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Visible-Light-Mediated α-Arylation of Enol Acetates Using Aryl Diazonium Salts

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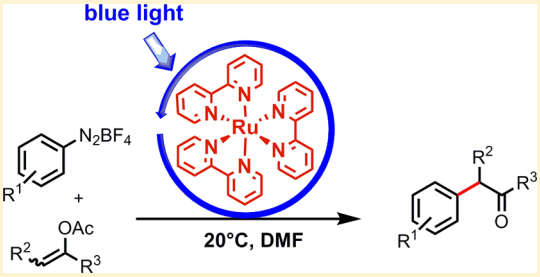
Supporting Information

ABSTRACT: Visible light mediates efficiently the α-arylation of enol acetates by aryl diazonium salts under mild conditions using $[Ru(bpy)_3]Cl_2$ as a photoredox catalyst. The broad scope of the reaction toward various diazonium salts and enol acetates was explored. The application of this reaction in the concise synthesis of 2-substituted indoles was demonstrated



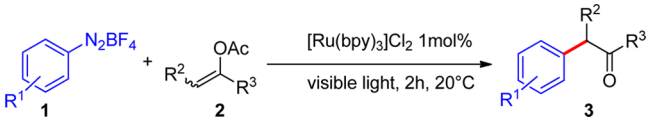
INTRODUCTION

The catalytic α-arylation of ketones as a method of C−C bond formation has been extensively studied over the past decades. This interest arises from the importance of α-aryl carbonyl moieties in many pharmaceuticals and bioactive molecules,[1] including well-known drugs such as ibuprofen and the β-blocker atenolol. 1,2-Diarylated ethanones (deoxybenzoines) can serve as valuable building blocks for the synthesis of heterocycles such as oxazoles,[2] pyrazoles,[3] diazepines,[4] and indoles,[5] which are common functionalities in various drug molecules.

In addition to only a few examples for base-promoted reactions,[6] especially transition metal[5a,7] (Pd, Ni, Cu, Fe)-catalyzed reactions proved to be highly effective. In particular Pd-catalyzed arylations pioneered by Buchwald and Hartwig offer access to many interesting products.[5c,7a,b] In the context of efficient synthesis, visible light can be considered the ideal "reagent" since it is abundant and nontoxic and generates no waste. The great potential of photoredox chemistry to perform essential organic transformations by irradiation with visible light was impressively demonstrated in recent publications by the groups of MacMillan, Yoon, Rüping, Blechert, Bach, Stephenson, and others.[8]

Reactive radical intermediates have unique features and are therefore widely employed in organic synthesis.[9] The highly reactive aryl radical, for instance, is easily accessible through one-electron reduction of aryl diazonium salts[10] and reacts with versatile unsaturated compounds.[8g] Detailed investigations on these reactions were done by Heinrich et al.,[11] who used $TiCl_3$ as a stoichiometric reductant for the generation of the aryl radical. An elegant and ecofriendly approach to aryl radicals is the catalytic reduction of aryl diazonium salts by photoinduced electron transfer (PET) using $[Ru(bpy)_3]Cl_2$. This was first described by Cano-Yelo and Deronzier. They used an intramolecular cyclization known as the Pschorr reaction for the synthesis of phenanthrene derivatives.[12] Our group has elaborated this concept to perform intermolecular direct C−H bond arylation of heteroarenes[8j] and double bonds.[8k] Herein we now report a mild method for the α-arylation of ketones in visible light by PET-mediated arylation of enol acetates (Scheme 1); the reaction proceeds at room temperature without the need for any bases or toxic metal enolates.

Scheme 1. Photocatalytic Approach for α-Arylation of Ketones in Visible Light



RESULTS AND DISCUSSION

Initial studies showed that under irradiation at 440 nm the reaction of *p*-nitrobenzenediazonium tetrafluoroborate **1a** with isopropenyl acetate **2a** and 1 mol % $[Ru(bpy)_3]Cl_2$ in DMSO gave the α-arylated ketone **3a** in high yields. The possibility to replace $[Ru(bpy)_3]Cl_2$ by photocatalytic active organic dyes[13] was investigated, and the results of the screening are presented in Table 1. We observed no catalytic enhancement for 5 mol % Eosin B or Rose Bengal (entries 5 and 6) compared to the control reaction without catalyst (entries 3 and 1). Eosin Y (5 mol %) increased the yield slightly, reaching a yield of 50% (entry 4) with 10 mol % Eosin Y. The much shorter lifetime of the excited states of the organic dyes[13a,14] in comparison to $[Ru(bpy)_3]Cl_2$ may explain why the ruthenium complex is the best photoredoxcatalyst for the reaction.

To optimize the reaction conditions we screened different solvents, catalyst loadings, and irradiation times (Table 2). Dry

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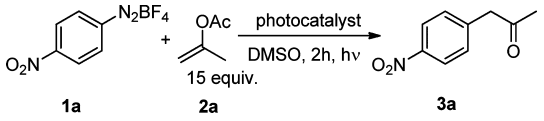
Table 1. Screening of Different Photocatalysts[a]



entry	catalyst	mol %	yield (%)[b]
1			33[c]
2	$[Ru(bpy)_3]Cl_2$	1	80
3	Eosin Y	5	43
4	Eosin Y	10	50
5	Eosin B	5	35
6	Rose Bengal	5	32

[a]The reaction was performed using 0.3 mmol of **1a,** with 15 equiv of **2a** in DMSO and irradiation time of 2 h. [b]Yield determined by gas chromatography. [c]Experiment was conducted in DMF (see ref 8(g) p 775 for details on the background reaction).

Table 2. Optimization of Reaction Conditions[a]

entry	conditions	yield (%)[a]
1	**2a** (15 equiv), DMSO dry, 2 h	80
2	**2a** (5 equiv), DMSO dry, 2 h	75–70
3	**2a** (15 equiv), DMSO dry, 6 h	70
4	**2a** (15 equiv), DMSO dry, 2 mol % cat.	70
5	**2a** (15 equiv), 2:1 DMSO/H_2O, 2 h	47
6	**2a** (15 equiv), MeCN, 2 h	56
7	**2a** (15 equiv), MeCN dry, 2 h	62
8	**2a** (15 equiv), DMF dry, 2 h	95–100
9	**2a** (10 equiv), DMF dry, 2 h	93
10	**2a** (5 equiv), DMF dry, 2 h	73
11	**2a** (15 equiv), DMF dry, no light, 2 h	15

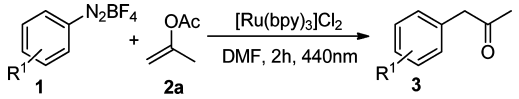
[a]Yield determined by gas chromatography.

DMF as a solvent, 2 h irradiation time, and 1 mol % $[Ru(bpy)_3]Cl_2$ provided the highest yields (entry 9). The excess of the enol acetate **2a** was needed for an efficient product formation (entries 8–10). Most of the unreacted substrate could be recovered during the workup, and we assume that the high concentration of **2** is required to trap the very reactive aryl radical efficiently. We observed no significant conversion without irradiation (entry 11).

With these optimized conditions in hand, we explored the scope of the reaction of **2a** with different aryl diazonium salts (Table 3). A variety of different substituents were tested, and the desired product **3** was obtained in all cases. In accordance with their higher reduction potentials[10] electron-deficient aryl diazonium salts (entries 1–5 and 7) showed the highest yields. However, a strong dependence on the position of the substituents was observed (entries 1–3), probably due to steric hindrance. Neutral or electron-donating substituents gave moderate to good yields. It is advantageous that halogen substituents are tolerated on the aromatic ring as this opens up possibilities for facile subsequent synthetic modifications (entries 7 and 8).

Having established the broad scope of the diazonium salts in this α-arylation, we varied the substituents on the enol. As Table 4 shows, the reaction was very effective for terminal enols regardless of the substituent (entries 1–6). Aliphatic as well as aromatic and heterocyclic groups are tolerated for terminal enols. Excellent yields can be obtained with aromatic enol acetates (entries 3–5), because a well stabilized benzylic radical is formed upon addition of the aryl radical (see Scheme 3, intermediate **7**). However, a substituent on the enol's double bond decreases the yield significantly (entries 7 and 8). Due to subsequent aldol reaction low or no yields are observed with enol acetates of aldehydes (entries 9[15] and 10).

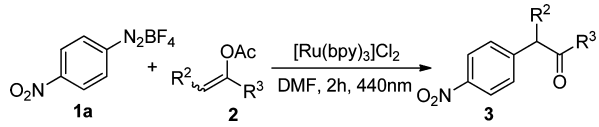
Table 3. Screening of Different Diazonium Tetrafluoroborates[a]



entry	R^1	diazonium salt	product	yield (%)[b]
1	4-NO_2	**1a**	**3a**	90
2	2-NO_2	**1b**	**3b**	60
3	3-NO_2	**1c**	**3c**	55
4	2-CF_3	**1d**	**3d**	59
5	2-CN	**1e**	**3e**	75
6	4-COOEt	**1f**	**3f**	50
7	4-Cl	**1g**	**3g**	61
8	4-Br	**1h**	**3h**	57
9	4-MeO	**1i**	**3i**	40
10	4-CH_3	**1j**	**3j**	47

[a]The reaction was performed using 0.3 mmol **1** with 10 equiv **2a** and 0.003 mmol of $[Ru(bpy)_3]Cl_2$ in DMF and 2 h of irradiation at 440 nm. [b]Yield after purification over silica gel.

Table 4. Scope of Enol Acetates[a]



entry	R^3	R^2	enol acetate	product	yield (%)[b]
1	Me	H	**2a**	**3a**	90
2	*tert*-butyl	H	**2b**	**3k**	75
3	Ph	H	**2c**	**3l**	95
4	4-Br- Ph	H	**2d**	**3m**	92
5	4-OMe- Ph	H	**2e**	**3n**	96
6	thienyl	H	**2f**	**3o**	79
7	Et	Me	**2g**	**3p**	33
8[c]	$-(CH_2)_4-$		**2h**	**3q**	35
9	H	H	**2i**	**3r**	26
10	H	C_6H_{13}	**2j**	**(3s)**	(only traces)

[a]The reaction was performed using 0.3 mmol of **1a** with 10 equiv of **2** and 0.003 mmol of $[Ru(bpy)_3]Cl_2$ in DMF and 2 h of irradiation at 440 nm. [b]Yield after purification over silica gel. [c]Enol acetate derived from cyclohexanone.

Our investigations have shown that visible light photoredox catalysis can serve as a viable method to promote organic transformations. To further illustrate its applicability, we performed the synthesis of 2-substituted indoles. As shown in Scheme 2 we used the developed photochemical arylation as a first step, followed by the iron-catalyzed reductive cyclization described by Raucher et al.[5b] The ketone **3** carrying an *ortho*-NO_2-substituted benzene in the α-position is easily accessible through the photoreaction of 2-nitro aryl diazonium salt **1b** with any enol acetate. In situ reduction of the nitro group leads to amine **4**, which undergoes iron-directed condensation to give indole **5**. This synthesis avoids regioselectivity problems observed in Fischer indole synthesis[16] and allows the introduction of synthetically valuable halogen substituents on the indoles benzene ring as well as on the substituent.

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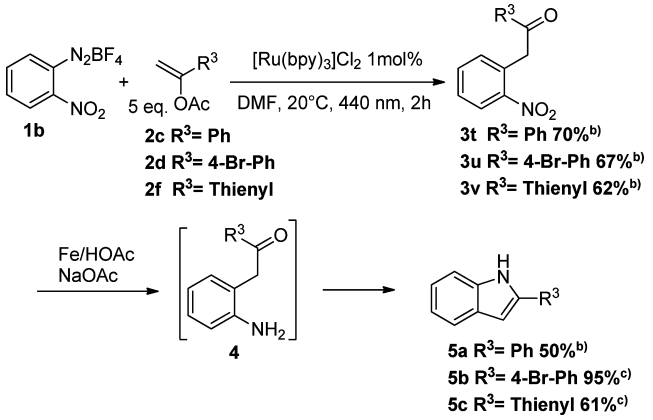
Scheme 2. Application of the Photoreaction in the Synthesis of Substituted Indoles through Photochemical Arylation Followed by Reductive Cyclization[a]



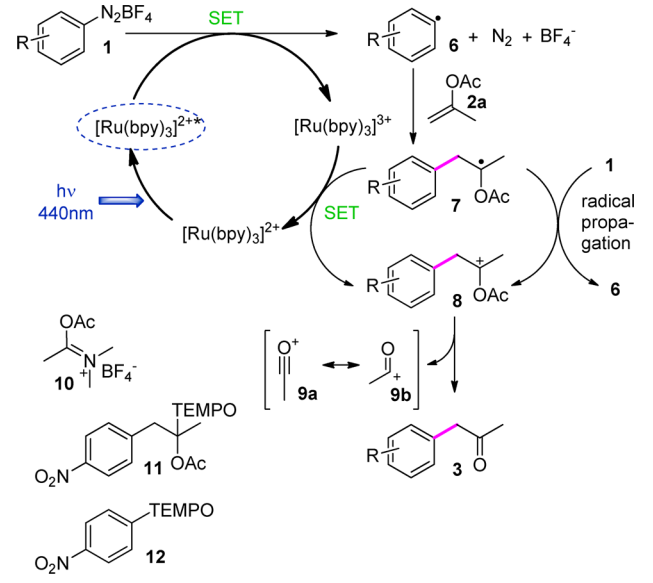
[a]Reaction was performed using 0.5 mmol of ketone **3**, 3.5 equiv of iron powder, 1 equiv NaOAc, and 7 equiv HOAc in 4:1 ethanol/water.[5b]

[b]Yield after purification over silica gel.

[c]Yield determined by NMR.

Scheme 3 depicts a plausible mechanism for the described arylation based on our investigation and recent literature reports.[8h,11] The cycle is initiated by photoexcitation of the catalyst, which is oxidatively quenched by the diazonium salt **1** to give aryl radical **6**.[17] The radical **6** can attack the enol double bond to form radical intermediate **7**. Compound **7** can be oxidized to the cationic species **8** by two possible pathways: (a) single electron transfer (SET) to $[Ru(bpy)_3]^{3+}$ thus closing the catalytic cycle or (b) reduction of **1** to the aryl radical **6** initiating a radical chain process. To yield the observed product **3**, an acyl cation **9** has to be transferred to a nucleophile, e.g., the solvent DMF, to give the stable salt **10** in analogy to the first step of the Vilsmeier–Haack reaction.[18] While the TEMPO adducts **11** and **12** support the presence of intermediates **7** and **6** in the reaction cycle, we could not detect compounds arising from acyl cation **9**.

Scheme 3. Proposed Mechanism for the Photocatalyzed α-Arylation of Enol Acetates



CONCLUSION

In conclusion, we described a mild method for the α-arylation of ketones by reacting aryl diazonium salts with enol acetates using visible light photoredox catalysis. The reaction proceeds smoothly at room temperature without the need of bases, expensive patented ligands, or toxic metal enolates and is compatible with a broad range of functional groups. Thus it provides an environmentally benign synthesis of α-arylated ketones catalyzed by photoinduced electron transfer (PET) as an alternative to conventional synthetic procedures. Furthermore, we obtained synthetically valuable indoles in a simple two-step process, introducing first an *ortho*-nitro-substituted aryl moiety on a ketone by our photochemical arylation followed by reductive cyclization to the indole. Further studies on the exact mechanism of the arylation are ongoing in our group.

EXPERIMENTAL SECTION

General Experimental Details. Commercial reagents and starting materials were purchased and used without further purification. Solvents were used either as p.a. grade or dried and distilled according to literature known procedures.[19] NMR spectroscopy was carried out on either a 400 MHz (^{1}H, 400.13 MHz; ^{13}C, 101 MHz, T = 300 K) or a 300 MHz Spectrometer (^{1}H, 300.13 MHz; ^{13}C, 75 MHz, T = 295 K). GC measurements were done with following parameters: injector temperature (split injection, 40:1 split) was 250 °C, detection temperature was 300 °C (FID) with a capillary column 30 m × 0.25 mm/0.2 μm film. The GC oven temperature program was adjusted as follows: initial temperature 40 °C was kept for 3 min, the temperature was increased at a rate of 15 °C/min over a period of 16 min until the final temperature (280 °C) was reached and kept for 5 min. Naphthalene was used as an internal standard. Irradiation was performed with high power LEDS (blue, λ_{max} = 455 ± 15 nm, 700 mA, 3.0 W) for blue light or (green, λ = 520 ± 15 nm, 145 lm @700 mA, 1.0 W) for green light.

General Procedure A: Preparation of Aryl Diazonium Tetrafluoroborates. Compounds were prepared according to literature.[20] In a mixture of 4 mL of distilled water and 3.4 mL of 50% hydrofluoroboric acid was dissolved 10 mmol of the appropriate aniline. After the reaction mixture was cooled to 0 °C using an ice bath, a solution of sodium nitrite in distilled water (0.69 g in 1.5 mL) was added dropwise. The suspension was stirred for an additional 40 min and then filtered, and the resulting solid was redissolved in a minimum amount of acetone. Diethyl ether was added until precipitation of diazonium tetrafluoroborate, which was filtered, washed several times with diethyl ether, and dried under vacuum.

General Procedure B: Preparation of Enol Acetates. Compounds were prepared according to literature.[7k] To a mixture of the ketone (50 mmol) and 2-propenyl acetate (250 mol) was added *p*-toluenesulfonic acid (3.6 mmol). The resulting mixture was refluxed overnight and afterward cooled to rt. The solvent was evaporated in vacuo. Diethyl ether (100 mL) was added, and the organic layer was subsequently washed with H_2O (3 × 50 mL), dried over Na_2SO_4, and concentrated in vacuo. The resulting crude mixture was purified by column chromatography on SiO_2 (50% CH_2Cl_2 in hexane) for aromatic products and by fractionated distillation under reduced pressure for aliphatic products.

1-Phenylvinyl Acetate (2c).[7n] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.43 (m, 2H), 7.38–7.32 (m, 3H), 5.49 (d, J = 2.2 Hz, 1H), 5.04 (d, J = 2.2 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 153.0, 134.3, 129.0, 128.6, 124.9, 102.2, 21.0.

1-(4-Bromophenyl)vinyl Acetate (2d).[7n] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.41 (m, 2H), 7.40–7.28 (m, 2H), 5.47 (d, J = 2.4 Hz, 1H), 5.06 (d, J = 2.4 Hz, 1H), 2.27 (s, 3H).

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1-(4-Methoxyphenyl)vinyl Acetate (2e).[7n] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.32 (m, 2H), 6.90−6.73 (m, 2H), 5.35 (d, J = 2.2 Hz, 1H), 4.91 (d, J = 2.2 Hz, 1H), 3.81 (s, 3H), 2.27 (s, 3H).

1-(Thiophen-2-yl)vinyl Acetate (2f).[21] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−7.19 (m, 1H), 7.10 (dd, J = 3.7, 1.2 Hz, 1H), 6.98 (dd, J = 5.0, 3.7 Hz, 1H), 5.39 (d, J = 2.5 Hz, 1H), 4.94 (d, J = 2.5 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 147.6, 138.2, 127.5, 125.8, 124.7, 101.2, 20.9.

3,3-Dimethylbut-1-en-2-yl Acetate (2b).[22] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (d, J = 2.0 Hz, 1H), 4.63 (d, J = 2.0 Hz, 1H), 2.17 (s, 3H), 1.09 (s, 9H).

Pent-2-en-3-yl Acetate (2g).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23−4.96 (m, 1H), 2.41−2.03 (m, 5H), 1.63 (d, J = 7.1 Hz, 1H), 1.47 (dd, J = 6.8, 1.4 Hz, 2H), 1.00 (m, 3H).

Cyclohex-1-en-1-yl Acetate (2h).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (ddd, J = 5.3, 2.6, 1.5 Hz, 1H), 2.16−2.06 (m, 7H), 1.72 (dtd, J = 12.2, 6.3, 2.8 Hz, 2H), 1.58 (dtd, J = 9.2, 6.0, 2.9 Hz, 2H).

Oct-1-en-1-yl Acetate (2j).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (dt, J = 12.4, 1.4 Hz,1H), 6.99 (dt, J = 6.4, 1.5 Hz,0.7H), 5.40 (dt, J = 12.4, 7.5 Hz, 1H), 4.86 (dd, J = 13.9, 7.4 Hz, 0.7H), 2.12 (d, J = 14.9 Hz, 7H), 1.99 (ddd, J = 9.6, 8.8, 5.9 Hz, 2H), 1.45−1.13 (m, 20H), 0.99−0.72 (m, 9H).

General Procedure C: Photocatalytic Arylation of Enol Acetates. In a 5 mL snap vial 0.3 mmol of the aryl diazonium tetrafluoroborate, 3.0 mmol (10 equiv) of the enol acetate, and 0.01 equiv $[Ru(bpy)_3]Cl_2$ were dissolved in 670 μL dry DMF. The vial was sealed with a septum and degassed via the "freeze-pump-method" (3×). The reaction mixture was stirred at 20 °C and irradiated for 2 h using blue LEDs (440 nm). After the irradiation time the mixture was diluted with water and washed three times with diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuum. The resulting crude product was further purified by column chromatography using a 3:1 mixture of petrol ether/ethyl acetate as an eluent (R_f value changes from 0.4 to 0.6 for all products). For GC analysis the samples were taken directly after irradiation, diluted in a 1:1 mixture with the internal standard solution and submitted to GC without further purification.

1-(4-Nitrophenyl)propan-2-one (3a).[6b] Yield 90% (49 mg, 0.27 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.09 (m, 2H), 7.32 (dd, J = 9.0, 2.2 Hz, 2H), 3.80 (s, 2H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.1, 147.1, 141.5, 130.5, 123.8, 50.1, 29.9.

1-(2-Nitrophenyl)propan-2-one (3b).[6b] Yield 60% (36 mg, 0.20 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 8.2, 1.2 Hz, 1H), 7.60 (td, J = 7.5, 1.2 Hz, 1H), 7.53−7.39 (m, 1H), 7.38−7.17 (m, 1H), 4.12 (s, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.6, 133.6, 133.6, 130.4, 128.5, 125.3, 48.6, 30.0.

1-(3-Nitrophenyl)propan-2-one (3c).[24] Yield 55% (30 mg, 0.17 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18−8.08 (m, 1H), 8.06 (s, 1H), 7.57−7.47 (m, 2H), 3.85 (s, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.4, 148.4, 135.9, 135.9, 129.5, 124.5, 122.2, 49.7, 29.9.

1-(2-(Trifluoromethyl)phenyl)propan-2-one (3d).[6b] Yield 59% (39 mg, 0.19 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.4 Hz, 1H), 3.91 (d, J = 0.9 Hz, 2H), 2.21 (s, 3H).

2-(2-Oxopropyl)benzonitrile (3e).[6b] Yield 75% (36 mg, 0.23 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 7.7, 1.1 Hz, 1H), 7.55 (td, J = 7.7, 1.4 Hz, 1H), 7.43−7.33 (m, 1H), 7.33−7.27 (m, 1H), 3.97 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.5, 138.2, 132.9, 132.8, 130.9, 127.7, 117.8, 113.4, 48.6, 30.1.

Ethyl 4-(2-Oxopropyl)benzoate (3f).[7l] Yield 50% (34 mg, 0.15 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11−7.94 (m, 2H), 7.31−7.17 (m, 2H), 4.36 (q, J = 7.1 Hz, 2H), 3.75 (s, 2H), 2.16 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.3, 166.4, 139.2, 129.9, 129.5, 129.4, 61.0, 50.7, 29.5, 14.3.

1-(4-Chlorophenyl)propan-2-one (3g).[6b] Yield 61% (31 mg, 0.18 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.27 (m, 2H), 7.16−7.04 (m, 2H), 3.67 (s, 2H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.6, 133.1, 132.6, 130.8, 128.9, 50.1, 29.4.

1-(4-Bromophenyl)propan-2-one (3h).[25] Yield 57% (40 mg, 0.17 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.35 (m, 2H), 7.06−6.96 (m, 2H), 3.61 (s, 2H), 2.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.5, 133.1, 131.8, 131.2, 121.1, 50.1, 29.5.

1-(4-Methoxyphenyl)propan-2-one (3i).[26] Yield 40% (22 mg, 0.13 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.05 (m, 2H), 6.91−6.82 (m, 2H), 3.79 (s, 3H), 3.63 (s, 2H), 2.13 (s, 3H).

1-(*p*-Tolyl)propan-2-one (3j).[6b] Yield 47% (24 mg, 0.16 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 3.65 (s, 2H), 2.34 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.7, 136.7, 131.2, 129.5, 129.3, 50.7, 29.2, 21.1.

3,3-Dimethyl-1-(4-nitrophenyl)butan-2-one (3k). Compound is an orange oil. Yield 75% (50 mg, 0.23 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 3.92 (s, 2H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 146.9, 142.5, 130.6, 123.6, 44.9, 42.9, 26.3. HRMS (EI-MS) m/z: $[M]^+$ calcd for $C_{12}H_{15}NO_3$ 221.1052; found 221.1056.

2-(4-Nitrophenyl)-1-phenylethanone (3l).[27] Yield 95% (69 mg, 0.29 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.16 (m, 2H), 8.01 (dd, J = 8.4, 1.3 Hz, 2H), 7.61 (d, J = 7.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 4.42 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 142.0, 136.2, 133.8, 130.7, 128.9, 128.5, 123.8, 45.0.

1-(4-Bromophenyl)-2-(4-nitrophenyl)ethanone (3m).[28] Yield 92% (88 mg, 0.28 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35−8.05 (m, 2H), 7.96−7.77 (m, 2H), 7.72−7.56 (m, 2H), 7.42 (d, J = 8.8 Hz, 2H), 4.38 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.0, 141.5, 134.9, 132.3, 130.6, 130.0, 123.9, 44.9.

1-(4-Methoxyphenyl)-2-(4-nitrophenyl)ethanone (3n).[28] Yield 96% (78 mg, 0.29 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25−8.11 (m, 2H), 8.06−7.89 (m, 2H), 7.44−7.35 (m, 2H), 7.05−6.90 (m, 2H), 4.35 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 163.9, 146.9, 142.5, 130.8, 130.5, 129.1, 123.6, 114.0, 55.5, 44.6.

2-(4-Nitrophenyl)-1-(thiophen-2-yl)ethanone (3o).[28] Yield 79% (0.59 mg, 0.24 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.14 (m, 2H), 7.81 (dd, J = 3.8, 1.1 Hz, 1H), 7.71 (dd, J = 5.0, 1.1 Hz, 1H), 7.48 (d, J = 8.8 Hz, 2H), 7.18 (dd, J = 4.9, 3.8 Hz, 1H), 4.32 (s, 2H).

2-(4-Nitrophenyl)pentan-3-one (3p). Compound is a colorless to pale yellow oil. Yield 33% (21 mg, 0,10 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.10 (m, 2H), 7.47−7.33 (m, 2H), 3.91 (q, J = 7.0 Hz, 1H), 2.42 (qd, J = 7.3, 4.1 Hz, 2H), 1.44 (d, J = 7.0 Hz, 3H), 0.99 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.8, 148.1, 147.1, 128.7, 124.0, 52.3, 34.9, 17.7, 7.8. HRMS (EI-MS) m/z: $[M]^+$ calcd for $C_{11}H_{13}NO_3$ 207.0895; found 207.0895.

2-(4-Nitrophenyl)cyclohexanone (3q).[5a] Yield 35% (23 mg, 0.11 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.13 (m, 2H), 7.36−7.27 (m, 2H), 3.73 (dd, J = 12.6, 5.3 Hz, 1H), 2.61−2.43 (m, 2H), 2.31 (ddd, J = 13.0, 5.5, 3.0 Hz, 1H), 2.26−2.16 (m, 1H), 2.11−1.94 (m, 2H), 1.93−1.75 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.7, 145.9, 145.3, 128.6, 122.5, 56.3, 41.2, 34.2, 26.7, 24.3.

2-(4-Nitrophenyl)acetaldehyde (3r).[29] Yield 26% (13 mg, 0.08 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.19 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 8.7 Hz, 2H), 3.83 (d, J = 1.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 139.3, 130.6, 124.1, 50.0.

2-(2-Nitrophenyl)-1-phenylethanone (3t).[30] Yield 70% (51 mg, 0.21 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.8 Hz, 1H), 8.04 (d, J = 7.4 Hz, 2H), 7.62 (t, J = 7.4 Hz, 2H), 7.50 (dd, J = 14.9, 7.4 Hz, 3H), 7.35 (d, J = 7.5 Hz, 1H), 4.74 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 136.5, 134.0, 133.7, 133.5, 130.7, 128.9, 128.8, 128.4, 128.3, 127.8, 125.33, 77.5, 77.0, 76.6, 44.2.

1-(4-Bromophenyl)-2-(2-nitrophenyl)ethanone (3u). Compound is a pale yellow solid. Mp: 83−86 °C. Yield 67% (46 mg, 0.56 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 8.2, 1.2 Hz, 1H), 7.95−7.86 (m, 2H), 7.70−7.64 (m, 2H), 7.62 (dd, J = 7.5, 1.3 Hz, 1H), 7.56−7.47 (m, 1H), 7.39−7.31 (m, 1H), 4.69 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 148.9, 135.2, 133.7, 133.66, 132.1, 130.3, 129.8, 128.7, 128.6, 125.4, 44.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{10}NO_3BrNa$ 341.9741 ; found 341.9736.

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2-(2-Nitrophenyl)-1-(thiophen-2-yl)ethanone (3v). Compound is an orange oil. Yield 62% (65 mg, 0.20 mmol) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 8.2, 1.0 Hz, 1H), 7.86 (dd, J = 3.8, 0.8 Hz, 1H), 7.69 (dd, J = 4.9, 0.8 Hz, 1H), 7.62 (m, 1H), 7.56−7.43 (m, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.19 (dd, J = 4.8, 3.9 Hz, 1H), 4.67 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.1, 143.3, 134.1, 133.7, 133.5, 132.4, 123.0, 128.6, 128.2, 125.3, 44.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}NO_3BrH^+$ 248.0376 ; found 248.0381.

General Procedure D: Reductive Cyclization. Indoles were prepared using a procedure described by Raucher and Koolpe.[5b] In a 50 mL round-bottom flask were dissolved 0.5 mmol of the ketone, 1.7 mmol (3.5 equiv) iron powder, and 0.5 mmol (1 equiv) sodium acetate in 3.5 mmol (7 equiv) acetic acid and 10 mL of 80:20 (v/v) ethanol/water. The mixture was heated to reflux under an atmosphere of nitrogen. After a reaction time of 2 h, the reaction mixture was cooled to room temperature, ethanol was evaporated, and the residue was extracted three times with dichloromethane. The organic layer were combined, washed with water and brine, and dried over potassium carbonate. Dichloromethane was evaporated, and the crude product was purified by column chromatography using a 1:1 mixture of hexane/dichloromethane containing 1−2% triethylamine as an eluent. To extract the residual triethylamine, the collected fraction was washed with 2 M HCl.

2-Phenyl-1*H*-indole (5a).[31] Yield 50% (48 mg, 0.25 mmol). ^{1}H NMR (400 MHz, DMSO) δ 11.19 (s, 1H), 7.88 (dd, J = 8.3, 1.1 Hz, 2H), 7.45 (m, 5H), 7.19 (m, 1H), 7.11−6.97 (m, 1H), 6.64 (d, J = 0.6 Hz, 1H).

2-(4-Bromophenyl)-1*H*-indole (5b).[32] Yield 95% (determined by NMR, corresponds to 0.47 mmol). ^{1}H NMR (400 MHz, DMSO) δ 11.45 (s, 1H), 7.91−7.81 (m, 2H), 7.71−7.63 (m, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.43 (dd, J = 8.2, 0.7 Hz, 1H), 7.24−7.14 (m, 1H), 7.09−7.01 (m, 1H), 6.68 (d, J = 0.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 135.5, 135.4, 131.4, 130.1, 129.4, 122.7, 121.9, 120.8, 120.2, 119.7, 108.8, 96.3.

2-(Thiophen-2-yl)-1*H*-indole (5c).[33] Yield 61% (determined by NMR, corresponds to 0.31 mmol). ^{1}H NMR (400 MHz, DMSO) δ 11.56 (s, 1H), 7.52 (ddd, J = 10.7, 6.5, 4.6 Hz, 3H), 7.36 (dt, J = 21.1, 10.5 Hz, 1H), 7.15 (m, 1H), 7.13−7.05 (m, 1H), 7.00 (td, J = 7.5, 1.0 Hz, 1H), 6.67 (d, J = 1.4 Hz, 1H).^{13}C NMR (101 MHz, DMSO) δ 136.7, 135.4, 132.3, 128.4, 128.0, 125.0, 123.4, 121.6, 119.8, 119.4, 111.0, 98.6.

TEMPO Trapping of Reactive Radical Intermediates. *Intermediate* ***12.*** To a 5 mL snap vial with a stirring bar were added 0.3 mmol *p*-nitrobenzene diazonium tetrafluoroborate, 5 mol % $[Ru(bpy)_3]Cl_2$, and 670 μL DMF. Quickly 1.2 equiv TEMPO was added, and the vial was sealed with a septum and degassed three times via "freeze-pump" method. The reaction mixture was stirred at 15 °C and irradiated for 2 h using blue LEDs (440 nm). After the irradiation the reaction mixture was worked up according to General Procedure C. ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.14 (d, J = 9.5 Hz, 2H), 7.4−7.1 (m, 2H), 1.67−1.56 (m, 5H), 1.46−1.42 (m, 1H), 1.23 (s,6H), 0.98 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.6, 141.0, 125.5, 114.1, 60.8, 39.6, 32.2, 20.4, 16.8. ESI-MS: 279.16 (MH+).

Intermediate ***11.*** To a 5 mL snap vial with a stirring bar were added with 0.3 mmol *p*-nitrobenzene diazonium tetrafluoroborate, 10 equiv isopropenyl acetate, 5 mol % $[Ru(bpy)_3]Cl_2$, and 670 μL DMF. Quickly 1.2 equiv TEMPO was added, the vial was sealed with a septum and degassed three times via "freeze-pump" method. The reaction mixture was stirred at 15 °C and irradiated for 2 h using blue LEDs (440 nm). After the irradiation the reaction mixture was submitted to mass spectroscopy (LC−MS) without further workup. ESI-MS: 380.2 (5), 379.2 (21), 268.1 (31), 266.1 (100).

■ ASSOCIATED CONTENT

Supporting Information

Mass spectra of the trapped intermediates, reduction potentials of several aryl diazonium salts, and NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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