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Synthesis of Diarylaminoacridinium Photocatalysts by Halogen-Metal Exchange Combined with Directed *ortho* Metalations

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Abstract: Photostability is an essential design aspect for the overall performance of photocatalysts, particularly as groups introduced to adjust redox properties often constitute sites of potential reactivity. Herein, we describe a modular and flexible synthetic approach to incorporate diarylamino moieties with increased photostability that allow to efficiently tune the redox behavior of a new generation of organic acridinium photocatalysts. A series of cross-coupling reactions gave access to precursors for halogen metal exchange reactions combined with directed *ortho*-metalations to provide reagents that allow the formation of acridinium salts with adjustable redox properties and enhanced photostability in good yields.

Keywords: acridinium salts; cross-coupling; photocatalysis; photostability; sustainability

While photocatalysis is a rapidly evolving field with an increasing demand for suitable catalysts,^[1–5] the majority of employed photocatalysts remains to be based on Ru or Ir polypyridyl transition metal complexes.^[6–9] As alternative to these metals of low natural abundance, a range of organic photoredox catalysts were developed and successfully employed.^[10–14] In the case of acridinium based photocatalysts introduced by Fukuzumi and broadly utilized by the Nicewicz and other groups,^[15–20] several opti-

mizations allowed to widen the range of application and improve performance.^[21–24] To efficiently access adjustable organic photocatalysts, we set our focus on synthetic strategies to obtain aminoacridiniums,^[22,24] as these have shown to be particularly tunable and compatible with various reaction conditions. To further increase the photostability, we here report a procedure to replace *N*-alkyl groups, allowing to access a new generation of acridinium photocatalysts with enhanced endurance for irradiation (Figure 1). Based on reagents obtained by halogen metal exchange reactions ($X \rightarrow M$) combined with a directed *ortho* metalation (DoM), esters could be directly converted into the diarylamino acridinium salts upon addition of HBr.^[24]

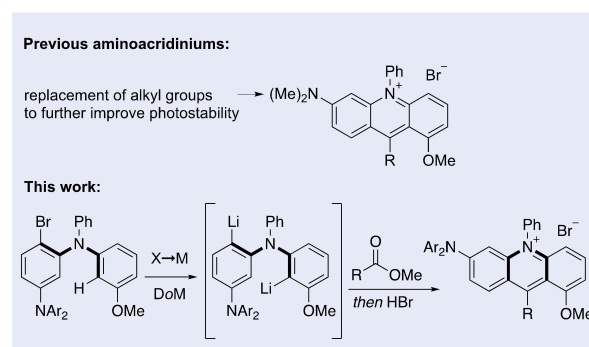
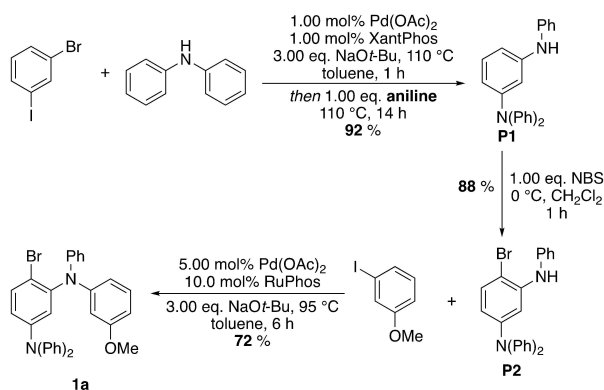


Figure 1. Previous dialkyl aminoacridiniums and the direct transformation of esters into diarylamino acridinium photocatalysts with enhanced photostability.

However, the synthesis of the precursors for 1,5-dilithium organyls with two triaryl amines proved to be a particular challenge and only substantial optimization of sequential Buchwald-Hartwig aminations^[25] allowed to synthesize the required building block **1a** in high yields within a short synthetic sequence (Scheme 1).



Scheme 1. Synthesis of building block **1a**.

Table 1. Synthesis of 6-diphenylamino-acridiniums.^[a]

Entry	Product ^[b]	Entry	Product ^[b]
1		4	
2		5	
3			

^[a] Reactions performed with ester (100 μmol) and **2a** (140 μmol) at RT followed by aqueous work-up (HBr 8.8 mol L⁻¹);

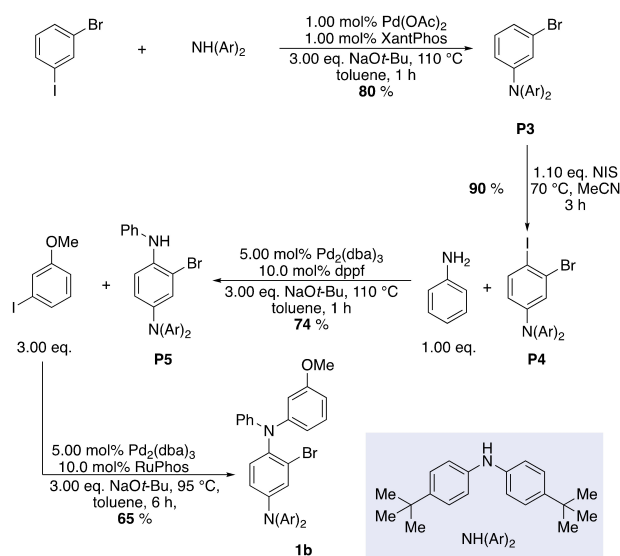
^[b] Yields of isolated products.

Notably, after the coupling of 3-bromoiodobenzene and diphenylamine, an ensuing addition of aniline gave direct access to a secondary amine **P1** which was selectively brominated with NBS followed by a final C–N cross-coupling with 3-iodoanisole to give precursor **1a**.

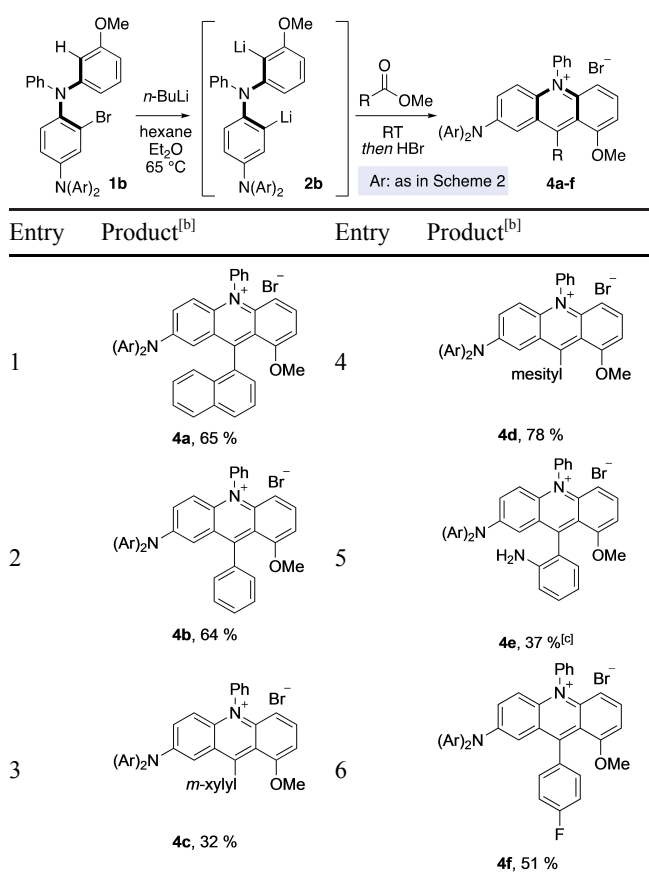
We next examined the twofold lithiation of precursor **1a**, which indicated that the exposure to *n*-BuLi at 65 °C for 5 h resulted in a smooth formation of the lithiated reagent **2a** by the X→M/DoM strategy.^[22] With the precursor synthesis and the metalation protocol developed, we set out to explore the synthesis of different diphenylacridinium salts (Table 1). Methyl 1-naphthoate was treated with 1.40 eq. of the *in situ* prepared reagent **2a** at room temperature followed by aqueous workup with HBr to form the acridinium bromide **3a** in 65% yield. In order to access a spectrum of acridinium salts, a variety of carboxylic acid esters was examined towards their reactivity with **2a**. Analogous results were observed for the synthesis **3e**, while **3c** was prepared with a somewhat lower efficiency. Conversely, the esters leading to the diaryl acridiniums **3b** and **3d** were converted with slightly increased yields (71%).

Having prepared 6-diphenyl acridinium salts **3a–e**, we next investigated the influence of the position of diphenylamine group by a modified synthetic pathway of the reagent precursor (Scheme 2 and Table 2).

Starting from 3-bromoiodobenzene, the C–N cross-coupling with bis(4-(*tert*-butyl)phenyl)amine was thus followed by an iodination, while an ensuing double cross-coupling with aniline and 3-iodoanisole consequently gave access to building block **1b**. Halogen metal exchange and directed *ortho* metalation was subsequently performed with building block **1b** to



Scheme 2. Synthesis of building block **1b**.

Table 2. Synthesis of 7-diaryl-amino-acridiniums.^[a]

^[a] Reactions performed with ester (100 μmol) and **2b** (140 μmol) at RT followed by aqueous work-up (HBr 8.8 mol L^{-1});

^[b] Yields of isolated products;

^[c] With 240 μmol mmol of **2b**.

give reagent **2b**, which was exposed to the carboxylic acid esters to obtain acridinium salts **4a–f**. To test if also protic substrates convert to acridinium products, an increased amount of reagent **2b** (2.40 eq.) was added to confirm that the transformation of methyl anthranilate to the corresponding acridinium salt **4e** was feasible.

Having synthesized both sets of 6- and 7- substituted acridinium photocatalysts, we characterized and compared the properties of the diarylamino acridiniums (Table 3). While 6-diaryl-amino catalysts **3a–e** show more intense absorption peaks at ~ 510 nm, substitution at the 7-position led to bathochromic shift (~ 600 nm). Overall, the introduction of amine moieties led to suitably attenuated excited state reduction potentials, whereas the impact of diarylamino groups is consistently reduced compared to the N-alkylated systems (Table 4).^[24,26]

To study the photostability of the new photocatalysts, we next intensively irradiated 6- and 7-substituted aminoacridiniums under defined conditions using a 405 nm laser during which the decay of the absorption was measured by UV-Vis spectroscopy (Figure 2). Gratifyingly, 6-diphenylamine substituted catalyst **3a** showed an outstanding stability when compared to its dimethylamine bearing analogue (Figure 2, grey vs red line). After 15 h, a decay of only 12% was observed, whereas the absorption of the dimethylamine bearing catalyst was reduced by 86% after the same amount of time, potentially through the formation of α -aminoradicals. These results prompted us to further examine the photostability of 7-substituted catalysts at 405 nm. As before, catalyst **4a** showed a significantly higher stability compared to the dimethylamine analogue (Figure 2, blue vs green line).

However, both catalysts indicated a lower stability at 405 nm irradiation compared to 6-amino substituted catalysts and we thus exposed both 7-substituted

Table 3. Photophysical properties of acridinium dyes.

Entry	Acridinium Salt	λ_{abs} [nm]	λ_{em} [nm]	ϵ_{abs} [$\text{L mol}^{-1} \text{cm}^{-1}$]	Stokes Shift [nm]	$E_{0,0}$ [eV] ^a	$E_{1/2}(\text{P}/\text{P}^-)$ [V] ^a	$E_{1/2}(\text{P}^*/\text{P}^-)$ [V]
1	3a	512	536	1.41×10^4	24	2.36	-0.74	+1.62
2	3b	509	540	1.52×10^4	31	2.33	-0.77	+1.57
3	3c	509	529	1.23×10^4	20	2.37	-0.73	+1.64
4	3d	509	536	1.16×10^4	27	2.36	-0.76	+1.60
5	3e	511	539	1.39×10^4	28	2.33	-0.74	+1.60
6	4a	601	648	5.82×10^3	47	1.95	-0.63	+1.32
7	4b	595	674	6.58×10^3	79	1.95	-0.65	+1.30
8	4c	600	657	6.18×10^3	57	1.97	-0.65	+1.32
9	4d	601	649	6.28×10^3	48	1.96	-0.66	+1.30
10	4e	601	669	7.55×10^3	68	1.92	-0.66	+1.27
11	4f	594	679	6.67×10^3	85	1.95	-0.61	+1.34

^[a] Measured in MeCN;

^[b] Measured in 100 $\mu\text{mol L}^{-1}$ $n\text{-Bu}_4\text{NPF}_6$ in degassed, dry MeCN against SCE.

Table 4. Comparison of photophysical properties of selected acridinium dyes.

Entry	-N(R') ₂	λ_{abs} [nm]	λ_{em} [nm]	$E_{1/2}(\text{P}^*/\text{P}^-)$ [V]
1 ^[a]	6-N(Ph) ₂ (3b)	509	540	+1.57
2 ^[a]	6-N(Me) ₂	511	576	+1.40
3 ^[a]	–	479	637	+1.69
4 ^[b]	6-N(Ph) ₂ (3b)	512	536	+1.62
5 ^[b]	6-N(Me) ₂	516	578	+1.40
6 ^[b]	–	480	635	+1.73
7 ^[c]	7-N(4- <i>t</i> -Bu-Ph) ₂ (4d)	601	669	+1.30
8 ^[c]	7-N(Me) ₂	583	723	+1.23
9 ^[c]	–	479	632	+1.68
10 ^[b]	7-N(4- <i>t</i> -Bu-Ph) ₂ (4d)	601	648	+1.32
11 ^[b]	7-N(Me) ₂	590	755	+1.19

^[a] R = phenyl;

^[b] R = naphthyl;

^[c] R = mesityl.

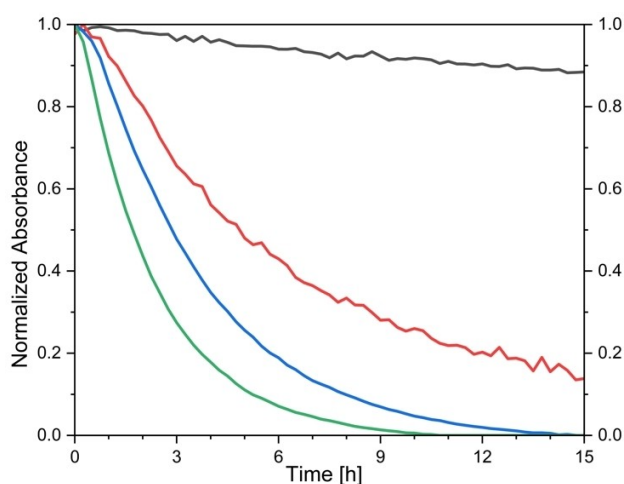


Figure 2. Decay of absorbance of the 6- and 7-substituted catalysts at 405 nm irradiation with a 526 mW laser. 500 $\mu\text{mol L}^{-1}$ solution in MeCN; 405 nm laser; grey-line: catalyst **3a**; red-line: NMe₂ analogue of catalyst **3a**; blue-line: catalyst **4a**; green-line: NMe₂ analogue of catalyst **4a**.^[26]

catalysts to irradiation at 532 nm. Under these conditions, catalyst **4a** showed considerably higher photostability (Figure 3, grey line) as the dimethylamine system (red line).

The new photocatalysts were furthermore examined in a benchmarking Ni-photosensitized catalytic esterification (Table 5).^[27] While both alkyl and aryl 6-substituted catalysts showed yields exceeding 80%, a significant increase in yield was observed for 7-substituted catalysts (see Supporting Information for details) and the highest yield (93%) was obtained with the 4-

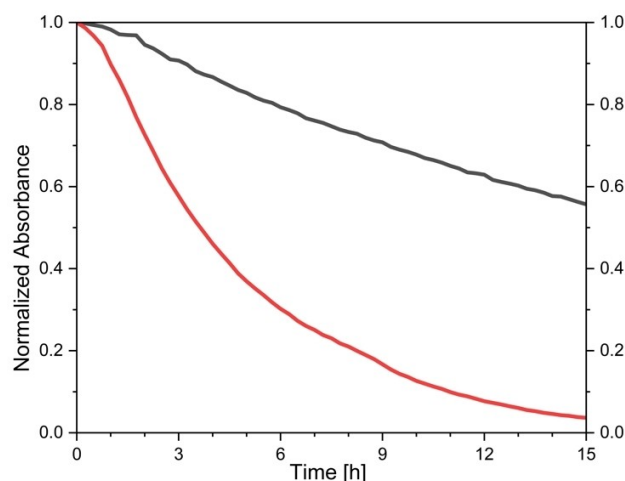


Figure 3. Decay of absorbance of 7-substituted catalysts at 532 nm irradiation with a 500 mW laser. 500 $\mu\text{mol L}^{-1}$ solution in MeCN; 532 nm laser; grey-line: catalyst **4a**; red-line NMe₂ analogue of catalyst **4a**.^[26]

Table 5. Ni-photosensitized catalytic esterification.

Entry	Photo-catalyst	Loading [mol%]	Time [h] ^[a]	Yield [%] ^[b]
1	3a	1.00	16	81
2	3b	1.00	16	85
3	3d	1.00	16	81
4	4a	1.00	16	81
5	4f	1.00	16	93

^[a] 50.0 μmol scale, 3.0 mL DMF,

^[b] Yield determined by ¹H-NMR.

fluorophenyl bearing 7-substituted catalyst **4f** (entry 5).

Conclusion

In conclusion, we describe an efficient synthetic preparation of eleven different diarylamino acridinium photocatalysts based on C–N cross couplings and halogen metal exchange combined with directed *ortho* metalations. The photophysical properties were determined and the photostabilities evaluated under laser irradiation at different wavelengths. When comparing the diarylamino to dialkylamino acridinium catalysts, the tunability of photophysical properties remained feasible, while a significantly increased photostability was observed. Furthermore, the utility of 6- and 7-

substituted catalysts in a Ni-photosensitized catalytic esterification was confirmed.

Experimental Section

General Procedure for the Synthesis of Diarylamino Acridinium Photocatalysts

To a 7.0 mL microwave vial equipped with a stir bar was added either precursor **1a** or **1b** (140 μmol , 1.40 eq.). The vial was evacuated and back filled with argon. Anhydrous Et_2O (170 μL) and *n*-hexane (1.70 mL) were added and the mixture was stirred for 5 minutes. A solution of *n*-BuLi in hexane (180 μL , 1.60 mol L^{-1} , 280 μmol , 2.80 eq.) was added and the mixture was stirred for 5 h at 65 °C. After cooling to RT, a solution of carboxylic acid ester (100 μmol , 1.00 eq.) in anhydrous THF (360 μL) was added dropwise, the reaction was stirred overnight and aq. HBr (1.0 mL, 48%) was added. The mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4 , concentrated *in vacuo* and the residue purified by column chromatography with CH_2Cl_2 100% to CH_2Cl_2 :MeOH 10:1 to yield the desired acridinium salt.

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