

## Electronic Supplementary Information

### Synthesis of unsymmetrical NH-pyrroles from biomass feedstock in the confined space of metal-organic frameworks

Deng-Yue Zheng,<sup>a</sup> Tianjian Zhang,<sup>a</sup> Rongxian Bai,<sup>a</sup> Minghao Li,<sup>a</sup> Ruifeng Wang\*<sup>b</sup> and Yanlong Gu\*<sup>a,c,d</sup>

- a Key Laboratory of Material Chemistry for Energy Conversion and Storage, Ministry of Education, Hubei Key Laboratory of Material Chemistry and Service Failure, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, 1037 Luoyu road, Hongshan District Wuhan 430074, China. E-mail: [klgyl@hust.edu.cn](mailto:klgyl@hust.edu.cn) (Y. Gu)
- b Ordos Institute of Technology, Ordos, Inner Mongolia, 017000, PR China.
- c School of Chemistry and Chemical Engineering, Shihezi University, Shihezi, Xinjiang 832003, China
- d State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Lanzhou 730000, China

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## 1. Materials and general methods

All chemical reagents were purchased from commercial sources and, unless specially indicated, were used as received without further purification. Organic solvents used in this work were further dried following standard procedures before use. N<sub>2</sub> sorption curves were obtained by Micromeritics ASAP 2420-4MP Plus automated sorption analyzer under 77 K. The powder X-ray diffraction (PXRD) patterns were collected by Cu-K $\alpha$  radiation ( $\lambda = 1.5406 \text{ \AA}$ ) at a Rigaku SmartLab-SE X-ray diffractometer. <sup>1</sup>H NMR spectra were performed on a Bruker Advance III 400 MHz.

## 2. Catalyst preparation

### Synthesis of MIL-101-NH<sub>2</sub>

MIL-101-NH<sub>2</sub> was obtained by reduction of MIL-101-NO<sub>2</sub>.<sup>[1]</sup> CrCl<sub>3</sub>·6H<sub>2</sub>O (334 mg, 1.25 mmol), nitroterephthalic acid (265 mg, 1.25 mmol), and deionized water (30 mL) were blended and briefly sonicated resulting in a blue-colored suspension. After putting the suspension into a 50 mL Teflon-lined stainless-steel autoclave, crystallization was conducted for 8 h at 220 °C, and the resultant fine blue MIL-101-NO<sub>2</sub> crystals were separated from water using a centrifuge and washed with water and methanol. MIL-101-NO<sub>2</sub> (100 mg) and SnCl<sub>2</sub>·2H<sub>2</sub>O (700 mg) were added to 20 mL ethanol. The mixture was heated at 70 °C for 6 h for the reduction of —NO<sub>2</sub> into the —NH<sub>2</sub> group. After the recovery of the solid product with filtration, the product was put into 12 M HCl (100 mL) for 2 min. The solid product was recovered by filtration and was washed three times with ample water and methanol; and dried at room temperature for 12 h.

### Synthesis of MIL-101

MIL-101 was synthesized according to the literature with some modifications.<sup>[2]</sup> In a typical procedure, CrCl<sub>3</sub>·6H<sub>2</sub>O (533 mg) and H<sub>2</sub>BDC (333 mg) were dispersed in 12 mL H<sub>2</sub>O. After vigorous stirring at room temperature for 3 min, the mixed solution was transferred into a Teflon-lined stainless-steel autoclave and heated at 210 °C for

24 h. As mentioned previously, a significant amount of nonreacted terephthalic acid is present both outside and within the pores of MIL-101. The solution was centrifuged at 1000 rpm for 3 min to remove H<sub>2</sub>BDC. After filtration, the collected MIL-101 was washed twice with DMF. The crystalline MIL-101 product in the solution was doubly filtered off using two glass filters with a pore size between 200 μm to remove the free terephthalic acid. Then a solvothermal treatment was sequentially performed using ethanol (95 % EtOH with 5 % water) at 80 °C for 24 h. The solid was finally dried overnight at 150 °C under an air atmosphere.

### **Synthesis of UiO-66**

The UiO-66 sample was synthesized using ZrCl<sub>4</sub> and terephthalic acid (H<sub>2</sub>BDC) as reactants according to the reported method with minor modifications.<sup>[3]</sup> Typically, 5 mL of dimethylformamide (DMF) solution of ZrCl<sub>4</sub> (40.8 mg) and 5 mL of DMF solution of H<sub>2</sub>BDC (26.6 mg) were mixed in a 20 mL glass vial. Following that, 0.5 mL of acetic acid was added, then sealed, and allowed to react at 120 °C for 24 h without stirring. The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, UiO-66 was dried at 60 °C under a vacuum overnight.

### **Synthesis of UiO-66-NH<sub>2</sub>**

The UiO-66-NH<sub>2</sub> sample was synthesized using ZrCl<sub>4</sub> and 2-aminoterephthalic acid as reactants.<sup>[4]</sup> Typically, 15 mL of DMF solution of ZrCl<sub>4</sub> (1232 mg) and 15 mL of DMF solution of 2-aminoterephthalic acid (924 mg) were mixed in a 50 mL glass vial. Following that, then sealed, and allowed to react at 120 °C for 24 h with stirring. The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, UiO-66-NH<sub>2</sub> was dried at 60 °C under a vacuum overnight. The yield of UiO-66-NH<sub>2</sub> is 96% (based on ZrCl<sub>4</sub>).

### **Synthesis of Zr-ATA**

The synthesis of Zr-ATA originates from the failed synthesis of UiO-66-NH<sub>2</sub>. Zr-ATA samples were also synthesized using ZrCl<sub>4</sub> and 2-aminoterephthalic acid as reactants. Similarly, 20 mL of DMF solution of ZrCl<sub>4</sub> (480 mg) and 20 mL of DMF solution of 2-aminoterephthalic acid (372 mg) were mixed in a 50 mL glass vial. Following that, then sealed, and allowed to react at 120 °C for 12 h without stirring.

The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, Zr-ATA was dried at 60 °C under a vacuum overnight.

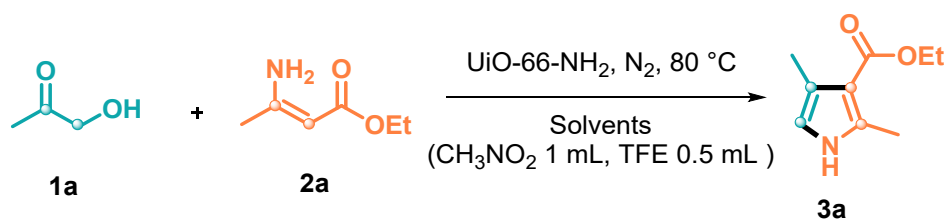
### Synthesis of IRMOF-3

IRMOF-3 was synthesized according to the literature.<sup>[5]</sup> Zn(NO<sub>3</sub>)<sub>2</sub>·4H<sub>2</sub>O (1568 mg) and 2-aminoterephthalic acid (332 mg) was dissolved in DMF (30 mL) in a vial. The mixture was heated to 100 °C and kept for 24 h to yield large cubic crystals of IRMOF-3. After cooled down to room temperature, the cubic crystals were repeatedly washed with DMF and anhydrous chloroform, and then soaked in anhydrous chloroform for 12 h. The final product was filtered and dried at 120 °C under vacuum for 10 h.

### 3. General procedure for MOF-catalyzed synthesis of unsymmetrical substituted NH-pyrroles.

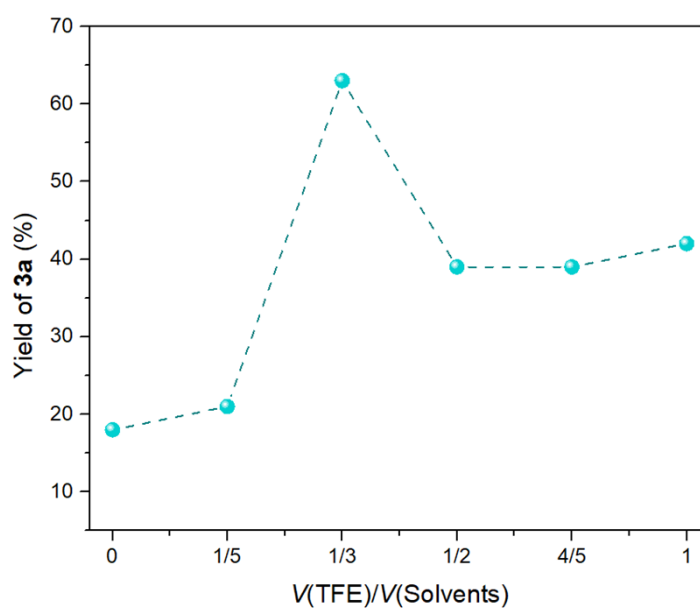
A Schlenk tube of 25 mL equipped with a magnetic stir bar was charged with MOFs catalysts (50 mg) in non-aqueous 1.5 mL solvents (1.0 mL CH<sub>3</sub>NO<sub>2</sub> and 0.5 mL TFE); then, hydroxyacetone **1** (0.20 mmol) and enaminones **2** (0.30 mmol) were added. Then the mixture was sonicated for 10 min and the tube was purged with N<sub>2</sub> gas 10 times and maintained atmospheric pressure at room temperature. The reaction mixture was stirred at 80 °C for 24 h. After completion of the reaction, the catalyst was separated by centrifugation, thoroughly washed with methanol several times, and then the catalyst was recovered by washing with an amount of methanol and exchanged with fresh methanol 3 times, before being dried under vacuum for reuse. The yield of the product was analyzed by preparative thin-layer chromatography (TLC) using a mixture of ethyl acetate and petroleum ether as eluent.

### Solvent optimization process



Entry	Deviation from conditions	Yield (%)
1	none	63
2	CH <sub>3</sub> CN	11
3	CH <sub>3</sub> OH	<5
4	THF	13
5	TFE	42
6	1,4-dioxane	15
7	CH <sub>3</sub> NO <sub>2</sub>	18

Isolated yields. TFE = 2,2,2-trifluoroethanol.

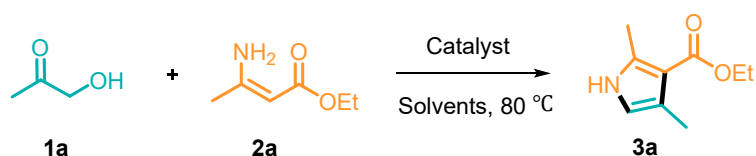


After many experiments and verification, we found that only nitromethane and TFE are the best solvent combination. The figure above shows the effect of the proportion of TFE in the solvent combination on the reaction yield.

#### 4. Model reactions catalyzed by homogeneous Lewis acid catalysts

A Schlenk tube of 25 mL equipped with a magnetic stir bar was charged with metal salts catalysts (0.03 mmol) in non-aqueous 1.5 mL solvents (1.0 mL CH<sub>3</sub>NO<sub>2</sub> and 0.5 mL TFE); then, hydroxyacetone **1** (0.20 mmol) and enaminones **2** (0.30 mmol) were added. Then the mixture was sonicated for 10 min and the tube was purged with N<sub>2</sub> gas 10 times and maintained atmospheric pressure at room temperature. The reaction mixture was stirred at 80 °C for 24 h. After completion of the reaction, the yield of the product was analyzed by preparative thin-layer chromatography (TLC) using a mixture of ethyl acetate and petroleum ether as eluent.

**Table S1.** Cyclization of hydroxyacetone and ethyl crotonate to pyrrole catalyzed by homogeneous catalysts <sup>a</sup>



Entry	Catalyst	Yield ( <b>3a</b> ) <sup>b</sup>
1	CrCl <sub>3</sub>	15
2	CuCl <sub>2</sub>	trace
3	FeCl <sub>3</sub>	trace
4	AlCl <sub>3</sub>	9
5	ZrCl <sub>4</sub>	18
6	ZnCl <sub>2</sub>	24
7	Al(OTf) <sub>3</sub>	12
8	Bi(OTf) <sub>3</sub>	21

<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst 0.03 mmol, CH<sub>3</sub>NO<sub>2</sub> (1.0 mL), TFE (0.5 mL), 80 °C, N<sub>2</sub>, 24 h. <sup>b</sup> Isolated yields. TFE = 2,2,2-trifluoroethanol.

## 5. Gram scale reaction

A Round-bottomed flask of 250 mL equipped with a magnetic stir bar was charged with MOFs catalysts (1.5 g) in non-aqueous 75 mL solvents (50 mL CH<sub>3</sub>NO<sub>2</sub> and 25 mL TFE); then, hydroxyacetone **1** (20 mmol) and enaminones **2** (30 mmol) were added. The mixture was then sonicated to uniformly disperse the catalyst, and the reaction flask was exchanged with N<sub>2</sub> and kept at atmospheric pressure at room temperature. The reaction mixture was stirred at 80 °C for 24 h. After completion of the reaction, the catalyst was separated by centrifugation, thoroughly washed with methanol several times, and then the catalyst was recovered by washing with an amount of methanol and exchanged with fresh methanol 3 times, before being dried under vacuum for reuse. After collecting the reaction and catalyst-washing liquid, the liquid was evaporated to dryness with a rotary evaporator, and the obtained solid was separated by column chromatography.

## 6. Calculation of TON and TOF

Turnover frequency (TOF): The number of reactant molecules converted on each active center per unit time, which describes the intrinsic catalytic activity of the catalyst.

$$\begin{aligned} TOF &= \frac{\text{mol of reactants(conv.)}}{\text{mol of catalytic active sites} \times \text{reaction time}} \\ &= \frac{20 \text{ mmol}}{3 \text{ mmol(Zr sites)} \times 24 \text{ h}} = 0.27 \text{ h}^{-1} \end{aligned}$$

Turnover number (TON): It reflects the maximum number of reactant molecules that can be converted by a catalytic active center under a certain condition.

$$\begin{aligned} TON &= TOF \times \text{reaction time} \\ &= 0.27 \text{ h}^{-1} \times 24 \text{ h} = 6.5 \end{aligned}$$

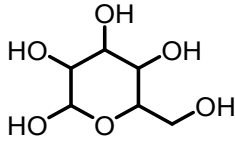
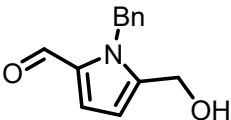
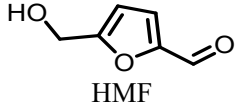
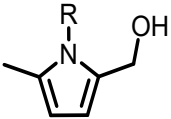
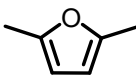
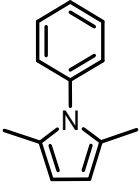
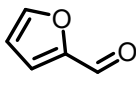

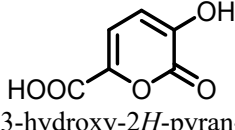
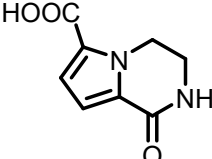
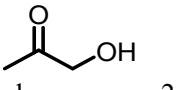
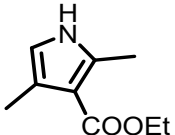
## 7. Computational study

The calculated structure was built from its single crystal structures. The GFN2-xTB<sup>[6]</sup> was adopted for geometry optimization calculations with Grimme's xtb program.<sup>[7]</sup> The Zr atoms keep their positions unchanged, and other atoms were optimized. Then, the interaction energy between hydroxyacetone,  $\alpha$ -hydroxyacetophenone, and UiO-66-NH<sub>2</sub>, respectively, were calculated by the following formula:

$$E_{\text{bind}} = E_{\text{complex}} - (E_{\text{partA}} + E_{\text{partB}})$$

## 8. Synthesis of pyrrole heterocycles from biomass materials

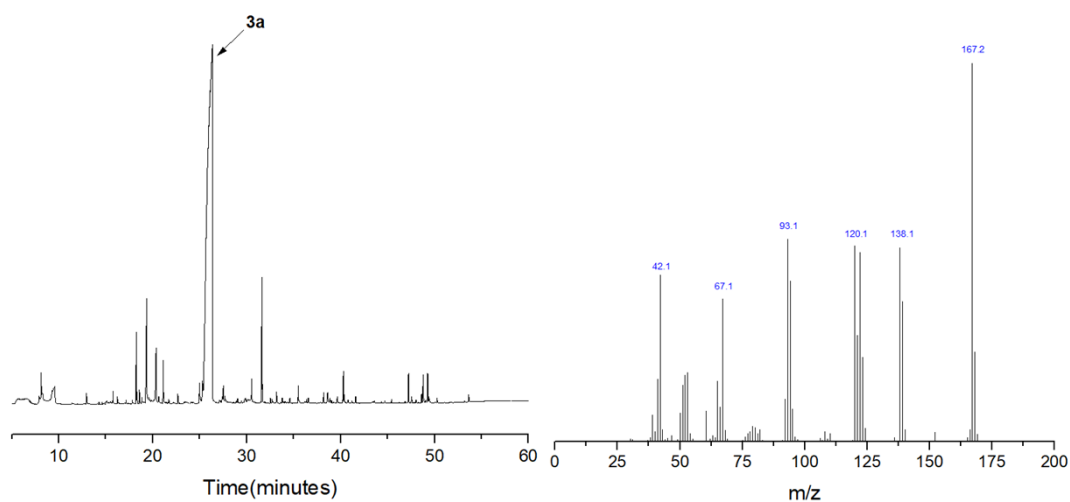
**Table S2** Synthesis of different pyrrole molecules from various biomass materials.

Biomass molecules	Catalyst	Reaction conditions	Product	Ref.
 D-glucose (OH)	(COOH) <sub>2</sub>	DMSO, 90 °C,		<i>J. Org. Chem.</i> <b>2015</b> , 80, 7693
 HMF	Iridium complex	60 bar H <sub>2</sub> , 140 °C, PBS (two steps)		<i>Eur. J. Org. Chem.</i> <b>2018</b> , 2009
 2,5-dimethylfuran	Hf/SBA-15	DMF, 150 °C		<i>ACS Sustainable Chem. Eng.</i> <b>2020</b> , 8, 12161
 furfural	Pd@S-1	NH <sub>3</sub> , H <sub>2</sub> , 460 °C		<i>Angew. Chem. Int. Ed.</i> <b>2020</b> , 59, 19846
 3-hydroxy-2H-pyran-2-one	--	50 °C, H <sub>2</sub> O		<i>ACS Sustainable Chem. Eng.</i> <b>2022</b> , 10, 12763
 1-hydroxypropan-2-one	UiO-66-NH <sub>2</sub>	80 °C, CH <sub>3</sub> NO <sub>2</sub>		This work

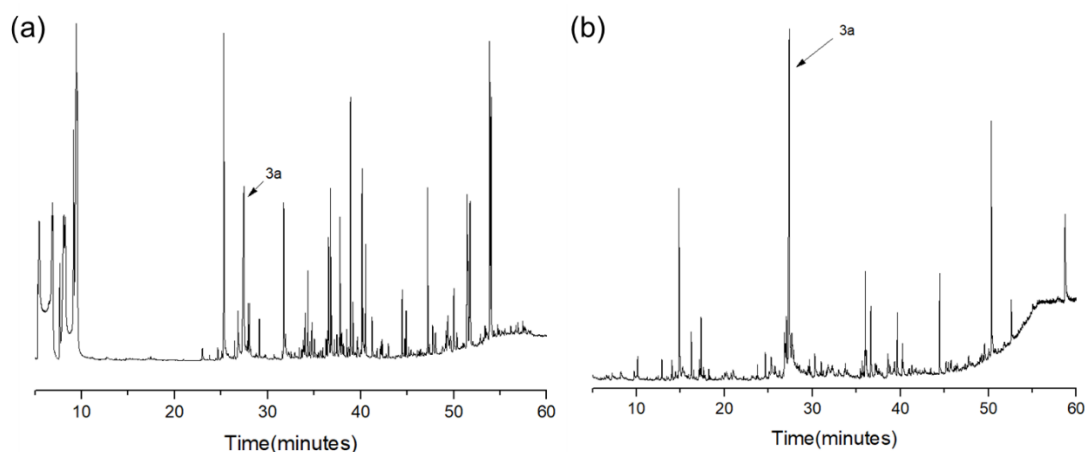




## 9. GC-MS measurement



GC-MS measurement of reaction solution (with catalyst filtered out) under general reaction conditions.  $m/z_{(3a)} = 167.2$



GC spectrum of the reaction solution: The product **3a** (20 mg) reacts with 0.2 mmol of **1a** (a) and **2a** (b), respectively, under the catalysis of  $ZrCl_4$  (0.02 mmol). Reaction conditions: 80 °C,  $CH_3NO_2$  1mL, TFE 0.5 mL, 12 h. The GC spectrum indicates that the target product **3a** can react with the substrates under Lewis catalysis to generate many products that are difficult to separate and judge.

## 10. Evaluation of green metrics

Atomic economy considers how many atoms of the starting material get into the product in a chemical reaction. It is usually expressed by atom economy (AE), which is the ratio of the molar mass of the target product to the sum of the molar masses of all reactants. This concept was first proposed by Professor Barry M. Trost<sup>[8]</sup> of Stanford University in 1991, and he also won the academic award in the 1998 US "Presidential Green Chemistry Challenge Award".

$$\text{Atom economy (AE)} = \frac{MW(\text{Product}) \times 100}{\sum MW(\text{Raw materials}) + \sum MW(\text{Redgents})} \%$$

Reaction mass efficiency is also an indicator to measure the utilization rate of raw materials, which refers to how much mass of raw materials is converted into products.<sup>[9]</sup>

$$\text{Reaction mass efficiency} = \frac{m(\text{Product}) \times 100}{\sum m(\text{Raw materials})} \%$$

In a chemical reaction, the largest component of the most intensively used is due to reaction and work-up solvents. Solvent intensity is an indicator of solvent utility in chemical reactions.<sup>[10]</sup>

$$\text{Solvent intensity} = \frac{\sum m(\text{Solvents})}{m(\text{Product})} \%$$

In 1992, Roger A. Sheldon of Delft University of Technology in the Netherlands proposed the concept of environmental factors to examine the impact of the whole process of chemical manufacturing on the environment. The environmental factor (EF) is defined as the ratio of the mass of all wastes to the mass of the target product in the whole process of product production. It covers not only by-products, reaction solvents, and auxiliaries, but also various wastes generated during product purification. Later EF develops into simple *E* factors (sEF) and complete *E* factors (cEF).<sup>[11]</sup> The sEF does not consider solvent and water and is more suitable for early route exploration activities, while cEF considers all process materials, including solvent and water, assuming no recycling, and is more suitable for total waste stream analysis.

$$cEF = \frac{\sum m(\text{Raw materials}) + \sum m(\text{Reagents}) + \sum m(\text{Solvents}) + m(\text{Water}) - m(\text{Product})}{m(\text{Product})}$$

Internationally, carbon footprint is usually used to measure the amount of greenhouse gas (GHG) released by an organization or product, which is mainly defined by annual carbon emissions, that is, carbon consumption. Calculating the carbon efficiency of chemical conversion processes is a quantitative analysis method to measure the carbon footprint of chemical feedstocks.<sup>[12]</sup>

$$\text{Carbon efficiency} = \frac{m(\text{Carbon in product}) \times 100}{\sum m(\text{Carbon in raw materials})} \%$$

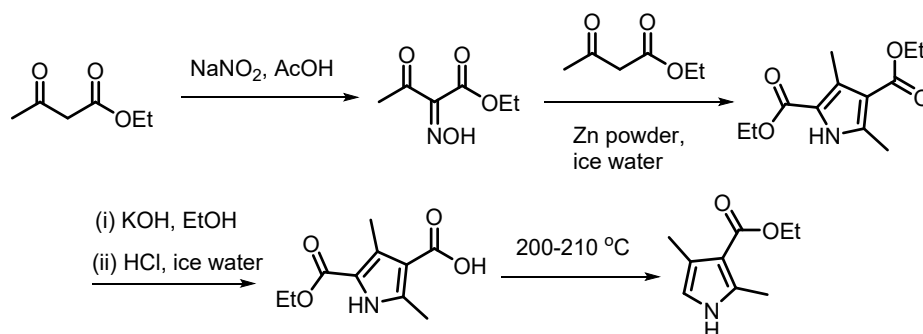
**Table S3.** Calculation of green metrics for the synthesis of **3a**.<sup>a</sup>

Process efficiency metrics	Zhiguo Zhang <sup>[13]</sup>	Koichi Takeya <sup>[14]</sup>	Yan Lou <sup>[15]</sup>	Jason W. Chin <sup>[16]</sup>	This work
<i>E</i> -factor	132.10	2023.16	3442.04	218.96	50.5
Reaction mass efficiency	12.89%	9.4%	1.58%	19.67%	35.9%
Carbon efficiency	16.95%	59.8%	6.5%	50.64%	42.9%
Atom economy	50.76%	81.46%	45.26%	46.75%	82.27%
Solvent intensity	115.2	2012.17	3378.2	213.2	47.86
Steps to obtain product	3	2	3	3	1
Whether the catalyst is reusable	NO	NO	NO	NO	YES
Catalyst cost <sup>b</sup> (CNY/per gram of product)	8.52	113.14	598.52	2.8	1.35

<sup>a</sup>Unless otherwise noted, only model products in references were calculated and assessed.

<sup>b</sup>The prices of catalysts refer to Sigma-Aldrich Co. LLC.

(1) Meng, G.; Liu, C.; Qin, S.; Dong, M.; Wei, X.; Zheng, M.; Qin, L.; Wang, H.; He, X.; Zhang, Z., *Res. Chem. Intermed.* 2015, 41, 8941-8954.



Reagent	Amount
Ethyl 3-oxobutanoate	1.03 g/mL×30.0 mL=30.85 g
Acetic acid	1.05 g/mL×60.0 mL=63 g
Sodium nitrite NaNO <sub>2</sub>	85 g/mol×0.12 mol =9.99 g
Zinc powder	15.4 g
KOH	3.92 g
Ethanol	0.79 g/mL×42 mL = 33.18 g
Water	420 g
Total	596.31 g
Product	4.48 g
Steps to obtain product	3
Whether the catalyst is reusable	No
Catalyst cost (CNY/per gram of product)	(Zn power)¥2,477.91/Kg×10 <sup>-3</sup> ×(15.4÷4.48)= 8.52 KOH(ignore)

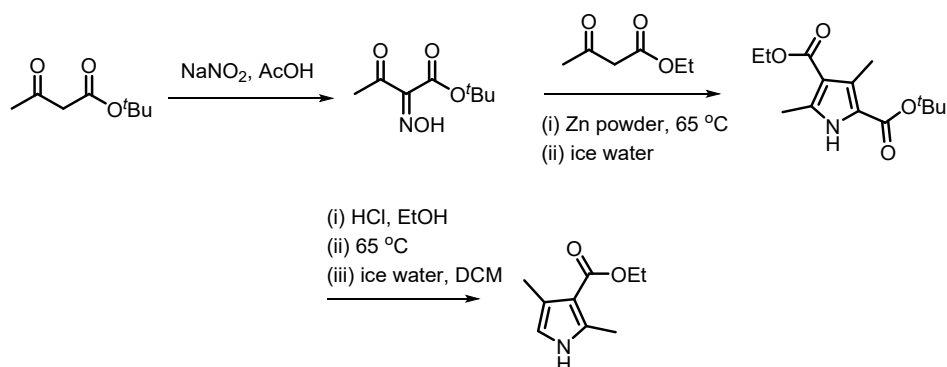
$$E\text{-factor} = (596.31 - 4.48) \text{ g} / 4.48 \text{ g} = 132.10$$

$$\text{Reaction mass efficiency} = (4.48 \text{ g} / 34.74 \text{ g}) \times 100\% = 12.89\%$$

$$\text{Carbon efficiency} = (4.48/167 \text{ g/mol}) \times 9 / (30.85/130.0 \text{ g/mol} \times 6) = 16.95\%$$

$$\text{Solvent intensity} = 115.2$$

(2) Tsai, Y.-H.; Essig, S.; James, J. R.; Lang, K.; Chin, J. W., *Nat. Chem.* 2015, 7, 554-561



Reagent	Amount
<i>tert</i> -Butyl acetoacetate	10 g
Acetic acid	1.05 g/mL×70.0 mL=73.5 g
Sodium nitrite NaNO <sub>2</sub>	85 g/mol×0.126 mol =11.97 g
Ethyl acetoacetate	14.4 g
Zinc powder	8.2 g
HCl	1.15 g/mL×17 mL=19.55 g
Ethanol	0.79 g/mL×600 mL = 474 g
DCM	1.33 g/mL×600.0 mL=798 g
Water	1000 g
Total	2409.62 g
Product	11 g
Steps to obtain product	2
Whether the catalyst is reusable	No
Catalyst cost (CNY/per gram of product)	(Zn power)¥2,477.91/Kg×10 <sup>-3</sup> ×8.2 = 20.35 (HCl)¥608/L×10 <sup>-3</sup> ×17 mL = 10.34 (20.35 + 10.34)/11 = 2.8

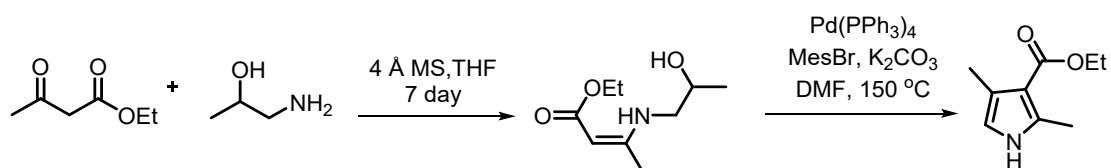
$$E\text{-factor} = (2409.62 - 11) \text{ g} / 11 \text{ g} = 218.96$$

$$\text{Reaction mass efficiency} = (11 \text{ g} / 55.92 \text{ g}) \times 100\% = 19.67\%$$

$$\text{carbon efficiency} = (11 / 167 \text{ g/mol}) \times 9 / (10 / 158.2 \text{ g/mol} \times 8 + 14.4 / 130.0 \text{ g/mol} \times 6) = 50.64\%$$

$$\text{Solvent intensity} = 213.2$$

(3) Aoyagi, Y.; Mizusaki, T.; Shishikura, M.; Komine, T.; Yoshinaga, T.; Inaba, H.; Ohta, A.; Takeya, K., *Tetrahedron* 2006, 62, 8533-8538.



Reagent	Amount
Ethyl 3-oxobutanoate	7.9 mmol×130.0 g/mol=1.03 g
THF	0.89 g/mL×30.0 mL=26.7 g
4 Å MS	5 g
Amino-2-propanol	9.4 mmol×75.1 g/mol=0.706 g
Mesityl bromide	1.33 g
Pd(PPh <sub>3</sub> ) <sub>4</sub>	0.17 g
K <sub>2</sub> CO <sub>3</sub>	1.79 g
DMF	0.95 g/mL×33 mL = 31.52 g
Water	132 g
Et <sub>2</sub> O	0.71 g/mL×2112 mL = 1500 g
Total	1700.29 g
Product	0.84 g
Steps to obtain product	2
Whether the catalyst is reusable	No
Catalyst cost (CNY/per gram of product)	(4 Å MS)¥1,601.75/Kg×10 <sup>-3</sup> ×5=8 (Pd(PPh <sub>3</sub> ) <sub>4</sub> )¥511.98/g×0.17=87.04 (87.04+8)/0.84=113.14

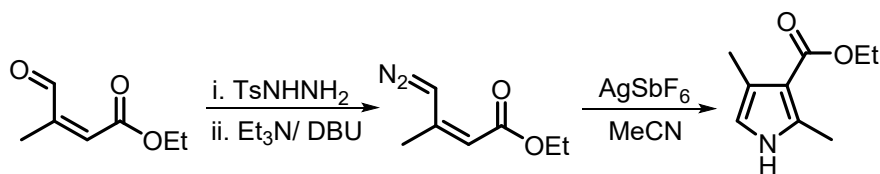
$$E\text{-factor} = (1700.29 - 0.84) \text{ g} / 0.84 \text{ g} = 2023.16$$

$$\text{Reaction mass efficiency} = (5.04 \text{ g} / 53.57 \text{ g}) \times 100\% = 9.4\%$$

$$\text{carbon efficiency} = (0.84 / 167 \text{ g/mol}) \times 9 / ((0.75 / 75.1 \text{ g/mol}) \times 3 + 1.03 / 130 \text{ g/mol} \times 6) = 59.8\%$$

$$\text{Solvent intensity} = 2012.17$$

(4) Billedeau, R. J.; Klein, K. R.; Kaplan, D.; Lou, Y., *Org. Lett.* 2013, 15, 1421-1423.



Reagent	Amount
( <i>E</i> )-3-methyl-4-oxo-but-2-enoic acid ethyl ester	2.0 g
DCM	1.33 g/mL × 635.0 mL = 844.55 g
Triethylamine	0.73 g/mL × 3.92 mL = 2.86 g
<i>p</i> -Toluenesulfonyl hydrazide	2.62 g
DBU	1.02 g/mL × 4.21 mL = 4.29 g
CH <sub>3</sub> CN	41 g/mol × 100 mmol = 4.1 g
AgSbF <sub>6</sub>	343.62 g/mol × 1 mmol = 0.34 g
Total	860.76 g
Product	0.25 g
Steps to obtain product	3
Whether the catalyst is reusable	No
Catalyst cost (CNY/per gram of product)	(AgSbF <sub>6</sub> ) ¥440.08/g × 0.34 = 149.63 149.63/0.25 = 598.52

$$E\text{-factor} = (860.76 - 0.25) \text{ g} / 0.25 \text{ g} = 3442.04$$

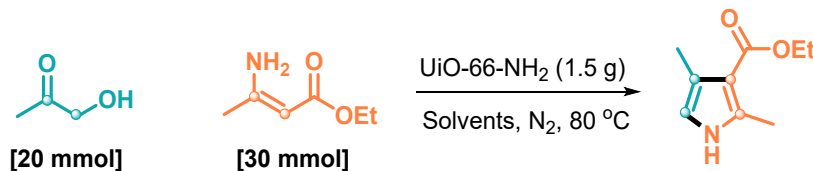
$$\text{Reaction mass efficiency} = (0.25 \text{ g} / 15.87 \text{ g}) \times 100\% = 1.58\%$$

$$\text{Carbon efficiency} = (0.25 / 167 \text{ g/mol}) \times 9 / (2 / 184 \text{ g/mol} \times 3 + 4.1 / 41 \text{ g/mol} \times 6) = 6.5\%$$

$$\text{Solvent intensity} = 3378.2$$



**This work:** We use gram scale scale-up reactions to calculate green chemistry process metrics. Yield is the average yield of ten cycles (56%), other conditions are consistent with gram-scale reaction conditions.



Reagent	Amount
Hydroxyacetone	1.4 g
Ethyl(Z)-3-aminobut-2-enoate	3.8 g
CH <sub>3</sub> NO <sub>2</sub>	50 mL × 1.13 g/mL = 56.5 g
TFE	25 mL × 1.32 g/mL = 33 g
UiO-66-NH <sub>2</sub>	1.5 g
Total	96.2 g
Product (Calculated with an average yield of 56% for ten reuses)	1.87 g
Steps to obtain product	1
Whether the catalyst is reusable	Yes
Catalyst cost (CNY/per gram of product, the catalyst can be reused ten times)	1.5g catalyst per synthesis: (ZrCl <sub>4</sub> ) ¥1,889.81/Kg × 10 <sup>-3</sup> × 0.9 = 1.7 (2-ATA) ¥5600/Kg × 10 <sup>-3</sup> × 0.69 = 3.8 (DMF) ¥656 × 10 <sup>-3</sup> × 30 = 19.68 (1.7 + 3.8 + 19.68)/1.87 = 13.5 13.5/10 = 1.35

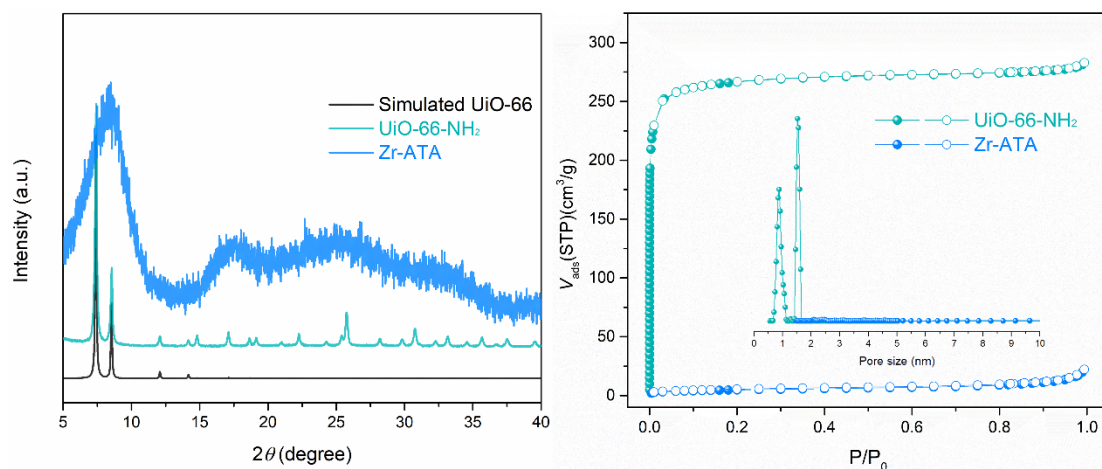
$$E\text{-factor} = (96.2 - 1.87) \text{ g} / 1.87 \text{ g} = 50.5$$

$$\text{Reaction mass efficiency} = (1.87 \text{ g} / 5.2 \text{ g}) \times 100\% = 35.9\%$$

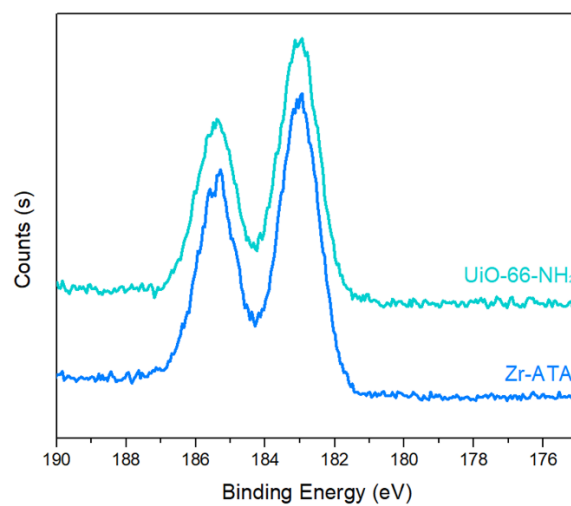
$$\text{carbon efficiency} = (1.87 / 167 \text{ g/mol}) \times 9 / (1.4 / 74 \text{ g/mol} \times 3 + 3.8 / 129 \text{ g/mol} \times 6) = 42.9\%$$

$$\text{Solvent intensity} = (56.5 + 33) / 1.87 = 47.86$$

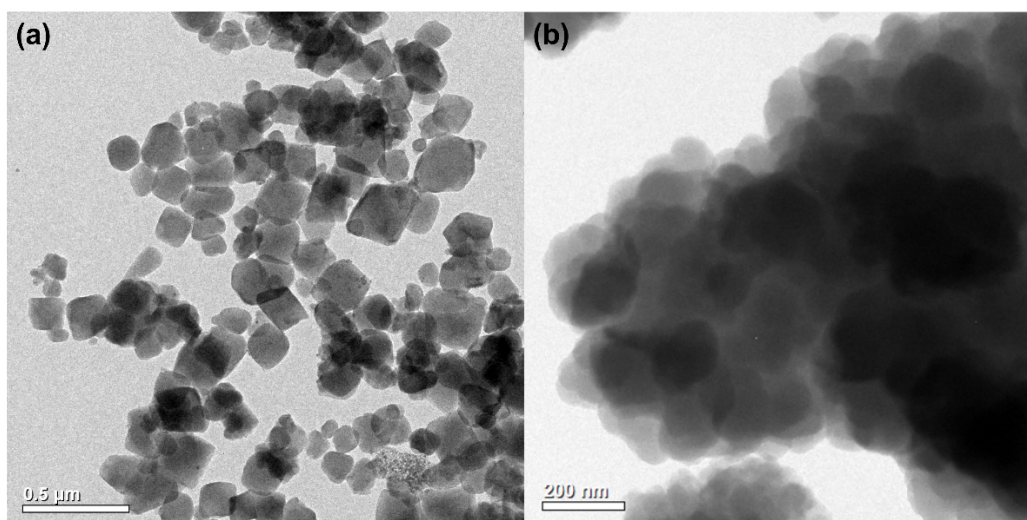
## 11. Catalyst structure characterization



**Fig. S1.** PXR (left) patterns and N<sub>2</sub> sorption isotherms (right) at 77 K of UiO-66-NH<sub>2</sub> and Zr-ATA

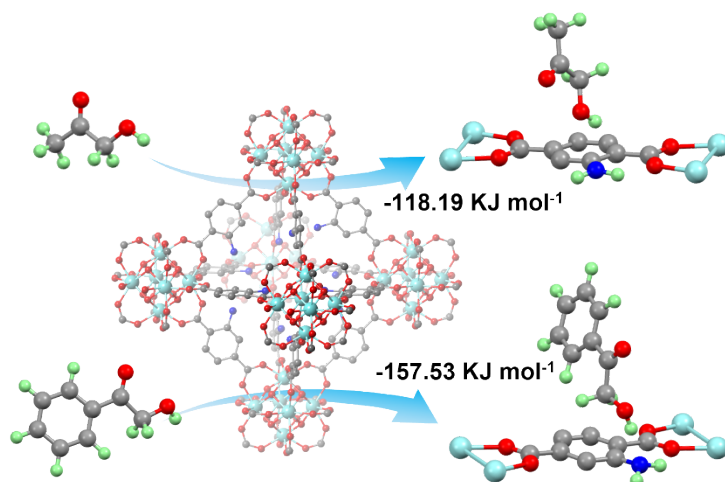


**Fig. S2** XPS spectrum of UiO-66-NH<sub>2</sub> and Zr-ATA.

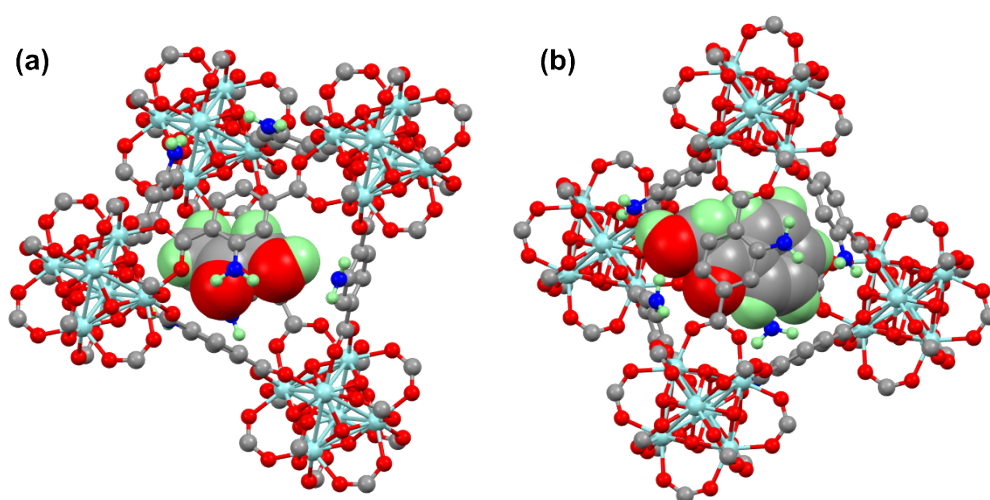


**Fig. S3.** TEM images of (a) UiO-66-NH<sub>2</sub> as-synthesized and (b) Zr-ATA.

## 12. DFT adsorption energy calculation

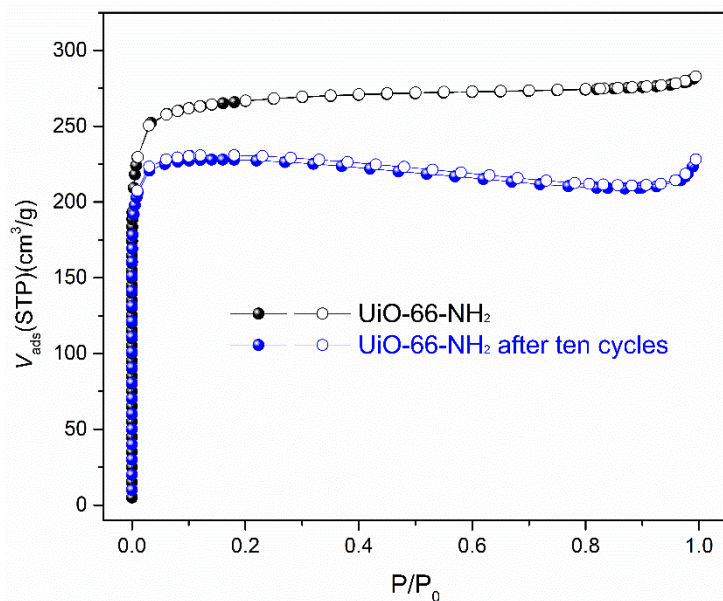


**Fig. S4.** DFT-calculated adsorption energies of UIO-66-NH<sub>2</sub> for hydroxyacetone and  $\alpha$ -hydroxyacetophenone, respectively. Gray C; Light green H; light blue Zr; red O; blue N.

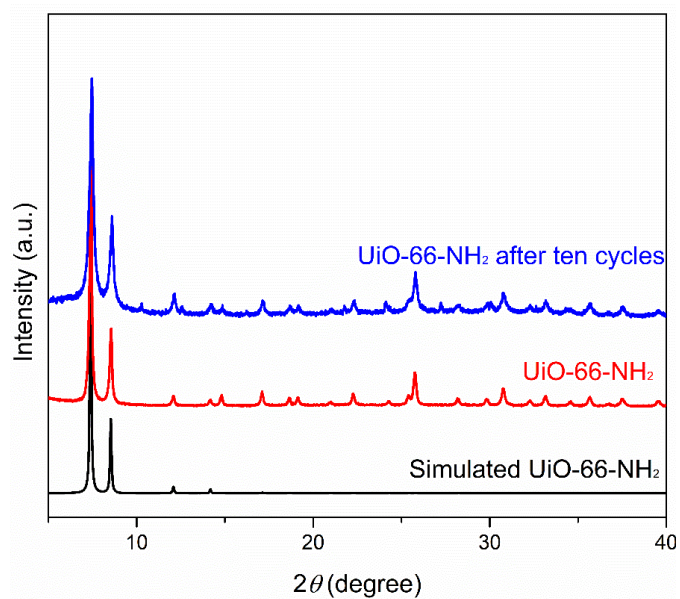


**Fig. S5.** Theoretical models of the interaction of hydroxyacetone (a) and  $\alpha$ -hydroxyacetophenone (b) on a UiO-66-NH<sub>2</sub> catalyst. Gray C; Light green H; light blue Zr; red O; blue N.

### 13. Catalyst recycling characterization



**Fig. S6.** N<sub>2</sub> sorption isotherms for UiO-66-NH<sub>2</sub> before reaction and after ten catalytic cycles at 77 K.

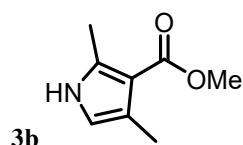


**Fig. S7.** PXRD pattern of UiO-66-NH<sub>2</sub> as synthesized (red) and after ten (blue) reaction cycles.

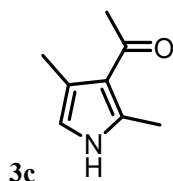
## 14. References

- [1] M. Lammert, S. Bernt, F. Vermoortele, D. E. De Vos, N. Stock, *Inorg. Chem.* **2013**, 52, 8521-8528.
- [2] G. Férey, C. Mellot-Draznieks, C. Serre, F. Millange, J. Dutour, S. Surblé, I. Margiolaki, *Science* **2005**, 309, 2040-2042.
- [3] J. H. Cavka, S. Jakobsen, U. Olsbye, N. Guillou, C. Lamberti, S. Bordiga, K. P. Lillerud, *J. Am. Chem. Soc.* **2008**, 130, 13850-13851.
- [4] S. J. Garibay, S. M. Cohen, *Chem. Commun.* **2010**, 46, 7700-7702.
- [5] M. Eddaoudi, J. Kim, N. Rosi, D. Vodak, J. Wachter, M. O'Keeffe, M. Yaghi Omar, *Science* **2002**, 295, 469-472.
- [6] C. Bannwarth, S. Ehlert, S. Grimme, *J. Chem. Theory Comput.* **2019**, 15, 1652-1671.
- [7] C. Bannwarth, E. Caldeweyher, S. Ehlert, A. Hansen, P. Pracht, J. Seibert, S. Spicher, S. Grimme, *WIREs Computational Molecular Science* **2021**, 11, e1493.
- [8] B. M. Trost, *Science* **1991**, 254, 1471-1477.
- [9] F. Roschangar, R. A. Sheldon, C. H. Senanayake, *Green Chem.* **2015**, 17, 752-768.
- [10] A. D. Curzons, D. J. C. Constable, D. N. Mortimer, V. L. Cunningham, *Green Chem.* **2001**, 3, 1-6.
- [11] R. A. Sheldon, *Green Chem.* **2017**, 19, 18-43.
- [12] D. J. C. Constable, A. D. Curzons, V. L. Cunningham, *Green Chem.* **2002**, 4, 521-527.
- [13] G. Meng, C. Liu, S. Qin, M. Dong, X. Wei, M. Zheng, L. Qin, H. Wang, X. He, Z. Zhang, *Res. Chem. Intermed.* **2015**, 41, 8941-8954.
- [14] Y. Aoyagi, T. Mizusaki, M. Shishikura, T. Komine, T. Yoshinaga, H. Inaba, A. Ohta, K. Takeya, *Tetrahedron* **2006**, 62, 8533-8538.
- [15] R. J. Billedeau, K. R. Klein, D. Kaplan, Y. Lou, *Org. Lett.* **2013**, 15, 1421-1423.
- [16] Y.-H. Tsai, S. Essig, J. R. James, K. Lang, J. W. Chin, *Nat. Chem.* **2015**, 7, 554-561.

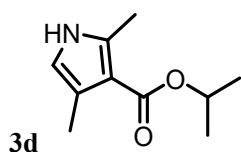
## 15. Characterization data of products



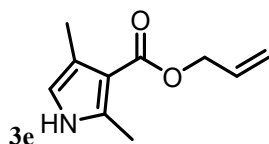
Methyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (**3b**): light yellow solid (21 mg, 67% yield), mp: 70–72 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.11 (s, 1 H), 6.21 – 6.15 (m, 1 H), 3.78 (s, 3 H), 2.48 (s, 3 H), 2.19 (s, 3 H). δ<sub>C</sub> (101 MHz, Chloroform-*d*) δ = 166.24, 134.43, 125.69, 111.26, 107.40, 50.69, 13.10, 12.63; HRMS (ESI, TOF) *m/z*: calcd for C<sub>8</sub>H<sub>12</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 154.0868, found 154.0869.



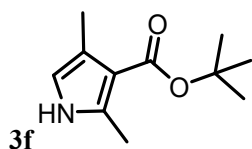
1-(2,4-Dimethyl-1*H*-pyrrol-3-yl)ethan-1-one (**3c**): white solid (11 mg, 39% yield), mp: 137–139 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.46 (s, 1 H), 6.21 – 6.10 (m, 1 H), 2.50 (s, 3 H), 2.37 (s, 3 H), 2.21 (s, 4 H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 195.24, 134.08, 125.54, 120.84, 107.86, 29.39, 13.87, 12.58; HRMS (ESI, TOF) *m/z*: calcd for C<sub>8</sub>H<sub>11</sub>NO, [M + H]<sup>+</sup> 138.0840, found 138.0840.



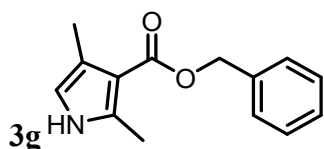
Isopropyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (**3d**): yellow solid (21 mg, 57% yield), mp: 85–87 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.07 (s, 1H), 6.23 – 6.15 (m, 1H), 5.14 (hept, *J* = 6.3 Hz, 1H), 2.47 (s, 3H), 2.19 (s, 3H), 1.30 (d, *J* = 6.3 Hz, 6H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 165.37, 134.04, 125.52, 112.04, 107.48, 66.25, 22.18, 13.18, 12.61; HRMS (ESI, TOF) *m/z*: calcd for C<sub>10</sub>H<sub>15</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 182.1102, found 182.1100.



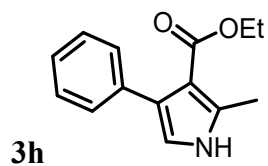
Allyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (**3e**): light yellow solid (26 mg, 73% yield), mp: 71–73 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.30 – 7.98 (m, 1H), 6.22 (d, *J* = 3.0 Hz, 1H), 6.09 – 5.90 (m, 1H), 5.43 – 5.15 (m, 2H), 4.71 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.48 (s, 3H), 2.19 (s, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 165.40, 134.60, 133.17, 125.72, 117.16, 111.23, 107.52, 64.00, 13.19, 12.62.; HRMS (ESI, TOF) *m/z*: calcd for C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 180.0946, found 180.0946.



*tert*-Butyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (**3f**): yellow solid (17 mg, 43% yield), mp: 72–74 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.01 (s, 1 H), 6.20 – 6.10 (m, 1 H), 2.45 (s, 3 H), 2.18 (s, 3 H), 1.54 (s, 9 H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 165.34, 133.48, 125.30, 113.18, 107.63, 79.07, 28.51, 13.24, 12.61; HRMS (ESI, TOF) *m/z*: calcd for C<sub>11</sub>H<sub>17</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 196.1292, found 193.1291.



Benzyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (**3g**): colorless solid (26 mg, 56% yield), mp: 115–117 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.12 – 7.92 (m, 1H), 7.43 – 7.30 (m, 5H), 6.24 (d, 1H), 5.25 (s, 2H), 2.47 (s, 3H), 2.18 (s, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 165.47, 137.10, 134.64, 128.45, 127.82, 127.76, 127.01, 125.69, 111.28, 107.63, 65.05, 13.25, 12.63; HRMS (ESI, TOF) *m/z*: calcd for C<sub>14</sub>H<sub>15</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 230.1136, found 230.1137.

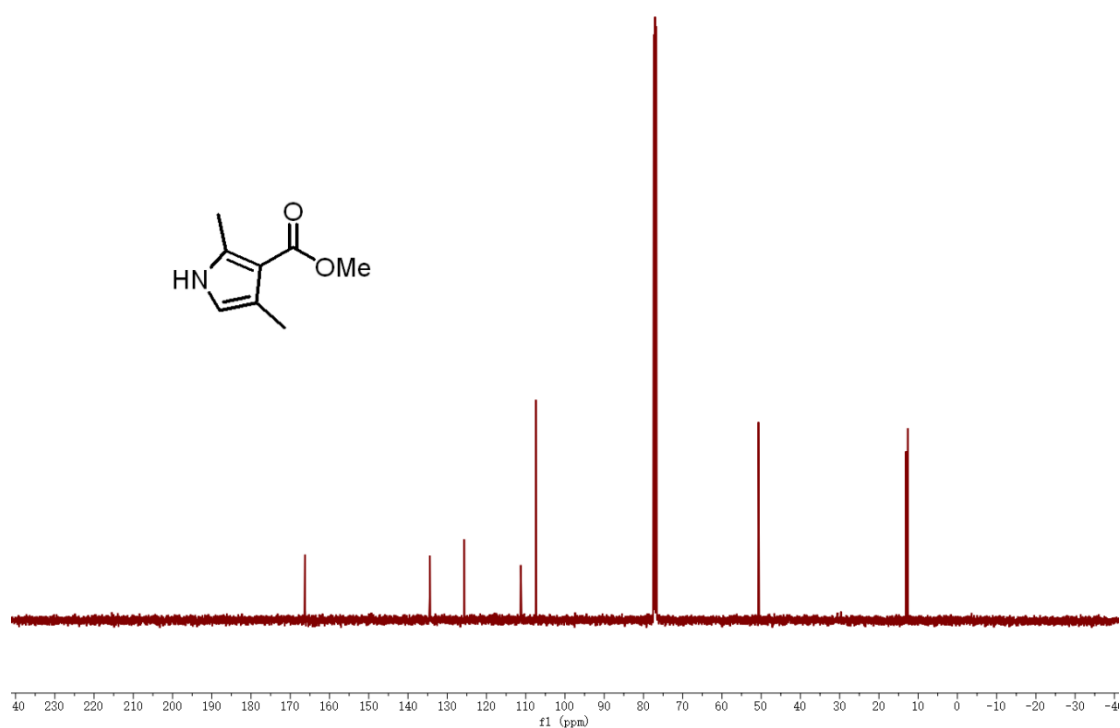
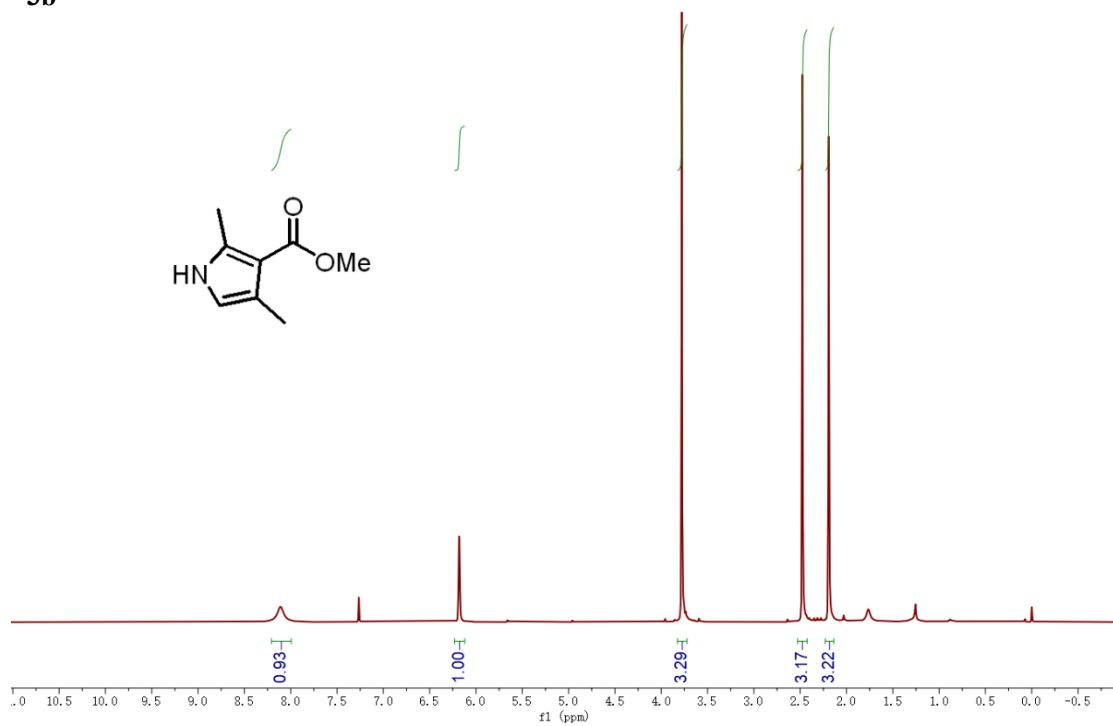


Ethyl 2-methyl-4-phenyl-1*H*-pyrrole-3-carboxylate (**3h**): yellow solid (21 mg, 46% yield), mp: 107–109 °C; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ = 8.50 (s, 1H), 7.48 – 7.42 (m, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.25 – 7.19 (m, 1H), 6.84 (d, *J* = 2.9 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.59 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ = 165.55, 136.13, 131.83, 128.96, 126.59, 123.68, 113.45, 107.38, 59.54, 14.54, 13.42; HRMS (ESI, TOF) *m/z*: calcd for C<sub>14</sub>H<sub>15</sub>NO<sub>2</sub>, [M + H]<sup>+</sup> 230.1102, found 230.1104.

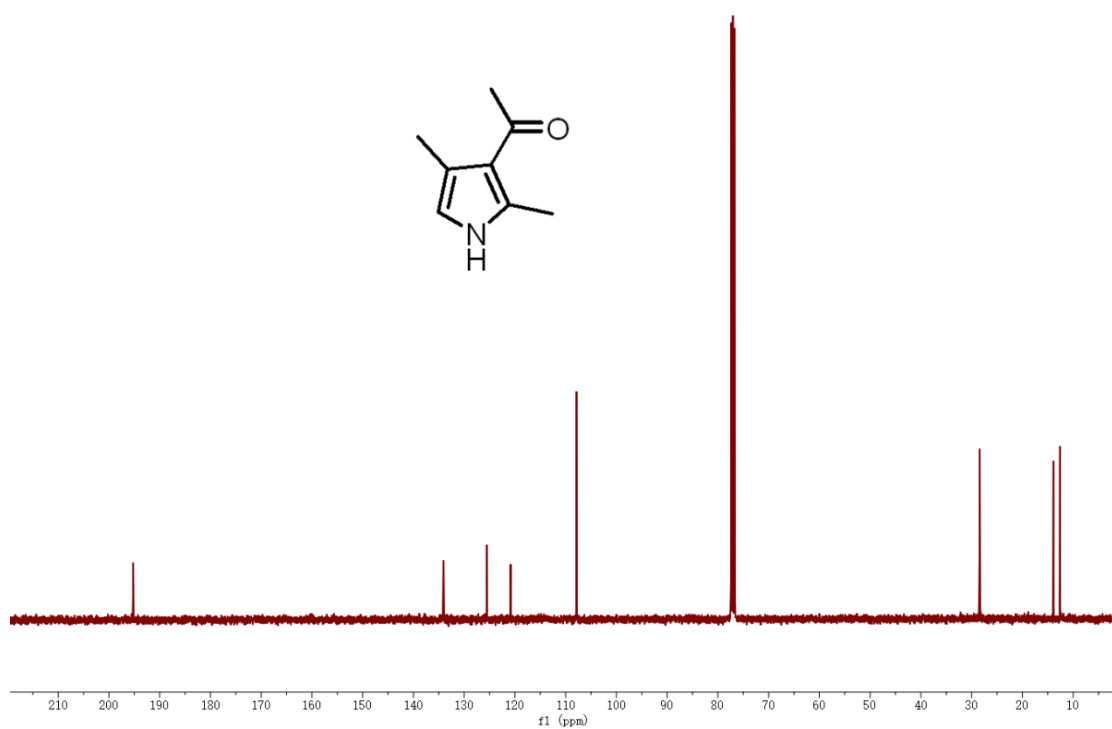
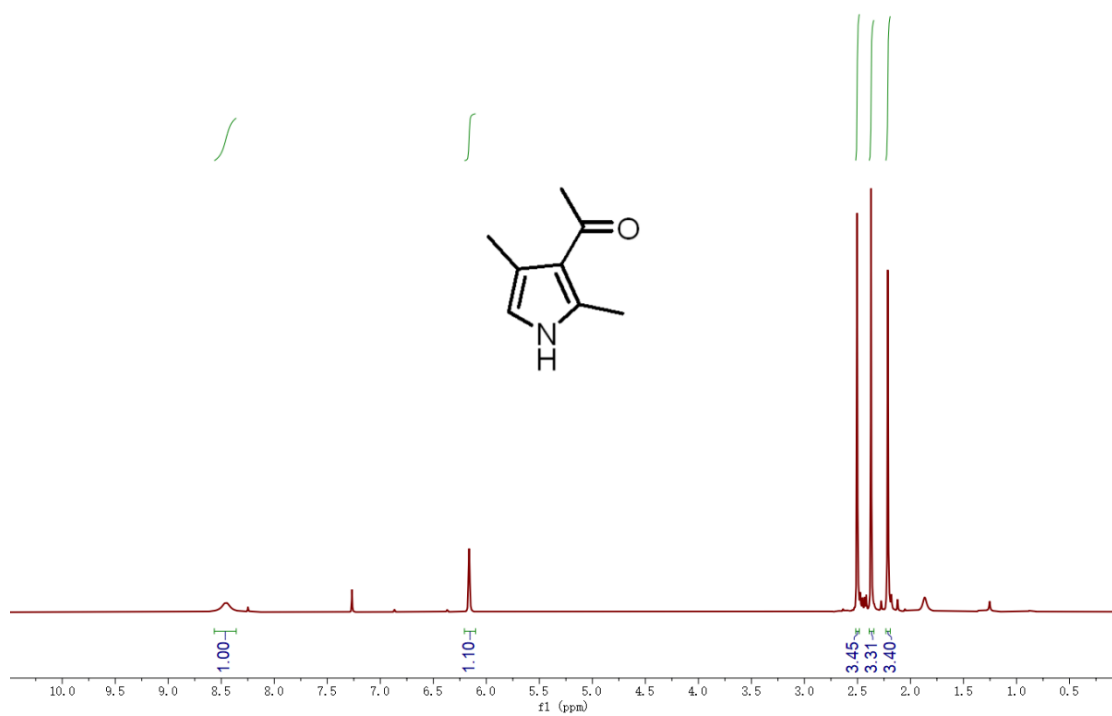


## 16. Copies of NMR spectra

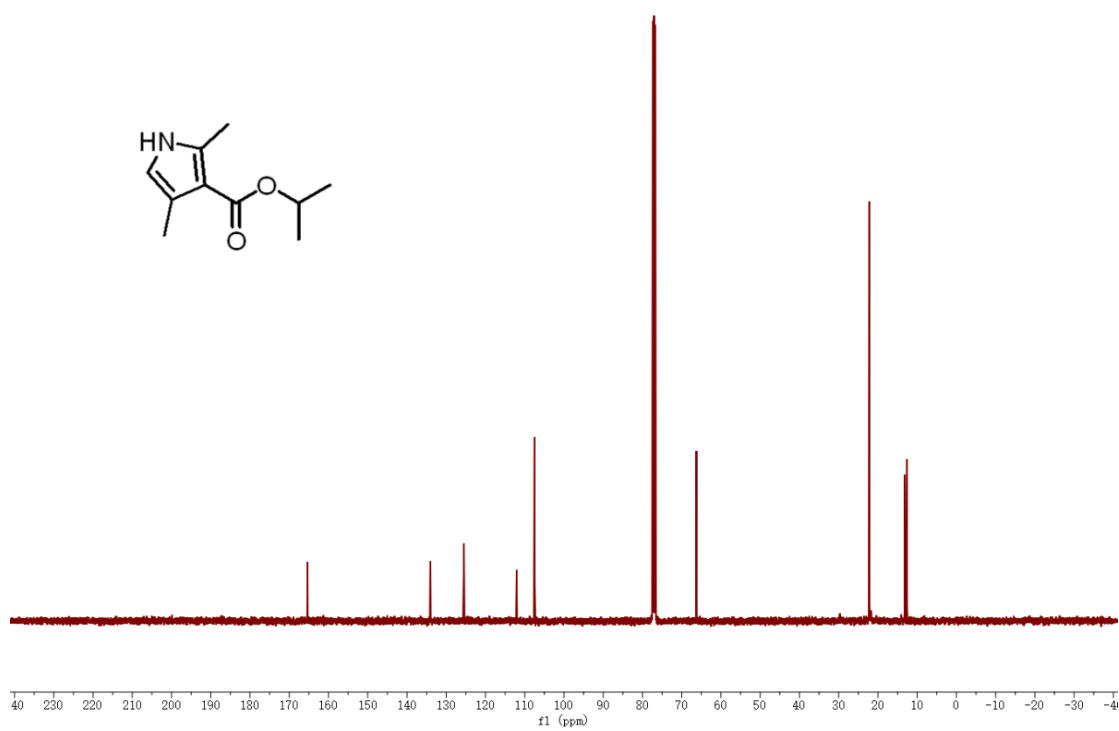
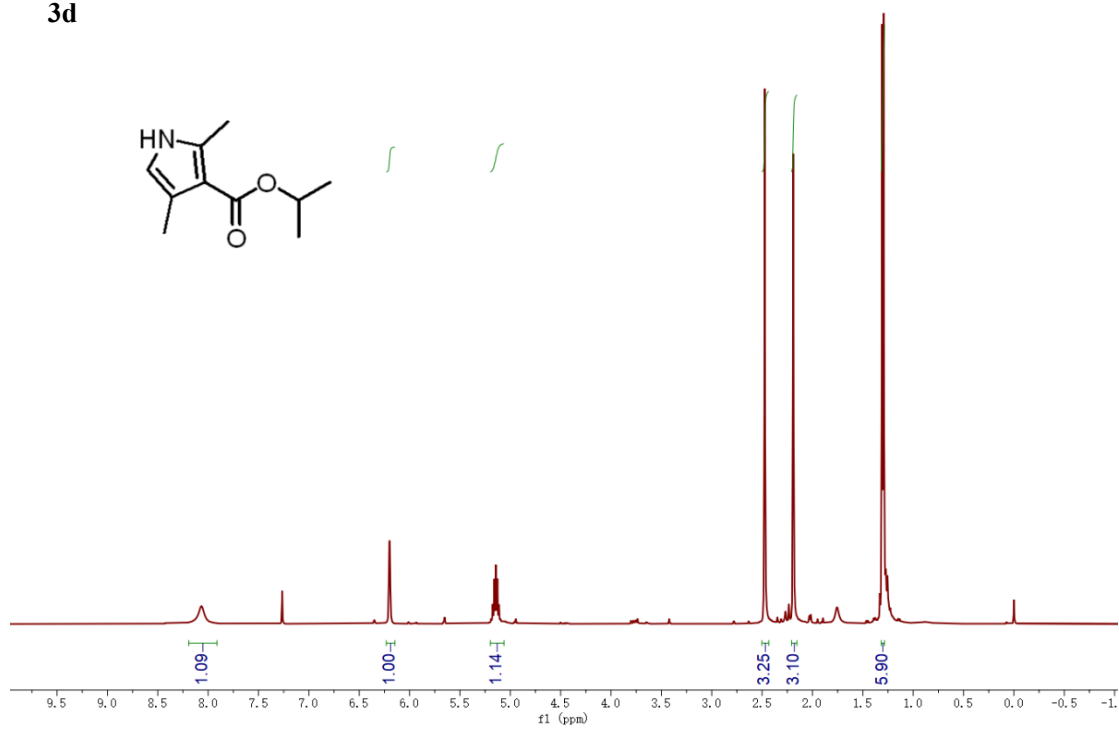
3b



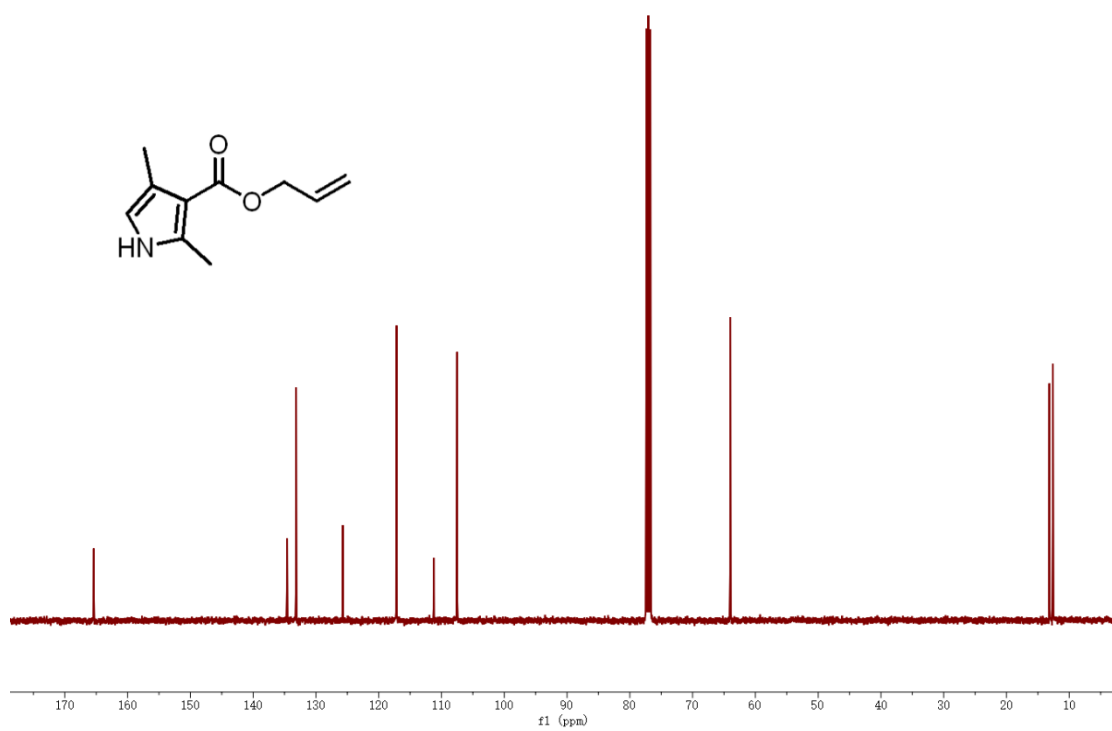
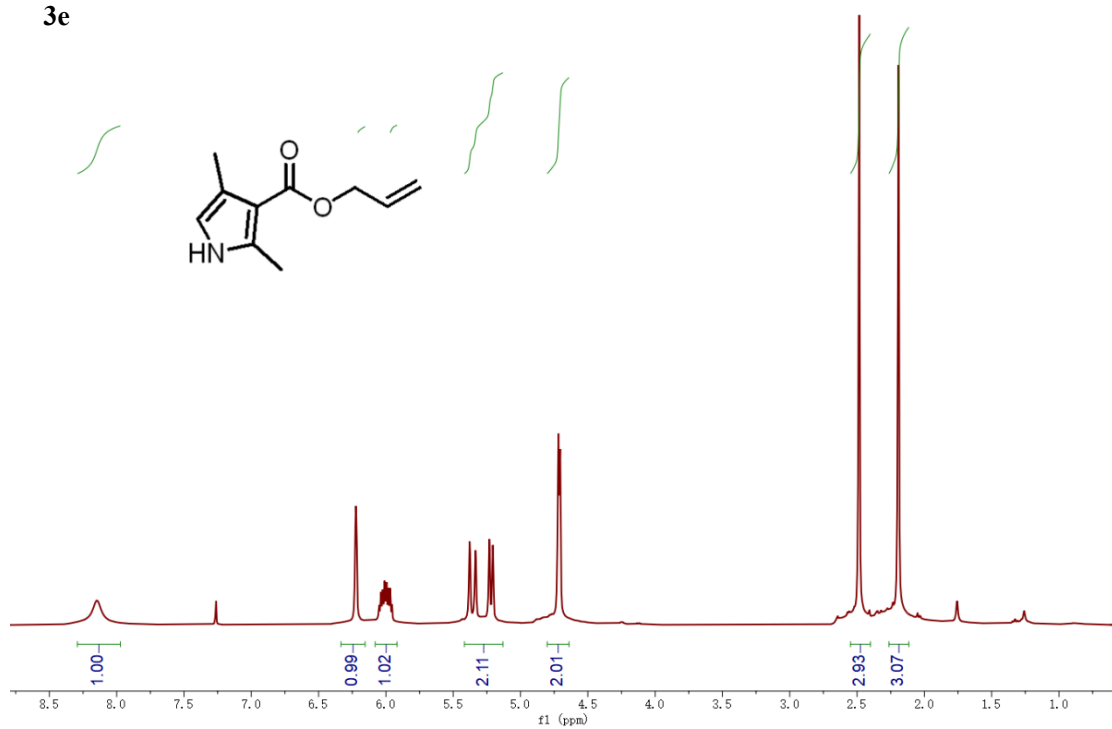
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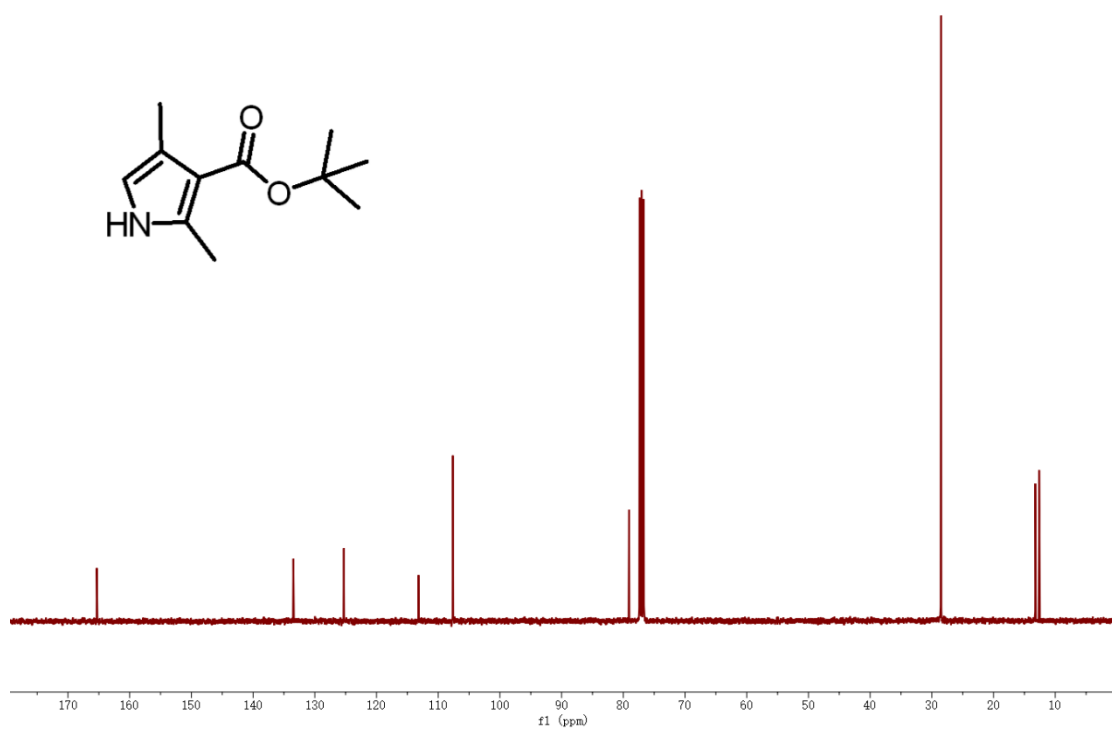
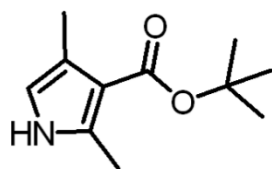
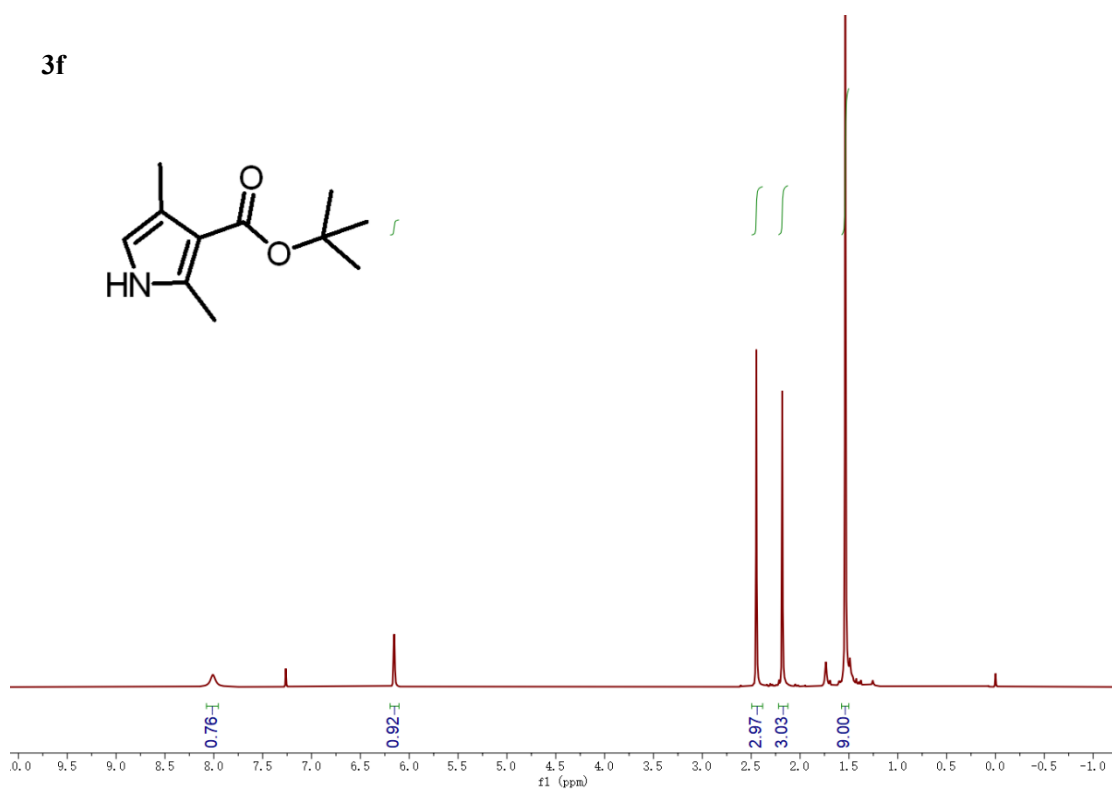
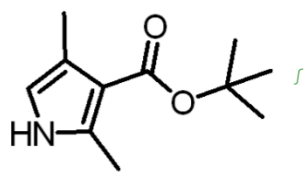
3d



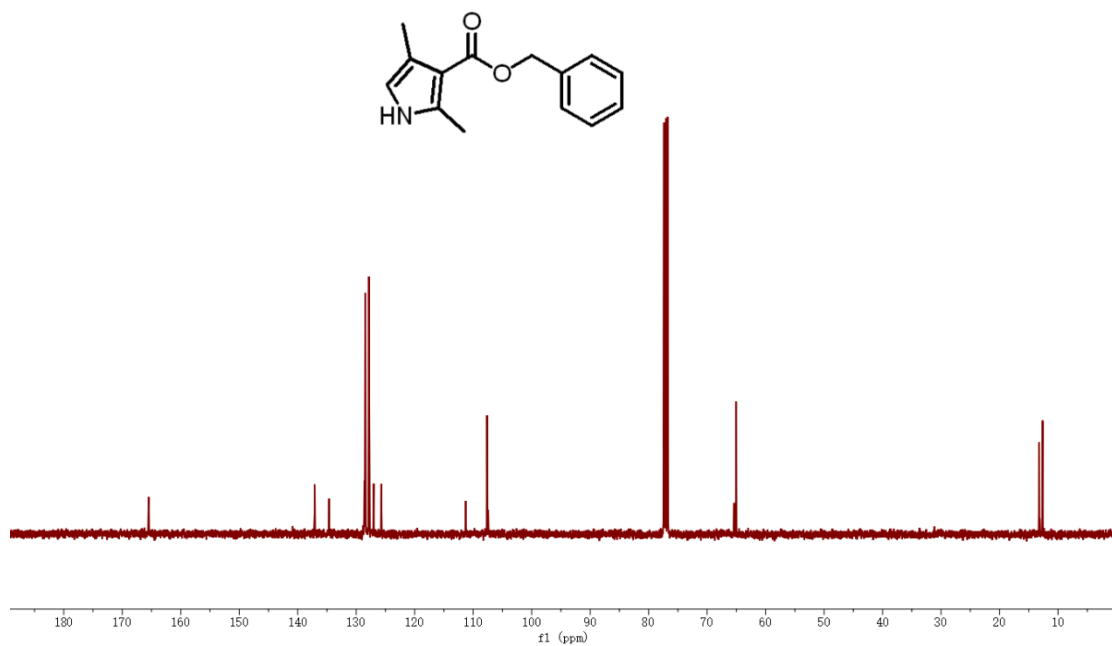
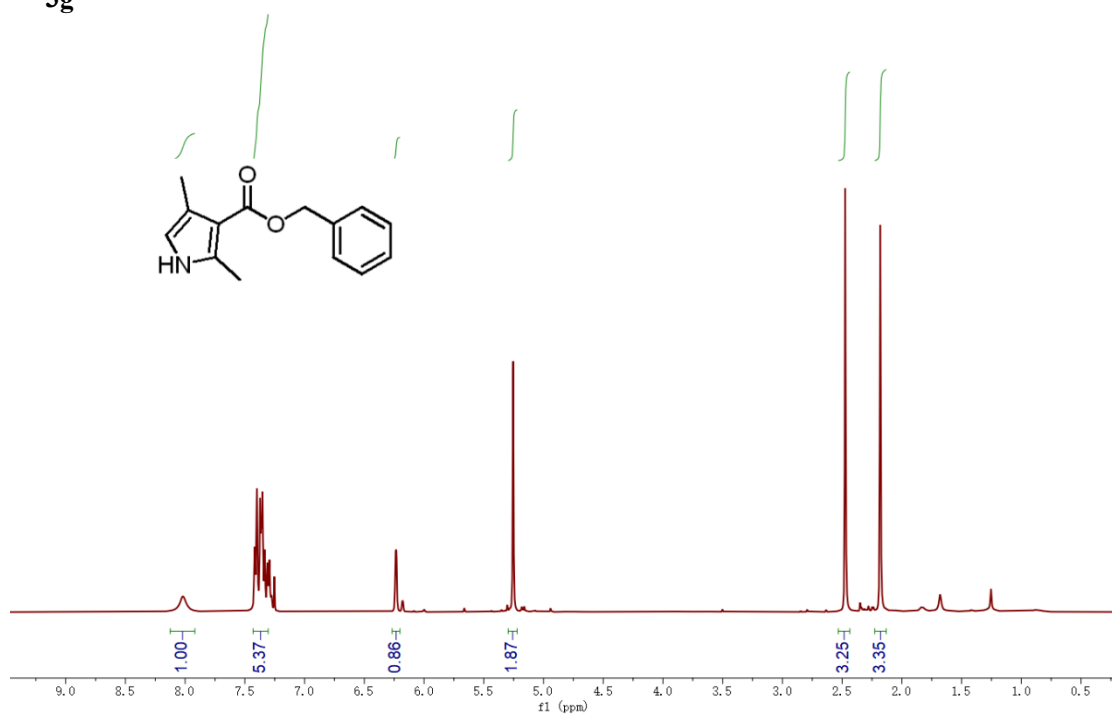
3e



3f



3g



3h

