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Photoredox Catalysis

Visible-Light Photoredox Alkylation of Heteroaromatic Bases Using Ethyl Acetate as Alkylating Agent

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Abstract: An efficient room-temperature visible-light photoredox α-acyloxyalkylation reaction of *N*-heteroarenes is reported, which relies on the use of ethyl acetate as a cheap and non-conventional radical source. The direct C(sp^2)-C(sp^3) coupling was extended to a diverse set of mono-, bi-, and tricyclic of *N*-heteroaromatics, and the optimized photoredox protocol was successfully performed on a multigram scale. The scope of the alkylating agent was also explored and a plausible mechanism was proposed, involving photoinduced single-electron transfer and hydrogen-atom transfer processes.

The strategy of using common organic solvents as radical precursors, however appealing, is only infrequently applied in organic synthesis.[1] Some examples utilizing toluene,[2–7] various ether and alcohol,[8–19] acetonitrile,[20–25] and *N*,*N*-dimethylformamide[26–30] derived radical synthons were reported. The common features of these transformations, besides the radical-chain mechanism, are the use of strong external oxidants, a stoichiometric amount of transition metals, and elevated temperatures respectively, resulting in narrow substrate scope and poor isolated yields.[1] It should be noted, that ethyl acetate as a radical source in organic reactions has barely been exploited so far.[31,32]

The pioneering work of Minisci and co-workers described the oxidative radical functionalization of lepidine via a cross-dehydrogenative coupling (CDC) using ethyl acetate, 1,4-dioxane, and methanol as coupling agents.[33] In general, solvents possessing a C(sp^3)-H bond adjacent to an oxygen atom (alcohol, ether, or ester) can be cleaved via a hydrogen atom transfer (HAT) process, and the corresponding radical can react with the heteroarenes directly (Figure 1a).[34–42]

Visible-light photoredox catalysis permits the mild and efficient generation of radicals. The Merck Research Laboratories developed a direct C–H functionalization of heteroarenes employing hydroxymethyl radicals generated from methanol under photoredox conditions (Figure 1b).[43] Upon alkoxyl radical formation and addition, various alcohols were found to undergo radical elimination of H_2O via Spin-Center-Shift (SCS) mechanism, resulting in alcohol C–O bond cleavage and the formation of a carbon-centered radical. Subsequent proton-coupled electron transfer (PCET) led to alkylated products instead of hydroxyalkyl derivatives (Figure 1c).[44,45]

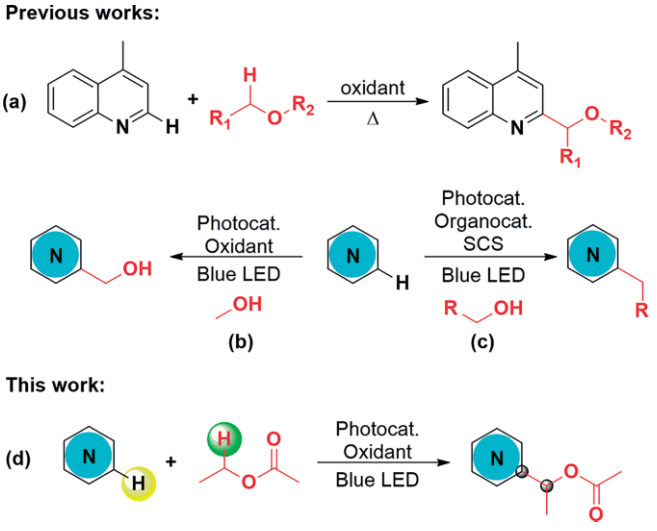

Figure 1. Cross-dehydrogenative couplings with solvents.

Based on this concept, Jin and MacMillan exploited the SCS-elimination for the photo- and organocatalyzed alkylation of heteroarenes using primary alcohols.[46] Their studies indicate that alkoxy radical generation under photoredox conditions is a viable option for the direct functionalization of heteroarenes. Our objective was to extend the photo-CDC-coupling to esters and suppressing the SCS-elimination obtain α-acyloxy-alkylated *N*-heterocycles that can serve as valuable synthetic intermediates (Figure 1d).

Our selected model reaction was the CDC coupling of lepidine (**1a**) with ethyl acetate (**2a**). First, we investigated the effect of the photocatalysts and the peroxide on the conversion and selectivity of the transformation in the presence of TFA. Among the catalysts tested, (Ir[dF(CF_3)ppy]$_2$(dtbpy))PF_6 (**PC-1**) showed the highest activity. Employing 2 equivalents of TFA

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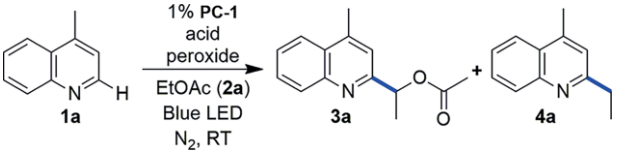
Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst	Peroxide	Acid	**3a** [%][b]	**3a/4a**[b]
1[a]	1 % **PC-1**	2 equiv. TBHP	2 equiv. TFA	28	4.6
2[a]	1 % **PC-1**	2 equiv. CHP	2 equiv. TFA	34	3.8
3[a]	1 % **PC-1**	2 equiv. TBPB	2 equiv. TFA	56	3.7
4[a]	1 % **PC-1**	2 equiv. TBPB	without TFA	0	–
5[a]	1 % **PC-1**	2 equiv. TBPB	0.2 equiv. TFA	67	17
6[a]	1 % **PC-1**	3 equiv. TBPB	0.2 equiv. CSA	21	25
7[a]	1 % **PC-1**	4 equiv. TBPB	0.2 equiv. CSA	99 [82][c]	60
8[d]	1 % **PC-1**	2 equiv. TBPB	0.2 equiv. CSA	0	–
9[e]	–	4 equiv. TBPB	0.2 equiv. CSA	12	n.d.
10[f]	1 % **PC-1**	4 equiv. TBPB	0.2 equiv. CSA	4	n.d.

[a] Reactions conditions: **1a** (0.5 mmol) in EtOAc (**2a**) (0.13 M), blue LEDs, N_2 atmosphere, room temperature, 1 h. [b] Conversion and selectivity were determined by HPLC using benzotrifluoride as internal standard. [c] Isolated yield on 3 mmol scale after 1 hour. [d] Absence of LED light, N_2 atmosphere, room temperature, 18 h. [e] Absence of PC-1, blue LEDs, N_2 atmosphere, room temperature, 18 h. [f] The reaction was performed in dark at 90 °C (closed vessel) for 1 h.

and *tert*-butyl hydroperoxide (TBHP) gave low conversion and selectivity for **3a** (Table 1, entry 1).

Changing the oxidizing agent to cumene hydroperoxide (CHP) did not improve the conversion, and the SCS-elimination as background reaction remained significant (Table 1, entry 2). In contrast, the treatment of **1a** with **2a** in the presence of *tert*-butyl peroxybenzoate (TBPB) and 2 equivalents of TFA under photoredox conditions resulted in an improved conversion, however, no further improvement of selectivity for **3a** was detected (Table 1, entry 3). Moreover, the reaction did not occur in the absence of TFA (Table 1, entry 4).

By decreasing the amount of TFA to 0.2 equivalent led to slightly improved conversion and good selectivity, although we still detected the formation of the SCS by-product **4a** (Table 1, entry 5). Furthermore, the application of 20 mol-% (1S)-(+)-10-camphorsulfonic acid (CSA) in the presence of 3 equivalents of TBPB led to lower conversion compared to entry 5 with moderately higher selectivity (Table 1, entry 6). By further increasing the amount of TBPB up to 4 equivalents, complete conversion, and an excellent product distribution profile was obtained, and **3a** was isolated in 82 % yield (Table 1, entry 7). Additional control experiments indicated that blue LED-light irradiation is essential for the α-acyloxyalkylation reaction, and in the absence of the photocatalyst a much slower conversion was observed (Table 1, entries 8–9). It should also be mentioned, that the alkylation occurs under thermal conditions with the exclusion of light, although at a significantly slower pace (Table 1, entry 10). Further details on the optimization studies including the photocatalyst, the nature and amount of the oxidant, the choice of the acid, and additional concentration studies are discussed in the Supporting Information.

With the optimized conditions in hand, we evaluated the scope of the photoredox α-acyloxyalkylation protocol. As shown in Scheme 1, a representative range of *N*-heteroaromatics was successfully converted to α-acyloxyalkylated products under mild conditions. It is important to note that the reaction rates varied from one substrate to the other, and the time required to reach high conversion (>90 %) is also presented on Scheme 1. Fortunately, we observed unremarkable levels of side reactions (SCS) in case of longer reaction times. The first set of compounds, 2,4-disubstituted, and condensed quinoline derivatives **3a**–**j** were isolated in moderate to good yields. For instance, 4-substituted quinolines (**1a**–**e**) were alkylated selectively in the 2-position. It was difficult to draw a direct correlation between the electron-donating ability of the substituents and the yields that varied in the range of 40–82 %. The best results were obtained for 4-methylquinoline (**1a**) and the condensed quinoline analog **1d**, and the corresponding products were isolated in 81 % and 65 % yield respectively. In the case of 2-substituted quinolines, the alkylation occurred in the 4-position selectively (**3f**–**j**). The electron-deficient 2-chloro analog gave the lowest yield (34 % for **3f**), while the 2-methyl derivatives gave similar yields (**3g**–**i**, 52–60 %) irrespective of the benzenoid substitution. 2-Phenylquinoline (**1j**) also fell into this category. Isoquinoline derivatives (**1k**–**p**) also performed well and showed regioselective coupling at C1, affording products **3k**–**3p** with yields up to 66 %. The isolated yields for most of the compounds covered a narrow range (48–66 %), while the most electron-rich dimethoxy analog (**1p**) was the only outlier providing product **3p** with a mediocre yield of 23 %. The procedure was also extended to the alkylation of bicyclic heteroarene scaffolds bearing two nitrogens (**1q**–**u**). 4-Chloroquinazoline derivatives with an electron-rich benzenoid part gave good yields (59 % for **3q** and 49 % for **3r**), whereas the less electron-rich analog (**3s**) was isolated in 33 % yield. Interestingly, we observed sequential radical alkylations during the photo CDC reactions in cases of **1t** and **1u** bearing two reactive positions. Quinazoline (**1t)** gave complete conversion after 18 hours, and a 1:20 mixture of monoalkylated and dialkylated products was formed along with a small amount of SCS side-products (less than 10 %) confirmed by LCMS. We were unable to isolate the monoalkylated product and **3t** was obtained in mediocre yield

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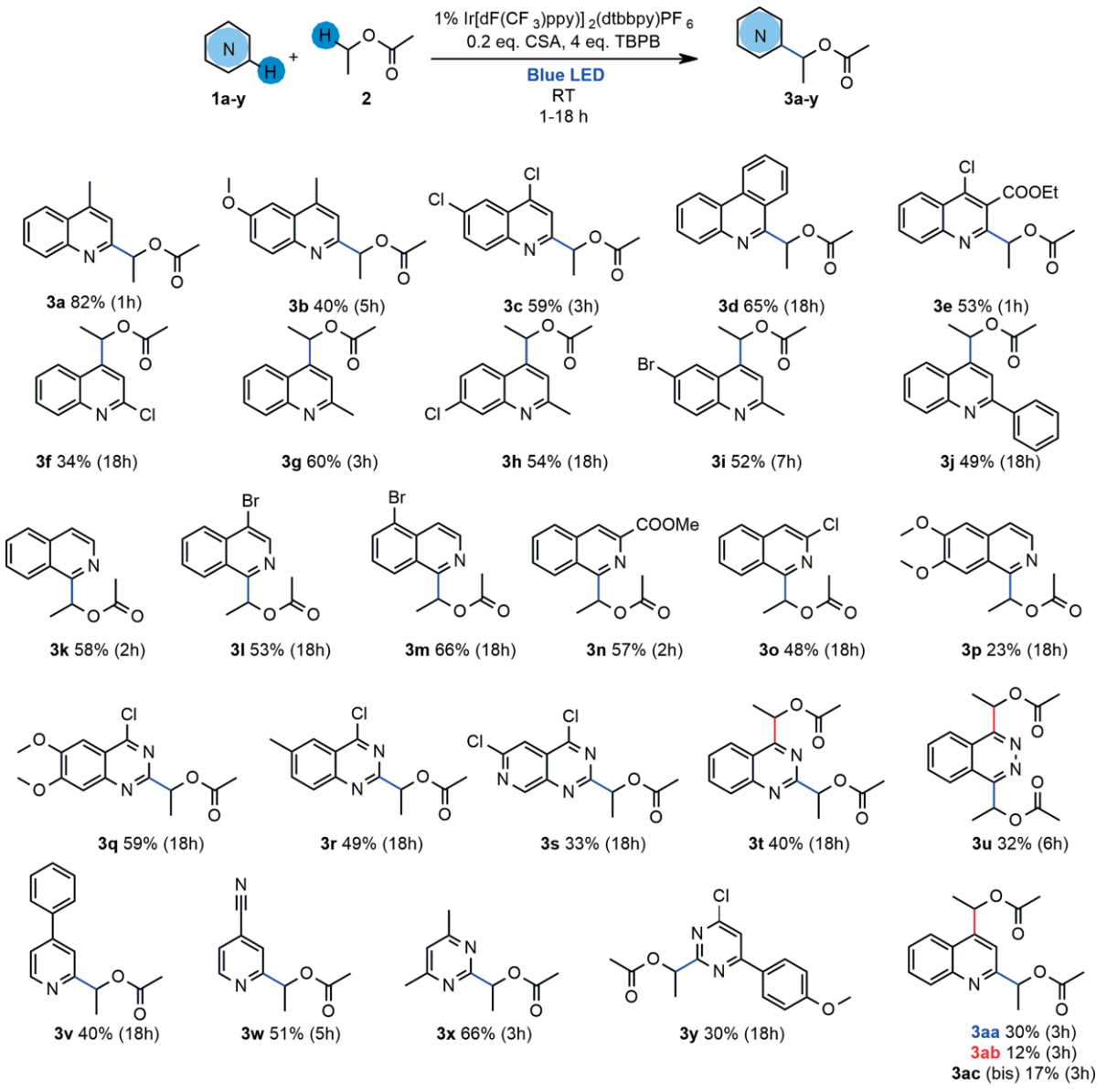
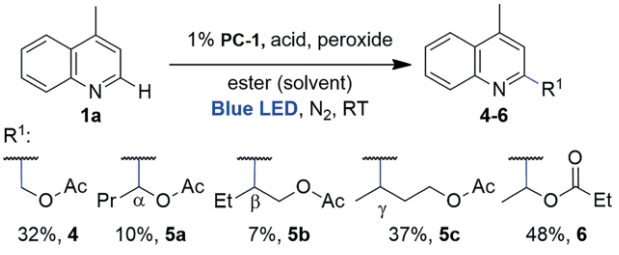


Scheme 1. Scope of the cross-dehydrogenative coupling of heteroarenes with EtOAc[a,b]; [a]Reactions conditions: **1** (2 mmol), TBPB (8 mmol) **PC-1** (0.02 mmol, 1 mol-%), CSA (0.2 mmol, 0.2 equiv.), EtOAc (12 mL), room temperature, 10 W blue LEDs, N_2. [b]Isolated yield.

(40 %). The reaction of **1u** was complete in 6 hours and a 37:63 mixture of monoalkylated and dialkylated products was formed, but only the dialkylated compound **3u** could be isolated in 32 % yield. Finally, six-membered α-acyloxyalkylated *N*-heterocycles, such as pyridine derivatives **3v** and **3w**, as well as pyrimidine derivatives **3x** and **3y** were isolated in 40–66 % yield. It is interesting to note that sequential dialkylation of **1y** that could have been anticipated following the example of **3t** was not observed; only the monoalkylated product **3y** was detected and isolated.

Having explored the scope of heteroaromatics we also examined the scope of esters as alkylating agents (Scheme 2.). Running the photo-CDC coupling of **1a** in methyl acetate furnished the expected α-acyloxyalkylated derivative **4** in 32 % yield.

However, when butyl acetate was employed as solvent and radical source, the photoalkylation resulted in a regioisomeric



Scheme 2. Alkylations with methyl-, butyl acetate, and ethyl propionate.

mixture. The product distribution (10 % C_α, 7 % C_β, 37 % C_γ) is in line with the fact that the less activated is the sp^3 CH-bond, the more preferred is the C-H abstraction.[47]

We also ran some control experiments to prove the radical nature of the transformation. In the presence of one equivalent

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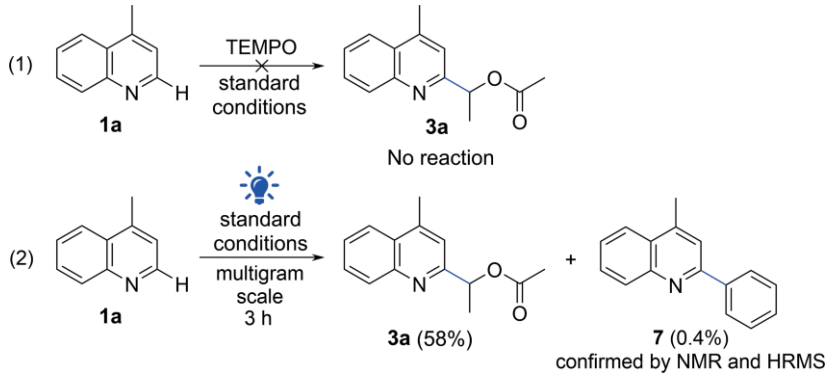
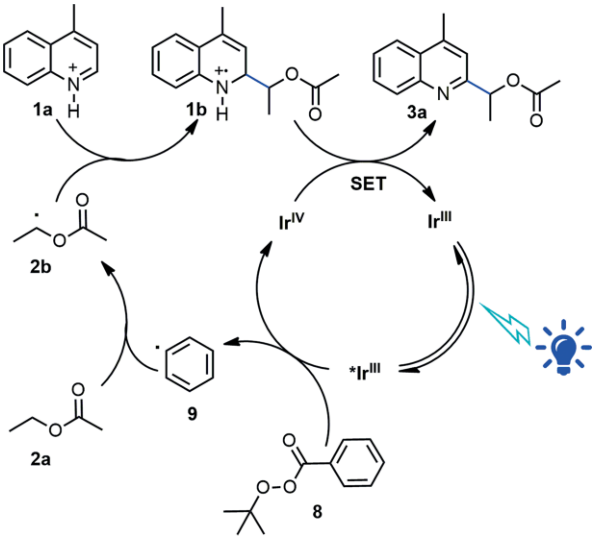


Scheme 3. Control experiments.

of TEMPO as a radical scavenger we didn't observe the formation of **3a** (Scheme 3.). To assess the robustness of the CDC photoalkylation reaction we devised a simple experimental setup (see Supporting Information for details) and performed the transformation of **1a** on the 5 g scale. The expected product (**3a**) was isolated in 58 % yield and 4-methyl-*2*-phenylquinoline (**7**) as minor by-product was isolated and confirmed by NMR and HRMS, supporting our proposed mechanism.

Based on the obtained experimental evidence and literature precedents we propose the mechanism for this coupling shown in Scheme 4. The excited state of Ir(III) complex may induce the photodecompostion of TBPB via single electron transfer (SET), resulting in the formation of a reactive phenyl radical species **9** and a transition Ir(IV) complex. Subsequent hydrogen atom transfer between **9** and ethyl acetate (**2a**) gives the α-acyloxyalkyl radical **2b**. Radical addition of **2b** to the heterocycle **1b** (activated by protonation), followed by a proton-coupled single electron transfer leads to product **3a** along with the regeneration of the Ir(III) complex.[43]



Scheme 4. Proposed mechanism for the HAT-induced α-acyloxyalkylation of heteroaromatic bases.

In summary, we have developed a photoredox α-oxyalkylation procedure using ethyl acetate as an unconventional radical source. Following the establishment of the optimal conditions and suppressing the undesired spin-center-shift elimination, a diverse collection of α-acyloxyalkylated *N*-heterocyclic compounds was synthesized and characterized. While methyl acetate gave a single product, using butyl acetate we obtained a multicomponent product mixture highlighting the limitations of this transformation. The robustness of the protocol was also demonstrated successfully running the transformation on the 5 g scale. Based on our observations and some control experiments a plausible mechanism was proposed, involving photoinduced SET and HAT processes.

Experimental Section

General Information: All reagents, solvents, and catalysts were commercially available and used without further purification. Purifications were carried out by forced-flow flash chromatography using pre-packed silica gel cartridges (RediSep R_f Gold) on a Teledyne CombiFlash RF 200 device. Thin-layer chromatography (TLC) was performed on TLC Silica gel 60 F_{254} 0.25 mm silica gel plates from Merck. Visualization of the developed chromatogram was performed by fluorescence quenching or $KMnO_4$ stain. Analytical LC-MS: Agilent HP1200 LC with Agilent 6140 quadrupole MS, operating in positive or negative ion electrospray ionization mode. Molecular weight scan range was 100 to 1350 *m/z*. Parallel UV detection was done at 210 nm and 254 nm. LCMS measurements Gemini-NX, 3 μm, C18, 50 mm × 3.00 mm i.d. column at 40 °C, at a flow rate of 1 mL/min using 5 mM aqueous NH_4HCO_3 solution and MeCN as eluents. Gas chromatography and low-resolution mass spectrometry were performed on Agilent 6850 gas chromatograph and Agilent 5975C mass spectrometer using 15 m × 0.25 mm column with 0.25 μm HP-5MS coating and helium as carrier gas. Ion source: EI^+, 70 eV, 230 °C, quadrupole: 150 °C, interface: 300 °C. UV purity of new compounds are >95 % unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance Ultrashield 500 (500 MHz ^1H and 124 MHz ^{13}C) instrument with Bruker Cryo Probe ATM and are internally referenced to residual protium solvent signals (note: [D_6]DMSO referenced at 2.52 and 39.98 ppm respectively). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. IR spectra were recorded with ATR mode on a Bruker Tensor 27 spectrometer and the spectra were reported in wavenumbers (cm^{-1}). High-resolution mass spectra were obtained on a Shimadzu IT-TOF mass spectrometer system, ion source temperature 200 °C, ESI +/–, ionization voltage: (+/–) 4.5 kV, mass resolution min. 10000.

OptiMelt MPA100 melting point apparatus was used for melting point measurements.

General Synthetic Procedure for Small Scale Reactions: An oven-dried 20 mL vial equipped with a septum and a Teflon magnetic stir bar was charged with $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (23.2 mg, 0.02 mmol, 0.01 equiv.), (1S)-(+)-10-camphorsulfonic acid (139 mg, 0.4 mmol, 0.2 equiv.) and heteroarene (2.00 mmol, 1.0 equiv.). The vial was evacuated and refilled with nitrogen three times before 12 mL of EtOAc (MeOAc or BuOAc) and *tert*-butyl peroxybenzoate (2.33 g, 2.3 mL, 8 mmol, 4 equiv.) were added by a syringe under constant nitrogen flow. The reaction mixture was degassed by sparging with nitrogen for 15 minutes at 10–15 °C. The mixture was then stirred vigorously and irradiated by a 10 W blue LED (approximately 0.5 cm between the light source and the vial) at room temperature. The progression of the reaction was monitored by LC-MS until no further conversion was detected (typically 18 hours). The reaction mixture was diluted with EtOAc (20 mL) and extracted with K_2CO_3 solution (20 mL, 10 m/m %). Then the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (1 × 20 mL), dried with Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel using a gradient program starting with heptane and gradually increasing the amount of added ethyl acetate to 20 % to afford the desired product.

Synthesis of Compound 3a on 5 g Scale: An oven-dried 250 mL Schlenk-tube equipped with a magnetic stir bar was charged with $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (392 mg, 0.35 mmol, 0.01 equiv.) and (1S)-(+)-10-camphorsulfonic acid (1.62 g, 7 mmol, 0.2 equiv.). The tube was sealed with a rubber septum, evacuated and refilled with nitrogen three times before adding dry EtOAc (250 mL), 4-methylquinoline (**1a**) (5.00 g, 4.6 mL, 35.0 mmol, 1.0 equiv.) and *tert*-butyl peroxybenzoate (27.2 g, 26.6 mL, 140 mmol, 4 equiv.) by a syringe under constant nitrogen flow. The reaction mixture was degassed by sparging with nitrogen for 15 minutes at 10–15 °C. The mixture was then stirred vigorously and irradiated by a blue LED source (see device B, approximately 5 cm between the light source and the Schlenk-tube) at room temperature. The reaction was monitored by LC-MS until no further conversion was detected (2–3 hours). The majority of the volatiles were removed to the volume of the mixture to 50 mL (***Caution: although we never experienced problem it is advised to carry out this operation behind a shield!***). The crude mixture was purified by flash chromatography on silica gel eluting with ethyl acetate/*n*-heptane gradient. Fractions containing **3a** were collected and evaporated to give the title compound **3a** (4.67 g, 20.3 mmol, 58 %) as a yellow oil.

Characterization Data for Compounds 3a–y, 4, and 5a–c

1-(4-Methyl-4-quinolyl)ethyl Acetate (3a): Following the General Synthetic Procedure starting from 4-methylquinoline (429 mg, 396 μL, 3 mmol), after 1 hour reaction time we obtained the title compound as yellow oil (563 mg, 82 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.10 (dd, *J* = 8.4 Hz and 1.0 Hz, 1H), 7.99 (dd, *J* = 8.4 Hz and 0.7 Hz, 1H), 7.77–7.74 (m, 1H), 7.63–7.60 (m, 1H), 7.44 (d, *J* = 0.8 Hz, 1H), 5.87 (q, *J* = 6.7 Hz, 1H), 2.71 (d, *J* = 0.9 Hz, 3H), 2.13 (s, 3H), 1.58 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.6, 161.0, 147.1, 145.9, 130, 129.8, 127.5, 126.8, 124.6, 119.1, 73.5, 21.5, 20.9, 18.8; IR: ν_{max} C=O 1734 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{14}H_{16}NO_2$: 230.1175, found 230.1175.

1-(6-Methoxy-4-methyl-2-quinolyl)ethyl Acetate (3b): Following the General Synthetic Procedure starting from 6-methoxy-4-methylquinoline (346 mg, 2 mmol), after 5 hours reaction time we obtained the title compound as white solid (204 mg, 40 % yield). ^{1}H NMR (500 MHz, DMSO): δ 7.89 (d, *J* = 9.2 Hz, 1H), 7.41–7.38 (m, 2H), 7.32 (d, *J* = 2.7 Hz, 1H), 5.84 (q, *J* = 6.7 Hz, 1H), 3.93 (s, 3H), 2.66 (s, 3H), 2.1 (s, 3H), 1.55 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.3, 157.9, 157.7, 144.4, 142.9, 131.2, 128.5, 122, 119.4, 102.9, 73.5, 56, 21.5, 20.9, 19.1; IR: ν_{max} C=O 1735 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{18}NO_3$: 260.1281, found 260.1287; Mp: 82.05–84.04 °C.

1-(4,6-Dichloro-2-quinolyl)ethyl Acetate (3c): Following the General Synthetic Procedure starting from 4,6-dichloroquinoline (396 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as white solid (334 mg, 59 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.19 (d, *J* = 2.3 Hz, 1H), 8.11–8.10 (m, 1H), 7.91 (dd, *J* = 2.3 Hz, *J* = 9.0 Hz, 1H), 7.89 (s, 1H), 5.87 (q, *J* = 6.7 Hz, 1H), 2.13 (s, 3H), 1.58 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.4, 162.1, 146.6, 141.6, 133.3, 132.2, 132.1, 126.1, 122.9, 120.2, 72.9, 21.4, 20.6; IR: ν_{max} C=O 1740cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{12}Cl_2NO_2$: 284.0240, found 284.0241; Mp: 97.11–99.14 °C.

1-Phenanthridin-6-ylethyl Acetate (3d): Following the General Synthetic Procedure starting from phenantridine (358 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as white solid (343 mg, 65 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.92 (d, *J* = 8.3 Hz, 1H), 8.81 (dd, *J* = 1.3 Hz and 8.2 Hz, 1H), 8.37 (d, *J* = 8.1 Hz, 1H), 8.08 (dd, *J* = 1.3 Hz and 8.2 Hz, 1H), 8.00–7.96 (m, 1H), 7.85–7.81 (m, 1H), 7.81–7.78 (m, 1H), 7.76–7.72 (m, 1H), 6.64 (q, *J* = 6.6 Hz, 1H), 2.1 (s, 3H), 1.72 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 131.1, 129.7, 129.0, 128.0, 127.4, 125.3, 123.1, 122.7, 70.0, 20.9, 19.3; IR: ν_{max} C=O 1733 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{17}H_{16}NO_2$: 266.1175, found 266.1182.

Ethyl 2-(1-Acetoxyethyl)-4-chloro-quinoline-3-carboxylate (3e): Following the General Synthetic Procedure starting from 4-chloroquinoline-3-carboxylate (472 mg, 2 mmol), after 1 hour reaction time we obtained the title compound as white solid (343 mg, 53 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.28–8.26 (m, 1H), 8.14–8.12 (m, 1H), 7.99–7.96 (m, 1H), 7.87–7.84 (m, 1H), 5.91 (q, *J* = 6.7 Hz, 1H), 4.51–4.40 (m, 2 H), 2.04 (s, 3H), 1.63 (d, *J* = 6.7 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.2, 165.4, 156.7, 147.3, 140, 132.8, 129.9, 129.8, 125.5, 124.6, 124.3, 72.5, 63.0, 21.1, 19.9, 14.3; IR: ν_{max} C=O 1740, 1722 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{17}ClNO_4$: 322.0840, found 322.0843; Mp: >300 °C (decomposition).

1-(2-Chloro-4-quinolyl)ethyl Acetate (3f): Following the General Synthetic Procedure starting from 2-chloroquinoline (326 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as colourless oil (170 mg, 34 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.23 (d, *J* = 8.7 Hz, 1H), 8.00 (dd, *J* = 0.8 Hz and 8.5 Hz, 1H), 7.88–7.84 (m, 1H), 7.74–7.70 (m, 1H), 7.53 (s, 1H), 6.47 (q, *J* = Hz 6.7 Hz, 1H), 2.15 (s, 3H), 1.6 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.2, 152.4, 150.4, 148, 131.5, 129.3, 128.1, 124.3, 124, 118.4, 68.3, 21.9, 21.3; IR: ν_{max} C=O 1733 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{13}ClNO_2$: 250.0629, found 250.0628; Mp: 83.00–86.34 °C.

1-(2-Methyl-4-quinolyl)ethyl Acetate (3g): Following the General Synthetic Procedure starting from 2-methylquinoline (286 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as yellow oil (274 mg, 60 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.10 (d, *J* = 8.5 Hz, 1H), 7.96 (dd, *J* = 8.5 Hz and 0.9 Hz, 1H), 7.75–7.71 (m, 1H), 7.59–7.56 (m, 1H), 7.41 (s, 1H), 6.45 (q, *J* = 6.6 Hz, 1H), 2.65 (s, 3H), 2.13 (s, 3H), 1.59 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.2, 159.2, 148.0, 147.8, 129.7, 129.6, 126.4, 123.6, 123.4, 118.0, 68.4, 25.4, 22.0, 21.4; IR: ν_{max} C=O 1736 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{14}H_{16}NO_2$: 230.1175, found 230.1174.

1-(7-Chloro-2-methyl-4-quinolyl)ethyl Acetate (3h): Following the General Synthetic Procedure starting from 7-chloro-2-methylquinoline (354 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as white solid (280 mg, 54 % yield). ^{1}H NMR (500 MHz, DMSO): δ ppm 8.17 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 2.2 Hz, 1H), 7.61 (dd, *J* = 9.0 and 2.2 Hz, 1H), 7.44 (s, 1H), 6.42 (q, *J* = 6.7 Hz, 1H), 2.66 (s, 3H), 2.13 (s, 3H), 1.57 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.2, 160.9, 148.6, 148.2, 134.4, 128.1, 127, 125.9, 122.1, 118.6, 68.4, 25.4, 22.0, 21.4; IR: ν_{max} C=O 1736 m^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{14}H_{15}ClNO_2$: 264.784, found 264.0787; Mp: 98.80–100.90 °C.

1-(6-Bromo-2-methyl-4-quinolyl)ethyl Acetate (3i): Following the General Synthetic Procedure starting from 6-bromo-2-methyl-quinoline (440 mg, 2 mmol), after 7 hours reaction time we obtained the title compound as white solid (319 mg, 52 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.34 (d, *J* = 2.0 Hz, 1H), 7.9 (d, 1H), 7.86 (dd, *J* = 8.9 Hz and 2.0 Hz, 1H), 7.45 (s, 1H), 6.43 (q, *J* = 6.7 Hz, 1H), 2.65 (s, 3H), 2.13 (s, 3H), 1.56 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.2, 160.0, 147.6, 146.7, 132.9, 131.8, 125.9, 124.8, 119.7, 119.0, 68.2, 25.4, 22.1, 21.4; IR: ν_{max} C=O 1731 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{14}H_{15}BrNO_2$: 308.0281, found 308.0275; Mp: 82.30–84.80 °C.

1-(2-Phenyl-4-quinolyl)ethyl Acetate (3j): Following the General Synthetic Procedure starting from 2-phenylquinoline (410 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as yellow oil (283 mg, 49 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.28–8.26 (m, 2 H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.13 (dd, *J* = 8.2 Hz and 0.8 Hz, 1H), 8.05 (s, 1H), 7.83–7.80 (m, 1H), 7.68–7.64 (m, 1H), 7.59–7.50 (m, 3H), 6.55 (q, *J* = 6.7 Hz, 1H), 2.16 (s, 3H), 1.68 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 169.8, 156.0, 148.6, 147.8, 138.5, 130.0, 129.9, 129.7, 128.9, 127.3, 126.8, 123.7, 123.3, 114.4, 68.4, 21.5, 20.9; IR: ν_{max} C=O 1737 cm^{-1}; HRMS (GC-TOF): *m/z* ([M]$^+$) calcd. for $C_{19}H_{17}NO_2$: 292.1259, found 292.1264.

1-(1-Isoquinolyl)ethyl Acetate (3k): Following the General Synthetic Procedure starting from isoquinoline (258 mg, 2 mmol), after 2 hours reaction time we obtained the title compound as colourless oil (248 mg, 58 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.47 (d, *J* = 5.7 Hz, 1H), 8.27 (d, *J* = 8.6 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.81–7.78 (m, 2H), 7.74–7.70 (m, 1H), 6.59 (q, *J* = 6.6 Hz, 1H), 2.04 (s, 3H), 1.64 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.3, 158.7, 141.9, 130.8, 128.3, 128.0, 124.7, 121.2, 70.1, 21.3, 20.0; IR: ν_{max} C=O 1732 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{14}NO_2$: 216.1019, found 216.1016.

1-(4-Bromo-1-isoquinolyl)ethyl Acetate (3l): Following the General Synthetic Procedure starting from 4-bromoisoquinoline (416 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as light yellow oil (310 mg, 53 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.74 (s, 1H), 8.37 (d, *J* = 8.5 Hz, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.00–7.97 (m, 1H), 7.87–7.83 (m, 1H), 6.57 (q, *J* = 6.6 Hz, 1H), 2.04 (s, 3H), 1.63 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.3, 159.0, 143.5, 134.6, 132.7, 129.6, 126.8, 126.6, 125.5, 119.2, 69.8, 21.3, 20; IR: ν_{max} C=O 1736 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{13}BrNO_2$: 294.0124, found 294.0115.

1-(5-Bromo-1-isoquinolyl)ethyl Acetate (3m): Following the General Synthetic Procedure starting from 5-bromoisoquinoline (416 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as pale white solid (390 mg, 66 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.63 (d, *J* = 5.9 Hz, 1H), 8.35 (d, *J* = 8.6 Hz, 1H), 8.18 (dd, *J* = 7.6 Hz and 0.8 Hz, 1H), 7.95 (dd, *J* = 5.9 Hz and 0.8 Hz, 1H), 7.67–7.64 (m, 1H), 6.6 (q, *J* = 6.6 Hz, 1H), 2.05 (s, 3H), 1.63 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.3, 159.7, 143.7, 135.1, 134.7, 129.1, 126.7, 124.9, 121.9, 119.4, 70.0, 21.3, 20.2; IR: ν_{max} C=O 1721 cm^{-1}, -CH 2985 cm-1; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{13}BrNO_2$: 294.0124, found 294.0118; Mp: 70.63–72.96 °C.

Methyl 1-(1-Acetoxyethyl)isoquinoline-3-carboxylate (3n): Following the General Synthetic Procedure starting from methyl isoquinoline-3-carboxylate (402 mg, 2 mmol), after 2 hours reaction time we obtained the title compound as white solid (313 mg, 57 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.62 (s, 1H), 8.39–8.37 (m, 1H), 8.27–8.25 (m, 1H), 7.92–7.86 (m, 2H), 6.58 (q, *J* = 6.7 Hz, 1H), 3.93 (s, 3H), 2.06 (s, 3H), 1.67 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.4, 165.9, 159.3, 140.2, 136.4, 131.6, 130.7, 129.7, 126.8, 125.0, 124.4, 70.5, 52.9, 21.3, 19.9; IR: ν_{max} C=O 1734 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{16}NO_4$: 274.1074, found 274.1071; Mp: 113.45–115.62 °C.

1-(3-Chloro-1-isoquinolyl)ethyl Acetate (3o): Following the General Synthetic Procedure starting from 3-chloroisoquinoline (326 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as light yellow solid (240 mg, 48 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.32 (d, *J* = 8.7 Hz, 1H), 8.02 (s, 1H), 8.00 (s, 1H), 7.86–7.83 (m, 1H), 7.75–7.72 (m, 1H), 6.54 (q, *J* = 6.6 Hz, 1H), 2.06 (s, 3H), 1.62 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.3, 160.4, 143.8, 138.9, 132.0, 128.8, 127.5, 125.1, 124.3, 120.4, 69.6, 21.3, 20.0; IR: ν_{max} C=O 1732 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{13}ClNO_2$: 250.0629, found 250.0634; Mp: 86.24–89.34 °C.

1-(6,7-Dimethoxy-1-isoquinolyl)ethyl Acetate (3p): Following the General Synthetic Procedure starting from 6,7-dimethoxyisoquinoline (378 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as colourless oil (127 mg, 23 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.29 (d, *J* = 5.5 Hz, 1H), 7.63 (d, *J* = 5.5 Hz, 1H), 7.45 (s, 1H), 7.38 (s, 1H), 6.55 (q, *J* = 6.6 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 2.05 (s, 3H), 1.63 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.4, 155.8, 152.8, 150.4, 140.7, 133.5, 121.6, 120.1, 106.2, 103.0, 70.3, 56.2, 56.0, 21.3, 19.6; IR: ν_{max} C=O 1717 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{18}NO_4$: 276.1230, found 276.1227.

1-(4-Chloro-6,7-dimethoxy-quinazolin-2-yl)ethyl Acetate (3q): Following the General Synthetic Procedure starting from 4-chloro-6,7-dimethoxyquinazoline (449 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as white solid (364 mg, 59 % yield). ^{1}H NMR (500 MHz, DMSO): δ 7.45 (s, 1H), 7.39 (s, 1H), 5.76 (q, *J* = 6.8 Hz, 1H), 4.01 (s, 3H), 3.99 (s, 3H), 2.10 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.4, 162.5, 158.8, 157.5, 151.8, 149.1, 117.7, 107.4, 102.8, 72.8, 57.1, 56.7, 21.3, 19.9; IR: ν_{max} C=O 1735 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{14}H_{16}ClN_2O_4$: 311.0793, found 311.0802; Mp: 115.36–119.15 °C.

1-(4-Chloro-6-methyl-quinazolin-2-yl)ethyl Acetate (3r): Following the General Synthetic Procedure starting from 4-chloro-6-methylquinazoline (357 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as white solid (257 mg, 49 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.05 (s, 1H), 7.99–7.95 (m, 2H), 5.80 (q, *J* = 6.8 Hz, 1H), 2.58 (s, 3H), 2.11 (s, 3H), 1.60 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (124 MHz, [D$_6$]DMSO) *δ* = 170.4, 163.2, 161.7, 149.6, 140.4, 138.5, 128.5, 124.5, 122.3, 72.8, 21.7, 21.3, 19.8; IR: ν_{max} C=O 1734 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{14}ClN_2O_2$: 265.0738, found 265.0733; Mp: 166.00–181.63 °C.

1-(4,6-Dichloropyrido[3,4-d]pyrimidin-2-yl)ethyl Acetate (3s): Following the General Synthetic Procedure starting from 4,6-dichloropyrido[3,4-d]pyrimidine (400 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as light yellow solid (146 mg, 33 % yield). ^{1}H NMR (500 MHz, DMSO): δ 9.33 (s, 1H), 8.22 (s, 1H), 6.77 (q, *J* = 6.7 Hz, 1H), 2.08 (s, 3H), 1.60 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): *δ* = 170.2, 163, 162/141.6, 155.2, 146.9,

129.6, 117.4, 67.8, 21.2, 19.9; IR: ν_{max} C=O 1731 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{11}H_{10}Cl_2N_3O_2$ 286.0144, found 286.0144; Mp: 163.66–177.08 °C (decomposition).

1-[2-(1-Acetoxyethyl)quinazolin-4-yl]ethyl Acetate (3t): Following the General Synthetic Procedure starting from quinazoline (260 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as yellow oil (242 mg, 40 % yield); ^{1}H NMR (500 MHz, DMSO): δ 8.34 (d, *J* = 8.4 Hz, 1H), 8.04–7.99 (m, 2H), 7.78–7.74 (m, 1H), 6.54–6.47 (m, 1H), 5.92–5.82 (m, 1H), 2.13 (d, *J* = 5.5 Hz, 3H) 2.09 (s, 3H), 1.67–1.59 (m, 6H); ^{13}C NMR (124 MHz, DMSO): δ = 170.4/170.3/170.2, 169.6/169.3, 164.2/164.0, 150.4/150.3, 135.0/129.0, 128.6/128.5, 124.9/124.8, 120.6/120.5, 73.1/73.0, 69.7/69.6, 21.3/21.1/21.0, 20/19.8; IR: ν_{max} C=O 1736 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{19}N_2O_4$: 303.1339, found 303.1341.

1-[4-(1-Acetoxyethyl)phthalazin-1-yl]ethyl Acetate (3u): Following the General Synthetic Procedure starting from phthalazine (260 mg, 2 mmol), after 6 hours reaction time we obtained the title compound as yellow oil (195 mg, 32 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.37–8.33 (m, 2 H), 8.10–8.07 (m, 2 H), 6.63–6.59 (m, 2 H), 2.07 (s, 6 H), 1.71 (d, *J* = 6.7 Hz, 6 H); ^{13}C NMR (124 MHz, DMSO): δ = 170.4, 158.2, 133.4, 124.6, 124.3, 69.7, 21.3, 19.9. IR: ν_{max} C=O 1724 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{19}N_2O_4$: 303.1339, found 303.1331.

1-(4-Phenyl-2-pyridyl)ethyl Acetate (3v): Following the General Synthetic Procedure starting from 4-phenylpyridine (310 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as yellow oil (192 mg, 40 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.59 (dd, *J* = 5.3 Hz and 0.6 Hz, 1H), 7.81–7.79 (m, 2H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.64 (dd, *J* = 5.2 and *J* = 1.8 Hz, 1H), 7.56–7.47 (m, 3H), 5.83 (q, *J* = 6.7 Hz, 1H), 2.09 (s, 1H), 1.55 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.3, 161.2, 150.1, 148.5, 137.7, 129.8, 129.7, 127.4, 120.9, 118.2, 73.0, 21.5, 20.9; IR: ν_{max} C=O 1731 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{16}NO_2$: 242.1176, found 242.1176.

1-(4-Cyano-2-pyridyl)ethyl Acetate (3w): Following the General Synthetic Procedure starting from isonicotinonitrile (208 mg, 2 mmol), after 5 hours reaction time we obtained the title compound as yellow oil (185 mg, 51 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.80 (dd, *J* = 5.0 Hz and 0.8 Hz, 1H), 7.91–7.90 (m, 1H), 7.81 (dd, *J* = 5.0 Hz and 1.5 Hz, 1H), 5.79 (q, *J* = 6.7 Hz, 1H), 2.11 (s, 3H), 1.50 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.3, 162.1, 150.7, 125.2, 122.6, 120.7, 117.2, 72.3, 21.4, 20.7; IR: ν_{max} C=O 1732 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{10}H_{11}N_2O_2$: 191.0815, found 191.0814.

1-(4,6-Dimethylpyrimidin-2-yl)ethyl Acetate (3x): Following the General Synthetic Procedure starting from 4,6-dimethylpyrimidine (316 mg, 2 mmol), after 3 hours reaction time, and using 20 % ethyl acetate – 80 % heptane as eluent we obtained the title compound as light yellow oil (258 mg, 66 % yield). ^{1}H NMR (500 MHz, DMSO): δ 7.14 (s, 1H), 5.61 (q, *J* = 6.7 Hz, 1H), 2.39 (s, 6H), 2.05 (s, 3H), 1.48 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.3, 167.8, 167.1, 119.1, 73.1, 23.9, 21.3, 20; IR: ν_{max} C=O 1734 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{10}H_{15}N_2O_2$: 195.1128, found 195.1130.

1-[4-Chloro-6-(4-methoxyphenyl)pyrimidin-2-yl]ethyl Acetate (3y): Following the General Synthetic Procedure starting from 4-chloro-5-(4-methoxyphenyl)pyrimidine (440 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as yellow oil (132 mg, 30 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.24–8.22 (m, 2H), 8.13 (s, 1H), 7.12–7.09 (m, 2H), 5.69 (q, *J* = 6.8 Hz, 3H), 3.81 (s, 3H), 2.13 (s, 3H), 1.57 (q, *J* = 6.8 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.4, 169.4, 165.4, 162.9, 161.8, 129.9, 127.5, 115.0, 114.9, 72.6, 56.0, 21.3, 19.9; IR: ν_{max} C=O 1738 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{16}ClN_2O_3$: 307.0844, found 307.0849.

1-(2-Quinolyl)ethyl Acetate (3aa): Following the General Synthetic Procedure starting from quinoline (258 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as yellow oil (131 mg, 30 % yield). ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ 8.40 (d, *J* = 8.5, 1H), 8.00–7.94 (m, 2H), 7.78–7.75 (m, 1 H), 7.62–7.59 (m, 1 H), 7.57 (d, *J* = 8.6 Hz, 1 H), 5.91 (q, *J* = 6.8 Hz, 1 H), 2.12 (s, 3 H), 1.58 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (124 MHz, [D$_6$]DMSO) δ = 170.4, 161.1, 147.2, 137.7, 130.3, 129.1, 128.4, 127.6, 127.0, 118.8, 73.5, 21.4, 20.9. IR ν_{max} C=O 1737 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{14}NO_2$: 216.1019, found 216.1019.

1-(4-Quinolyl)ethyl Acetate (3ab): Following the General Synthetic Procedure starting from quinoline (258 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as yellow oil (50 mg, 12 % yield). ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ 8.89 (d, *J* = 4.5 Hz, 1 H), 8.19 (dd, *J* = 8.7 Hz and *J* = 0.8 Hz, 1 H), 8.07 (dd, *J* = 8.4 Hz and *J* = 0.8 Hz,1 H), 7.83–7.79 (m, 1 H), 7.70–7.66 (m, 1 H), 7.53 (d, *J* = 4.5 Hz, 1 H), 6.51 (q, *J* = 6.4 Hz, 1 H), 2.14 (s, 3 H), 1.61 (d, *J* = 4.5 Hz, 3 H); ^{13}C NMR (124 MHz, [D$_6$]DMSO) δ = 170.2, 151.0, 148.2, 148.0, 130.3, 129.9, 127.4, 125.0, 123.8, 117.4, 68.4, 22.0, 21.4. IR ν_{max} C=O 1734 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{14}NO_2$: 216.1019, found 216.1019.

[(1)-1-[2-[(1)-1-Acetoxyethyl]-4-quinolyl]ethyl] Acetate (3ac): Following the General Synthetic Procedure starting from quinoline (258 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as yellow oil (105 mg, 17 % yield). ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ 8.18 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.82–7.78 (m, 1H), 7.69–7.65 (m, 1H), 7.53 (d, *J* = 4.3 Hz, 1H), 6.53–6.48 (m, 1H), 5.96–5.88 (m, 1H), 2.15–2.13 (m, 6H), 1.62–1.58 (m, 6H). ^{13}C NMR (124 MHz, [D$_6$]DMSO) δ = 170.4/170.3, 170.2/170.1, 161.0/160.8, 149.2/149.0, 147.5/147.5, 130.2/130.1, 129.7/129.0, 127.4/127.4, 124.4/124.3, 123.8, 114.5/114.1, 73.4, 68.6, 22.0, 21.4/21.3, 20.7. IR ν_{max} C=O 1736 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{17}H_{20}NO_4$: 302.1387, found 302.1390.

(4-Methyl-2-quinolyl)methyl Acetate (4): Following the General Synthetic Procedure starting from 4-methylquinoline (283 mg, 2 mmol), after 18 hours reaction time we obtained the title compound as colourless oil (138 mg, 32 % yield.). ^{1}H NMR (500 MHz, DMSO): δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.78–7.74 (m, 1H), 7.64–7.61 (m, 1H), 7.41 (s, 1H), 5.26 (s, 2H), 2.7 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.7, 156.5, 147.2, 145.7, 130.1, 129.6, 127.5, 126.9, 124.7, 120.3, 67.1, 21.2, 18.8; IR: ν_{max} C=O 1737 cm-1; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{13}H_{14}NO_2$ 216.1019, found 216.1020.

The Reaction of 4-Methylquinoloine with Butyl Acetate

Following the General Synthetic Procedure starting from 4-methylquinoline (283 mg, 2 mmol), after 18 hours of reaction time we obtained the following compounds.

1-(4-Methyl-2-quinolyl)butyl Acetate (5a): colourless oil (51 mg, 10 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.08 (dd, *J* = 8.3 Hz and 0.8 Hz, 1H), 7.97 (dd, *J* = 8.4 Hz and 0.7 Hz, 1H), 7.77–7.73 (m, 1H), 7.63–7.60 (m, 1H), 7.39 (d, *J* = 0.8 Hz, 1H), 5.77–5.74 (m, 1H), 2.70 (d, *J* = 0.9 Hz, 3H), 2.12 (s, 3H), 1.92–1.87 (m, 2H), 1.41–1.28 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.6, 145.7, 129.9, 129.7, 124.6, 119.3, 76.8, 36.9, 21.4, 18.9, 18.7, 14.1; IR: ν_{max} C=O 1740 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{20}NO_2$ 258.1489, found 258.1481.

2-(4-Methyl-2-quinolyl)butyl Acetate (5b): colourless oil (36 mg, 7 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.06 (dd, *J* = 8.3 Hz and

0.9 Hz, 1H), 7.95 (dd, *J* = 8.4 Hz and 0.7 Hz, 1H), 7.73–7.70 (m, 1H), 7.60–7.56 (m, 1H), 7.34 (d, *J* = 0.8 Hz, 1H), 4.36 (d, *J* = 7.1 Hz, 2H), 3.19–3.12 (m, 1H), 2.67 (d, *J* = 0.9 Hz, 3H), 1.91 (s, 3H), 1.83–1.75 (m, 2H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.8, 162.1, 147.7, 144.7, 129.6, 129.6, 127.2, 126.3, 124.6, 122.4, 67.1, 48.5, 24.8, 21.1, 18.7, 12.0; IR: ν_{max} C=O 1742 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{20}NO_2$ 258.1489, found 258.1493.

3-(4-Methyl-2-quinolyl)butyl Acetate (5c): colourless oil (190 mg, 37 % yield). ^{1}H NMR (500 MHz, DMSO): δ 8.04 (dd, *J* = 8.3 Hz and 0.9 Hz, 1H), 7.93 (dd, *J* = 8.4 Hz and 0.7 Hz, 1H), 7.72–7.69 (m, 1H), 7.58–7.54 (m, 1H), 7.33 (d, *J* = 0.8 Hz, 1H), 3.99–3.91 (m, 2H), 3.14–3.07 (m, 1H), 2.66 (d, *J* = 0.8 Hz, 3H), 2.19–2.12 (m, 1H), 1.97–1.90 (m, 4H), 1.30 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (124 MHz, DMSO): δ = 170.8, 165.5, 147.5, 144.9, 129.6, 129.5, 127.1, 126.1, 124.5, 121.4, 62.8, 39.0, 35.0, 21.2, 21.1, 18.7; IR: ν_{max} C=O 1739 cm^{-1}; HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{20}NO_2$ 258.1489, found 258.1492.

1-(4-Methyl-2-quinolyl)ethyl Propanoate (6): Following the General Synthetic Procedure starting from 4-methylquinoline (283 mg, 2 mmol), after 3 hours reaction time we obtained the title compound as colourless oil (235 mg, 48 % yield). ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ 8.09 (dd, *J* = 8.4 Hz and *J* = 1.0 Hz, 1H), 7.98 (dd, *J* = 8.4 Hz and *J* = 0.7 Hz, 1H), 7.78–7.74 (m, 1H), 7.64–7.61 (m, 1H), 7.42 (d, *J* = 0.8 Hz, 1H), 5.88 (q, *J* = 6.7 Hz, 1H), 2.71 (d, *J* = 0.8 Hz, 3H), 2.47–2.41 (m, 2H), 1.57 (d, *J* = 6.7 Hz, 3H), 1.06 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (124 MHz, [D$_6$]DMSO) δ = 173.6, 160.8, 147.1, 145.8, 130.0, 129.7, 127.5, 126.8, 124.6, 119.0, 73.4, 27.4, 21.0, 18.9, 9.5. IR ν_{max} C=O 1736 cm^{-1}, -CH 2982 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{15}H_{18}NO_2$: 244.1332, found 244.1332.

4-Methyl-2-phenylquinoline (7): Following the General Synthetic Procedure starting from 4-methylquinoline (5 g, 35 mmol), after 3 hours reaction time we obtained the title compound as colourless oil (31 mg, 0.4 % yield). ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ 8.29–8.27 (m, 2H), 8.12–8.05 (m, 3H), 7.80–7.76 (m, 1H), 7.65–7.61 (m, 1H), 7.58–7.51 (m, 3H), 2.78 (s, 3H); ^{13}C NMR (124 MHz, [D$_6$]DMSO) δ = 156.1, 147.9, 145.7, 139.2, 130.1, 130.0, 129.3, 127.6, 127.4, 126.8, 124.6, 119.7, 18.9. IR ν_{max} C=C 1598 cm^{-1}. HRMS: *m/z* ([M + H]$^+$) calcd. for $C_{16}H_{14}N$: 220.1121, found 220.1121.

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Keywords: Alkylation · C–H activation · Minisci reaction · Photocatalysis · Synthetic methods

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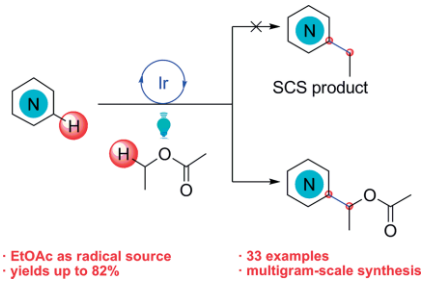
Photoredox Catalysis



The direct Csp^2-Csp^3 visible-light photoredox cross-dehydrogenative coupling of *N*-heteroaromatics with ethyl acetate via the generation of 1-acetoxyethan-1-yl radical is reported. This approach also uncovers ethyl acetate as a cheap and non-conventional radical source in photoredox related organic synthesis.

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