**RAPID COMMUNICATION**

# Green and mild production of 5-aminolevulinic acid from algal biomass

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**Abstract**–Algal biomass was converted into 5-aminolevulinic acid (5-ALA) in five chemical steps: conversion to 5-(chloromethyl)furfural (5-CMF), ammoniation, ring-opening (photo-oxidation), reduction, and hydrolyzation. Among them, we mainly focused on the 5-CMF production and the following ammoniation. To our knowledge, the mixed solvent catalytic system of deep eutectic solvent (DES) and low concentration hydrochloric acid is the first reported for the synthesis of 5-CMF from algal biomass, providing a 24.6% 5-CMF yield at 120 °C for 5 h. Potassium phthalimide (KPI) was employed as an ammoniation reagent with superb selectivity and activity instead of conventional sodium azide ($NaN_3$). Optimizing the experimental design, a 23.7% 5-ALA yield along with high purity (>96%) was achieved from 5-CMF, and the total 5-ALA yield was 5.8% from algal biomass. This work provides a green and mild pathway for 5-ALA production from algal biomass.

Keywords: 5-Aminolevulinic Acid, 5-(Chloromethyl)furfural, Deep Eutectic Solvent, Ammoniation, Algal Biomass

## INTRODUCTION

5-Aminolevulinic acid (5-ALA), as an essential intermediate, is the core structure of heme, porphyrins, vitamin B12, and chlorophyll [1,2]. 5-ALA is biodegradable, highly active, and non-toxic, so it has been widely applied in the agricultural field such as salt tolerance agent, cold temperature tolerance agent, herbicide, insecticide, and plant growth regulator [3-5]. Meanwhile, it has also been proposed for cosmetics, health care products, and photodynamic therapy or diagnostic drugs for various cancers [6,7].

Up to now, 5-ALA has been mainly synthesized by microbial routes [8-10]; however, it is difficult to carry out large-scale applications in a short time. On the other hand, chemical routes using furfurylamine, tetrahydrofurfurylamine, and 5-hydroxy-2-pyridon as starting materials have enormous challenges, such as commercial availability of the starting materials, rigorous conditions, and toxic intermediates [11,12]. Therefore, it is highly desirable to develop a green and sustainable 5-ALA production pathway.

Biomass used as starting material has gained the spotlight due to its availability, sustainability, and renewability [13-16]. Compared to terrestrial biomass, algal biomass is more appealing and considered as a potential alternative for land crops in the field of biorefinery because of its high growth rate, which is approximately 7-10 times than land crops [17]. Many studies have shown the potential of algal biomass in a biorefinery. For example, Lee's group reported that 30.13 wt% and 28.15 wt% levulinic acid (LA) yield could be obtained from *Nannochloropsis gaditana* and *Chlorella*, respectively [18]. The same group also proposed a chemical conversion way for ethyl levuli-

nate production through wet in situ transesterification of algal biomass [19,20]. What is more, several studies relating to biomass-derived platform chemicals employed as starting materials, like 5-hydroxymethylfurfural (5-HMF), LA, and methyl levulinate, were investigated for the production of 5-ALA [21-23]. However, these cases shared the same problems, such as poor yield direct from raw biomass. Unlike these platform chemicals, 5-(chloromethyl)furfural (5-CMF) preparation with high yield direct from raw biomass catalyzed by hydrochloric acid (HCl) was reported by several elegant studies [24-27]. As one of the most remarkable milestones on platform chemicals production in a biorefinery, Mascal and co-workers first reported a 5-ALA production method based on biomass derived 5-CMF, and employed $NaN_3$ as a nitrogen atom donor [24,28]. 92% yield intermediate product 5-(azidomethyl)furfural was obtained at 110 °C for 3, and total 5-ALA yield was 68% from 5-CMF *via* ring-opening (photo-oxidation), reduction, and hydrolyzation (Scheme S1). Inspired by this, developing a new way to synthesize 5-ALA from biomass *via* 5-CMF as an intermediate is of great significance, especially the steps of 5-CMF preparation and next ammoniation are sustainable and green.

Deep eutectic solvent (DES) is regarded as an emerging type of "designer" ionic liquid and has attracted much attention due to its excellent properties, including low vapor pressure, tunable polarity, biodegradability, easy of preparation, and economics [29-31]. Our previous work reported a novel 5-CMF production method based on choline chloride (ChCl)/fructose DES along with eliminating dependence on concentrated acid, providing a 50.3% CMF yield [32]. So DES-based CMF production method was further carried out. In addition, phthalimide potassium salt (KPI), as a non-toxic and green amination agent [33,34], was also used for the synthesis of 5-ALA.

In this work, an environment-friendly and mild synthesis route
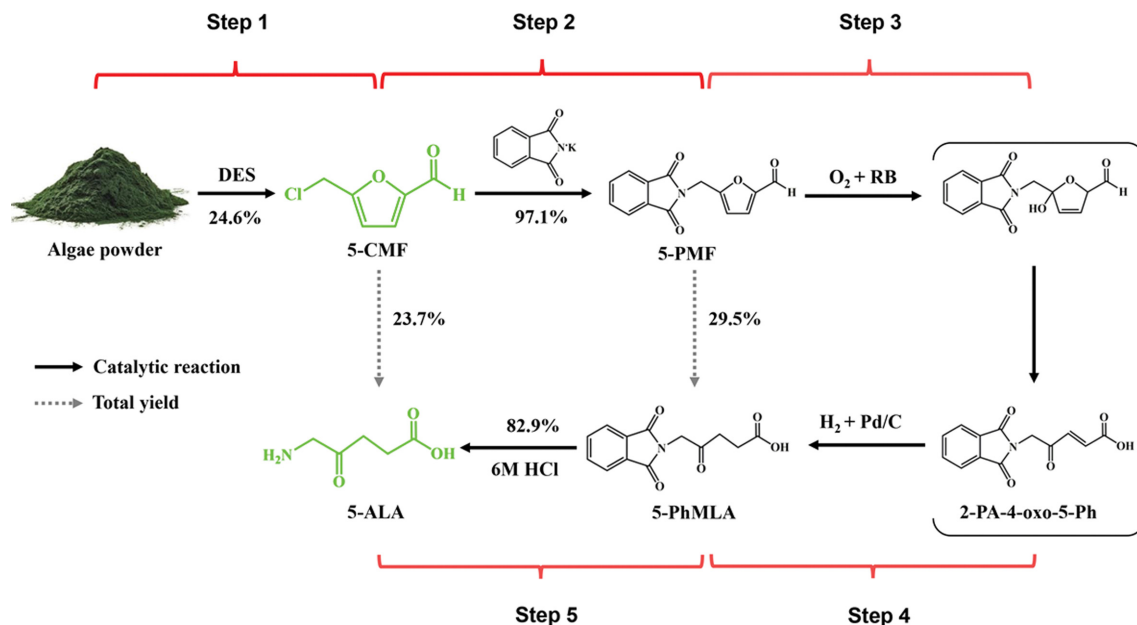
Scheme 1. Synthesis of 5-ALA from algal biomass in five chemical steps.

for 5-ALA production from algal biomass was proposed (Scheme 1). The mixed solvent catalytic system of deep eutectic solvent (DES) and low concentration hydrochloric acid (HCl) was first reported for the 5-CMF production from algae powder, providing a 24.6% 5-CMF yield at 120 °C for 5 h. KPI as a greener nitrogen donor was employed in the ammoniation process along with a 5-phthalimid-emethyl furfural (5-PMF) yield up to 97.1%. What is more, a detailed pathway including ring-opening (photooxidation), reduction, and hydrolyzation was also further discussed. The total 5-ALA yield of 23.7% with high purity (96%) was obtained from 5-CMF, and the total 5-ALA yield from algal biomass was 5.8%.

## MATERIAL AND METHODS

### 1. Material

Algae powder was obtained from Xi'an Shouhe Biotechnology Co., Ltd. Phthalimide potassium salt (KPI, >98%) was supplied by Aladdin (Shanghai, China). All other chemicals were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and used without any treatment or purification.

### 2. Experimental Procedure

2-1. The Procedure for the Synthesis of 5-CMF

The preparation of 5-CMF was carried out in a 50 mL round-bottom flask. The DES system was formed by a measurable mass ratio of ChCl to $AlCl_3 \cdot 6H_2O$, and algae powder (0.23 g) was introduced to the flask with $CrCl_3 \cdot 6H_2O$ (0.1 g) as a catalyst and methyl isobutyl ketone (MIBK, 12.5 mL) as extraction solvent. The flask equipped with a condenser was then placed in an oil bath preheated to the desired temperature (100-130 °C) with stirring (500 rpm). After the reaction was completed, the crude 5-CMF was obtained by filtration and extraction, and the light yellow 5-CMF was observed by further distillation (95% purity detected by GC-MS, Fig. S1). All experiments for 5-CMF production and the next other

reactions were repeated three times.

2-2. The Procedure for the Synthesis of 5-Phthalimidemethyl Furfural (5-PMF)

5-CMF (0.1 g), KPI (0.185 g) and N, N-dimethyl formamide (DMF, 30 mL) were added to a three-necked flask and stirred at 40 °C for 3 h. After the reaction was completed, deionized water was added to the mixture, and followed by filtration. A 5-PMF purity over 98% could be detected by GC-MS (Fig. S2).

2-3. Typical Procedure for the Synthesis of 2-Pentenoic Acid, 4-Oxo-5-phthalimido (2-PA-4oxo-5-Ph)

The procedure of ring-opening (photo-oxidation) was based on Takeya's work and Ha's work with small minor modifications [5, 35]: 5-PMF (2.3 g) and rose bengal (RB, 0.18 g) in DMF (30 mL) solution was irradiated with a metal halide lamp (250 W). During the irradiation, the dry oxygen was effervesced through the above solution. When 5-PMF was completely consumed, activated carbon was added to the reaction system to remove the color of the liquid products. Crude 2-pentenoic acid, 4-oxo-5-phthalimido (2-PA-4oxo-5-Ph) could be obtained after further removing solvent with the rotary evaporator (40 °C).

2-4. Typical Procedure for the Synthesis of Methyl 5-Phthalimide-levulinic Acid (5-PhMLA)

The procedure of reduction was based on Takeya's work and Ha's work with small minor modifications [5,35]: 1.2 g 2-PA-4-oxo-5-Ph, 0.4 g Pd/C, and 40 mL $CH_3OH$ were added and shaken under 2 MPa $H_2$ at the desired temperature (20-70 °C) for 2-7 h. After filtration and rotary evaporation, a light yellow crude 5-PhMLA could be detected by GC-MS with a purity of 90% (Fig. S3).

2-5. Typical Procedure for the Synthesis of 5-ALA

The procedure of hydrolyzation was based on our previously described procedure with small minor modifications [23]: 5-PhMLA (0.65 g) was boiled in 6 M HCl (15 mL) for 10 h, then the mixture was cooled to −23 °C. The by-products were collected by fil-

tration and dried, and 20 mL acetone was added to the mixture medium. The resulting precipitate was collected by filtration and then dried to yield whiteness 5-ALA with a purity of over 96% (detected by HPLC, Fig. S4).

## 3. Analytical Methods

The GC-MS (Thermofisher Trace 1300 & ISQ LT) equipped with a TR-5MS column (15.0 m×250 μm×0.25 μm) was used for qualitative analysis.

The yield of 5-ALA was determined by HPLC (Waters 2695) equipped with a ZORBAX Eclipse XDB-C18 column (250 mm× 4.6 mm) and the injection volume was 10 μL. The maximum absorption wavenumber for 5-ALA was 265 nm. The mobile phase was methanol : water=5 : 5 (v : v) with 1/1,000 (v : v) acetic acid and flow rate was at 0.6 mL/min.

The samples including 5-CMF, 5-PMF, 5-PhMLA, and 5-ALA were characterized by NMR (Bruker AV 600 MHz, Germany), and as shown in Fig. S5-S11.

The yields and conversion were calculated by external standard method following the equation:

$$5\text{-CMF yield (\%)} = \frac{\text{moles of 5-CMF produced}}{\text{moles of starting hexoses}} \times 100\%$$

$$\text{Yield}_x \text{ (\%)} = \frac{\text{moles of X produced}}{\text{moles of starting materials}} \times 100\%$$

(x stands for 5-PMF, 5-PhMLA, and 5-ALA)

$$\text{Conversion}_x \text{ (\%)} = \left(1 - \frac{\text{moles of 5-PMF in reaction mixture}}{\text{moles of starting materials}}\right) \times 100\%$$

(x stands for 5-CMF and 5-PMF)

## RESULTS AND DISCUSSION

## 1. Synthesis of 5-CMF from Algal Biomass

### 1-1. Effects of Additive

Encouraged by our previous study [32], we used DES (ChCl/ AlCl$_3$·6H$_2$O) to produce 5-CMF direct from algal biomass. As shown in Fig. 1(a), however, CMF yield was poor (only 4.6%) at 120 °C for 5 h. Some studies have revealed that metal-based or metal-containing ionic liquids and DES exhibited superior catalytic activity for the conversion of glucose and glucose polymers [36,37], so some metal chlorides were added into DES for further investigation. Compared to the control experiment, additional ZnCl$_2$, SnCl$_4$, and CrCl$_3$·6H$_2$O all promoted the isomerization process and the yield of 5-CMF was 5.2, 7.3, and 10.4%, respectively. The highest total furanic derivative yield (5-CMF and 5-HMF) was 25% catalyzed by in DES (ChCl/AlCl$_3$·6H$_2$O/CrCl$_3$·6H$_2$O). It was noted that even when CrCl$_3$·6H$_2$O was supported on the Amberlyst-15 resin (abbreviation for CrCl$_3$-Amb-15), the 5-CMF yield still could increase from 4.6 to 6.9%. However, the catalytic activity of CrCl$_3$-Amb-15 was inferior to that of single chromium salt, which may be ascribed to the fact that CrCl$_3$-Amberlyst-15 resin as a heterogeneous catalyst was not fully in contact with the reaction substrates in DES [38], so CrCl$_3$·6H$_2$O was employed for further experiment.

### 1-2. Effects of the Reaction Temperature and Reaction Time on Yield

The reaction temperature and reaction time had a significant influence on the yield of 5-CMF (Fig. 1(b)). When the reaction temperature (100 and 110 °C) was lower than the boiling point of the MIBK solvent (116 °C), the yield of 5-CMF increased gradually during the whole process. However, it was also observed that the yield of 5-CMF exhibited the tendency of rising first and then decreasing once the temperature increased to 120 or 130 °C. This phenomenon may be because the increase of temperature can accelerate the speed of molecular motion, which was conducive to the migration of 5-CMF to the extraction phase. However, the intense boiling of the extraction phase will lead to incomplete extraction at the higher temperature, which also promotes the aggravation of the undesirable side reaction (e.g. formation of humins and polymers) [39,40]. A darker reaction solution color at higher temperature was observed, which also proved that the side reactions occurred simultaneously at elevated temperature as well. Optimizing the reaction parameters, the maximum 5-CMF yield was 10.4% from algal biomass at 120 °C for 5 h.

### 1-3. Effects of HCl Content

Previous studies have demonstrated that concentrated acid can produce 5-CMF with a high yield direct from biomass [41]. To further improve the conversion and desired product selectivity, a small amount of HCl was introduced to the reaction system. As shown in Fig. 1(c), 5-CMF yield increased rapidly from 10.4 to 24.6% when the content of HCl increased from 0 to 100 μL. At the same time, the total furanic derivatives yield was up to 39.5% in DES with 100 μL HCl. The introduction of HCl obviously enhanced the behavior of DES, which may be because substrate hydrolysis and sugars dehydration were promoted due to the enhancement of Brønsted acidity (H$^+$) [42]. When HCl loading was further increased to 200 μL, the yield of 5-CMF was almost unchanged. However, the DES system was destroyed and the reaction system changed from biphasic system to single-phase system due to the introduction of a large amount of water (HCl aqueous solution), leading to an obstacle in the following separation and extraction process.

### 1-4. Reusability of DES

The reusability of DES is an important parameter for industrial production. After finishing the reaction, the extractant solvent (upper) containing the products was directly separated. The DES phase (bottom) did not require any treatment, and the new starting materials (0.23 g algae powder, 0.1 mL HCl, and 12.5 mL MIBK) were added for the next cycle (Fig. 1(d)). The yields of 5-CMF and 5-HMF reduced quickly in the first cycle, and a small amount of algae powder residue was clearly observed in the second cycle. But in our previous work, DES exhibited good stability when the starting materials were sugars [32,43]. This may be because the complicated algal biomass as substrate was easier to produce more byproducts compared to sugars, so the DES system was more likely to be contaminated.

### 1-5. Biphasic System for 5-CMF Production from Biomass

Fig. 1(e) shows a biphasic system for 5-CMF production from biomass, including the bottom layer of DES phase (ChCl/AlCl$_3$· 6H$_2$O/CrCl$_3$·6H$_2$O) with a small amount of HCl as the catalyst and the top layer of organic extraction phase (MIBK). According to the above analysis and previous studies [44,45], a plausible mechanism was provided (Scheme S2). In the DES phase, the algal biomass was hydrolyzed to glucose via Brønsted acidity (H$^+$), followed by isomerization to fructose via Lewis acidity (Al$^{3+}$ and Cr$^{3+}$). Next, fructose removed three molecules of water to 5-HMF and then
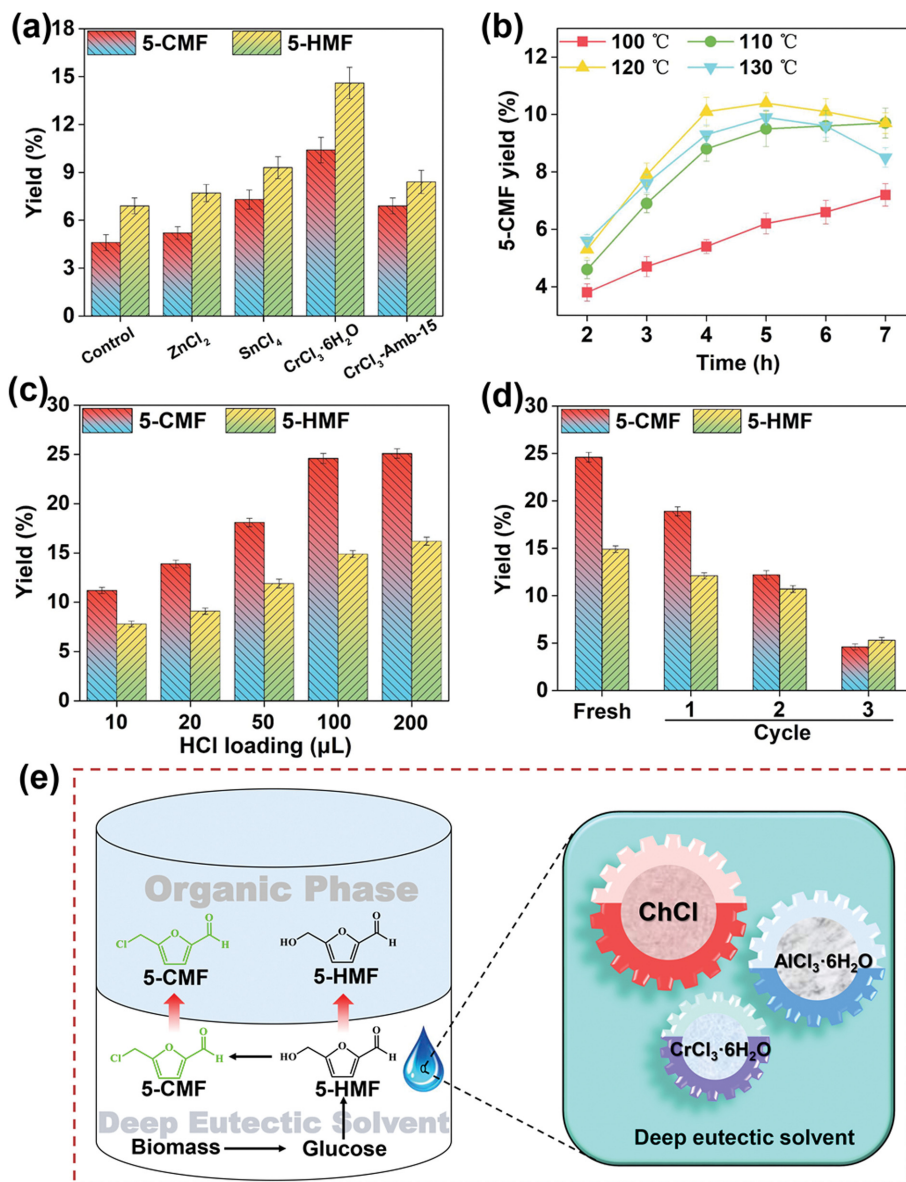
Fig. 1. (a) Yields of 5-CMF and 5-HMF obtained in the presence of various metal salts. (b) Effects of reaction time and temperature on 5-CMF yield. (c) Effects of different loading of HCl. (d) Reusability of DES. (e) Biphasic system for conversion of biomass into 5-CMF. Reaction conditions: 0.23 g algae powder, 0.9 g ChCl, 0.3 g AlCl₃·6H₂O, 12.5 mL MIBK. (a) 0.1 g metal salts, 120 °C, 5 h; (b) 0.1 g CrCl₃·6H₂O; (c) 0.1 g CrCl₃·6H₂O, 120 °C, 5 h; (d) 0.1 g CrCl₃·6H₂O, 100 μL HCl, 120 °C, 5 h.

was halogenated *via* the *in-situ* formation of HCl. These furanic derivatives (5-CMF and 5-HMF) were further extracted into the organic phase to prevent further degradation and condensation.
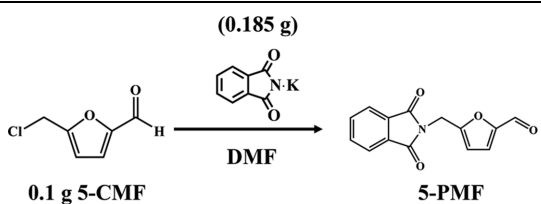
**2. Synthesis of 5-PMF from 5-CMF**

The first attempt to screen the ratio between 5-CMF and KPI is shown in Fig. 2. As we predicted above, the encouraging yield of the target product was up to 89.4% using KPI for the ammoniation process when the mole ratio of 5-CMF and KPI was 0.7 : 1. The reaction conditions, including time, temperature, and the volume of N, N-dimethyl formamide (DMF), were further optimized and shown in Table 1. It can be seen that the conversion of 5-CMF was near 100% under different conditions, suggesting that KPI possessed excellent activity in the whole ammoniation process. The 5-

PMF yield increased with the prolonging of the reaction, and a maximum yield (90.1%) was detected at 2 h. Nevertheless, the 5-PMF yield showed downward trends when the reaction time was over 2 h (Table 1, entries 1-6), indicating that longer reaction time was not conducive to the accumulation of the target product.

Meanwhile, the effects of reaction temperature showed similar regularity. With the reaction temperature increased from 20 to 120 °C, the yield of 5-PMF exhibited a trend of increasing first and then decreasing. It may be ascribed to the shift of equilibrium towards 5-PMF at elevated temperature. Meanwhile, the reactive collisions and miscibility were increased by raising the temperature, which promoted the formation of 5-PMF since facilitating mass transfer [46]. However, the excessive reaction temperature can lead to the

**Table 1. Effects of different reaction conditions on 5-PMF yield and 5-CMF conversion**



| Entry | Temperature (°C) | Time (h) | DMF volume (mL) | 5-PMF yield (%) | 5-CMF conversion (%) |
|---|---|---|---|---|---|
| 1 | 20 | 1 | 20 | 83.9±0.8 | >99.0 |
| 2 | 20 | 3 | 20 | 90.1±1.1 | >99.0 |
| 3 | 20 | 5 | 20 | 89.4±0.7 | >99.0 |
| 4 | 20 | 7 | 20 | 87.2±0.5 | >99.0 |
| 5 | 20 | 9 | 20 | 80.0±1.3 | >99.0 |
| 6 | 20 | 11 | 20 | 79.3±0.9 | >99.0 |
| 7 | 40 | 3 | 20 | 93.5±0.6 | >99.0 |
| 8 | 60 | 3 | 20 | 91.5±0.8 | >99.0 |
| 9 | 80 | 3 | 20 | 89.5±1.2 | >99.0 |
| 10 | 100 | 3 | 20 | 88.0±0.7 | >99.0 |
| 11 | 120 | 3 | 20 | 85.3±0.9 | >99.0 |
| 12 | 40 | 3 | 10 | 89.4±1.1 | >99.0 |
| 13 | 40 | 3 | 30 | 97.1±0.9 | >99.0 |
| 14 | 40 | 3 | 40 | 96.4±0.6 | >99.0 |
| 15 | 40 | 3 | 50 | 85.4±0.5 | >99.0 |
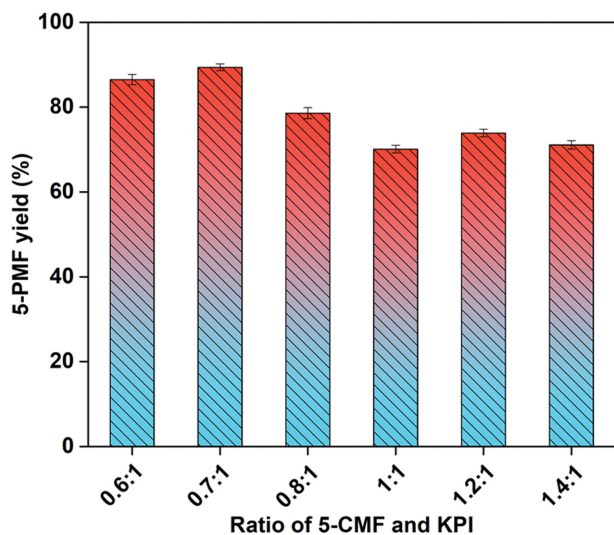


**Fig. 2. Effects of different ratio between 5-CMF and KPI on 5-PMF yield. Reaction conditions: 0.185 g KPI, 4 h, 20 °C.**

formation of more insoluble black sediment byproduct termed humins, which attenuate the yield of 5-PMF [47]. The maximum of the target product yield was 93.5% when the reaction temperature was 40 °C (Table 1, entries 7-12).

Furthermore, the corresponding 5-PMF yield increased quickly when the volume of DMF was increased from 10 to 30 mL, and 97.1% 5-PMF yield could be obtained at 30 mL. It can be clearly seen that the 5-PMF yield decreased when the volume of DMF

was further increased to 40 or 50 mL (Table 1, entries 13-17). This phenomenon can be attributed to the fact that the use of excessive solvent increases the molecular dispersion of the substrate to some extent, reducing the accessibility of substrate (5-CMF) towards nitrogen atom donor (KPI) [48]. An orthogonal test for 5-PMF optimization was also implemented (Table S1), and a high yield of 97.1% could be obtained in DMF at 40 °C for 3 h (analyzed by GC-MS, Fig. S2).

**3. Synthesis of 2-PA-4oxo-5-Ph from 5-PMF**

Considering the safety of the reaction, the reaction temperature was set at 20 °C, referring to Takeya's work and Ha's work [5,35], and the other reaction conditions concerning reaction solvent, solvent dosage, and reaction time were subsequently optimized (Table S2 and S3). Finally, the 5-PMF conversion was near 100% in DMF-CH₃OH (1 : 5) medium for 8 h. According to previous studies [5], a plausible mechanism for proposed photo-oxidation from 5-PMF was proposed (Scheme 2). It can be seen that the target photo-oxidation product existed in the form of conjugated compounds. After that, the photo-oxidation reaction products of 5-PMF were further analyzed, and the results showed that many byproducts will be formed in the photo-oxidation process (detected by GC-MS, Fig. S12).

**4. Synthesis of 5-PhMLA from 2-PA-4oxo-5-Ph**

5-PhMLA was produced with the oxidation of 5-PMF followed by hydrogenation reduction of 2-PA-4-oxo-5-Ph, and the reaction time and temperature were optimized (Table S4). The total 5-5-PhMLA yield from 5-PMF was 29.5% and high purity (>90%) was obtained (detected by GC-MS and NMR, Fig. S3, S8, and S9).
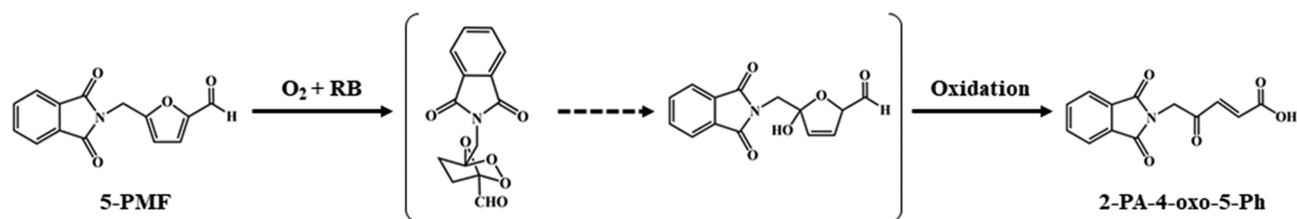
**Scheme 2. Plausible mechanism for the conversion of 5-PMF into 2-PA-4-oxo-5-Ph.**

## 5. Synthesis of 5-ALA from 5-PhMLA

After that, 6 M HCl was used as the catalyst for the acid hydrolysis process (Fig. S13). To avoid the polymerization of 5-ALA at high temperature, the crude product was further concentrated in a vacuum at 40 °C, and an encouraging 5-ALA yield of 85% could be achieved (determined by HPLC and NMR, Fig. S4 and S11).

## CONCLUSIONS

We have provided a green and mild 5-ALA production method (five steps) from algal biomass *via* 5-CMF as intermediate. The maximum 5-CMF yield of 24.6% and total furanic derivatives yield of 39.5% were obtained at 120 °C for 5 h in DES with a small content of HCl (0.1 mL). Although the yield of 5-CMF was low, it should be noted that the mixed solvent catalytic system was first reported for the 5-CMF production. Compared with conventional CMF production, our work not only eliminates the dependence on concentrated acid, but also shows green MIBK as an extractant solvent instead of toxic dichloroethane. In addition, KPI was employed as a nitrogen atom donor and had superb activity and selectivity (97.1%) instead of conventional $Na_3N$ (toxic), suggesting a new and efficient synthetic route for the ammoniation of 5-CMF. We believe that this work could shed some light on the 5-ALA production way from biomass.

## ACKNOWLEDGEMENTS

## CONFLICT OF INTEREST

There is no conflict to declare.

## SUPPORTING INFORMATION

Additional information as noted in the text. This information is available via the Internet at http://www.springer.com/chemistry/journal/11814.

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# Supporting Information

# Green and mild production of 5-aminolevulinic acid from algal biomass

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**Table S1. Results of 5-PMF yield in orthogonal experiment**

| Entry | $n_{(5-CMF)} : n_{(KPI)}$ | Temperature (°C) | Time (h) | Volume (mL) | 5-PMF yield (%) |
|---|---|---|---|---|---|
| 0 | 0.7 : 1 | 40 | 3 | 30 | 97.1 |
| 1 | 0.6 : 1 | 20 | 1 | 20 | 80.7 |
| 2 | 0.6 : 1 | 40 | 3 | 30 | 91.1 |
| 3 | 0.6 : 1 | 60 | 5 | 40 | 92.5 |
| 4 | 0.7 : 1 | 20 | 3 | 40 | 87.1 |
| 5 | 0.7 : 1 | 40 | 5 | 20 | 92.7 |
| 6 | 0.7 : 1 | 60 | 1 | 30 | 93.6 |
| 7 | 0.8 : 1 | 20 | 5 | 30 | 94.4 |
| 8 | 0.8 : 1 | 40 | 1 | 40 | 82.7 |
| 9 | 0.8 : 1 | 60 | 3 | 20 | 92.8 |
| Mean 1 | 88.1 | 87.4 | 85.7 | 88.7 | |
| Mean 2 | 91.1 | 88.8 | 90.3 | 93.0 | |
| Mean 3 | 89.9 | 92.9 | 93.2 | 87.4 | |
| R | 3.1 | 5.6 | 7.5 | 5.6 | $A_2B_3C_3D_2$ |

**Table S2. Effects of different solvents on the conversion of 5-PMF**

| Entry | Solvent | Time (h) | 5-PMF conversion (%) |
|---|---|---|---|
| 1 | $CH_3OH$ | 6 | 6.2±0.7 |
| 2 | DMF | 6 | <0.1 |
| 3 | $C_5H_5N$ | 6 | 75.1±1.1 |
| 4 | CHCOCH | 6 | 80.3±0.9 |
| 5 | $V_{DMF} : V_{CH_3OH}$ (1 : 1) | 6 | 78.5±1.3 |
| 6 | $V_{DMF} : V_{CH_3OH}$ (1 : 5) | 6 | 95.7±1.1 |

Reaction conditions: 2.3 g 5-PMF, 0.18 g RB, 120 mL solvent, 0.05 L/min $O_2$, 20 °C.

**Table S3. Effects of different conditions on the conversion of 5-PMF**

| Entry | Time (h) | Volume (mL) | 5-PMF conversion (%) |
|---|---|---|---|
| 1 | 6 | 40 | 70.1±0.9 |
| 2 | 6 | 60 | 85.3±1.6 |
| 3 | 6 | 80 | 91.1±1.3 |
| 4 | 6 | 120 | 95.4±0.8 |
| 5 | 2 | 120 | 29.7±1.3 |
| 6 | 4 | 120 | 73.8±1.2 |
| 7 | 8 | 120 | >99.0 |

Reaction conditions: 2.3 g 5-PMF, 0.18 g RB, solvent ($V_{DMF} : V_{CH_3OH}$=1 : 5), 0.05 L/min $O_2$, 20 °C.

**Table S4. Effects of different reaction conditions on 5-PhMLA yield**

| Entry | Time (h) | Temperature (°C) | 5-PhMLA yield (%) |
|-------|----------|------------------|-------------------|
| 1 | 2 | 40 | 6.4±0.5 |
| 2 | 3 | 40 | 8.5±1.1 |
| 3 | 4 | 40 | 10.4±0.9 |
| 4 | 5 | 40 | 8.7±0.8 |
| 5 | 6 | 40 | 7.6±0.6 |
| 6 | 7 | 40 | 6.2±0.9 |
| 7 | 4 | 20 | 7.1±0.7 |
| 8 | 4 | 30 | 8.4±0.5 |
| 9 | 4 | 50 | 26.2±0.7 |
| 10 | 4 | 60 | 29.5±1.1 |
| 11 | 4 | 70 | 25.1±1.3 |

Reaction conditions: 1.2 g 2-PA-4-oxo-5-Ph, 0.4 g Pd/C, 40 mL $CH_3OH$, 2 MPa $H_2$.
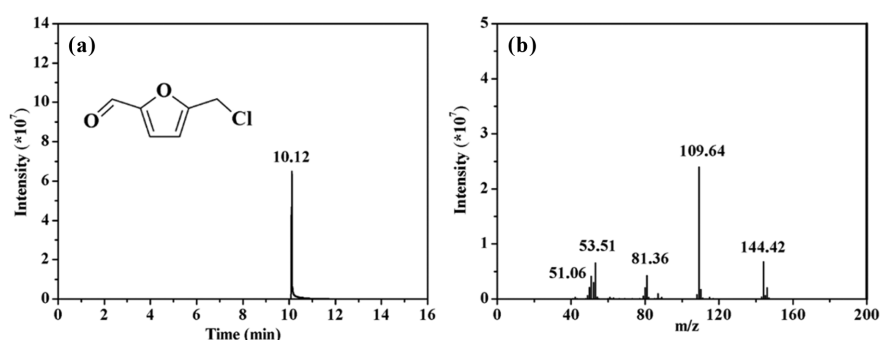


Fig. S1. GC-MS chromatogram of purified 5-CMF ((a) GC chromatogram of purified 5-CMF, (b) MS chromatogram of purified 5-CMF).
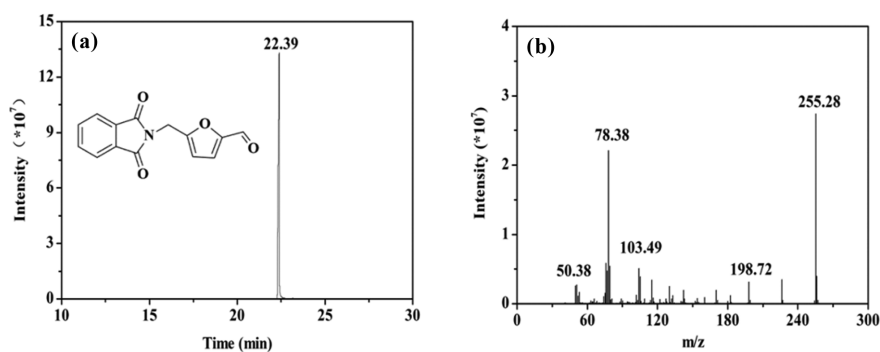


Fig. S2. GC-MS chromatogram of purified 5-PMF ((a) GC chromatogram of purified 5-PMF, (b) MS chromatogram of purified 5-PMF).
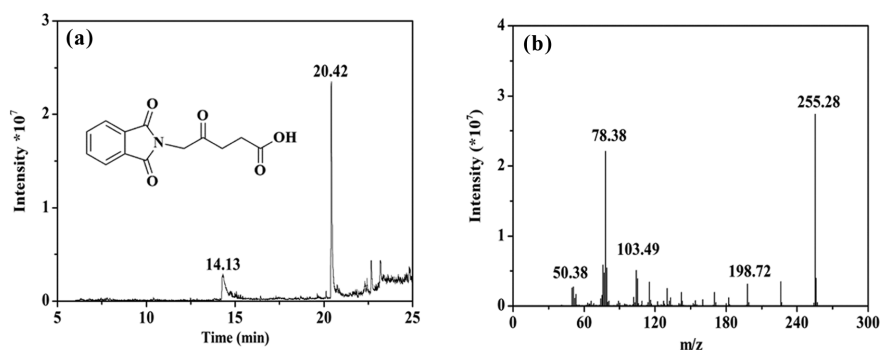


Fig. S3. GC-MS chromatogram of purified 5-PhMLA ((a) GC chromatogram of purified 5-PhMLA, (b) MS chromatogram of purified 5-PhMLA).
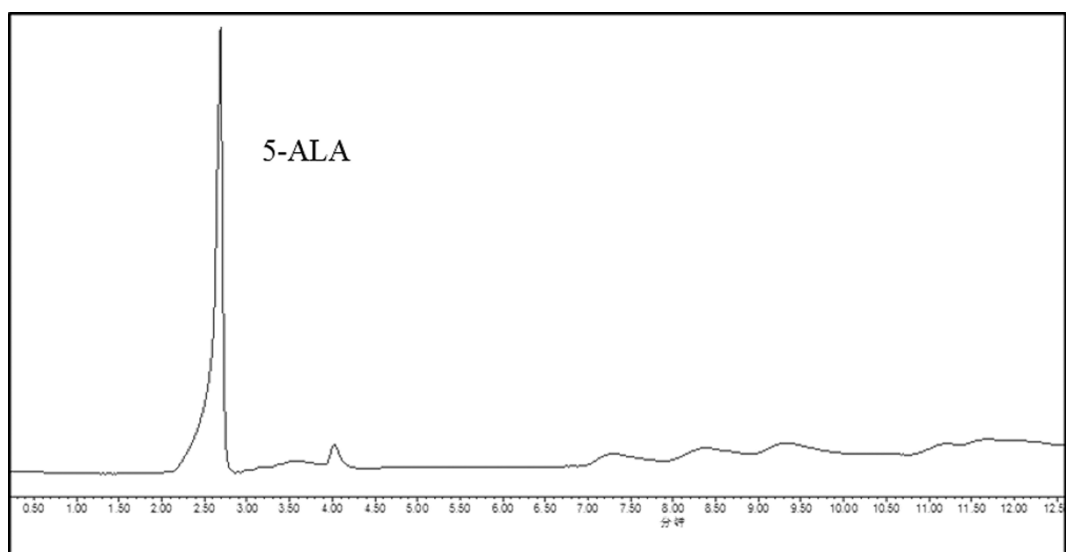
Fig. S4. HPLC spectrum of purified 5-ALA.
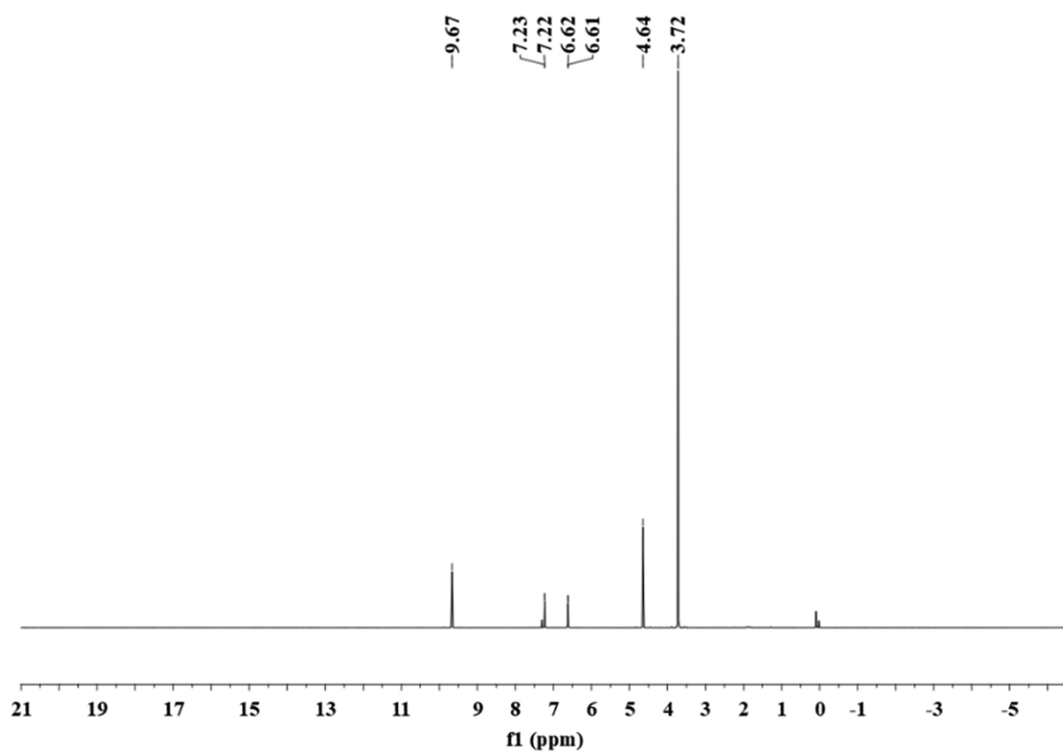


Fig. S5. ¹H-NMR spectrum of purified 5-CMF. $\delta$ (ppm): 4.64 (s, 2H), 6.61, 6.62 (s, 1H), 7.22, 7.23 (s, 1H), 9.67 ppm (s, 1H).
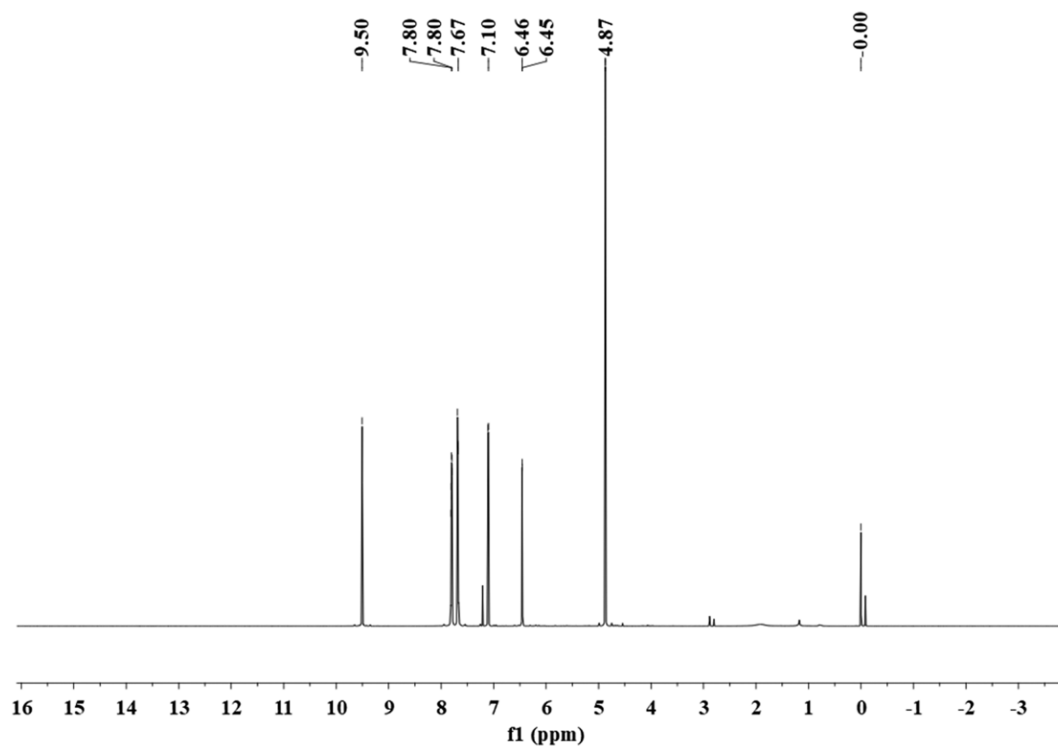
Fig. S6. ¹H NMR spectrum of purified 5-PMF. ¹H NMR (600 MHz, CDCl₃) $\delta$ (ppm): 4.87 (s, 2H), 6.46, 6.45 (s, 2H, J=6.5 Hz), 7.10, 7.80, 7.69, 7.67 (s, 2H, J=6.5 Hz), 9.50.
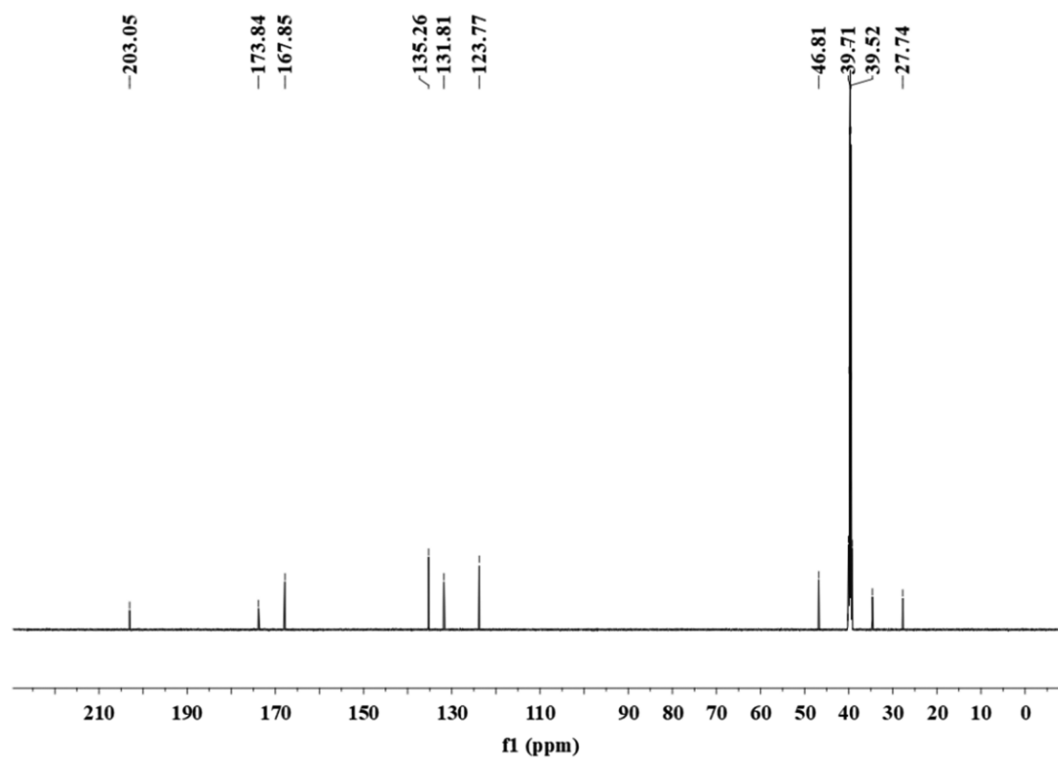


Fig. S7. ¹³C NMR spectrum of purified 5-PMF. ¹³C NMR (600 MHz, CDCl₃) $\delta$ (ppm): 203.05, 173.84, 167.85, 135.26, 131.81, 123.77, 46.81, 39.71, 39.52, 27.74.
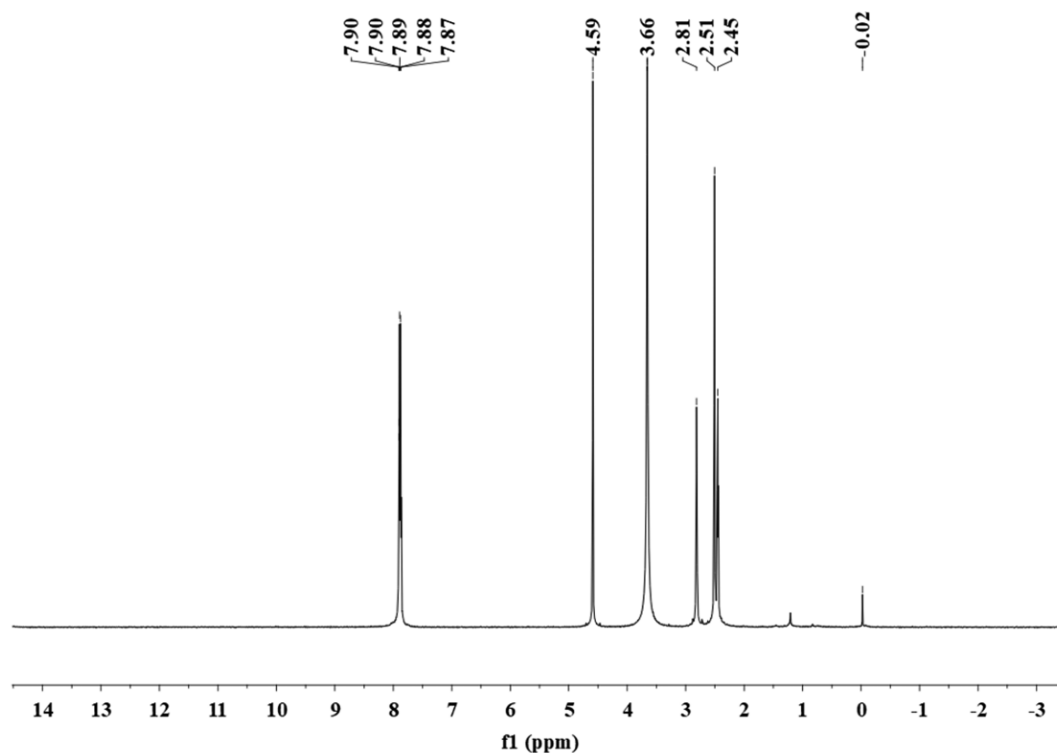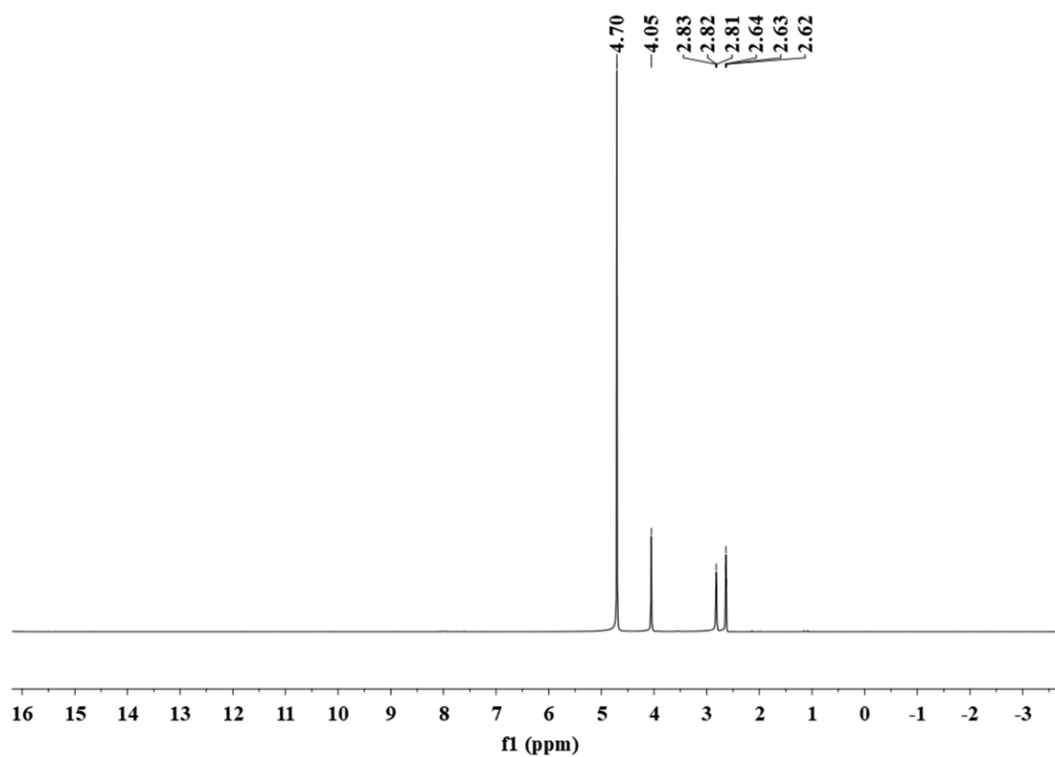
**Fig. S8.** $^1$H NMR spectrum of purified 5-PhMLA. $^1$H NMR (600 MHz, DMSO) $\delta$ (ppm): 7.89, 7.88 (s, 2H), 4.59 (s, 2H) 2.81, 2.80, (s, 2H, J= 6.8 Hz), 2.51, 2.45 (s, 2H, J=6.8 Hz).
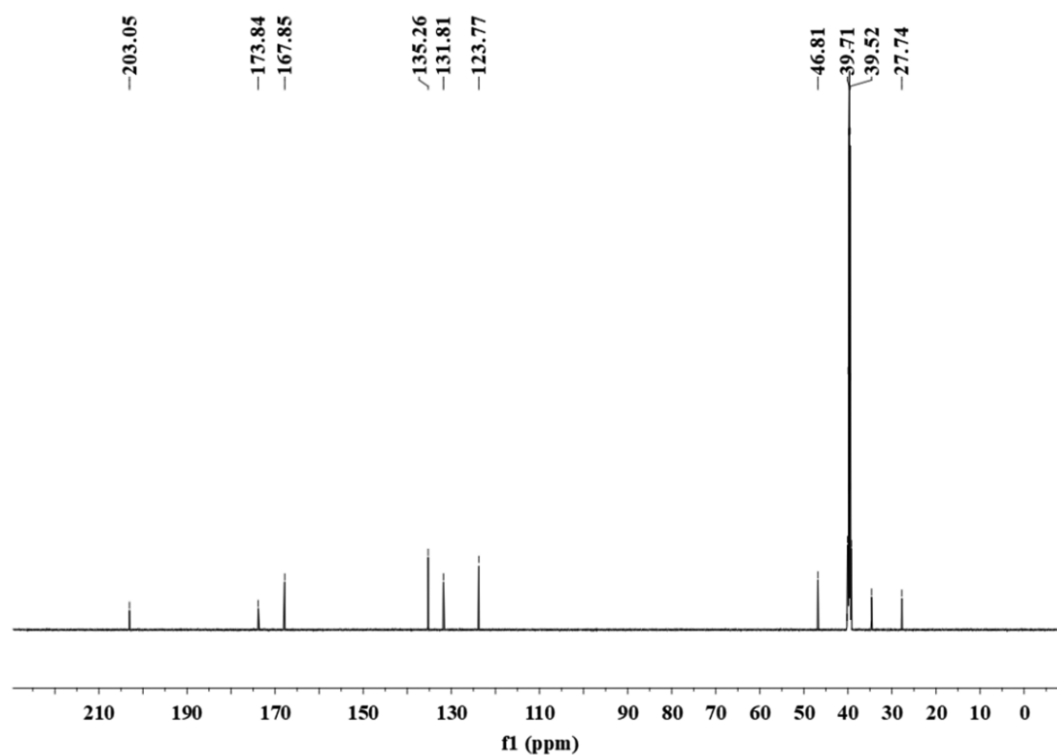


**Fig. S9.** $^{13}$C NMR spectrum of purified 5-PhMLA. $^{13}$C NMR (600 MHz, DMSO) $\delta$ (ppm): 203.05, 173.84, 167.85, 135.26, 131.81, 123.77, 46.81, 34.45, 27.74.

Fig. S10. $^1$H NMR spectrum of purified 5-ALA. $^1$H NMR (600 MHz, D$_2$O) $\delta$(ppm): 4.05 (s, 2H), 2.83, 2.82, 2.81 (s, 2H, J=6.5 Hz), 2.65, 2.64, 2.62 (s, 2H, J=6.5 Hz).
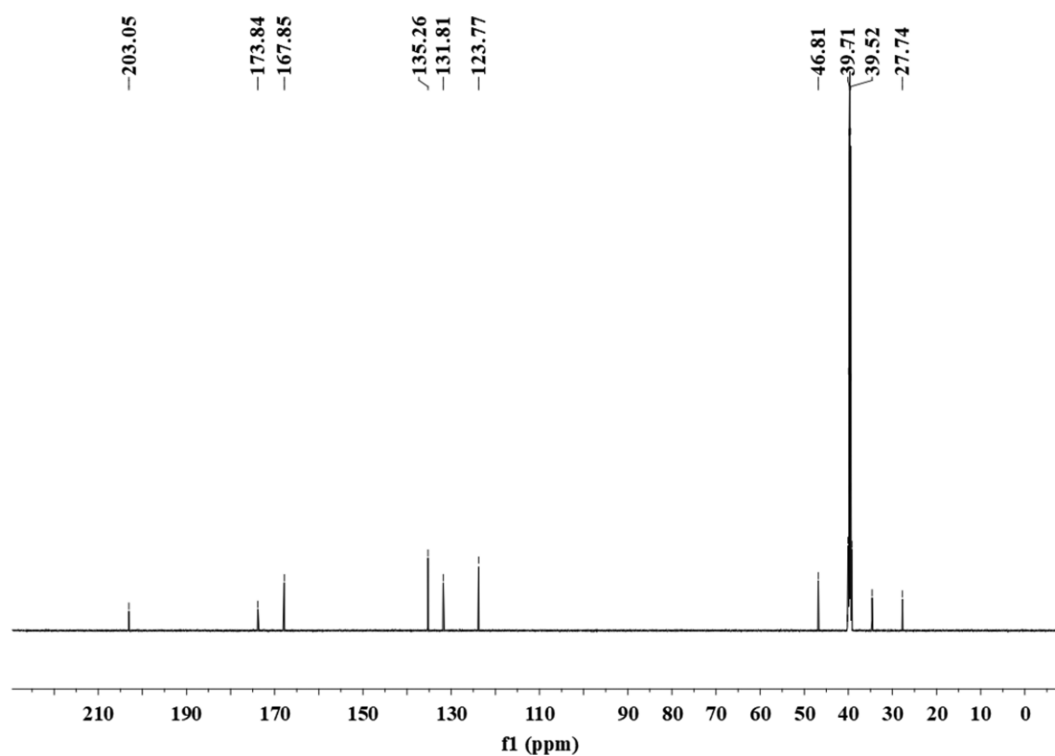


Fig. S11. $^{13}$C NMR spectrum of purified 5-ALA. $^{13}$C NMR (600 MHz, D$_2$O) $\delta$(ppm) 204.12, 176.76, 47.10, 34.33, 27.36.
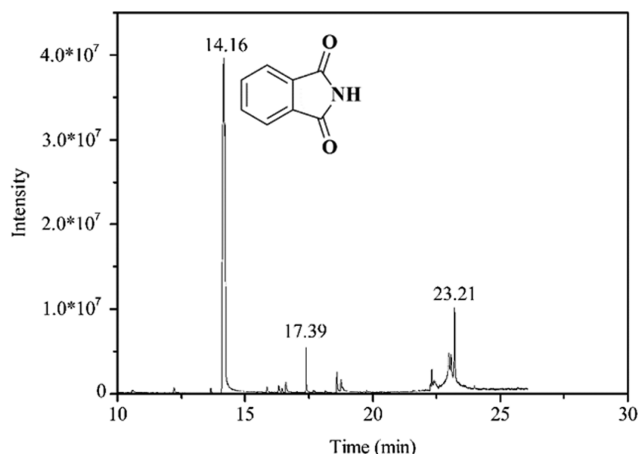
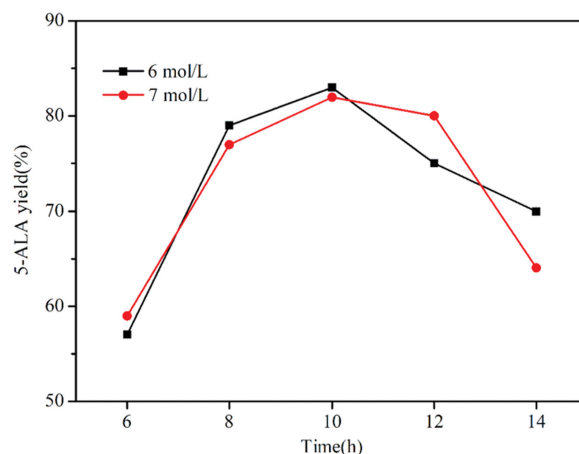**Fig. S12.** GC-MS chromatogram of photo-oxidation products.
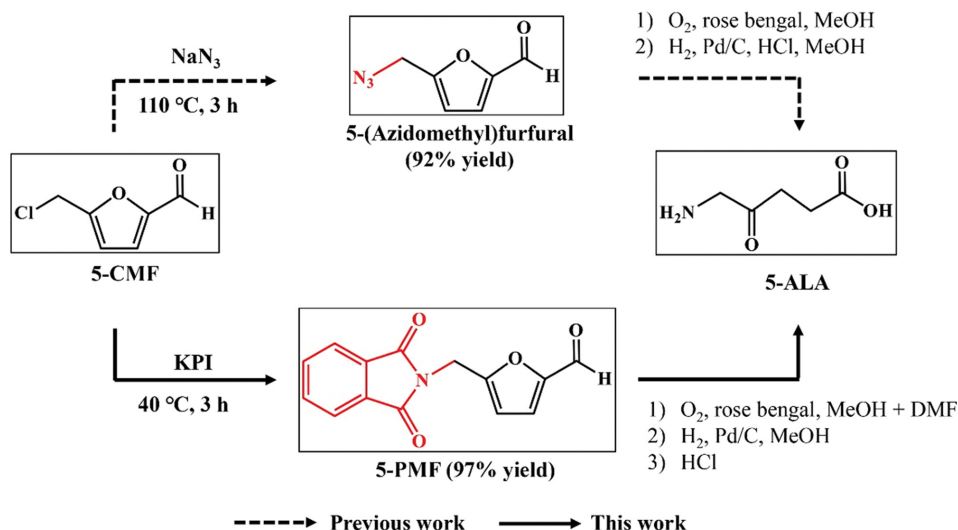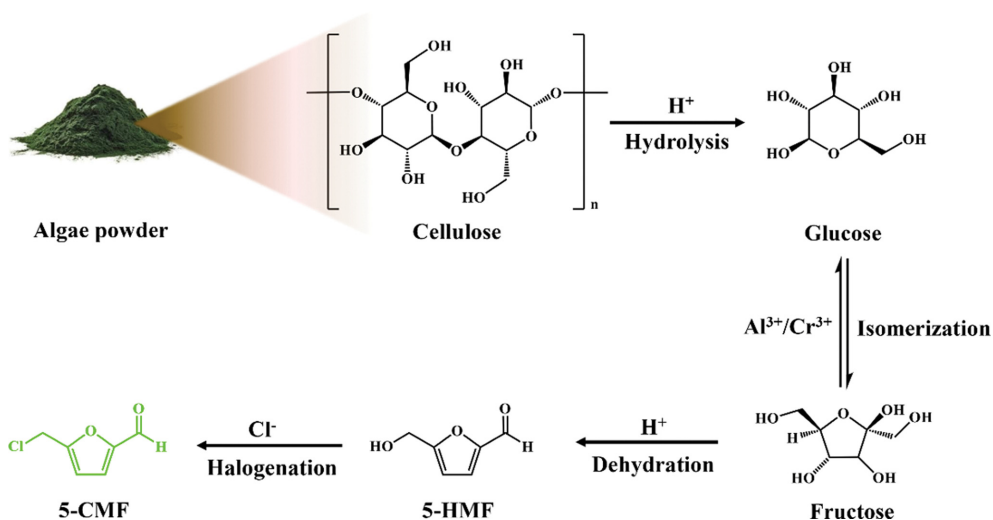


**Fig. S13.** Effects of reaction time and acid concentration on 5-ALA yield. Reaction conditions: 0.65 g 5-PhMLA, 15 mL HCl, 110 °C.



**Scheme S1.** Different ammoniation agents for catalytic conversion of 5-CMF to 5-ALA.



**Scheme S2.** Plausible mechanism for 5-CMF production from algal biomass in DES system.