

**Acid/Base-Steered Cascade Cyclization: An Efficient One-Pot  
Access to Diverse Isobenzofuranone and Isoindolobenzoxazinone  
Derivatives**

**Supplementary Materials**

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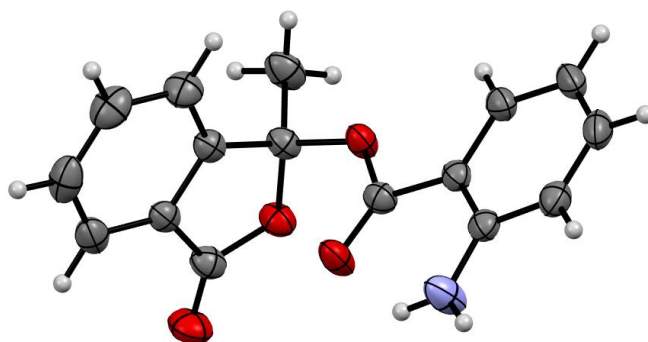
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## 1. General information

All chemicals were commercially available for direct use unless otherwise stated. Dried was treated with sodium according to standard procedures prior to use. Flash column chromatography was performed on silica gel (100-200). Reactions were monitored using pre-coated, glass-backed silica gel plates and visualized by means of UV irradiation (254 nm) or KMnO<sub>4</sub>, phosphomolybdic acid, ninhydrin, and pancaldi solution. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded using 500 MHz spectrometers at ambient temperature. Chemical shifts are reported in ppm with either tetramethylsilane or the residual solvent resonance used as an internal standard. Abbreviations are used in the description of NMR data as follows: chemical shift ( $\delta$ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant ( $J$ , Hz). High-resolution mass spectra (HRMS) were measured on a quadrupole time-of-flight mass spectrometer (Q-TOF-MS) using electrospray ionization (ESI) as an ionization method. Crystallographic data were collected on a Rigaku XtaLAB Synergy (Cu) X-ray single crystal diffractometer. All yields reported were isolated yields.

## 2. Crystallographic Data of **4aa**

High quality single crystals of **4aa** were cultivated from the evaporation of a solution of **4aa** in the mixture of EtOAc and *n*-hexane. As depicted below, the molecular structures was determined by X-ray diffraction analysis.



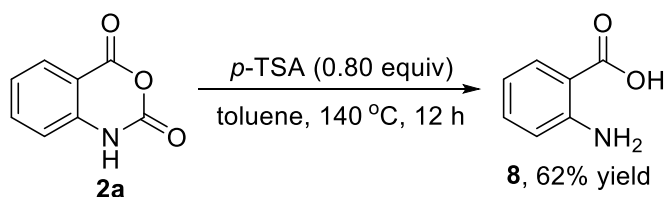
**Figure S1.** X-ray molecular structure of **4aa**. The molecular structure is depicted in an ellipsoid style at 50% probability level.

## 2.1 Crystallographic data and structure refinement of 4aa

CCDC Number	2226673
Empirical formula	C <sub>16</sub> H <sub>13</sub> NO <sub>4</sub>
Formula weight	283.27
Temperature	173.0 K
Wavelength	0.71073 Å
Crystal system	Tetragonal
Space group	P 41 21 2
a	9.6989 (6) Å
b	9.6989 (6) Å
c	29.7180 (2) Å
α	90 °
β	90 °
γ	90 °
Volumn	2795.5 (4) Å <sup>3</sup>
Z	8
Density (calculated)	1.346
Absorption coefficient	0.098 mm <sup>-1</sup>
F(000)	1184.0
Radiation type	MoK $\alpha$
Completeness to theta =30.761°	1.46/0.87
R (reflections)	0.0467 (2569)
wR2 (reflections)	0.0936 (3363)

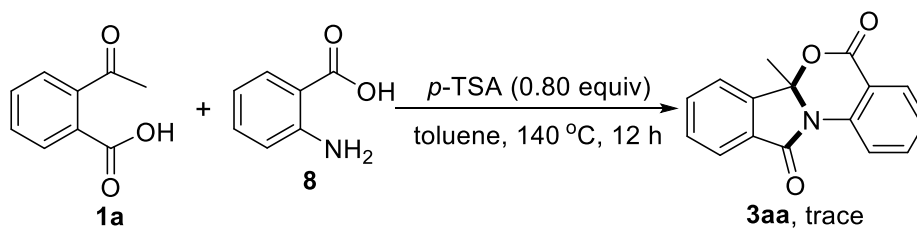
## 3. Mechanism Studies

### 3.1 The Reaction of Isatoic Anhydride under Standard Conditions



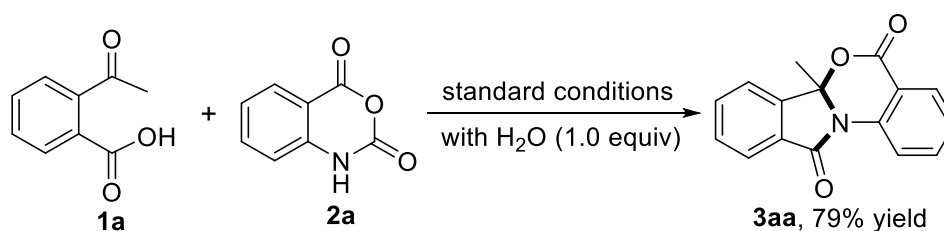
In a 5 mL reaction tube, isatoic anhydride **2a** (0.50 mmol, 82 mg), TsOH (0.4 mmol, 68.9 mg) and toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 12 h. After being cooled to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluted with a mixture of petroleum ether and ethyl acetate (1:1) to give the desired 2-aminobenzoic acid in 62% yield.

### 3.2 The Reaction of 2-Acetylbenzoic Acid and 2-Aminobenzoic Acid



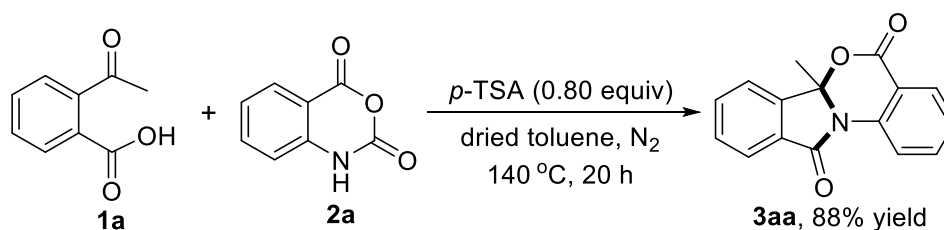
In a 5 mL reaction tube, 2-acetylbenzoic acid **1a** (0.5 mmol, 82.1 mg), 2-aminobenzoic acid **8** (0.5 mmol, 68.6 mg), TsOH (0.4 mmol, 68.9 mg) and toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 12 h. The target product **3aa** was not obtained and plenty of starting material remained.

### 3.3 The Reaction with an Additional Equivalent H<sub>2</sub>O



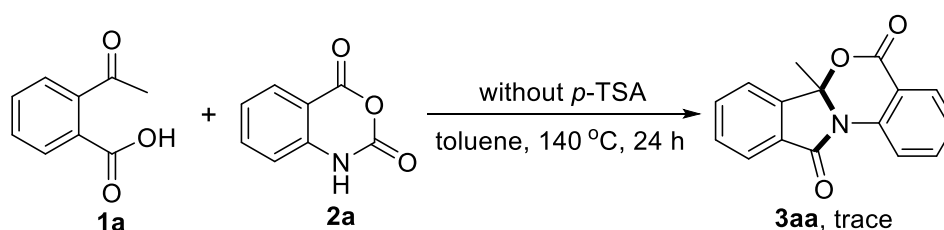
In a 5 mL reaction tube, 2-acetylbenzoic acid **1a** (0.5 mmol, 82.1 mg), isatoic anhydride **2a** (0.6 mmol, 97.8 mg), TsOH (0.4 mmol, 68.9 mg), H<sub>2</sub>O (0.5 mmol, 9.0 mg) and toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 12 h. After being cooled to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluted with a mixture of petroleum ether and ethyl acetate (2:1) to give the target product in 79% yield.

### 3.4 The Reaction in Dried Toluene



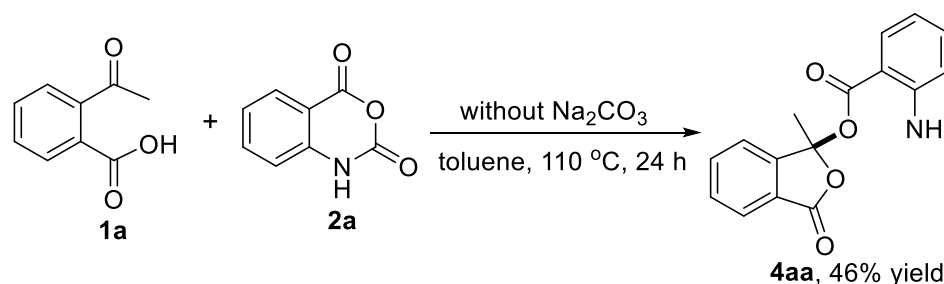
In a 5 mL reaction tube, 2-acetylbenzoic acid **1a** (0.5 mmol, 82.1 mg), isatoic anhydride **2a** (0.6 mmol, 97.8 mg), TsOH (0.4 mmol, 68.9 mg), and dried toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 12 h. After being cooled to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluted with a mixture of petroleum ether and ethyl acetate (2:1) to afford the target product in 88% yield.

### 3.5 The Reaction without *p*-TSA



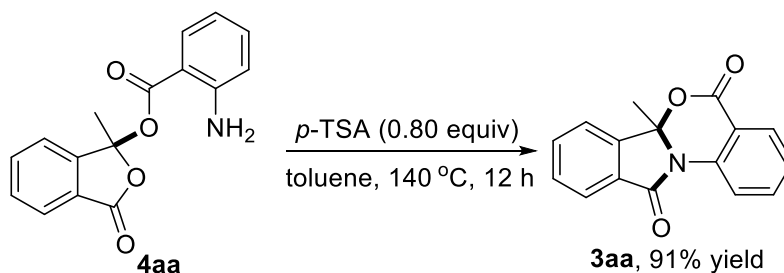
In a 5 mL reaction tube, 2-acetylbenzoic acid **1a** (0.5 mmol, 82.1 mg), isatoic anhydride **2a** (0.6 mmol, 97.8 mg) and toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 24 h. The target product **3aa** was not obtained and plenty of starting material remained.

### 3.6 The Reaction without Na<sub>2</sub>CO<sub>3</sub>



A solution of 2-acetylbenzoic acid **1a** (0.5 mmol, 82.1 mg) and isatoic anhydride **2a** (0.6 mmol, 97.8 mg) in toluene (2.5 mL) was held at reflux in oil bath for 12 h. After being cooled to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluted with a mixture of petroleum ether and ethyl acetate (2:1) to give the pure target product in 46% yield. .

### 3.7 The Transformation of 4aa at High Temperature with TsOH



In a 5 mL reaction tube, compound **4aa** (0.5 mmol, 141.6 mg), TsOH (0.4 mmol, 68.9 mg) and toluene (2.5 mL) were mixed. Then, the reaction tube was capped with a septum and allowed to stir at 140 °C in a pre-heated oil bath for 12 h. After being cooled to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluted with a mixture of petroleum ether and ethyl acetate (2:1) to give the target product in 91% yield.

**Chemical structure of 3aa:** CC1(C(=O)N1C(=O)c2ccccc2)C(=O)OC(=O)c3ccccc3

**<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>):**

Chemical Shift (ppm)	Integration
8.17, 8.15, 8.13, 8.12, 8.11	0.98
7.97, 7.96, 7.95, 7.78, 7.77, 7.76, 7.75, 7.74, 7.73, 7.68, 7.66, 7.65, 7.64, 7.63, 7.38, 7.37, 7.36, 7.35	0.99, 3.03, 1.01, 1.02
1.95	3.00
1.62	
1.26	



