Green Light to A Green Arylation

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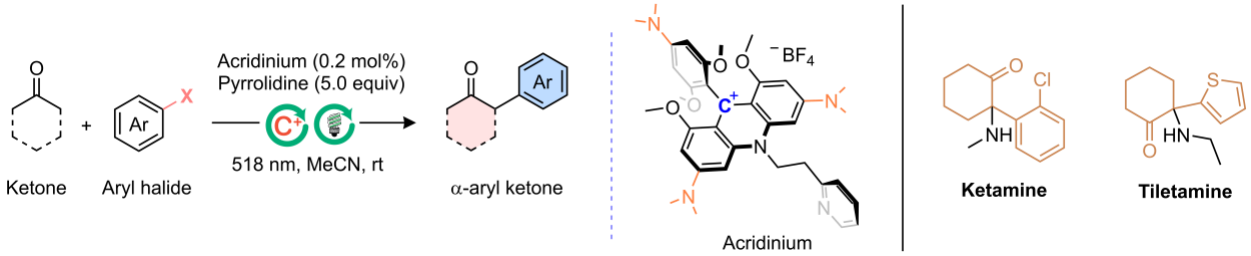


ORIGIN

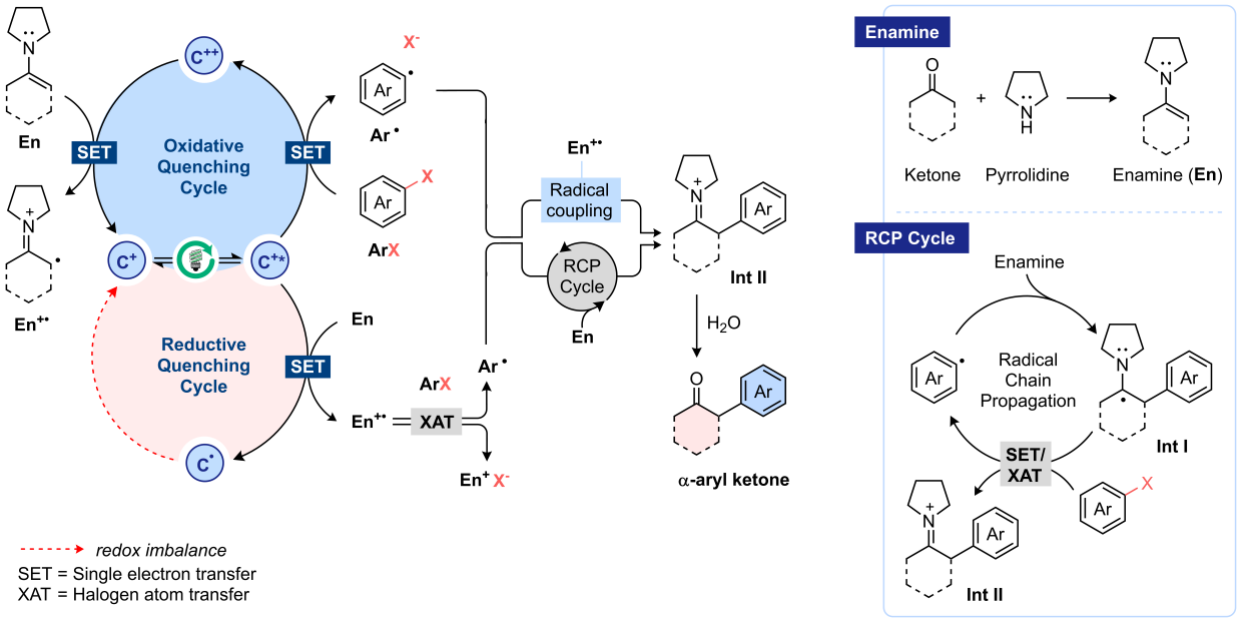
Photoactivation of C(sp^2)-X bond by an organic photocatalyst unveils the prospect of accelerated mild arylation at the α position of unbiased carbonyls. Transition-metal based approaches are ubiquitous while metal-free methods are scarce and heavily depend on activated carbonyls and/or electronically biased aryl halides. Our group developed electron rich acridiniums to catalyze direct α-arylation of ketones starting with unfunctionalized substrates in a low energy green-light-mediated photoredox protocol leading to myriad of bioactive and pharmaceutical agents.

REACTION MECHANISM

Electron rich acridiniums have a strong absorption cross section in the green light region (λ = 490 to 530 nm) of the visible light spectrum. Photophysical and electrochemical properties of this acridinium family confirmed their strong photoreduction [$E_{1/2}$ ($C^{\bullet+}$/C^{+*}) = -1.85 V vs SCE in MeCN] and photooxidation [$E_{1/2}$ (C^{+*}/ $C^{\bullet}$) = +1.15 V vs SCE in MeCN] capability in the excited state. A detailed mechanistic study unveiled the existence of both oxidative and reductive quenching cycle at play upon green light illumination.

Photoexcited acridinium **C^{+*}** can initiate oxidative quenching cycle via single-electron transfer (SET) with the aryl halide [($E_{1/2}^{red}$) ≈ -1.85 V vs SCE in CH_3CN]. That will result in aryl radical and the oxidized acridinium photocatalyst **$C^{\bullet+}$**. Then, electron deficient **$C^{\bullet+}$** radical dication [($E_{1/2}^{red}$) = +0.58 V vs SCE in CH_3CN] can readily accept an electron from the *in situ* formed enamine **En** [($E_{1/2}^{ox}$) ≤ +0.58 V vs SCE in CH_3CN] to generate the enaminyl/iminium radical cation **$En^{\bullet+}$** leading to the completion of the photocatalytic cycle. In case of reductive quenching cycle, the excited

state photocatalyst C^{+*} accepts an electron from enamine **En** to form $En^{+\bullet}$ radical cation and the reduced photocatalyst $C^{\bullet}$. The $En^{+\bullet}$ radical cation can act as a halogen atom abstractor to generate aryl radical from the corresponding aryl halide via halogen atom transfer (XAT). This aryl radical species can forge the new C(sp^3)-C(sp^2) bond by radical-radical coupling with iminium radical cation $En^{+\bullet}$ or initiate radical chain propagation (RCP) with the enamine **En**. In both cases, upon hydrolysis of the arylated iminium intermediate **Int II**, we expect the regeneration of the ketone functional group via the removal of the amine to furnish the final desired α-aryl ketone.



IMPORTANCE

The scope of α-arylation of ketones with non-prefunctionalized carbonyls and/or electronically biased aryl halides are of limited practicability if no metals are involved in the methodology. The organocatalyzed photoredox approach developed by our group addresses this classic challenging transformation with benchtop unbiased ketones and aryl halides. This methodology is tolerable to most organic functional groups while stand out as an operationally simple, mild and scalable protocol.

Literature

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