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Porphyrin-catalyzed photochemical C-H arylation of heteroarenes

Katarzyna Rybicka-Jasińska,[a] Burkhard König,[b] and Dorota Gryko*[a]

In memory of professor Teodor Silviu Balaban

Abstract: Organic dyes are a promising class of photoredox catalysts and offer a meaningful alternative to broadly applied Ru- and Ir-complexes. We have found that porphyrins with tuned physicochemical properties, via tailoring various substituents at the periphery of the macrocycle, are effective in catalyzing light-induced direct arylation of heteroarenes and coumarins with diazonium salts. Mechanistic studies confirmed that the reaction operates by an oxidative quenching pathway of the porphyrin.

Introduction

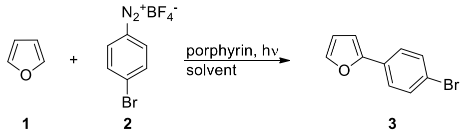
Photoredox catalysis is strongly associated with the use of Ru- and Ir-complexes.[1] Surprisingly, organic dyes, though interesting, have attracted much less attention.[2] The list of compounds used as metal-free photocatalysts collected by Romero and Nicewicz comprise of only 33 compounds.[3] But the structural diversity of organic chromophores, and their different redox and photochemical properties, may provide access to new and more efficient photocatalysts. To this end porphyrinoids, represented in nature by chlorophyll - the most efficient photocatalyst, offer unique opportunities. Due to stability issues, it is rarely applied as a catalyst in synthetic organic chemistry. However, fully aromatic porphyrins with well-established photophysical properties have already been used to harvest light energy for artificial photosynthesis, phototherapy, imaging etc.[4] Moreover, their metal complexes proved efficient in catalyzing various reactions, for example: C-H hydroxylation, cyclopropanation, alkylation, amination, epoxidation, olefination, oxidative Mannich reaction and oxidative amine coupling.[5] However, in photochemistry they are mainly associated with the generation of singlet oxygen or other oxygen reactive species.[6] Only recently, we have reported their use as photoredox catalysts in a C-C bond forming reaction.[7] Light induced α-alkylation of aldehydes with diazo reagents in the presence of morpholine afforded the desired products in satisfactory yield. Mechanistic studies revealed that once in the excited state, a porphyrin oxidizes an enamine to the cation radical that subsequently reacts with a carbene generated via a photo synthetic pathway. The resulting intermediate is reduced by back electron transfer from the porphyrin's anion radical thus regenerating the photocatalyst. This example represents a reductive quenching pathway of porphyrins.

We wondered, whether free-base porphyrins are also able to promote a direct arylation of heteroarenes by C-H bond activation via an oxidative quenching? Under light irradiation this reaction is effectively promoted by a ruthenium complex and eosin Y.[8] On the other hand, Kanai and co-workers found that porphyrins catalyze C(3)-H arylation of coumarins with aryl diazonium salts.[9] Intriguingly, the reaction was not affected by the presence or absence of light. However, only very electron rich porphyrins, namely tetra(4-diethylaminophenyl)porphyrin, catalyzed the reaction and less electron–rich tetra(4-methoxyphenyl)- or tetraphenylporphyrins were not effective. It was proposed that the porphyrin reduces the aryl diazonium tetrafluoroborate affording an aryl radical and nitrogen.

The thermodynamic driving force of a redox process is determined by the difference in redox potentials of the half reactions. As aryl diazonium salts' reduction potentials vary around 0.0-0.2 V vs. SCE, weak reductants should promote this reaction.[8c,10] Under light irradiation porphyrin reducing properties are altered, and based on the E_{ox} even tetraphenylporphyrin should facilitate the formation of the phenyl radical (Table 1, entry 1). Herein, we report that porphyrins in the excited state can indeed act as a reductant.

Results and Discussion

In the initial experiment, furan (**1**) was reacted with diazonium salt **2** in the presence of H_2TPP (**4**) under light irradiation (Scheme 1).



Scheme 1. Model reaction of furan with diazonium salts.

After 3 h the reaction furnished the desired product **3** in 80% yield (Table 1, entry 1). Background reactions clearly showed that both the porphyrin and light are required for effective production of arylated furan **3** (entries 2-4). In the absence of porphyrin, but under light irradiation product **3** formed in only 8% yield; this could be attributed to the direct, light-triggered heterolysis of starting material **2** followed by the reaction with furan (**1**) (entry 3). Surprisingly, tetra(4-diethylaminophenyl)-porphyrin (**5**), though a better electron donor, was less effective than porphyrin **4** (compare entries 1 and 6).

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Substituents, present at the periphery of the macrocycle, have a determinant role on redox properties of porphyrins.[11] Accordingly, various porphyrins were tested as catalysts in the model reaction (Chart 1, Table 2).

Table 1. Control experiments.[a]

Entry	Porphyrin	Light	Time (h)	Yield of **3** (%)[b]
1	H_2TPP (**4**)	yes	3	80
2	No	no	16	5
3	No	yes	3	8
4	No	yes	16	23
5	H_2TPP (**4**)	no	16	6
6	H_2(4- Et_2NP)P (**5**)	yes	3	23

[a] Reaction conditions: diazonium salt (**2**, 0.25 mmol), furan (**1**, 2.5 mmol, 10 equiv.), DMSO (2 mL), porphyrin (1 mol%), blue LED (455 nm). [b] Yield determined by GC.

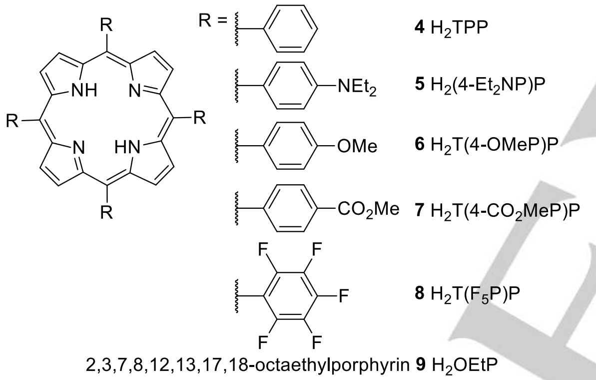

Figure 1. Porphyrins tested as photoredox catalysts.

Substituents, present at the periphery of the macrocycle, have a determinant role on redox properties of porphyrins.[11] Accordingly, various porphyrins were tested as catalysts in the model reaction (Chart 1, Table 2). Interestingly, the best result, was obtained from electron-poor tetra(pentafluorophenyl)porphyrin (**8**) (entry 4). Stern-Volmer quenching experiments showed that diazonium salt **2** quenches the luminescence of all porphyrins tested, though with different quenching rates (Figure 2). The highest quenching rate was observed for H_2TPP (**4**) that gave slightly lower yield than the best catalyst **8**. Notwithstanding, its oxidation potential in the excited states is 0.13 V higher than the potential of porphyrin **8** (compare entry 1 and 4). On the other hand porphyrin **9** with the lowest oxidation potential gave the product in 72% (entry 5). Plots of yields vs both quenching rates (k_q) and oxidation potentials in the exited state (E_{ox}*) clearly shows that for the arylation of heteroarenes with diazonium salts there is an optimal quenching rate and catalyst redox properties in the excited state (Figure 3 and 4). *This highlights the importance of fine tuning of both electro- and photochemical properties of a catalyst for reactions involving PET processes.* With the best photoredox catalyst selected, we optimized the reaction conditions with respect to solvent and catalyst loading. Various solvents, suitable for dissolving porphyrins, were studied: DMSO, DMF, DCM, and MeOH (see SI). DMSO assured product formation with the highest yield.

Table 2. Screening of photoredox catalysts.[a]

Entry	Porphyrin	E_{ox}*[$Por^{\bullet+}$/Por^*] (mV)	k_q ($M^{-1}s^{-1}$)	Yield of **3** (%)[b]
1	H_2TPP (**4**)	-0.91(S) -0.42(T)[12a]	$1.5x10^{10}$	80
2	H_2T(4-OMeP)P (**6**)	-0.99(S) -0.54(T)[12b]	$2.9x10^9$	41[c]
3	H_2T(4-CO_2MeP)P (**7**)	-0.81(S)[12c] -0.31(T)	-[e]	74
4	**H_2T(F_5P)P (8)**	**-1.04(S)** **-0.78(T)**[12d]	**$7.2x10^9$**	**86** **(81)[d]**
5	H_2OEtP (**9**)	-1.52(S) -1.15(T)[12e]	-[e]	72[d]

[a] Reaction conditions: diazonium salt (**2**, 0.25 mmol), furan (**1**, 10 equiv.), DMSO (2 mL), porphyrin (1 mol%), blue LED (455 nm), 3 h. [b] Yield determined by GC. [c] Catalyst loading was lower due to solubility issues. [d] Isolated yield. [e] k_q not provided due to solubility issues,

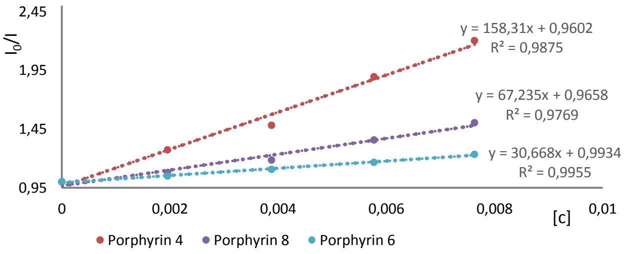

Figure 2. Stern-Volmer experiments for diazonium salt **2** and porphyrins **4**, **8**, and **6**.

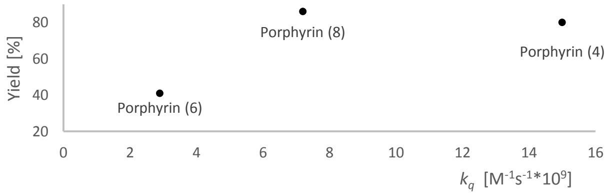

Figure 3. The correlation between *kq* and yield for porphyrins **4**, **6**, and **8**.

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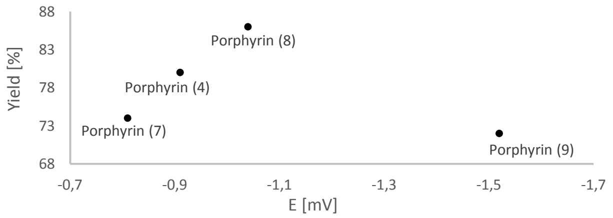


Figure 4. The correlation between E_{ox}*(S) and yield for porphyrins **4**, **7**, **8**, **9**.

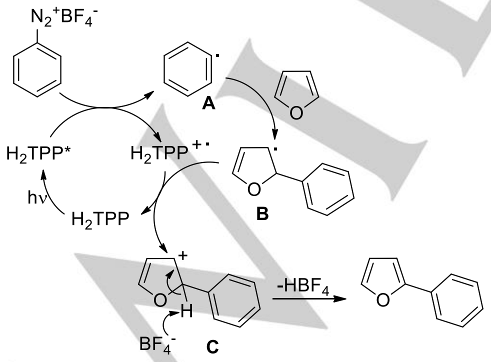
Gratifyingly, the best catalyst loading was as low as 1 mol% (Table 3, entry 2). Furthermore, we have also examined the amount of furan (**1**) used. As the concentration was diminished the yield gradually decreased with a 5-fold excess giving a satisfactory yield (Table 3, entries 2, 5-7).

Table 3. Optimization of the catalyst loading and furan equiv.[a]

Entry	Catalyst loading (mol%)	Furan (**1**) (equiv.)	Yield of **3** (%)[b]
1	1.5	10	78
2	1.0	10	86
3	0.8	10	71
4	0.1	10	42
5	1	15	71
6	1	5	76
7	1	2.5	41[c]

[a] Reaction conditions: diazonium salt (**2**, 0.25 mmol), furan (**1**, 10 equiv.), DMSO (2 mL), porphyrin (1 mol%), blue LED (455 nm), 3 h. [b] Yield determined by GC. [c] Isolated yield.

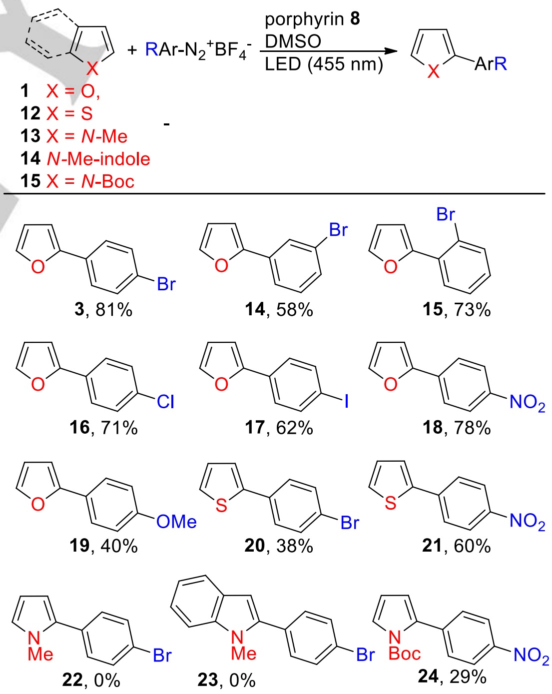
The mechanism of the photocatalytic, direct C-H arylation of heteroarenes with aryl diazonium salts catalyzed by eosin Y has been proposed by König and co-workers[8b] and studied in detail by Wangelin and Majek.[8c] The crucial step involves generation of an aryl radical via SET from the excited state eosin Y to the aryl diazonium salt and its subsequent addition to a heteroarene furnishing an aryl radical intermediate. We reasoned that in our case a similar mechanism should operate (Scheme 2).



Scheme 2. Plausible mechanism for photochemical arylation of heteroarenes with diazonium salts in the presence of porphyrin (ineffective chain propagation steps omitted for clarity).

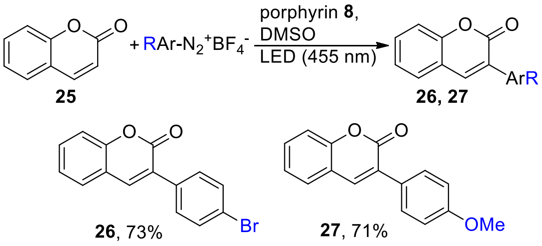
If so, the porphyrin in its excited state reduces the diazonium salt while forming a cation radical. Indeed, the Stern-Volmer experiment confirmed that diazonium salt **2** quenches the luminescence of the porphyrin contrary to furan (**1**) (Figure 1). We were also able to trap radical **A** as adduct with TEMPO and detect it by ESI MS (See SI). In the next step, radical **B** is oxidized to intermediate **C** that after proton elimination furnishes arylated product **3**. For this step two pathways were proposed: oxidation by a porphyrin cation radical or by another molecule of the starting material **2** in a radical chain reaction. In our case, oxidation by the porphyrin cation radical predominates as the reaction quantum yield was calculated to be Φ = 1.4 ± 0.8 (for details see SI). This is in contrast to the eosin Y-catalyzed reaction (4.7 ± 0.6).

Finally, the optimized conditions [diazonium salt (**2**, 0.25 mmol), furan (**1**, 10 equiv.), DMSO (2 mL), porphyrin **8** (1 mol%), blue LED (455 nm), 3 h,] were used exploring the scope and limitations of the reaction (Scheme 3). In general, the reaction gave moderate to good yields in arylation of furan (**1**) with diazonium salts with different functional groups being well tolerated (-Br, - Cl, - NO_2, -OMe). Notwithstanding, electron-donor substituted diazonium salts were found to be less efficient for arylation of furan (**10**) than electron-acceptor substituted ones.



Scheme 3. Arylation of heteroarenes with diazonium salts.

Porphyrin-catalyzed photochemical arylation was also effective for other compounds such as thiophene (**10**) and coumarin (**25**) (Scheme 2 and 3), but arylation of pyrrole derivatives (**11**) and (**12**) proved to be difficult under porphyrin catalysis. Supposably, porphyrin **8** reacts in the exited state faster with pyrrole or indole derivatives than with the diazonium salt **2** thus precluding the formation of the phenyl radical. Indeed, Stern-Volmer experiments showed that both *N*-methylpyrrole (**11**) and *N*-methylindole (**12**) effectively quenched the luminescence of the porphyrin contrary to furan and thiophene, likely via a reductive quenching (Figure 4).



Scheme 4. Arylation of coumarins with diazonium salts.

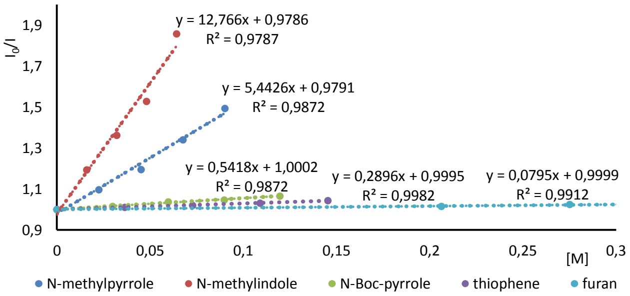


Figure 5. Stern-Volmer experiments for different heteroarenes and porphyrin **8**.

The obtained yields are in inverse proportion to the arene quenching rates. Hence, the prerequisite for an effective reaction is the lack of a reaction between an arene and a porphyrin in the excited state. To confirm our hypothesis, we performed the reaction of diazonium salt **2** with electron-poor *N*-Boc-pyrrole (**13**) for which the calculated quenching rate was similar to that of thiophene (**10**). Indeed, in this case the reaction afforded arylated product (**24**) in 29% yield.

Conclusions

Summing up, we have shown that porphyrins are suitable photoredox catalysts for the direct C-H arylation of heteroarenes. The reaction involves the generation of a phenyl radical via photoinduced electron transfer from a porphyrin in its exited state to a diazonium salt followed by the addition to a hetereoarene. The formed radical is oxidized by the porphyrin cation radical thus closing the catalytic cycle. A reaction quantum yield close to unity was determined; hence it is a photocatalytic process with only minor or ineffective chain propagation.

Under light irradiation exited porphyrins proved to be efficient electron donors and acceptors. Our work highlights the importance of the proper tuning of the photocatalyst redox behavior and photophysical properties for an efficient photocatalytic reaction. The porphyrins' electro- and photochemical properties can be easily changed by the proper substituent selection at the periphery of the macrocycle. Hence, this class of compounds represents a unique case as their photocatalytic properties can be adjusted to the reaction's need.

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Keywords: photocatalysis • porphyrins • C-H arylation • aryl diazonium salts • heteroarenes

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Photocatalysis*

*Katarzyna Rybicka-Jasińska, Burkhard König and Dorota Gryko**

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Porphyrin-catalyzed photochemical C-H arylation of heteroarenes

Porphyrins are suitable photoredox catalysts for direct C-H arylation of heteroarenes with aryl diazonium salts. The reaction involves PET from a porphyrin in its exited state to a diazonium salt.

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