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Visible light-mediated Direct Decarboxylative Acylation of Electron Deficient Heteroarenes using α-Ketoacids

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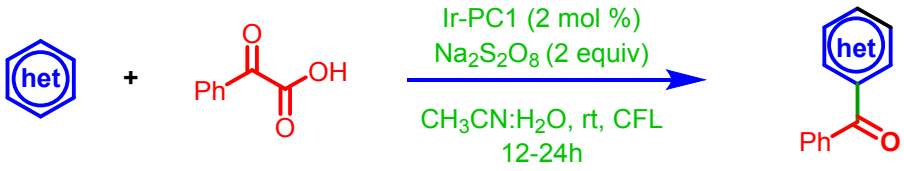


ABSTRACT: Acylation of electron deficient heteroaromatic compounds has been developed using visible light. α-Ketoacids have been used as an efficient source of acyl radicals under photoredox conditions. The in situ generated acyl radicals from α-ketoacids have been coupled to a wide variety of electron deficient heteroaromatic compounds in a Minisci type reaction. This method would be attractive to access biologically attractive molecules.

INTRODUCTION

Advances in photoredox catalysis are opening new avenues in organic synthesis as these methods offer excellent sustainability in functionalization of C-H bonds.[1] Formation of C-C bonds is facile in the light-mediated radical decarboxylation of carboxylic acids, which involves radical decarboxylative functionalization and extrusion of CO_2.[2] This method offers the advantage of using readily available acids. The initial and simultaneous efforts from MacMillan, Yoon and Stephenson groups' has made an emphatic emergence of the visible light mediated reactions in the field of synthetic organic chemistry.[3]

Acylation of heteroarenes has attracted chemists due to the occurrence of the acylated heterocyclic scaffold in various natural products and drugs (Fig 1).[4] While the acylation of electron-rich aryl system is facile and well established using metal catalysts,[5] acylation of heteroaromatic compounds is a challenging task.[6] Nevertheless, the acylation of heterocyclic compounds has been accomplished using acyl radicals employing Minisci reaction conditions.[7] The classical Minisci reaction involves the acylation of heteroarenes using α-keto acid under harsh reaction conditions, which limits its scope.[7] Therefore, several variations of Minisci reactions can be seen in the literature[5a, 8-10] for the acylation of heteroarenes. However, most of these reactions also involve harsh reaction conditions. There are many approaches to overcome these constraints with a varied degree of success (Scheme 1). Recently, Antonchick reported a metal-free CDC (cross dehydrogenative coupling) reaction of heteroarenes using $PhI(OCOCF_3)_2$ and $TMSN_3$.[5a] Soon after this report, our group has demonstrated acylation of

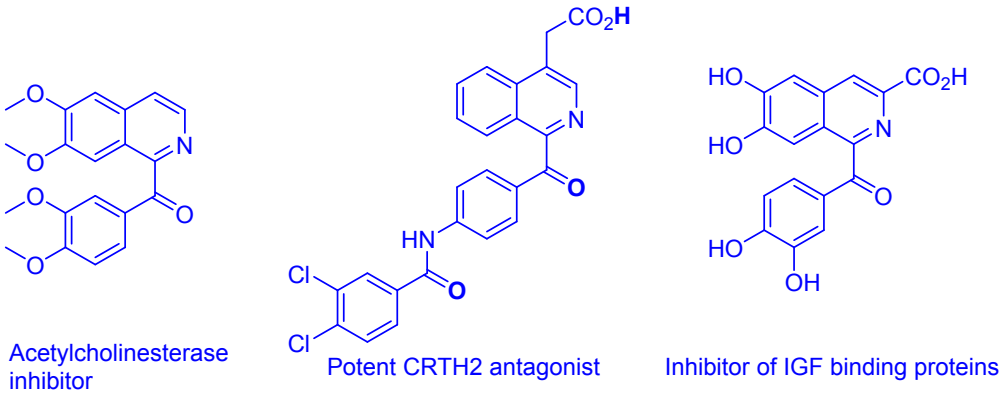
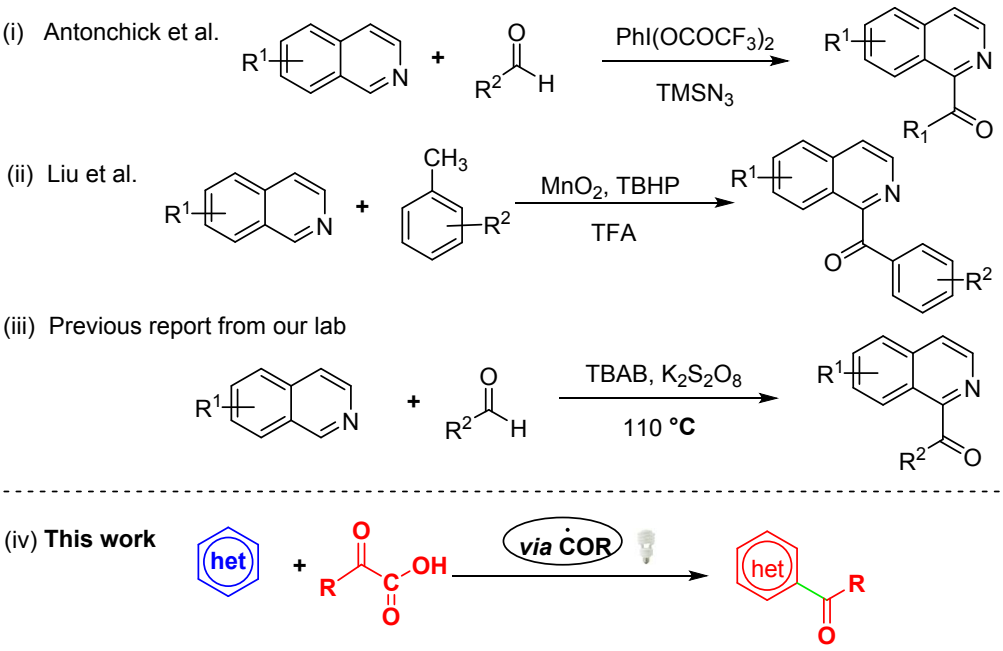


Figure 1. Bio-active Benzoyl Isoquinolines

electron- deficient heterocycles using TBAB/$K_2S_2O_8$ combination with aldehydes.[8] Subsequently there were a few more reports on acylation of electron deficient heteroarenes using aldehydes.[9] Liu and co-workers, as well as other groups, employed methyl arenes to acylate electron-deficient heteroarenes[10]. In order to achieve milder conditions, light-mediated reactions were designed which led to a variety of reactions such as the alkylation of heterocyclic compounds, C-C bond forming reactions, etc.[11] The transition-metal-catalyzed decarboxylative coupling strategies are attractive and useful reactions for the formation of C-C and C-hetero bonds. The Minisci reaction, generally, employs acyl radical,[12] but there are a few reports, which employed ketoacids as mild reactants for achieving the acylation of heterocyclic compounds.[12,13,14] We envisioned the utility of ketoacids as an effective source of the acyl radical under visible light conditions.

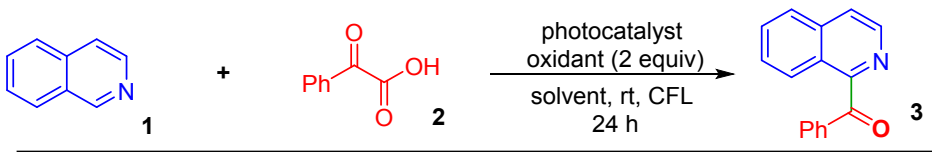
Scheme 1. Minisci C-H Acylation of *N*-Heteroarenes



RESULTS AND DISCUSSION

To verify this hypothesis, we subjected isoquinoline **1** to phenylglyoxalic acid **2** as an acylating reagent using 2 mol % of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**Ir-PC1,** $dF(CF_3)ppy$ = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine, dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine) as a photocatalyst and sodium persulfate as an oxidant under 5W blue LED irradiation using CH_3CN as a solvent (entry 1, Table 1). To our delight, the acylated isoquinoline **3** was obtained in 20% yield (^1H NMR yield). Further, solvent screening studies showed that a mixture of degassed CH_3CN and H_2O (1:1) is a better solvent system as it furnished the acylated product **3** in 65% yield (entries 2-6). The reaction of **1** with 2.4 equiv. of keto acid **2** furnished the product **3** in 66% yield (entry 7). The similar reaction of **1a** with **2** using $K_2S_2O_8$ for 24h furnished the product **3** in 64% yield (entry 8). The use of $[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$ (Ir-PC2) furnished the product **3** in 62% yield (entry 9). The reaction of **1** with **2** in the presence of Ir-PC1 using $K_2S_2O_8$ for 12h furnished the product **3** in 55% yield (entry 10). The similar reaction for 24h with low catalyst loading (1 mol%) resulted in the formation of the product **3** in 60% (entry 11), whereas increasing the catalyst loading to 3% was not of great use as this reaction rendered the product in 65% (entry 12). Ru(III)-Catalyst under the similar conditions furnished the product **3** in a low yield of 16% (entry 13). Oxidant screening studies showed that $Na_2S_2O_8$ is a better-suited oxidant whereas other oxidants such as $NH_4S_2O_8$, TBHP, benzoquinone, benzylperoxide, and $NaClO_2$ gave either diminished yields or furnished no product (entries 14). The reaction mixture, when irradiated under CFL, instead of blue LED, gave almost the same yield (65%, entry 15). Further control studies revealed that there was no reaction in the absence of light irradiation, or the oxidant, or the photocatalyst (entries 16-18).

Table 1. Optimization of the Decarboxylative Acylation of Isoquinoline[a]



entry	photocatalyst (mol %)	oxidant (2 equiv)	solvent	yield (%)[b]

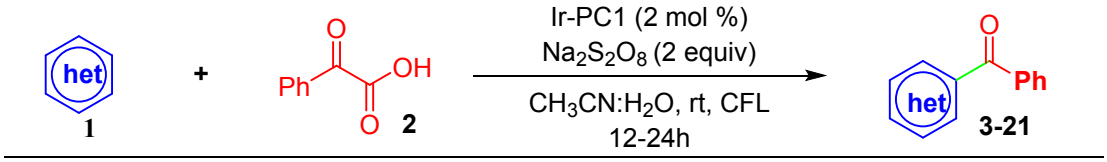
			(2 mL)	
1	Ir-PC1 (2)	$Na_2S_2O_8$	CH_3CN	20
2	Ir-PC1 (2)	$Na_2S_2O_8$	DMSO	12
3	Ir-PC1 (2)	$Na_2S_2O_8$	Toluene	5
4	Ir-PC1 (2)	$Na_2S_2O_8$	DCM	15
5	**Ir-PC1 (2)**	**$Na_2S_2O_8$**	**$CH_3CN:H_2O$ (1:1)**	**65 (56)[c]**
6	Ir-PC1 (2)	$Na_2S_2O_8$	$CH_3CH_2CN:H_2O$ (1:1)	54
7[d]	Ir-PC1 (2)	$Na_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	66
8	Ir-PC1 (2)	$K_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	64
9	Ir-PC2 (2)	$K_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	62
10 [e]	Ir-PC1(2)	$Na_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	55
11	Ir-PC1(1)	$K_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	60
12 [f]	Ir-PC1(3)	$K_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	65
13	$Ru(bpy)_3(PF_6)_2$ (2)	$K_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	16
14	Ir-PC1 (2)	other oxidants	$CH_3CN:H_2O$ (1:1)	trace[g]
15[h]	Ir-PC1 (2)	$Na_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	65
16[i,j]	Ir-PC1 (2)	$Na_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	4
17	Ir-PC1 (2)	none	$CH_3CN:H_2O$ (1:1)	0
18	none	$Na_2S_2O_8$	$CH_3CN:H_2O$ (1:1)	trace

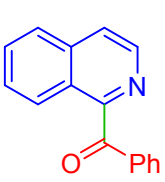
[a] General conditions: 1 (0.2 mmol, 1 equiv.), 2 (0.4 mmol, 2 equiv), **Ir-PC1** (0.004 mmol, 0.004 equiv.), oxidant (0.4 mmol, 2 equiv.) and $CH_3CN:H_2O$ (2 mL, 1:1 v/v). [b] Yields determined by ^1H NMR spectroscopy using terephthaldehyde as internal standard. [c] Isolated yield in the parentheses. [d] Ketoacid 2.5 equiv . [e]$Na_2S_2O_8$ 2.5 equiv. [f] Reaction time 12h. [g] $NH_4S_2O_8$, TBHP, BQ, BPO, and $NaClO_2$ furnished less than 15 % yields. [h].CFL light was used instead of LED. [i] Time: 6 h. [j] Reaction performed in the absence of light. (**Ir-PC1,** $dF(CF_3)ppy$ = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine, bpy = 2,2′-bipyridine). **Ir-PC2** = $[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$

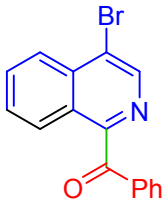
Having the optimized reaction conditions at hand (entry 2, Table 1), we explored the scope of the C-H acylation reaction with a variety of heteroarenes. As can be seen, electron-deficient heteroarenes were acylated at the most electrophilic position with phenylglyoxalic acid (Scheme 2). Isoquinoline with no substituent at the C4-position gave the desired product **3** in 56% isolated yield (entry 1), whereas 4-bromoisoquinoline and 5-bromoisoquinoline furnished the corresponding acylated products **4** and **5** in 70 and 76% yields, respectively. The reaction of 4-arylated isoquinolines with glyoxalic acid **2** was facile, and corresponding acylated products were obtained in good to excellent yields. Thus, 4-phenylisoquinoline furnished the acylated product **6** in 77% yield. The reaction of 4-(4-chlorophenyl)isoquinoline, 4-(4- ethylphenyl)isoquinoline, 4-(4-bromophenyl)isoquinoline, and 4-(4-(tert-butyl)phenyl)isoquinoline with glyoxalic acid was facile furnishing the corresponding acylated

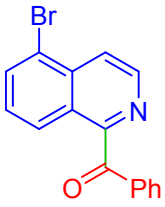
products **7**, **8**, **9**, and **10** in 76, 61, 54, , and 73% yields, respectively. The reaction of 4-(4-(phenylethynyl)phenyl)isoquinoline with **2** furnished the product **11** in 26% yield and the low yield may be attributed to the decomposition of the isoquinoline under the oxidative photoredox conditions. The reaction of 4-(2,4-difluorophenyl)isoquinoline, 4-(4-phenethylphenyl)isoquinoline, and 1-(4-(isoquinolin-4-yl)phenyl)ethan-1-one under the optimal reaction conditions furnished the corresponding acylated products **12**, **13**, and **14** in 89, 73, and 77% yields, respectively. Interestingly, the reaction of phenanthridine with glyoxalic acid was facile furnishing the corresponding acylated product **15** in 88% yield. The reaction was also successful with 4-(naphthalen-1-yl)isoquinoline furnishing the expected acylated product **16** in 79% yield. The acylation of the 4-cyanopyridine using the present strategy afforded the corresponding acylated product **17** 48% yield. Quiniloine derivatives underwent the acylation successfully. Thus, the acylation of 4,7-dichloroquinoline gave the corresponding acylated product **18** in 72% yield. 8-Methylisoquinoline was acylated successfully but furnished a mixture of mono- and diacylated products **19** and **20** in 46 and 35% yields, respectively. The acylation of quinoxaline is a difficult task. However, the acylation of quinoxaline under the optimal reaction conditions was facile furnishing the desired acylated product **21** in 47% yield. In most of the reactions wherein the yields are modest, it was observed that the starting materials were decomposed and no other side products were detected under the reaction conditions.

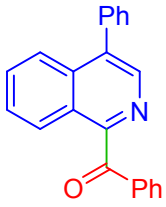
Scheme 2. Scope of Heteroarenes[a]

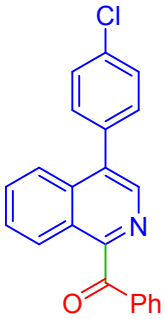


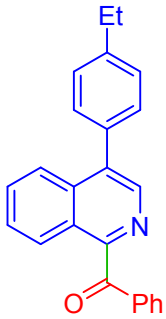

3, (56%)

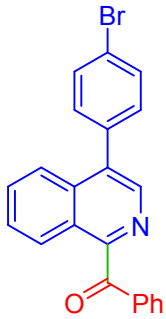

4, (70%, 67% [b])

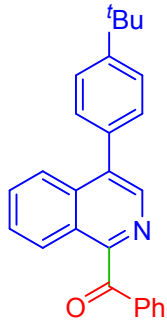

5, (76%)

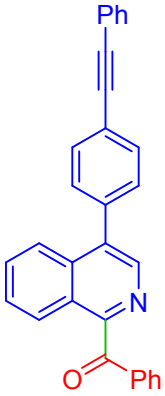

6, (77%)

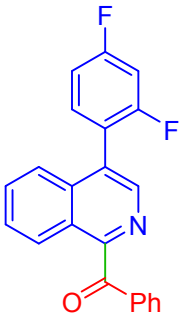

7, (76%)

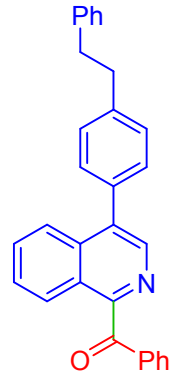

8, (61%)

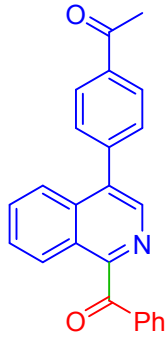

9, (54%)

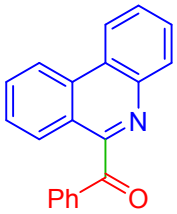

10, (73%)

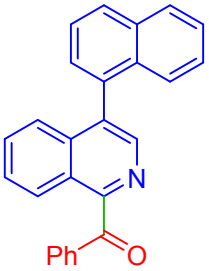

11, (26%)

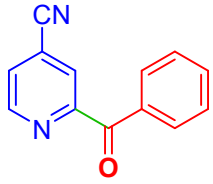

12, (89%)

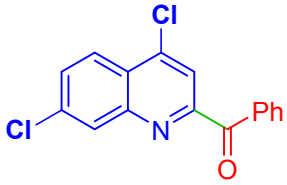

13, (73%)

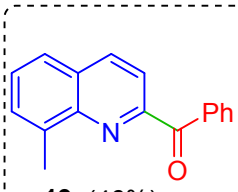

14, (77%)

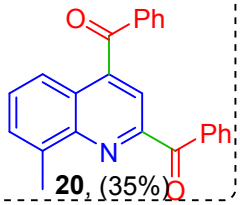

15, (88%)

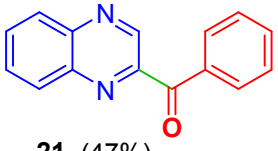

16, (79%)


17, (48%)


18, (72%)


19, (46%)

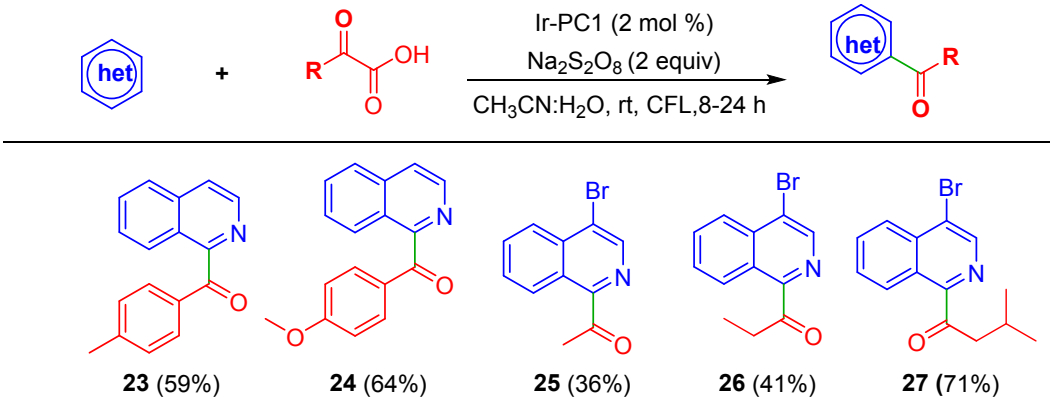

20, (35%)


21, (47%)

[a] Reaction conditions: Heteroarene (0.2 mmol), phenylglyoxalic acid (0.4 mmol), $Na_2S_2O_8$ (2 mmol), Ir-PC1 (0.004 mmol) in 2 mL CH_3CN:H_2O (1:1) under CFL for 24 h. [b] 5 mmol scale.

After exploring the scope for heteroarenes, we turned our attention to exploring the scope of the reaction with α-ketoacids for this decarboxylation reaction (Scheme 3). Thus, the reaction of 2-oxo-2-(*p*-tolyl)acetic acid and 2-(4-methoxyphenyl)-2-oxoacetic acid with isoquinoline under optimal reaction conditions gave the corresponding acylated products **22** and **23** in 59 and 64% yields, respectively. The reaction of aliphatic glyoxalic acids such as pyruvic acid, 2-oxobutyric acid ,and 4-methyl-2-oxovaleric acid with 4-bromoisoquinoline gave the corresponding acylated product **24, 25, 26** in 36, 41 and 71% yield respectively. The scaled up reaction of 4-bromoisoquinoline (5 mmol, 1.04 g) with phenylglyoxalic acid **2** (10 mmol, 1.50 g) under optimal reaction conditions afforded the acylated product **4** in 67% yield, which compares to the yield obtained on smaller scale (see Scheme 2).

Scheme 3. Scope of Glyoxalic acid[a]

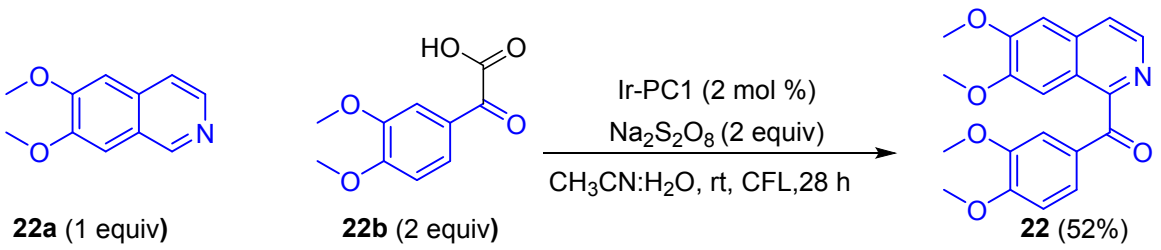


[a] Reaction conditions: Heteroarene (0.2 mmol), phenylglyoxalic acid (0.4 mmol), $Na_2S_2O_8$ (2 mmol), Ir-PC1 (0.004 mmol) in 2 mL CH_3CN:H_2O (1:1) under CFL for 24 h

To showcase the applicatioin of the methodology, we employed the present strategy to synthesize (6,7-dimethoxyisoquinolin-1-yl)(3,4-dimethoxyphenyl)methanone, which is a acetylcholinesterase inhibitor (Fig 1). Thus 6,7-dimethoxyisoquinoline (**22a**) was reacted with the keto acid 2-(3,4-dimethoxyphenyl)-

2-oxoacetic acid (22b**b**) under optimal conditions to obtain the acylated product **22** in 52% yield (Scheme 4).

Scheme 4. Synthesis of acetylcholinesterase inhibitor [a]

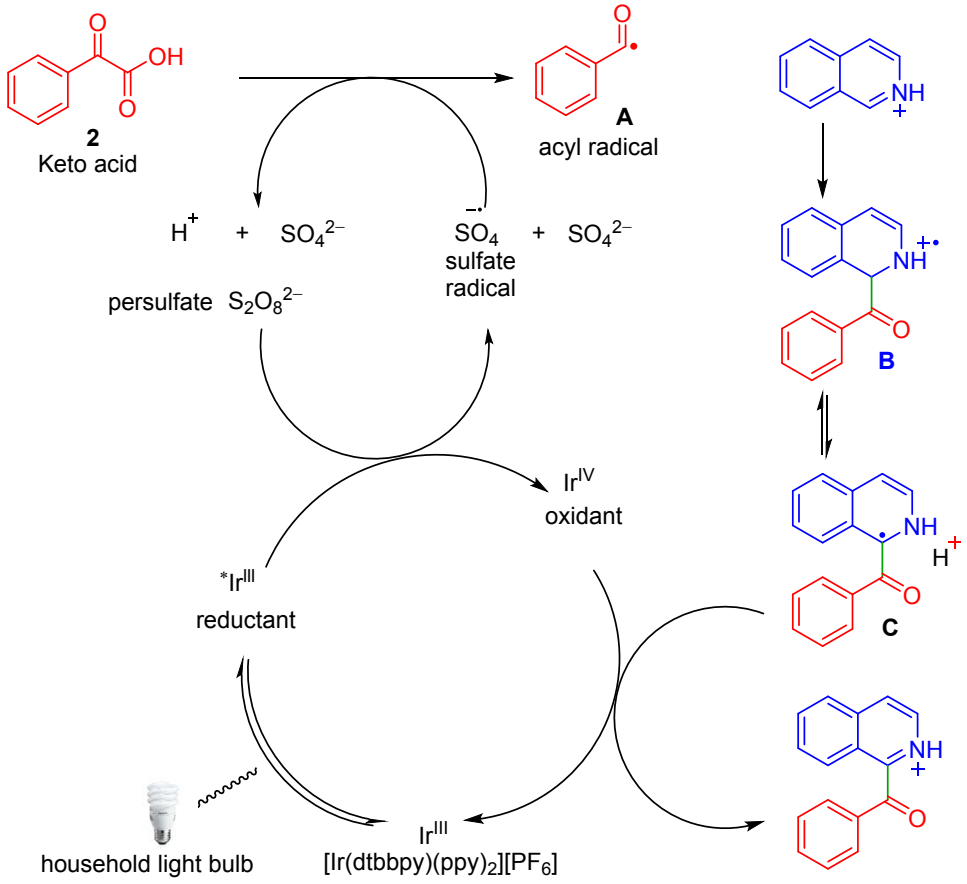


[a] Reaction conditions: **22a** (37.8 mg, 0.2 mmol), **22b** (84 mg, 0.4 mmol), $Na_2S_2O_8$ (95.6 mg, 2 mmol), Ir-PC1 (4.48 mg, 0.004 mmol) in 2 mL CH_3CN:H_2O (1:1) under CFL for 24 h

Once the scope of the reaction was explored, we attempted to understand the mechanism of this direct acylation reaction. A reaction of 4-bromoisoquinoline with phenylglyoxalic acid **2** in the presence of TEMPO (2 equiv) under optimal failed to furnish the expected product suggesting the possible involvement of acyl radical intermediate in the reaction. Based on the literature reports,[15] we present a tentative mechanism of the reaction here in Scheme 5. Photo-irradiation of photocatalyst $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**PC1**) under visible light from household light bulb (CFL) produces a long-lived photoexcited state $*[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$. The produced $*Ir^{III}$ is a strong reductant ($E_{1/2}^{IV/*III}$ = -0.88 vs SCE in MeCN/H_2O = 2:1)[16] and, it is capable of reducing the persulfate anion ($E_{1/2}$ = 1.75 V vs SCE)[17] to afford the oxidized iridium species (Ir^{IV}), sulfate dianion and sulfate radical anion. The acyl radical **A** is then generated through hydrogen-atom transfer (HAT) between the ketoacid **2** and the sulfate radical anion, followed by decarboxylation.[18] It was expected that the resulting acyl radical **A** would be sufficiently nucleophilic to add to the protonated (from the proton transfer between bisulfate anion and the heteroarene) electron deficient heteroarenes to produce the amine radical cation **B**. This cation **B** upon deprotonation would give α-amino radical **C**, which can take part in another

single electron transfer (SET) event with the oxidized iridium species Ir^{IV} ($Ir^{IV/III}$ = + 1.70V vs SCE in MeCN/H_2O = 2:1)[11] to regenerate the ground state photocatalyst and the desired acylated heteroarene.

Scheme 5. Proposed catalytic cycle



CONCLUSION

In summary, we have developed a photoredox catalytic approach to the direct acylation of electron deficient heteroarenes. This mild and efficient protocol can be applied to acylate a variety of isoquinoline, quinolone, phenanthridine, and pyridine derivatives. We anticipate this visible light mediated C-H functionalization protocol will find broad application in academic and pharmaceutical chemistry.

EXPERIMENTAL SECTION

General Information: All chemicals were purchased from commercial suppliers and used as delivered. $Pd(OAc)_2$ (product number: 10516) has been obtained from Alfa Aesar. Tricyclohexylphosphine (product number: 261971) was procured from Sigma Aldrich. THF (Finar AR dry grade) was used directly for all the procedures. ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm) and coupling constants in Hertz (Hz). Tetramethylsilane (TMS) (δ = 0.00 ppm) or residual $CHCl_3$ in $CDCl_3$ (δ = 7.26 ppm) served as internal standard for recording. ^1H NMR and the residual non-deuterated solvent signal of $CDCl_3$ (δ = 77.16 ppm) was used as internal standard for ^{13}C NMR (proton decoupled).[1,2] IR spectra were recorded using Perkin Elmer FT-IR instrument; Mass spectra (EI) were recorded using Shimadzu; and High-resolution mass spectra (HRMS) were recorded on Q-TOF (Micromass) spectrometer. Melting points of the product were determined on Buchi melting point apparatus. Flash column chromatography was carried out using commercially obtained silica gel and thin-layer chromatography (TLC) was performed using Merck silica gel 60 F_{254} TLC plates.

Preparation of starting isoquinolines

The isoquinoline (**3a**),[19a] and its derivatives 4-bromoisoquinoline (**4a**),[19b] 5-bromoisoquinoline (**5a**),[19c] phenanthridine (**15a**),[20a] isonicotinonitrile (**17a**),[20b] 8-methylquinoline (**19a**),[21] and quinoxaline (**21a**)[22] were procured from commercial sources and used as is. 4-Phenylisoquinoline (**6a**),[23a] 4-(4-chlorophenyl)isoquinoline (**7a**),[23b] 4-(4-ethylphenyl)isoquinoline (**8a**), 4-(4-bromophenyl)isoquinoline (**9a**),[23c] 4-(4-(tert-butyl)phenyl)isoquinoline (**10a**),[23a] 4-(phenylethynyl)isoquinoline (**11a**),[23d] 4-(2,4-difluorophenyl)isoquinoline (**12a**), 4-phenethylisoquinoline (**13a**),[23d] 1-(4-(isoquinolin-4-yl)phenyl)ethan-1-one (**14a**),[23e] 4-(naphthalen-1-yl)isoquinoline (**16a**),[23f] and 6,7-

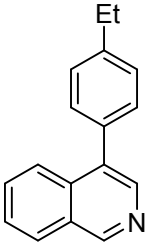
dimethoxyisoquinoline (**22a**)[8b] were prepared according to the modified reported methods, [23d,,23g] and the data were matched with reported values.

General procedure for preparation for 4-phenylisoquinolines

In an oven dried round bottom flask, 4-bromoisoquinoline (250 mg, 1.2 mmol, 1 equiv) was taken in a mixture of 1.5 mL of EtOH, 3 mL water and 6 mL toluene and degassed for 15 min. To the resulting mixture, phenylboronic acid (1.5 equiv), K_2CO_3 (4.8 mmol, 4 equiv) and $Pd(PPh_3)_4$ (0.06 mmol, 0.025 equiv) were added at r.t. The resulting mixture was stirred at 95 °C (oil bath) under argon atmosphere for 36h. The reaction mixture was cooled to r.t., quenched with saturated aq. NH_4Cl solution, extracted with CH_2Cl_2. The combined organic layer was collected, dried over Na_2SO_4, concentrated in vacuo to give crude product which was purified by flash column chromatography over silica using 20-30% EtOAc in petrolium ether as eluent to obtain 4-phenylisoquinolines as pure product.

Characterisation data for unknown 4-phenylisoquinolines:

4-(4-Ethylphenyl)isoquinoline (8a).

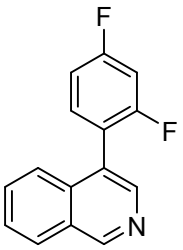


8a

Purified by silica gel (230-400 mesh) column chromatography using 20% EtOAc in petroleum ether. Reddish oil; Yield 83% (233.3 mg); R_f (20% EtOAc/Hexane) 0.4; **IR** (Neat, cm^{-1}) 2965, 1619, 1495, 1390; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.24 (s, 1 H), 8.48 (s, 1 H), 8.02 (d, J = 8.2 Hz, 1 H), 7.94 (d, J = 8.4 Hz, 1 H), 7.43 (d, J = 8 Hz, 2 H), 7.35 (d, J = 8 Hz, 2 H), 2.76 (q, J = 7.6 Hz, 2 H), 1.33 (t, J = 7.6 Hz, 3 H); **^{13}C NMR {^{1}H}** (100 MHz, $CDCl_3$): δ 151.7, 144.0, 142.8, 134.3, 134.2, 133.3, 130.4, 130.0,

129.4, 128.4, 128.1, 127.8, 127.0, 124.8, 28.6, 15.5; **HRESI-MS** (*m/z*) Calculated for $C_{17}H_{15}NH$ (M+H) 234.1283 found (M+H) 234.1285.

4-(2,4-Difluorophenyl)isoquinoline (12a).



12a

Purified by silica gel (230-400 mesh) column chromatography using 30% EtOAc in petroleum ether. Yellowish oil; Yield 89% (257.6 mg); R_f (20% EtOAc/Hexane) 0.3; **IR** (Neat, cm^{-1}) 3050, 1621, 1509; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.30 (s, 1 H), 8.47 (s, 1 H), 8.06-8.03 (m, 1 H), 7.71-7.62 (m, 3 H), 7.42-7.36 (m, 1 H), 7.07-6.98 (m, 2 H); **^{13}C NMR {^{1}H}** (100 MHz, $CDCl_3$): δ 163.1 (dd, J= 11.34, 248.7 Hz), 160.4 (dd, J=11.34, 248.7 Hz), 152.8, 143.5, 134.3, 133.0 (dd, J=4.9, 9.5 Hz), 130.8, 128.2, 127.9, 127.4, 126.6, 124.4, 120.5 (dd, J=4.1, 16.7 Hz), 111.7 (dd, J=3.8, 21.2 Hz) , 104.3 (dd, J=25.6, 25.6 Hz); **^{19}F NMR** (376 MHz,$CDCl_3$):δ 108.9 (d, *J* = 8.3 Hz), 109.2 (d, *J* = 8.3 Hz); **HRESI-MS** (*m/z*) Calculated for $C_{15}H_9F_2NH$ (M+H) 242.0781 found (M+H) 242.0785.

Typical general experimental procedure

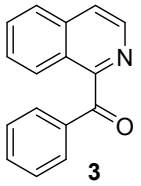
General procedure for visible light mediated acylation of heteroarenes: To an oven dried 8 mL vial containing a magnetic stirring bar, heteroarene (0.2 mmol, 1 equiv), arylglyoxalic acid (0.4 mmol, 2 equiv), sodium persulfate (0.4 mmol, 2 equiv) and $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (0.004 mmol, 2 mol%) were added. The vial was flushed with argon and closed with a PTFE cap followed by addition of 2 mL of CH_3CN:H_2O (1:1) to it via syringe. The resulted mixture was then degassed with argon for 15 min

and was kept stirring for 12 h under the irradiation of 2×27W Philips Tornado CFL bulb (at a distance of 5 cm from the bulb) with a fan above it. The mixture was then transferred in a round bottom flask with washing with EtOAc. CH_3CN were then removed under reduced pressure. To the residue, saturated $NaHCO_3$ was added and the aqueous phase was extracted 3 times with EtOAc. The combined organic layer was washed with brine followed by drying over sodium sulfate. The solvent was then removed under reduced pressure and the product was purified by flash column chromatography.

Experimental procedure for Scaling up reaction: To a oven dried 100 mL round bottom flask containing an oval shaped magnetic stirring bar, 4-bromoisoquinoline (5 mmol, 1 equiv), Phenylglyoxalic acid (10 mmol, 2 equiv), sodium persulfate (10 mmol, 2 equiv) and $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (0.1 mmol, 2 mol%) were added. The flask was flushed with argon and closed with a rubber septum followed by addition of 50 mL of CH_3CN:H_2O (1:1) to it via syringe. The resulted mixture was then degassed with argon for 20 min and was kept stirring for 24 h under the irradiation of 2×27W Philips Tornado CFL bulb with a fan above it. The mixture was then transferred in a round bottom flask with washing with EtOAc. CH_3CN were then removed under reduced pressure. To the residue, saturated $NaHCO_3$ was added and the aqueous phase was extracted 3 times with EtOAc. The combined organic layer was washed with brine followed by drying over sodium sulfate. The solvent was then removed under reduced pressure and the product was purified by flash column chromatography.

Characterization data for the products

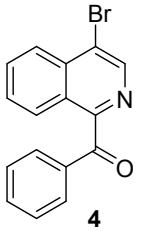
Isoquinolin-1-yl(phenyl)methanone (3).[24,25]



3

Prepared as described in the general experimental procedure. White solid; Yield 56% (26.1 mg); ***mp***: 74-76 °C (lit.[24] 74-75 °C); R_f (20%EtOAc/Hexane) 0.6; **IR** (KBr, cm^{-1}) 2923, 1670; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 5.3 Hz, 1 H), 8.22 (d, *J* = 8.2 Hz, 1 H), 7.96-7.92 (m, 3 H), 7.81 (d, *J* = 5.81 Hz, 1 H), 7.76-7.73 (m, 1 H), 7.64-7.59 (m, 2 H), 7.49-7.46 (m, 2 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ 194.7, 156.4, 141.1, 136.7, 136.6, 133.7, 130.7, 130.4, 128.5, 128.3, 127.1, 126.4, 126.2, 122.6; **HRESI-MS** (*m/z*) Calculated for $C_{16}H_{11}NONa$ (M+Na) 256.0738 found (M+Na) 256.0742.

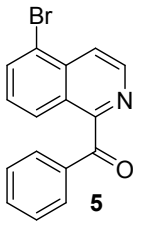
(4-Bromoisoquinolin-1-yl)(phenyl)methanone (4).



4

Prepared as described in the general experimental procedure. White solid; Yield 70% (43.6 mg); ***mp***: 131 °C (lit.[25] 129-130 °C) ; R_f (20%EtOAc/Hexane) 0.6; **IR** (KBr, cm^{-1}) 2962, 1666; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.80 (s, 1 H), 8.29 (d, *J* = 8.46 Hz, 1 H), 8.23 (d, *J* = 8.46 Hz, 1 H), 7.95-7.93 (m, 2 H), 7.88-7.84 (m, 1 H), 7.71-7.66 (m, 1 H), 7.64-7.60 (m, 1 H), 7.50-7.46 (m, 1 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ193.9, 155.7, 142.9, 136.3, 135.5, 133.9, 132.0, 130.7, 129.2, 128.5, 127.5, 126.6, 126.4, 121.7; **HRESI-MS** (*m/z*) Calculated for $C_{16}H_{10}BrNONa$ (M+Na) 333.9843 found (M+Na) 333.9845.

(5-Bromoisoquinolin-1-yl)(phenyl)methanone (5).

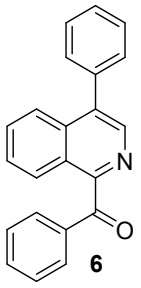


5

Prepared as described in the general experimental procedure. Colorless liquid; Yield 76% (47.5 mg); R_f (20%EtOAc/Hexane) 0.7; **IR** (KBr, cm^{-1}) 2922, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.71 (d, *J* =

5.69 Hz, 1 H), 8.20-8.17 (m, 2 H), 8.03 (d, *J* = 7.4 Hz, 1 H), 7.94-7.92 (m, 2 H), 7.64-7.60 (m, 1 H), 7.50-7.45 (m, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ 194.3, 156.8, 142.5, 136.3, 135.7, 134.4, 133.9, 130.7, 128.6, 128.5, 127.4, 125.9, 122.0, 121.4; **HRESI-MS** (*m/z*) Calculated for $C_{16}H_{10}BrNONa$ (M+Na) 333.9843 found (M+na) 333.9840.

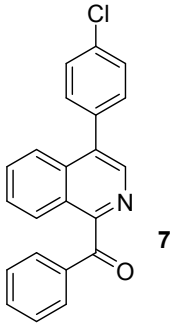
Phenyl(4-phenylisoquinolin-1-yl)methanone (6).[8]



6

Prepared as described in the general experimental procedure. Yellow liquid; Yield 77% (47.6 mg); R_f (20%EtOAc/Hexane) 0.6; **IR** (Neat, cm^{-1}) 2922, 1663; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.56 (s, 1 H), 8.30 (d, *J* = 8.32 Hz, 1 H), 8.03-7.99 (m, 3 H), 7.72-7.68 (m, 1 H), 7.64-7.60 (m, 2 H), 7.57-7.56 (m, 4 H), 7.53-7.48 (m, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.8, 140.9, 136.6, 136.5, 135.3, 135.1, 133.7, 130.8, 130.1, 128.7, 128.5, 128.3, 128.1, 126.3, 126.2, 125.4; **HRESI-MS** (*m/z*) Calculated for $C_{22}H_{15}NONa$ (M+Na) 332.1051 found (M+Na) 332.1053.

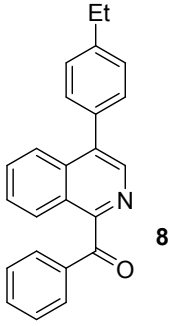
(4-(4-Chlorophenyl)isoquinolin-1-yl)(phenyl)methanone (7).



7

Prepared as described in the general experimental procedure. White solid; Yield 76% (52.3 mg); ***mp***: 148 °C; R_f (10%EtOAc/Hexane) 0.5; **IR** (Neat, cm^{-1}) 2924, 1656; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.52 (s, 1 H), 8.29 (d, *J* = 8.43, 1 H), 8.02-8.0 (m, 2 H), 7.96-7.94 (m, 1 H), 7.75-7.71 (m, 1 H), 7.67-7.61 (m, 2 H), 7.56-7.49 (m, 6 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.7, 156.1 , 140.9, 136.6, 135.0, 134.9, 134.6, 134.1, 133.8, 131.4, 131.0, 130.8, 129.0, 128.5, 128.2, 126.5, 126.2, 125.0; **HRESI-MS** (*m/z*) Calculated for $C_{15}H_{12}FNOH$ (M+H) 242.0981 found (M+H) 242.0981.

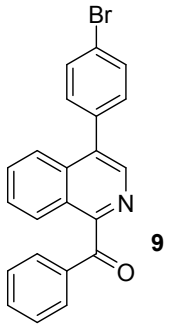
(4-(4-Ethylphenyl)isoquinolin-1-yl)(phenyl)methanone (8).



8

Prepared as described in the general experimental procedure. Yellow liquid; Yield 61% (41.2 mg); R_f(20%EtOAc/Hexane) 0.6; **IR** (KBr, cm^{-1}) 2964, 1668; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.55 (s, 1 H), 8.29 (d, *J* = 8.35 Hz, 1 H), 8.05-8.01 (m, 3 H), 7.71-7.68 (m, 1 H), 7.64-7.60 (m, 2 H), 7.54-7.47 (m, 4 H), 7.41-7.35 (m, 2 H), 2.78 (q, *J* = 7.52 Hz), 1.34 (t, *J* = 7.53 Hz); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ 194.9, 144.5, 141.0, 136.7, 135.4, 135.2, 133.8, 133.6, 130.8, 130.6, 130.1, 128.5, 128.2, 128.0, 126.3, 126.3, 125.5, 28.6, 15.5; **HRESI-MS** (*m/z*) Calculated for $C_{24}H_{19}NONa$ (M+Na) 360.1364 found (M + Na) 360.1366.

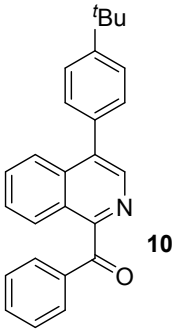
(4-(4-Bromophenyl)isoquinolin-1-yl)(phenyl)methanone (9).



9

Prepared as described in the general experimental procedure. Yellowish solid; Yield 54% (41.9 mg); ***mp***: 157 °C*;* R_f (20%EtOAc/Hexane) 0.7; **IR** (Neat, cm^{-1}) 3059, 1669; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.43 (s, 1 H), 8.20 (d, *J* = 8.33 Hz, 1H), 7.92-7.86 (m, 2 H), 7.85 (d, *J* = 8.47 Hz, 1H), 7.61-7.53 (m, 3 H), 7.42-7.40 (m, 2 H), 7.38-7.35 (m, 2 H), 7.33-7.16 (m, 2 H);; **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.6, 156.1, 140.8, 136.5, 135.4, 134.8, 134.0, 133.7, 131.9, 131.6, 131.0, 130.7, 128.5, 128.2, 126.4, 126.1, 124.9, 122.7; **HRESI-MS** (*m/z*) Calculated for $C_{16}H_{15}NOH$ (M+ H) 238.1232 found (M+H) 238.1232.

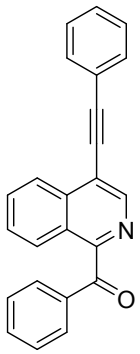
(4-(4-(*tert*-Butyl)phenyl)isoquinolin-1-yl)(phenyl)methanone (10).



10

Prepared as described in the general experimental procedure. White sticky liquid; Yield 73% (53.4 mg); R_f (20%EtOAc/Hexane) 0.7; **IR** (Neat, cm^{-1}) 2962, 1670; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.56 (s, 1 H), 8.29 (d, *J* = 8.44 Hz, 1 H), 8.06 (d, *J* = 8.41 Hz, 1 H), 8.03-8.01 (m, 2 H), 7.71-7.67 (m, 1 H), 7.63-7.57 (m, 4 H), 7.51-7.47 (m, 4 H), 1.42 (s, 9 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.8, 155.4, 151.3, 141.0, 136.7, 135.3, 135.1, 133.6, 130.8, 130.6, 129.8, 128.4, 128.0, 126.3, 125.6 125.5, 34.7, 31.3; **HRESI-MS** (*m/z*) Calculated for $C_{26}H_{23}NONa$ (M+Na) 388.1677 found (M+Na) 388.1674.

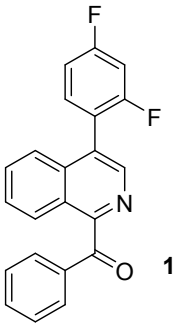
Phenyl(4-(phenylethynyl)isoquinolin-1-yl)methanone (11).



11

Prepared as described in the general experimental procedure. Yellow liquid; Yield 26% (17.3 mg); R_f (10%EtOAc/Hexane) 0.5; **IR** (Neat, cm^{-1}) 2922, 1666; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.83 (s, 1 H), 8.47 (d, J = 8.45 Hz, 1 H), 8.28 (d, J = 8.41 Hz, 1 H), 7.98-7.96 (m, 2 H), 7.88-7.84 (m, 1 H), 3.71-7.67 (m, 3 H), 7.61-7.61 (m, 1 H), 7.51-7.48 (m, 2 H), 7.46-7.43 (m, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.3, 155.3 , 144.4, 136.5, 136.4 , 133.8 , 131.9 , 131.4, 129.2 , 128.8, 128.6, 128.5 , 126.5, 125.7 , 125.6 122.5, 118.1, 98.3, 84.3; **HRESI-MS** (*m/z*) Calculated for $C_{24}H_{15}NONa$ (M+Na) 356.1051 found (M+Na) 356.1054.

(4-(2,4-Difluorophenyl)isoquinolin-1-yl)(phenyl)methanone (12).

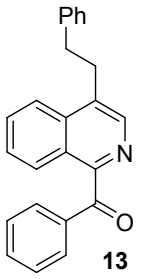


12

Prepared as described in the general experimental procedure. Brown liquid; Yield 89% (61.5 mg); R_f (20%EtOAc/Hexane) 0.6; **IR** (KBr, cm^{-1}) 3065, 1669; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.53 (s, 1 H), 8.28 (d, J = 8.50 Hz, 1 H), 8.02-8.00 (m, 2 H), 7.74-7.73 (m, 2 H), 7.66-7.61 (m, 2 H), 7.52-7.48 (m, 2 H), 7.46-7.42 (m, 1 H), 7.12-7.03 (m, 2 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.5, 163.3 (dd, J=12.0, 250.7 Hz), 160.3 (dd, J=12.7, 250.9 Hz), 156.6, 141.7, 136.4, 135.2, 133.7, 132.9 (dd, J = 5.1, 9.3 Hz),

131.0, 130.7, 128.5, 128.4, 128.2, 126.4, 126.0, 124.9 (d, J=1.05 Hz), 120.1 (dd, J=5.7, 14.7 Hz), 111.8 (dd, J=4.3, 20.9 Hz), 104.4 (dd, J=25.6 Hz); **^{19}F NMR** (376 MHz,DMSO-d_6):δ 108.62 (d, *J* = 8.2 Hz), 108.8 (dd, *J* = 8.2 Hz) **HRESI-MS** (*m/z*) Calculated for $C_{22}H_{13}F_2NONa$ (M+Na) 368.0863 found (M+Na) 368.0866.

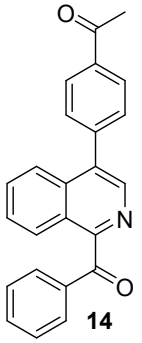
(4-Phenethylisoquinolin-1-yl)(phenyl)methanone (13).



13

Prepared as described in the general experimental procedure. Colorless liquid; Yield 73% (49.3 mg); R_f(10%EtOAc/Hexane) 0.6; **IR** (Neat, cm^{-1}) 2931, 1664; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.38 (s, 1 H), 8.28 (d, *J* = 8.56 Hz, 1 H), 8.13 (d, *J* = 8.52 Hz, 1 H), 7.94 (d, *J* = 7.54, 2 H), 7.80-7.76 (m, 1 H), 7.64-7.58 (m, 2 H), 7.48-7.44 (m, 2 H), 7.33-7.29 (m, 2 H), 7.24-7.21 (m, 3 H), 3.41 (t, *J* = 7.45 Hz, 2 H), 3.09 (t, *J* = 8.54 Hz, 2 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.8, 155.0, 140.9, 136.8, 135.3, 133.5, 133.0, 130.7, 130.6, 128.5, 128.4, 128.3, 127.8, 126.9, 126.3, 126.2, 123.1, 36.7, 32.3; **HRESI-MS** (*m/z*) Calculated for $C_{24}H_{19}NONa$ (M+Na) 360.1364 found (M+Na) 360.1365.

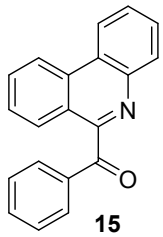
1-(1-Benzoylisoquinolin-4-yl)ethan-1-one (14).



14

Prepared as described in the general experimental procedure. Yellowish liquid; Yield 77% (54.1 mg); R_f(40%EtOAc/Hexane) 0.6; **IR** (KBr, cm^{-1}) 2962, 1670; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.56 (s, 1 H), 8.30 (d, *J* = 8.39 Hz, 1 H), 8.16 (d, *J* = 8.05 Hz, 2 H), 8.02-8.00 (m, 2 H), 7.95 (d, *J* = 8.42 Hz, 1 H), 7.76-7.72 (m, 1 H), 7.69-7.62 (m, 4 H), 7.51 (t, *J* = 7.81 Hz, 2 H), 2.71 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 197.6, 194.6, 156.4, 141.4, 140.8, 136.8, 136.5, 134.7, 134.1, 133.8, 131.1, 130.7, 110.4, 128.7, 128.5, 128.3, 126.5, 126.1, 124.9, 26.7; **HRESI-MS** (*m/z*) Calculated for $C_{24}H_{17}NO_2Na$ (M+Na) 374.1157 found (M+Na) 374.1156.

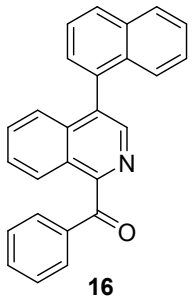
Phenanthridin-6-yl(phenyl)methanone (15).



15

Prepared as described in the general experimental procedure. Colorless liquid; Yield 88% (49.9 mg); R_f (10%EtOAc/Hexane) 0.6; **IR** (Neat, cm^{-1}) 2927, 1673; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.69 (d, *J* = 8.47 Hz, 1 H), 8.63 (d, *J* = 8.08 Hz, 1 H), 8.21 (d, *J* = 7.40 Hz, 1 H), 8.13 (d, *J* = 8.18 Hz, 1 H), 8.03 (d, *J* = 8.05 Hz, 2 H), 7.89-7.85 (m, 1 H), 7.70-7.73 (m, 2 H), 7.66-7.59 (m, 2 H), 7.48-7.45 (m, 2 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.7, 157.4, 142.6, 136.1, 134.0, 133.2, 131.2, 126.5, 130.8, 130.6, 129.1, 128.8, 128.5, 128.1, 127.8, 127.3, 124.4, 123.7, 122.3, 122.1; **HRESI-MS** (*m/z*) Calculated for $C_{20}H_{13}NONa$ (M+Na) 306.0895 found (M + Na) 306.0895.

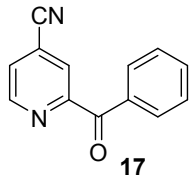
(4-(Naphthalen-1-yl)isoquinolin-1-yl)(phenyl)methanone (16).



16

Prepared as described in the general experimental procedure. Yellow liquid; Yield 79% (56.8 mg); R_f(20%EtOAc/Hexane) 0.8; **IR** (KBr, cm^{-1}) 2927, 1669; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.63 (s, 1 H), 8.33 (d, *J* = 8.25 Hz, 1 H), 8.08 (d, *J* = 8.4 Hz, 1 H), 8.03-7.96 (m, 2 H), 7.65-7.59 (m, 3 H), 7.56-7.49 (m, 6 H), 7.44-7.42 (m, 1 H), 7.38-7.34 (m, 1 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.8, 156.1, 141.9, 136.6, 136.4, 134.1, 133.9, 133.7, 133.5, 132.6, 130.8, 130.7, 128.9, 128.5, 128.4, 128.3, 128.2, 126.5, 126.3, 126.2, 126.0, 125.4; **HRESI-MS** (*m/z*) Calculated for $C_{26}H_{17}NOH$ (M+H) 360.1388 found (M+H) 360.1385.

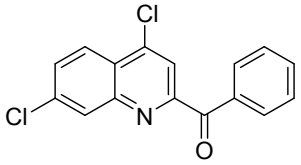
2-Benzoylisonicotinonitrile (17).[12]



17

Prepared as described in the general experimental procedure. Yellow liquid; Yield 48% (19.9 mg); R_f (30%EtOAc/Hexane) 0.4; **IR** (Neat, cm^{-1}) 2927, 1669; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.91 (d, *J* = 4.89 Hz, 1 H), 8.28 (s, 1 H), 8.09-8.06 (m, 2 H), 7.73 (dd, J_1 = 4.94 Hz, J_2 = 1.45 Hz, 1 H), 7.65 (t, *J* = 7.46 Hz, 1 H), 7.54-7.50 (m, 2 H); **^{13}C {^{1}H} NMR** (100 MHz, $CDCl_3$):δ 191.6, 156.1, 149.4, 135.1, 133.6, 131.0, 128.4, 127.2, 126.4, 121.9, 115.8; **HRESI-MS** (*m/z*) Calculated for $C_{13}H_8N_2ONa$ (M+Na) 231.0534 found (M+Na) 231.0543.

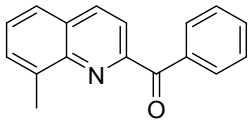
(4,7-Dichloroquinolin-2-yl)(phenyl)methanone (18).



18

Prepared as described in the general experimental procedure. White solid; Yield 72% (43.5 mg); ***mp***: 148-149 °C; R_f (10%EtOAc/Hexane) 0.7; **IR** (KBr, cm^{-1}) 3071, 1656; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.24-8.18 (m, 5 H), 7.70-7.62 (m, 2 H), 7.54-7.50 (m, 2H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 192.0, 155.3, 147.8, 143.9, 137.1, 135.4, 133.4, 131.3, 130.3, 129.6, 128.2, 125.5, 125.4, 121.1; **HRESI-MS** (*m/z*) Calculated for $C_{16}H_9Cl_2NOH$ (M+H) 302.0139 found (M+H) 302.0138.

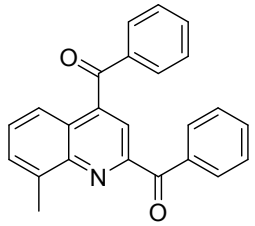
(8-Methylquinolin-2-yl)(phenyl)methanone (19).[25]



19

Prepared as described in the general experimental procedure. Colorless liquid; Yield 46% (22.7 mg); ***mp***: 71 °C (lit.[25] 63-64 °C) ; R_f (20%EtOAc/Hexane) 0.5; **IR** (KBr, cm^{-1}) 2921, 1659; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.36 (d, *J* = 7.35 Hz, 2 H), 8.31 (d, *J* = 8.44 Hz, 1 H), 8.18 (d, *J* = 8.45 Hz, 1H), 7.75-7.70 (m, 1 H), 7.64-7.60 (m, 2 H), 7.57-7.50 (m, 3 H), 2.78 (s, 3H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 193.5, 153.0, 145.8, 138.8, 137.2, 136.5, 132.7, 132.4, 131.7, 130.9, 130.1, 129.0, 128.8, 128.3, 127.8, 125.5, 120.4, 17.9; **HRESI-MS** (*m/z*) Calculated for $C_{17}H_{13}NONa$ (M+Na) 270.0895 found (M+Na) 270.0889.

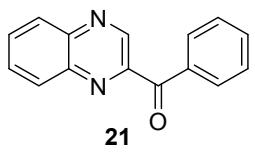
(8-Methylquinoline-2,4-diyl)bis(phenylmethanone) (20).



20

Prepared as described in the general experimental procedure. Yellow liquid; Yield 35% (24.6 mg); ***mp***: 138 °C; **IR** (KBr, cm^{-1}) 2922, 1664; R_f (40% EtOAc/Hexane) 0.6; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.37 (d, J = 7.38 Hz, 2 H), 8.19 (s, 1 H), 7.88 (d, J = 7.53 Hz, 2 H), 7.78 (d, J = 8.25 Hz, 1 H), 7.69-7.63 (m, 3 H), 7.55-7.47 (m, 5 H), 2.83 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 196.0, 192.7, 152.1, 146.2, 145.7, 139.4, 136.4, 136.1, 134.3, 132.9, 131.6, 130.6, 130.3, 129.4, 128.8, 127.9, 125.7, 123.1, 118.9, 18.3; **HRESI-MS** (*m/z*) Calculated for $C_{24}H_{17}NO_2Na$ (M+Na) 374.1157 found (M+Na) 374.1161.

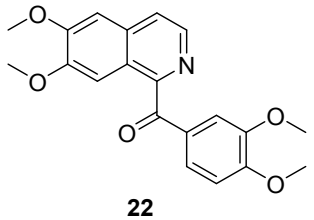
Phenyl(quinoxalin-2-yl)methanone (21).[25]



21

Prepared as described in the general experimental procedure. Colorless liquid; Yield 47% (22 mg); **IR** (KBr, cm^{-1}) 2928, 1726; R_f (40% EtOAc/Hexane) 0.6; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 9.50 (s, 1 H), 8.26-8.23 (m, 3 H) 8.21-8.20 (m, 1 H), 7.94-7.87 (d, 2 H), 7.70-7.66 (m, 1 H), 7.57-7.53 (m, 2 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 192.3, 148.7, 145.3, 143.1, 140.4, 135.5, 133.6, 132.0, 131.2, 130.8, 130.4, 129.4, 128.4; **HRESI-MS** (*m/z*) Calculated for $C_{15}H_{10}N_2ONa$ (M+Na) 257.0691 found (M+Na) 257.0692.

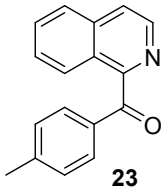
(4,7-Dichloroquinolin-2-yl)(phenyl)methanone (22).[8a]



22

Prepared as described in the general experimental procedure. White solid; Yield 52% (36.7 mg); ***mp***: 204-206 °C (lit.[8a] 205-207 °C); R_f (50% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}) 2938, 1680; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.46 (d, *J* = 8.4 Hz, 1 H), 7.71 (d, *J* = 2 Hz, 1 H), 7.65 (d, *J* = 5.2 Hz, 1 H), 7.55 (s, 1 H), 7.44 (d, *J* = 2 Hz, 1 H), 7.41 (d, *J* = 2 Hz, 1 H), 7.15 (s, 1 H), 6.87 (d, *J* = 8.4 Hz, 1 H), 4.06 (s, 3 H), 3.96 (s, 6 H), 3.95 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 193.9, 153.8, 153.7, 153.2, 150.9, 149.0, 140.0, 133.9, 129.9, 126.8, 122.8, 121.2, 111.8, 109.9, 104.8, 104.0, 56.1, 56.0, 55.9; **HRESI-MS** (*m/z*) Calculated for $C_{20}H_{19}NO5H$ (M+H) 354.1341 found (M+H) 354.1342.

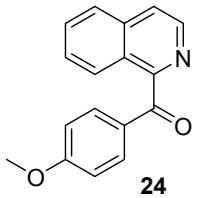
Isoquinolin-1-yl(p-tolyl)methanone (23).[25]



23

Prepared as described in the general experimental procedure. Yellowish liquid; Yield 59% (29.2 mg); **IR** (Neat, cm^{-1}) 2926, 1718; R_f(20% EtOAc/Hexane) 0.6; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.59 (d, *J* = 5.61 Hz, 1 H), 8.19 (d, *J* = 8.54 Hz, 1 H), 7.91 (d, *J* = 8.21, 2.4 Hz, 1 H), 7.85 (d, *J* = 8.06 Hz, 2 H), 7.79 (d, *J* = 5.64 Hz, 1 H), 7.74-7.71 (m, 1 H), 7.62=7.58 (m, 1 H), 7.27 (d, *J* = 7.54 Hz, 2 H), 2.42 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 194.5, 156.8, 144.7, 141.1, 136.6, 134.0, 130.8, 130.6, 129.2, 128.2, 127.0, 126.3, 126.2, 122.4, 21.8; **HRESI-MS** (*m/z*) Calculated for $C_{17}H_{13}NONa$ (M+Na) 270.0895 found (M+Na) 270.0893.

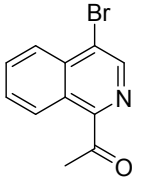
Isoquinolin-1-yl(4-methoxyphenyl)methanone (24).[25]



24

Prepared as described in the general experimental procedure. Yellowish liquid; Yield 64% (33.5 mg); R_f (20% EtOAc/Hexane) 0.4; **IR** (Neat, cm^{-1}) 1687, 2964; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 8.59 (d, J = 5.57 Hz, 1 H), 8.15 (d, J = 8.35 Hz, 1 H), 8.05 (d, J = 7.79 Hz, 1 H), 7.83-7.78 (m, 4 H), 6.99-6.97 (d, J = 8.68 Hz, 2 H), 3.86 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$):δ 193.3, 157.0, 141.0, 136.6, 133.1, 130.7, 129.8, 129.4, 128.1, 127.0, 126.2, 122.3, 113.5, 55.3; **HRESI-MS** (*m/z*) Calculated for $C_{17}H_{13}NO_2Na$ (M+Na) 286.0844 found (M+H) 286.0846.

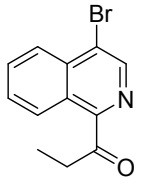
(1-(4-Bromoisoquinolin-1-yl)ethan-1-one (25).



25

Prepared as described in the general experimental procedure. Yellow liquid; Yield 36% (18 mg); R_f (10%EtOAc/Hexane) 0.7; **IR** (Neat, cm^{-1}) 1621;**^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.99 (d, J = 8.58 Hz, 1 H), 8.78 (s, 1 H), 8.25 (d, J = 8.29 Hz, 1 H), 7.86-7.82 (m, 1 H), 7.77-7.73 (m, 1 H), 2.84 (s, 3 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ197.6, 151.8, 142.9, 135.6, 131.6, 130.0, 127.3, 126.3, 124.0, 28.6; **HRESI-MS** (*m/z*) Calculated for $C_{11}H_8BrONNa$ (M+Na) 271.9687 found (M+Na) 271.9685.

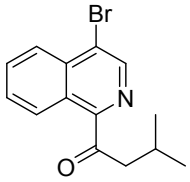
(1-(4-Bromoisoquinolin-1-yl)ethan-1-one (26).



26

Prepared as described in the general experimental procedure. Yellow solid; Yield 41% (21.6 mg); ***mp***: 82-84 °C R_f(10%EtOAc/Hexane) 0.7; **IR** (Neat, cm^{-1}) 2975, 1693; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.88 (d, *J* = 8.8 Hz, 1 H), 8.76 (s, 1 H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.85-7.81 (m, 1 H), 7.75-7.71 (m, 1 H), 3.32 (q, *J* = 7.2 Hz, 2 H), 1.26 (t, *J* = 7.6 Hz, 1 H); **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ204.6, 152.4, 142.9, 135.6, 131.5, 129.7, 127.2, 126.8, 126.2, 123.5; **HRESI-MS** (*m/z*) Calculated for $C_{12}H_{10}BrNOH$ (M+H) 264.0024 found (M+H) 264.0023.

(1-(4-Bromoisoquinolin-1-yl)ethan-1-one (27).



27

Prepared as described in the general experimental procedure. Yellow liquid; Yield 71% (41.4 mg); R_f(10%EtOAc/Hexane) 0.8; **IR** (Neat, cm^{-1}) 2958, 2924, 2869, 1695; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.85 (d, *J* = 8.4 Hz, 1 H), 8.75 (s, 1 H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.84-7.80 (m, 1 H), 7.74-7.70 (m, 1 H), 3.17 (t, *J* = 7.2 Hz, 2 H), 2.37-2.27 (m, 1 H), 1.02 (d, *J* = 6.8 Hz, 6 H) ; **^{13}C NMR{^{1}H}** (100 MHz, $CDCl_3$): δ203.9, 152.8, 142.9, 135.6, 131.5, 129.7, 127.1, 126.8, 126.3, 123.4, 49.1, 25.0, 22.7; **HRESI-MS** (*m/z*) Calculated for $C_{14}H_{14}BrNOH$ (M+H) 292.0337 found (M+H) 292.0336.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Photoreactor set-up, ^{1}H NMR and ^{13}C spectra for all compounds (PDF).

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Notes

The authors declare no competing financial interests.

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