

Supporting Information

An iodine-promoted one-pot and metal-free access to indolin-2-ones

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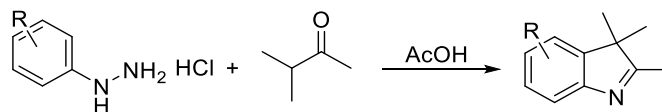
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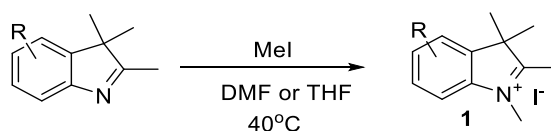
1. General procedure for the synthesis of starting materials

1.1 Preparation of the 3*H*-indoles



3*H*-indoles used in the experiment were prepared according to the reported literatures.¹⁻⁵ A three-necked, round-bottomed flask, fitted with a reflux condenser, was charged with substituted phenylhydrazine hydrochloride (20 mmol) in acetic acid (30 mL). Then 3-methyl-2-butanone (30 mmol) was added to the reaction mixtures. The resulting mixture was heated to 90 °C and stirred for 12 hours. When the reaction was complete (monitored by TLC), the hot solution was cooled to 0-5 °C in an ice-bath. With water added to the solution, the mixture was extracted with ethyl acetate (3 times). The combined organic layers were washed with saturated NaHCO₃ solution and brine solution, then dried by Na₂SO₄ and evaporated in vacuum to afford the crude product, which was used for the next step without further purification.

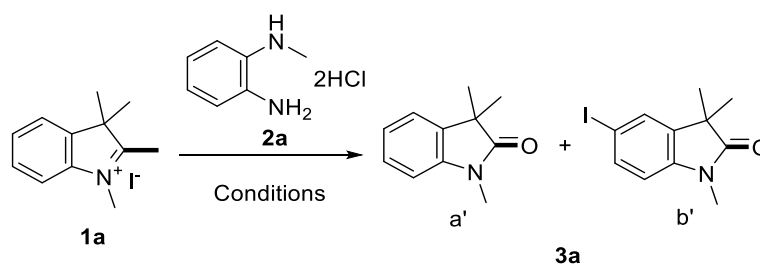
1.2 Preparation of the indolium iodide **1**^{4,5}



In a round-bottom flask charged with a solution of crude indoles from above step (20 mmol) in dry THF or DMF (40 mL) at room temperature, iodomethane (40 mmol) was added and then the solution was stirred for 12 hours at 40 or 70 °C. After the reaction was completed, the solution was cooled to 5 °C in an ice-bath. The solid was washed with cold THF (10mL) after filtration. The resulting solid was dried under high vacuum to give the pure quaternary salt.

2. Further optimization of the reaction

To further optimize this reaction, we explored the influence of different solvents (Table S1, entries 1-6). However, these reactions failed to produce desired products. Moreover, when these solvent was added to DMSO (entries 7-9), only trace amount of product was obtained, revealing the unusual role of DMSO as oxidant in these conditions.

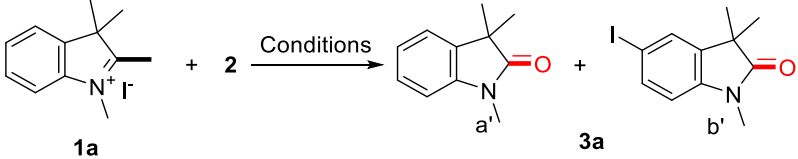
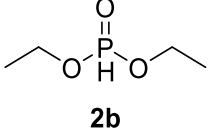
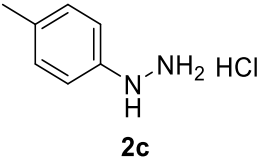
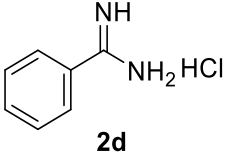
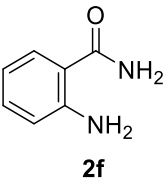
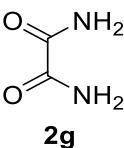
Table S1. Comparison of various solvents^a

Entry	Solvent	I ₂ (equiv)	Temp (°C)	Time (h)	Yield (%) ^b
1	THF	2	70	0.5	0
2	acetonitrile	2	70	0.5	0
3	toluene	2	70	0.5	0
4	DMF	2	70	0.5	0
5	1,4- dioxane	2	70	0.5	0
6	water	2	70	0.5	0
7	THF/DMSO ^c	2	70	0.5	trace
8	acetonitrile/DMSO ^c	2	70	0.5	trace
9	1,4- dioxane/DMSO ^c	2	70	0.5	trace

^a Reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol) and DMSO (3 mL). ^b Isolated yield of **3a**. ^c Other solvents (1 mL) was added into DMSO (3mL).

Then we explored the influence of different additives (Table S2). When the diethyl phosphonate **2b** (Table S2, entry 1), p-tolylhydrazine hydrochloride **2c** (Table S2, entry 2) and benzimidamide hydrochloride **2d** (Table S2, entry 3) were employed, the desired product **3a** was obtained in 35%-39% yields, which shows no further improvement comparing to **2a** (Table 1, entry 6). Additives, such as thiourea **2e**, 2-aminobenzamide **2f** and oxalamide **2g** have little effect on the reactions (Table S2, entries 4-6). Nevertheless, as shown in Table S1, additives have a great influence on the ratio of indolin-2-one to its iodide product (Table S2, entries 1-3).

Table S2. Comparison of various additives in the reaction

				
Entry	Additive	Reaction conditions	Ratio a'/b' ^a	Yield (%) ^b
1	 2b	1a (1.0 mmol), 2b (1.6 mmol) and I ₂ (3.0 mmol) in DMSO (3 mL) at 100 °C for 2h	5:1 ^c	35
2	 2c	1a (1.0 mmol), 2c (1.2 mmol) and I ₂ (3.0 mmol) in DMSO (3 mL) at 100 °C for 2h	0.55:1 ^c	39
3	 2d	1a (1.0 mmol), 2d (1.2 mmol) and I ₂ (3.0 mmol) in DMSO (3 mL) at 100 °C for 2 h	34:66	36
4	 2e	1a (1.0 mmol), 2e (2 mmol) and I ₂ (3.0 mmol) in DMSO (3 mL) at 70 °C for 1.5 h	n.d.	trace
5	 2f	1a (1.0 mmol), 2f (1.2 mmol) and I ₂ (2.0 mmol) in DMSO (3 mL) at 100 °C for 1 h	n.d.	trace
6	 2g	1a (1.0 mmol), 2g (1.2 mmol) and I ₂ (2.0 mmol) in DMSO (3 mL) at 100 °C for 2 h	n.d.	trace

^a Ratio of a' to b' in the isolated product is determined by HPLC. ^b Isolated yield. n.d. = not determined. ^c Ratio of a' to b' in the isolated product is determined by ¹H-NMR spectroscopy.

3. Reaction process monitored by ¹H NMR

According to the reaction of Table 1 (entry 1), a lower yield as 25% was obtained without N-methyl-1,2-benzenediamine dihydrochloride (**2a**). In order to gain insight into the mechanism of reaction, the demonstration reaction of **1a** (0.2 mmol) with I₂ (0.4 mmol) in DMSO-*d*₆ was tracked by ¹H NMR (Figure S1). The signals at 2.79 and 3.99 ppm are assigned to 2-CH₃ and N-CH₃ groups of indolium iodide (**1a**), respectively.

The signal at 3.11 ppm is assigned to the characteristic peak of **3a**. Within 20 minutes, the characteristic peaks of **1a** gradually disappeared, and new peaks for **3a** started to appear, indicating the conversion of starting materials to product (Figure S1). Moreover, as the reaction proceeds, the signal around 10 ppm rapidly appeared, indicating the existence of an aldehyde group due to the release of formaldehyde in the reaction system.

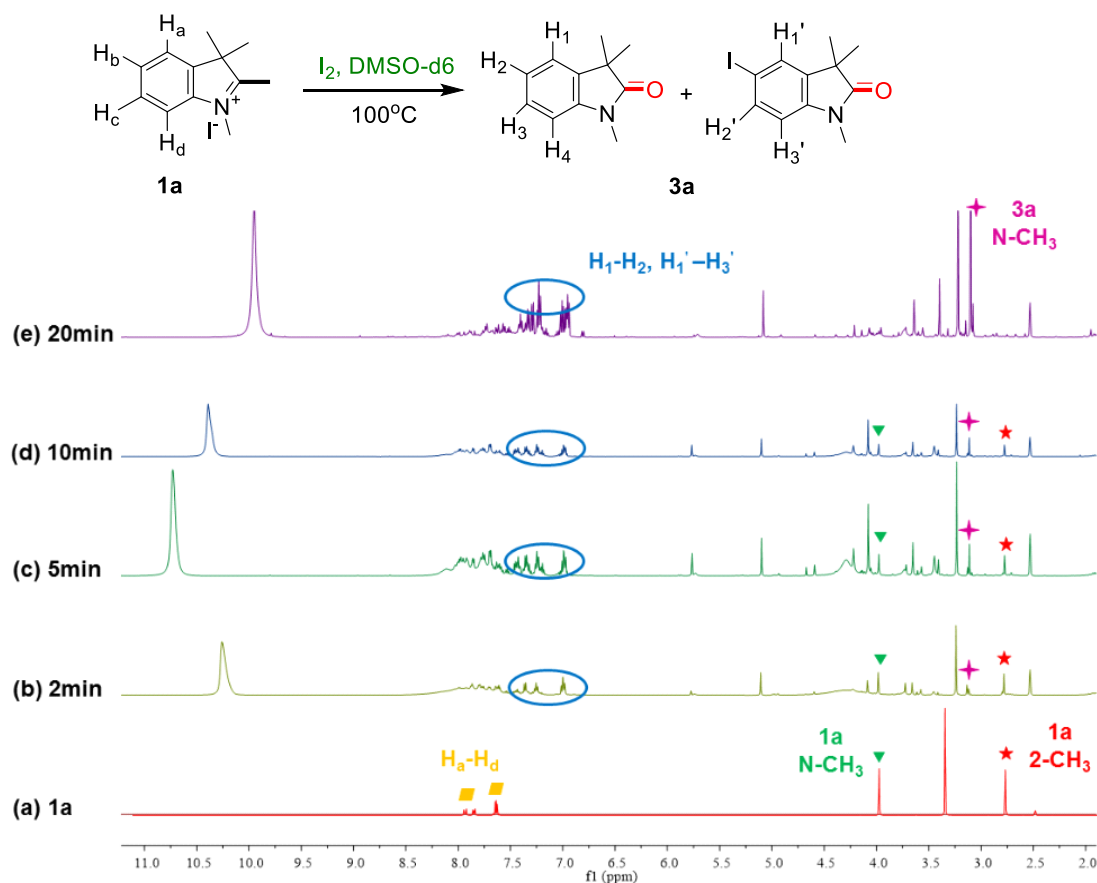


Figure S1. The reaction process of **1a** (0.2 mmol) with I_2 (0.4 mmol) monitored by 1H NMR (500 MHz, $DMSO-d_6$, 298 ± 0.5 K) over time.

4. References

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5. ^1H and ^{13}C NMR Spectra

