counter DIPEA radical cation does not absorb in this
Unfortunately, 10f shows a significant photodecomposition at prolonged intense illumination. On an analytic scale, after 20 min of irradiation in the absence of halogenarene, 10f photodecomposed completely. The main decomposition product could be assigned to 8-methoxydeazaflavin 10g (iso-H) by MS and 'H NMR (see Figures S25, S26, and S38 as well as further details in the Supporting Information) and yielded 32% in the preparative ansatz (Scheme 3). To note, when using 8 mol% of the photocatalyst, a higher yield for the dehalogenation of 14 after 24 h of illumination was achieved with 10g compared to 10f (see Table 1). However, considering that 10f photodecomposes with 32% into 10g, we performed the photodehalogenation with 2.6 mol% of 10g (equal to 32% of the 8 mol% standard condition) which resulted in a similar course of the reaction and product yield as compared to the reaction with 8 mol% 10f (see Figure S31). Thus, it is tempting to speculate that the other decomposition products (not identified) of 10f do not contribute to the dehalogenation reaction. 10e (iso-Cl) also showed a significant amount of photodecomposition (see Figures S27 and S28 in the Supporting Information). In contrast, the dFls 10c (p-Br) and 10d (o-Br), i.e., with the halogen atom on the phenyl ring, show only a small amount of the dehalogenated compound 10a (H) after 20 min of irradiation (see Figures S29 and S30 in the Supporting Information). Thus, although 10f provides the most beneficial photophysical characteristics compared to the other dFls, as its bromine electron density participates in the electronic transitions to the excited states providing efficient triplet formation (see Figure S8 in the Supporting Information), the decomposition pathway via dissociation of the labile bromine group represents a drawback in the preparative usage.

As a compromise between photostability and triplet yield, 10d and 10e both perform very efficient in the debromination of bromoarenes. However, dechlorination is significantly less photostable for 10e (Table 1). Since 10e consists of only one MeO group in the deazaaisoalloxazine core, it is tempting to speculate that this structural difference will impact on other unproductive side reactions such as disproportionation, re-oxidation by molecular oxygen, eT from the excited state intermediate radical dFl to the substrate, and its lower photostability. The origin of the differential performance caused by the different structural motives is currently investigated in our labs and will be addressed elsewhere.

Avoiding the loss channel via the S1 reaction by reduced concentration of the sacrificial electron donor. The diffusion-controlled bi-molecular rate constants for the unproductive S1 reaction between DIPEA and the S1 of 10a (H), 10d (o-Br), 10g (iso-H), and 10e (iso-Cl) were determined via fluorescence quenching in the low concentration limit to (1.13 ± 0.02) · 10−3 M−1·s−1, (7.64 ± 0.05) · 10−3 M−1·s−1, (1.15 ± 0.03) · 10−3 M−1·s−1, and (9.6 ± 0.1) · 10−3 M−1·s−1, respectively (see Figure S22 and further information in the Supporting Information). Comparison of these rates with the theoretical totally diffusion controlled bi-molecular rate constants estimated by the Smoluchowski theory (see Table S3 in the Supporting Information), may indicate a preference on reactive encounters in all cases as only 62%, 42%, 64%, and 53%, respectively, of collisions lead to a reaction. To note, bromination in the ortho position of the phenyl ring, as in 10d, reduces the eT reaction efficiency on encounter with DIPEA by ca. 10–20% compared to the other dFls. Since this unproductive reaction is entirely reversible, the amount of DIPEA will not be consumed by this reaction but the overall conversion velocity of the actual substrate will be significantly slowed down and will eventually stop at very high DIPEA concentrations. To demonstrate this, we determined the photodehalogenation efficiency of all relatively photostable dFl after 1 h illumination as a function of the DIPEA concentration for the exemplary conversion of 14 to 22 (Figure 4). The dFls 10e and 10g with only one MeO group in the deazaaisoalloxazine core show the lowest performance with a broad optimal range between 90 and 230 mM at a maximal conversion of around 15%. The dFls with a second MeO group in the deazaaisoalloxazine core perform consistently better reaching maxima of ca. 25% for 10a and 10c and of ca. 35% for 10d. While the efficiency curve of 10c shows a broad optimal range as obtained for 10g and 10e, the curve is significantly narrower and its maxima peak at around 60 mM (ca. 1 eq of 14) for 10a and 10d. Although 10a and 10c underlie similar photophysical characteristics (see Supporting Information), the structural difference, i.e., the bromine in para position of the phenyl moiety, impacts on other unproductive side reactions as also discussed above. 10d shows the best performance at optimal conditions in agreement with its altered photophysics and eT with DIPEA, as becomes obvious in a longer excited singlet state lifetime, a higher triplet yield, and a 20% less effective eT efficiency in the S1 reaction with DIPEA.
To point out, all dFls clearly show a bell-shaped dependence, where the optimal DIPEA concentration lies below 240 mM, upon which the efficiency decreases due to contributions of the unproductive S₁ reaction via a singlet-born radical pair. Such a behaviour clearly indicates the involvement of the triplet state as a key intermediate in the underlying conPET reaction, thus, demonstrating the importance of the concentration conditions rather than considering only the equivalents of the sacrificial electron donor used in the system.

Conclusion

Here, we describe the successful synthesis of 5-aryldeazaflavins with Br or Cl substituents on different structural positions, i.e., on the phenyl side group or on the deazaisoalloxazine moiety, via three-component reactions and show their efficient usage as reductive photocatalysts enabling dehalogenation of bromo- and chloroarenes with electron-donating methoxy and alkyl groups even under aerobic conditions. The reductive power of the novel dFls is comparable to that of sodium and lithium as demonstrated by the defluorination of 1,2-difluorobenzene and dechlorination of chlorobenzenes whose reduction is deactivated by methoxy and alkyl groups.

The synthesis was guided by mechanistic investigations aiming to increase ISC by the IHAE within the dFls, since the triplet state of the dFls is the first crucial intermediate in the productive photocatalytic reaction based on the conPET mechanism, while the excited singlet state undergoes unproductive eT reactions with the sacrificial electron donor via a spin-correlated singlet-born radical pair that recombines faster than it is formed (Figure 5).231 Introducing a bromine into the deazaisoalloxazine core has optimal impact on the triplet formation, i.e., almost 100%, but simultaneously also causes photo-instability and enhances other unproductive side reactions losing the advantage of the improved triplet yield. In contrast, positioning a bromine on the phenyl-side group did not affect the photostability by impacting on the triplet yield in dependence on the location within the phenyl ring. While a bromine in para position of the phenyl side group does not provide significant SOC to the system resulting in unaltered ISC, substitution on the ortho position resulted in a decent increase of the triplet yield, thus, providing – in a compromise between photostability and improved triplet yield formation – the best performance. Importantly, the performance of the photocatalytic process is further optimised by reducing the concentration of the sacrificial electron donor so that the unproductive S₁ reaction and the productive T₁ reactions are maximally avoided and enforced, respectively. This last point demonstrates the importance of the concentration conditions rather than equivalent relations of the sacrificial electron donor. Thus, in preparative applications the reductive conversions described here should be conducted under continuous addition of the sacrificial electron donor maintaining its actual concentration on a constant optimal level for maximal efficiency.

Another aspect of general importance for all conPET type reactions, as we have already stated in our previous work,232 is the specific timing of the two differently coloured intense photons necessary to be absorbed by the two key photocatalytic forms of the deazaflavins, where one is formed from the other having a distinct lifetime in the ns regime. Further experiments that provide insights for improvement on the

Figure 5. Photocatalytic reaction mechanism in a Jablonski type diagram (left, vertical axis represents a relative energy scale) and the structures of photocatalysts with increasing IHAE (right). DIPEA as a sacrificial electron donor (SSac) reacts either with the excited singlet or triplet state of the deazaflavin initiating either the unproductive (red) or productive (blue) pathway. In the unproductive pathway a singlet-born spin-correlated radical pair, [dFlₓ₋₁..SSac*], is formed after eT, which recombines faster than it is formed. In contrast, in the productive pathway eT to the triplet state results in a triplet-born radical pair, [dFlₓ₋₁..SSac*], allowing the accumulation of the considerably stable dFlₓ₋₁. A second photon can be absorbed by dFlₓ₋₁ enabling a consecutive photo-induced electron transfer from dFlₓ₋₁ to the substrate, (EDG)Ar-Br/CIF, regenerating dFlₓ in its ground state, closing the photocatalytic cycle, and initiating dehalogenation. The concentration of SSac is decisive on the systems’ reaction pathway, where the enhancement of the ISC by the IHAE promotes the productive pathway via the triplet manifold. Bromine in the deazaisoalloxazine moiety provides maximal ISC, but photodissociates after prolonged illumination.
efficiency in terms of external experimental conditions are currently performed in our labs and will be published elsewhere.

This study demonstrates the importance of a detailed mechanistic understanding for the cost efficient and sustainable development of photocatalysts of the next generation. By our newly engineered deazaflavin photocatalysts, we expanded the photocatalytic toolbox for reductive conversions, where reduction powers comparable to that of sodium and lithium are required. Furthermore, the in-depth elucidation of the underlying mode of action of the conPET reaction will allow the projection onto other systems ensuring their significant improvement.

Experimental Section

Extended information on materials and methods are described in the Supporting Information including detailed descriptions of the synthesis, NMR/Mass characterisation, time-resolved spectroscopic experimental setups and conditions, analysis, computational studies, extended references, and further supportive experimental work and collected data.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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