

Modular Assembly of Acridines by Integrating Photo-Excitation of *o*-Alkyl Nitroarenes with Copper-Promoted Cascade Annulation

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Acridines play pivotal roles in natural products, pharmaceuticals, molecular probes, and optoelectronic devices.¹ However, conventional synthetic methodologies often require the use of specialized starting materials, anaerobic and moisture-free procedures, as well as multiple sequential steps for disparate functional group installations.²

Recently, a research team led by Professor Yu-Mei Lin at Xiamen University (P. R. of China) has developed an innovative and modular approach to the synthesis of acridine derivatives, leveraging the synergistic combination of photo-excitation of *o*-alkyl nitroarenes with copper-mediated cascade annulation (Scheme 1). “This method significantly simplifies the synthesis of a diverse array of acridine compounds and expands the range of possible structures, including unsymmetric and multi-substituted derivatives (Scheme 2),” explained Professor Lin. She continued: “The method starts with the photo-excitation of *o*-alkyl nitroarenes, progressing through intramolecular hydrogen atom transfer and oxygen relocation steps to generate crucial amine intermediates. A subsequent copper-induced cascade – encompassing Chan–Lam amination, Friedel–Crafts acylation, and aromatization – completes the one-pot formation of diverse acridine derivatives. The *o*-alkyl nitroarene precursors are easily obtained through the coupling of alkyl halides with *o*-nitroaryl boronic acids.”

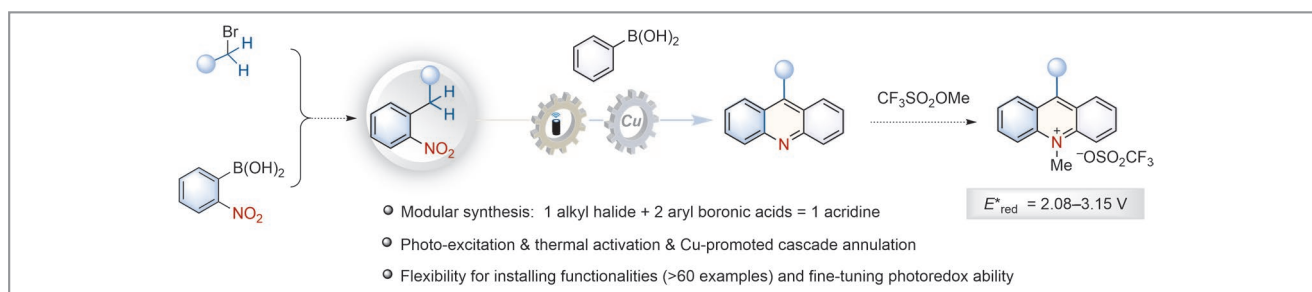
Through further assembly, a structurally diverse library of acridinium salts (more than 30 types) can be synthesized through a streamlined, single-step methylation process using the derived acridine precursors (Scheme 3). “Significantly, several of these acridinium salts, including compounds **94–100**, have not been previously synthesized nor document-

ed in the previous literature,” said Professor Lin, who told SYNFORM that the synthesized acridinium salts have shown extraordinary oxidative strength in their excited states, with reduction potentials spanning from 2.08 to 3.15 V, outperforming many known photocatalysts³ (Scheme 3). “This unique characteristic designates them particularly suitable for catalyzing oxidative transformations, making them promising candidates for photochemical reactions,” remarked Professor Lin. She concluded: “This research represents a significant advance in the field of acridine chemistry, providing a versatile and efficient method for synthesizing structurally diverse acridine compounds. The ease of incorporating substitutions in precursors and the exceptional properties of the resulting acridinium salts open up new possibilities for the development of advanced photocatalysts and pharmaceuticals.”

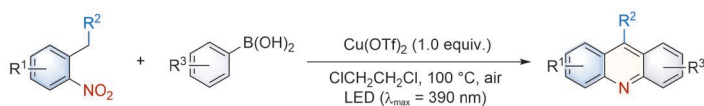
Matthew Farnok

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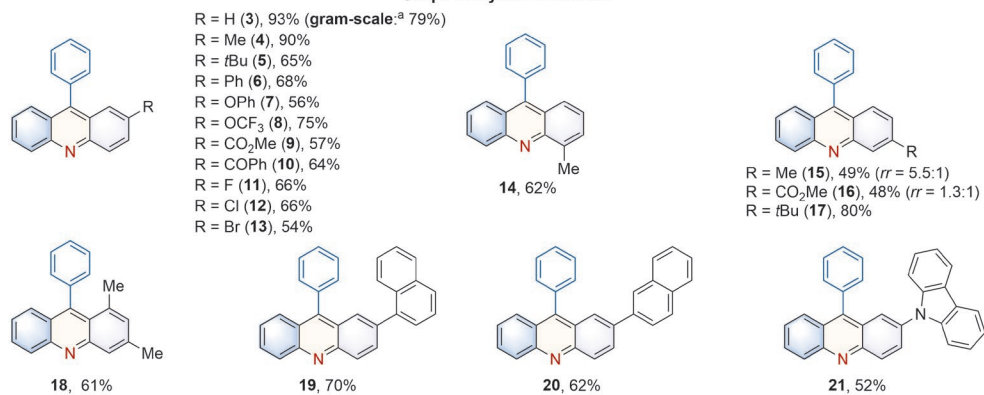
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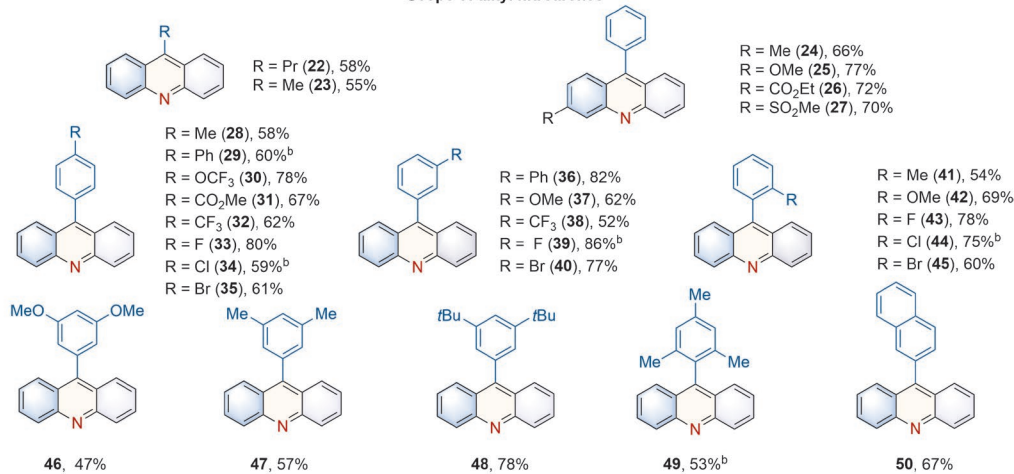
Scheme 1 Modular assembly of acridines and their N-methylation



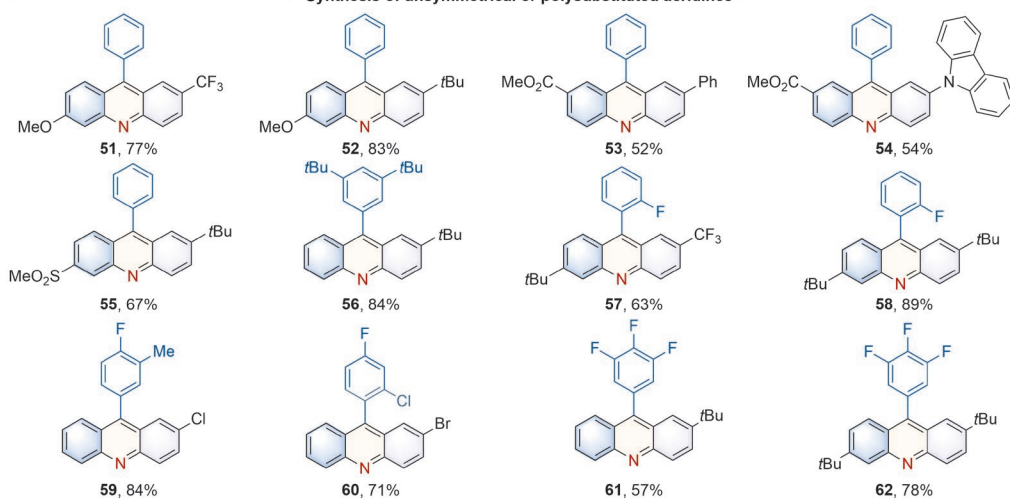
Scope of aryl boronic acids



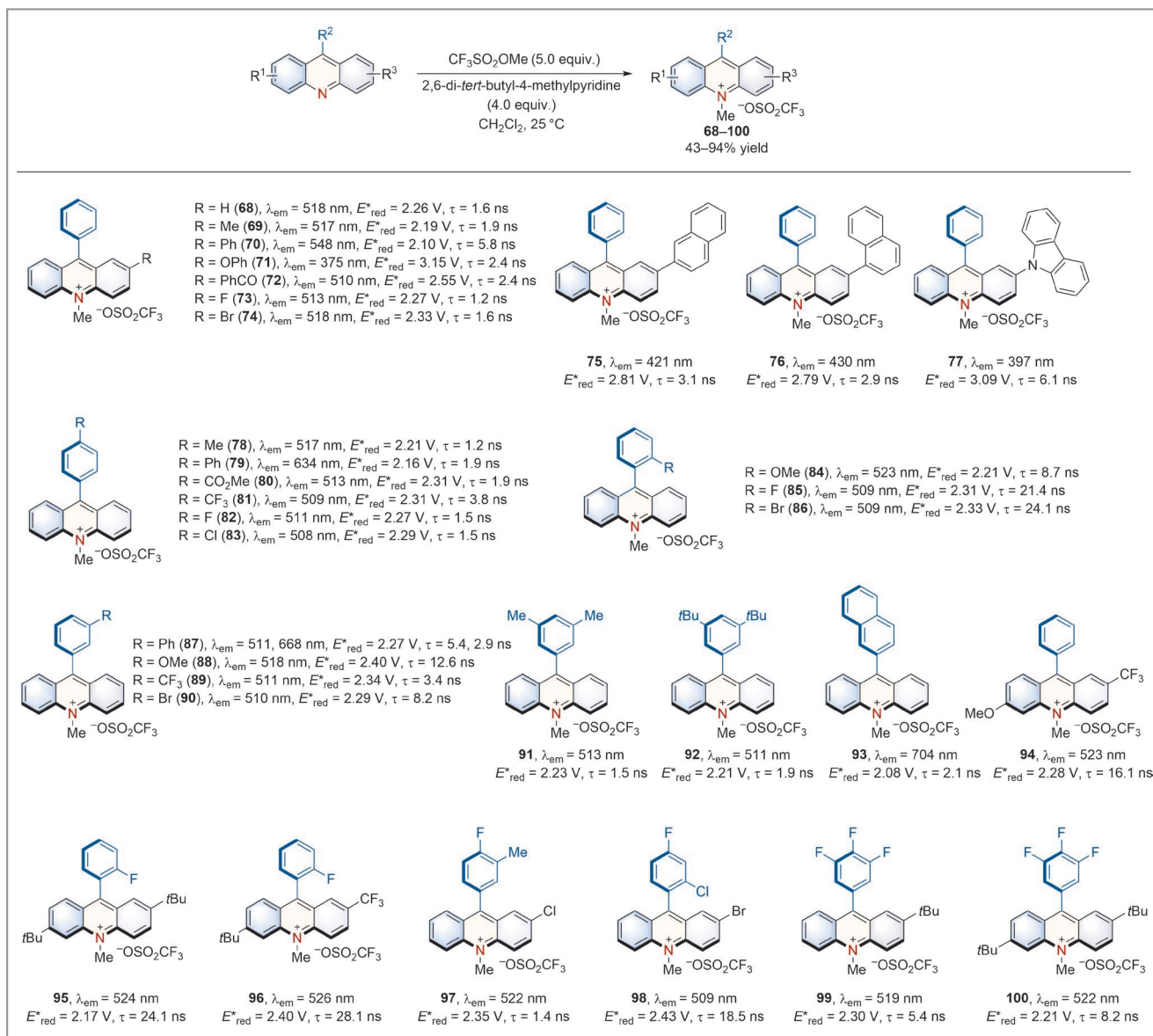
Scope of alkyl nitroarenes



Synthesis of unsymmetrical or polysubstituted acridines

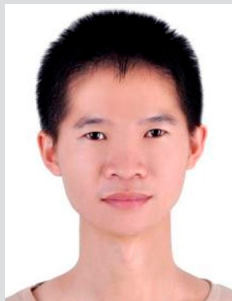


Scheme 2 Substrate scope. ^a Reaction performed with two 50 W LED lamps ($\lambda_{\text{max}} = 390 \text{ nm}$). ^b Reaction performed using $\text{Cu}(\text{OTf})_2$ (0.12 mmol).



Scheme 3 Synthesis of acridinium-based photocatalysts and their photophysical properties

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Yu-Mei Lin received her Ph.D. from Xiamen University (P. R. of China) in 2010, directed by Prof. Haiping Xia. Then, she worked with Prof. Stefanie Dehnen at Philipps-University Marburg (Germany), as a Humboldt Alexander fellow. She joined Xiamen University as an Associate Professor in 2013 and was promoted to Professor in 2023. Her research focuses on transition-metal carbene chemistry and the design of new photocatalysts.