

# Light-Induced Synthesis for C5-Nitro Indolines

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### Keywords

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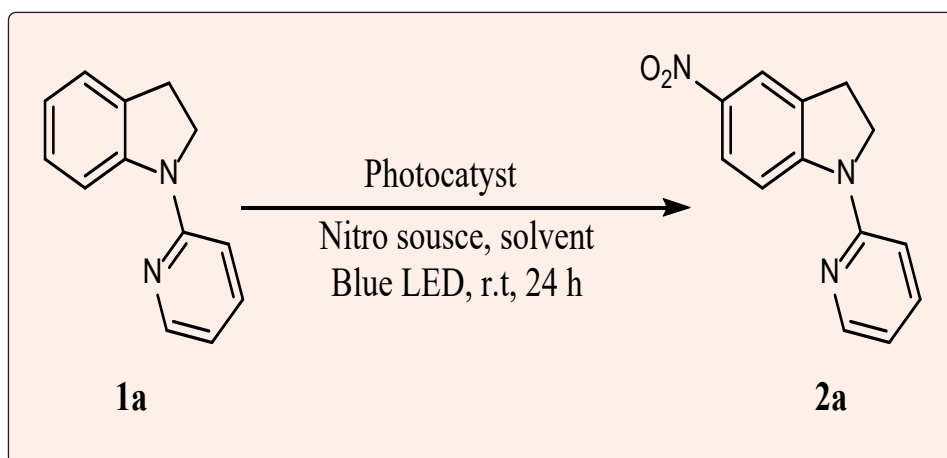
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### Opinion

Indoline, especially C5-nitro indoline is a kind of widely used nitrogen-containing compounds with high chemical reactivity, which can be used to prepare a variety of pharmaceutical or pesticide chemicals. Particularly, they demonstrated a wide range of biological and physiological activities in anti-tumor, anti-virus, anti-malaria, sterilization and other aspects. Therefore, various methods have been developed to prepare this valuable framework. However, excessive Lewis acids and bases are generally needed. Which make massive waste and poor functional group tolerance [1-6]. In recent years, the light-induced organic synthesis has received considerable attention [7-15]. Also, it has gained fast development and emerged as one of most promising concepts for nitrification reactions [16-23]. Here in, we describe the light-induced synthesis of C5-nitro indoline, which should provide inspiration for the development of the photochemical organic synthesis. We started to investigate the nitration of *N*-pyridyl indoline (**1a**) with Tert-Butyl Nitrite (TBN) under CeCl<sub>3</sub> catalysis. To our delight, this Ce-catalysed C-H nitration occurred at the C5 position of *N*-pyridyl indoline (**1a**) to afford 5-nitro-*N*-pyridyl indoline product (**2a**). MeCN was the most efficient solvent among those solvents tested for this C5-nitration process (Table 1, entries 1-5). The photocatalyst affected the C-H nitration conspicuously. CeBr<sub>3</sub> demonstrated the best catalytic activity and give the corresponding product in 89% yield. The use of AgNO<sub>3</sub> and Fe(NO<sub>3</sub>)<sub>3</sub> as the nitro surrogates could not give any product. However, the C5 nitration products were obtained in moderate yield when employing Cu(NO<sub>3</sub>)<sub>2</sub> as the nitro source (Entry 11). The control reaction suggested the photocatalyst is essential for this process (Entry 12).

Table 1: Optimization of reaction conditions

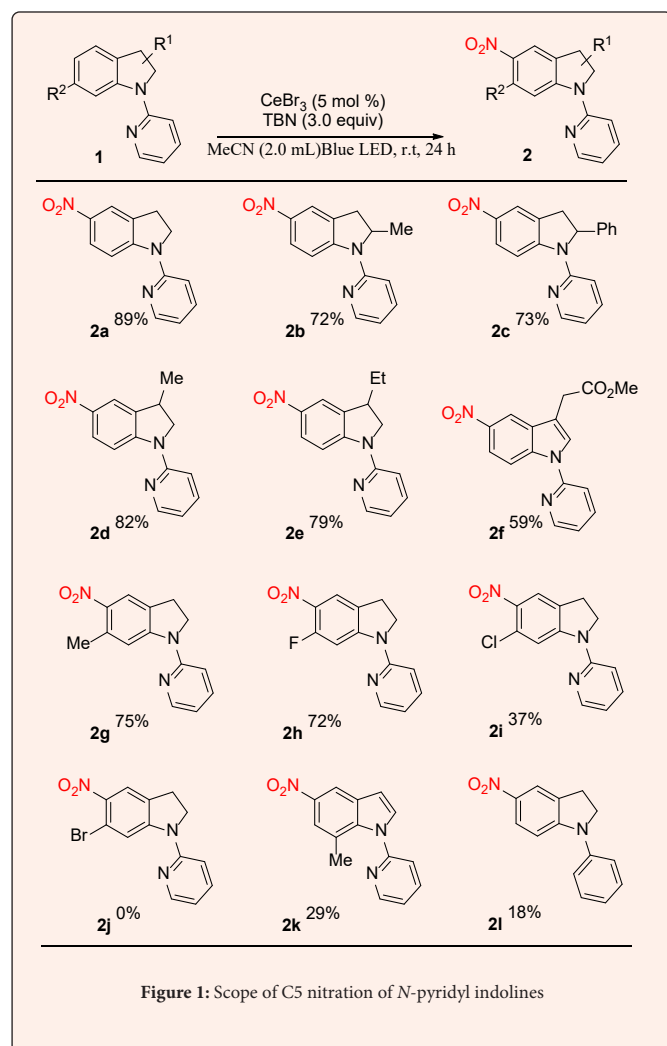
Entry	Cat (mol %)	Nitro source	Solvent	Yield
1	CeCl <sub>3</sub> (5)	TBN (3.0)	1,4-dioxane	17
2	CeCl <sub>3</sub> (5)	TBN (3.0)	DCE	22
3	CeCl <sub>3</sub> (5)	TBN (3.0)	THF	11
4	CeCl <sub>3</sub> (5)	TBN (3.0)	DMSO	Trace
5	CeCl <sub>3</sub> (5)	TBN (3.0)	MeCN	47
6	TBADT (5)	TBN (3.0)	MeCN	32
7	Eosin Y (5)	TBN (3.0)	MeCN	70
8	CeBr <sub>3</sub> (5)	TBN (3.0)	MeCN	89
9	CeCl <sub>3</sub> (5)	AgNO <sub>3</sub> (4.0)	MeCN	0
10	CeCl <sub>3</sub> (5)	Fe(NO <sub>3</sub> ) <sub>3</sub> (4.0)	MeCN	Trace
11	CeCl <sub>3</sub> (5)	Cu(NO <sub>3</sub> ) <sub>2</sub> (4.0)	MeCN	36
12	-	TBN (3.0)	MeCN	0



**Reaction conditions:** **1a** (0.2 mmol), nitro source and photocatalyst, stirring in solvent (2.0 mL) at room temperature (25°C), Blue LED (4 W) for 24 h, Isolated yield.

With the optimized condition in hand, the substrate scope of *N*-pyridyl indoline was examined. The functionalities, methyl, phenyl, ethyl and ester, at C<sub>2</sub> or C<sub>3</sub> position were well tolerated, furnishing the corresponding C5-nitrated products in good yields (**2b-2f**). Indoline with methyl substituent at C6 position was also found to be good substrate in this reaction, giving the desired product **2g** in 75% yield. Substrates with C6 fluoride and chlorine atoms led to C5 nitration products **2h** and **2i** in 72% and 37%, respectively. To our surprise, C6 bromo indoline cannot give the desired product possibly due to the steric hindrance (**2j**). Interestingly, the efficiency of this nitration significantly decreased when replacing the pyridine with a non-coordinate benzene ring on the *N* atom (**2l**).

**Reaction conditions:** **1a** (0.2 mmol), nitro source and photocatalyst, stirring in solvent (2.0 mL) at room temperature (25°C), Blue LED (4 W) for 24 h, Isolated yield.



In summary, we have developed a new light-induced nitration reactions of indolines under mild conditions. To best of our knowledge, this is the first example for photochemical organic synthesis of C5-nitro indoline. The method displays merits including green, safety, low-cost and simplistic operation. The frequently used substituted indoline substrates including *N*-pyridyl and *N*-phenyl can be well tolerated in our procedure. We believed this protocol should provide some inspiration for the development of environment-friendly organic transformation processes. The investigations on the mechanism and further application of our strategy are still ongoing in our laboratory.

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