Supporting Information

Experimental Section

Materials

$CuBr_2$ (99%) was purchased from Shanghai Macklin Biochemical Co. Ltd (Shanghai, China). Methyl levulinate (>99%), phthalimide potassium salt (>98%) were purchased from Aladdin (Shanghai, China). All other chemicals were supplied by Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and used without any treatment or purification.

Typical procedure for the bromination of ML

ML (0.33 g, 2.5 mmol), $CuBr_2$ (1.67 g, 7.5 mmol) and methanol/chloroform (1:1 volume ratio, 30 mL) were added to a three-necked flask and stirred at 40°C for 5 h, note that $CuBr_2$ was added 4 times in 30 mins. After the reaction, the crude product of M5B was obtained by vacuum distillation and extraction ($CHCl_3$, 30 mL×3). A mixture of ethyl ether/ cyclohexane (20 mL, ethyl ether/ cyclohexane ratio 1:1) was applied for recrystallization, and affording M5B with a purity over 95% (detected by GC-MS, Fig. S3).

Typical procedure for the ammoniation of M5P

In a round-bottom flask with a magnet, KPI (0.83 g, 4.5 mmol), N, N-dimethylformamide (DMF, 25 mL) and M5B (0.52 g, 2.5 mmol) were heated at 40°C for 4 h. The concentrated mixture under reduced pressure was diluted with deionized water (8 mL) and then extracted with dichloromethane (4 mL×3). After moving the aqueous phase, the organic phase was washed with 10% NaOH solution and deionized water for three times, respectivily, and then dried with anhydrous $MgSO_4$. Finally, the resulting brown substances were treated by vacuum distillation, recrystallization and filtration, achieving M5P with purity over 98% (detected by GC-MS Fig. S4).

Typical procedures for the acidolysis of M5P

M5P (0.69 g, 2.5 mmol) was boiled in 6 M HCl (10 mL) for 10 h, then the mixture was cold to -23℃. The precipitate *o*-phthalic acid was collected by filtration and dried, and 15 mL acetone was added to the mixture solution, the resulted precipitate was collected by filtration and then dried to yield whiteness 5-ALA with purity over 98% (detected by HPLC Fig. S5).

Typical reactions for eliminating free radical

ML (0.33 g, 2.5 mmol), TEMPO (0.39 g, 2.5 mmol), and BHT (1.10 g, 5mmol) were dissolved in methanol / chloroform (1:1 volume ratio, 30 mL) in a three-necked flask. $CuBr_2$ (1.67 g, 7.5 mmol) was then added in batches every 10 min for 4 times and the resulting solution was stirred at 40°C for 3 h. No M5B was detected by GC-MS

during the reaction process.

Characterization

The GC-MS analysis was performed with Themofisher Trace 1300 & ISQ LT GC-MS instrument with a TR-5MS column (15.0 m × 250 μm × 0.25 μm). MS was used to certify the structure of the compounds M5B and M5P. The retention time of M5B and M5P in GC-MS is 11.3 and 22.10 min, respectively.

The yield of 5-ALA was determined by HPLC analysis and was performed on a Waters 2695 Separation Module equipped with a UV-vis detector and Agilent SB-C18 column (250mm × 4.6mm). The maximum absorption wavenumber for 5-ALA is 265 nm. The mobile phase was methanol: water =5:5 (v: v) with 1/ 1000 (v: v) acetic acid. External standard method was used for quantitative analysis.

Samples were characterized by NMR, including M5B, M5P and 5-ALA (Fig. S6- S12). All the NMR experiments were recorded on a Bruker AV 600 MHz NMR spectrometer (Germany).

M5B, M5P and 5-ALA were calculated by external standard method following the equation:

$$\text{Yield}_{X} = \frac{\text{Mole of X in the products}}{\text{Initial mole of one equivalent of raw materal}} \times 100\%$$

, (X stands for M5B, M5P and 5-ALA.)

Tables and Figures

Table S1. Effect of solvent dosage on the bromination reaction

Entry	ML (g)	$CuBr_2$ (g)	$V_{CH3OH/CHCl3}$ (mL)	Yield (%)
1	0.33	1.68	10	62
2	0.33	1.68	20	71
3	0.33	1.68	30	80
4	0.33	1.68	40	59
5	0.33	1.68	50	57

Reaction Condition: temperature = 40°C , time = 3 h.

Table S2. Effect of $CuBr_2$ dosage on the bromination reaction

Entry	ML (g)	$CuBr_2$ (g)	Material ratio ML: $CuBr_2$(mol /mol)	$V_{CH3OH/CHCl3}$ (mL)	Yield (%)
1	0.33	0.56	1:1	30	43
2	0.33	0.84	1:1.5	30	45
3	0.33	1.12	1:2	30	70
4	0.33	1.41	1:2.5	30	76
5	0.33	1.68	1:3	30	80
6	0.33	1.95	1:3.5	30	69
7	0.33	2.23	1:4	30	59

Reaction condition: CH_3OH /$CHCl_3$ = 1:1, temperature = 40°C, time = 3 h.

Table S3. Effect of the ratio of KPI and M5B on the ammoniation

Entry	KPI (g)	M5B (g)	Material ratio KPI: M5B (mol /mol)	Yield (%)
1	0.46	1.05	0.5:1	78
2	0.46	0.94	0.6:1	82
3	0.46	0.73	0.7:1	84
4	0.46	0.63	0.8:1	83

5	0.46	0.52	1.0:1	75
6	0.56	0.52	1.2:1	82
7	0.65	0.52	1.4:1	86
8	0.74	0.52	1.6:1	87
9	0.83	0.52	1.8:1	88
10	0.93	0.52	2.0:1	88

Reaction condition: DMF = 25 mL, temperature =40℃, time = 4 h.

Table S4. Optimization of the reaction conditions on 5-ALA production

Entry	T. (°C)	t. (h)	DMF volume (mL)	Yield (%)
1	40	2	25	83
2	40	4	25	88
3	40	6	25	86
4	40	8	25	84
5	40	10	25	83
6	40	12	25	83
7	30	2	5	69
8	30	2	15	75
9	30	2	25	77
10	30	2	35	75
11	30	2	45	70
12	20	2	25	67
13	40	2	25	83
14	60	2	25	75
15	80	2	25	73
16	100	2	25	70
17	110	2	25	73
18	130	2	25	71

Reaction condition: KPI = 0.83 g, M5B = 0.52 g.

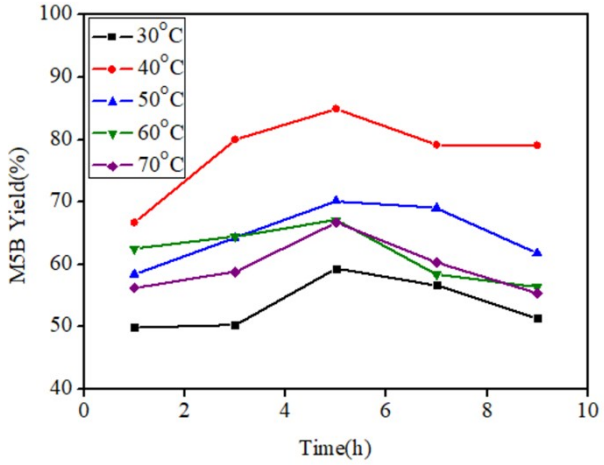

Fig S1 Effect of reaction time and temperature on M5B production

Reaction condition: ML = 0.33 g, $CuBr_2$ = 1.67 g, CH_3OH =15 mL, $CHCl_3$ = 15 mL.

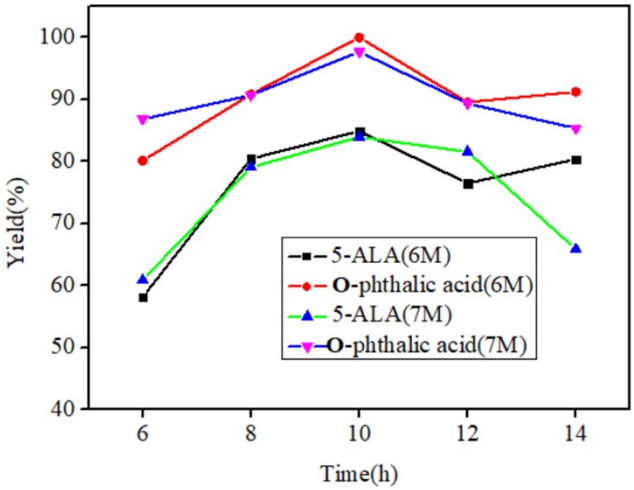

Fig S2 Effect of different time and concentrations of HCl solution on the 5-ALA production.

Reaction condition: M5P = 0.7 g, HCl = 10 mL, temperature =110°C.

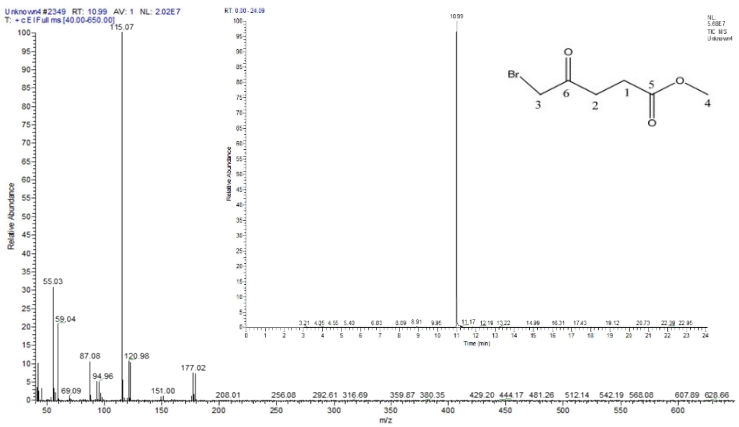

Fig. S3 GC-MS spectrum of the dehydration of fructose to M5B catalyzed by CH_3OH.

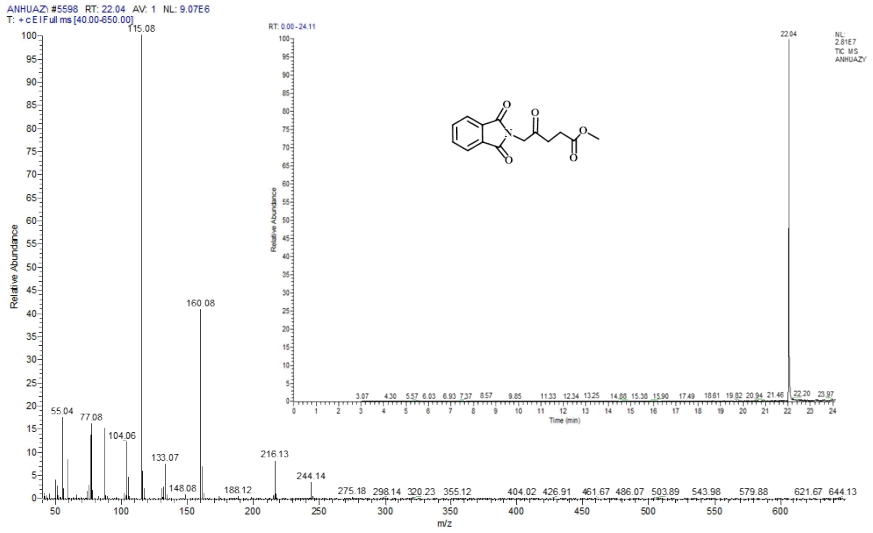

Fig. S4 GC-MS spectrum of the dehydration of fructose to M5P catalyzed by DMF.

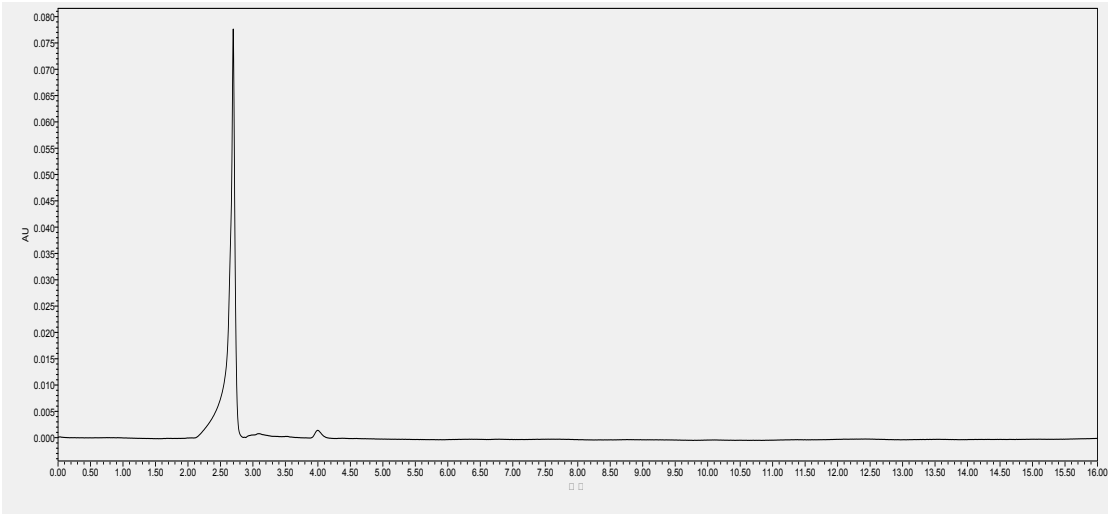

Fig. S5 HPLC of 5-ALA.

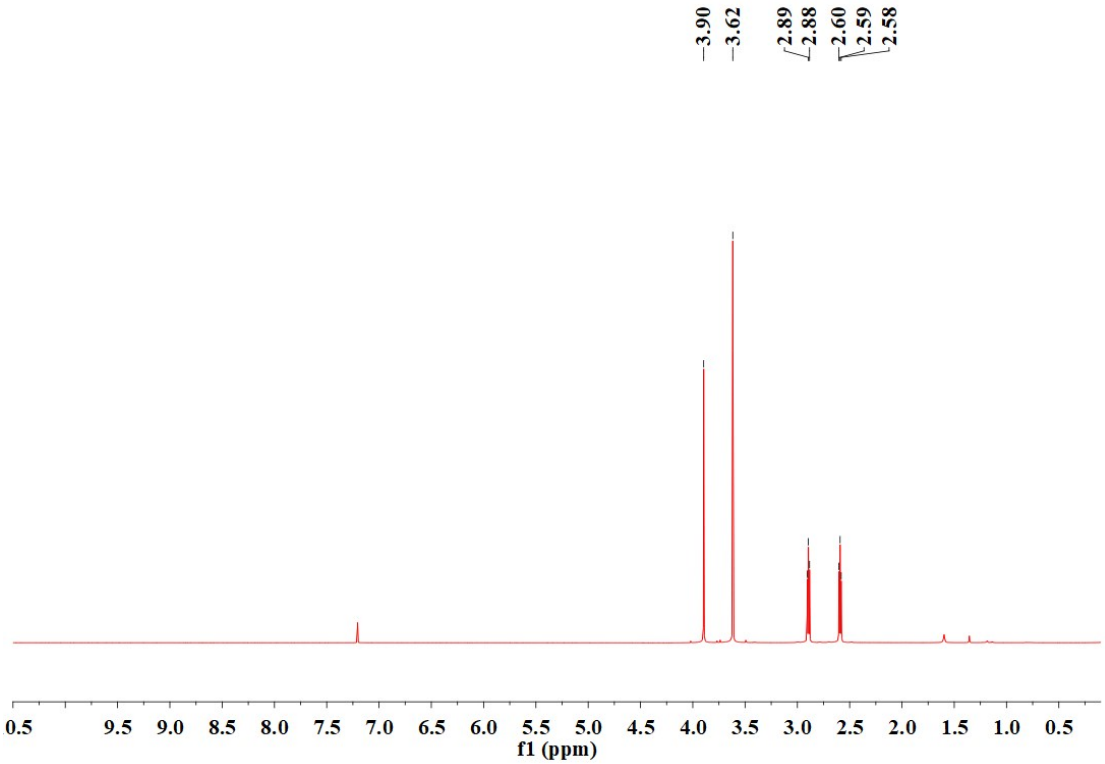

Fig. S6 ^{1}H NMR spectrum of M5B. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm): 3.90 (s, 2H), 3.62, (s, 3H), 2.89, 2.88, 2.87 (s, 2H, J=6.5Hz), 2.60, 2.59, 2.58 (s, 2H, J=6.5Hz).

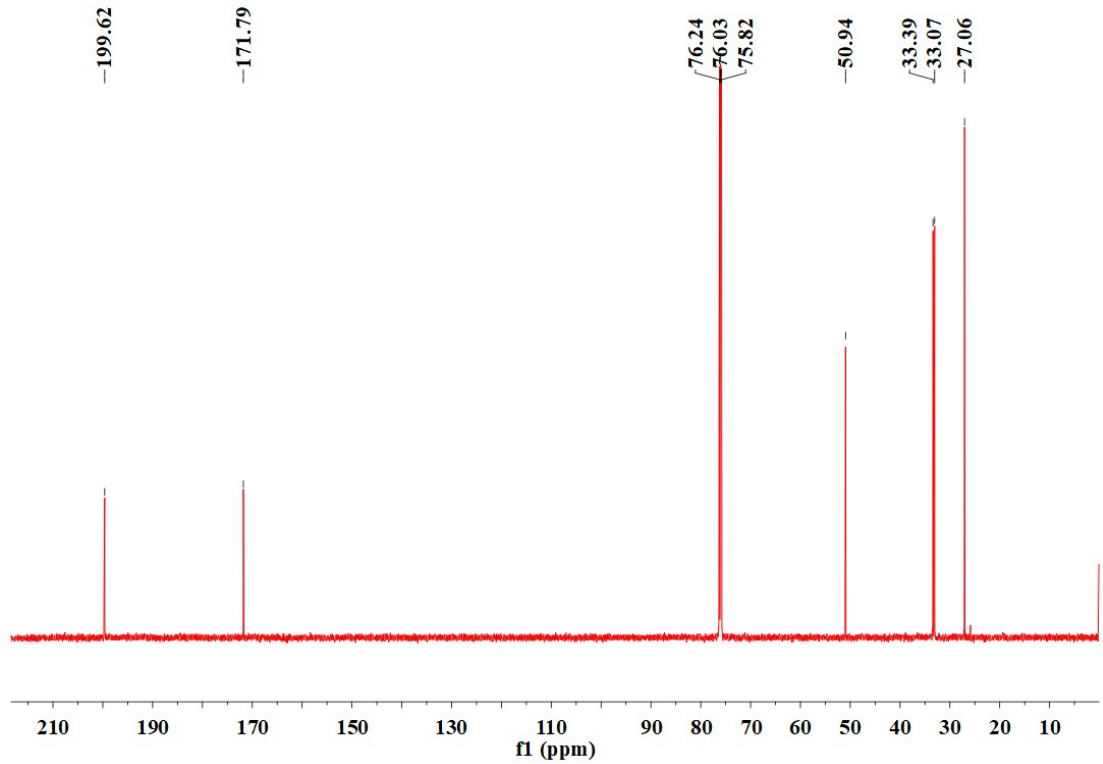

Fig. S7 ^{13}C NMR spectrum of M5B. ^{13}C NMR (600 MHz, $CDCl_3$): δ (ppm): 199.62, 171.79, 50.94, 33.39, 33.07, 27.06.

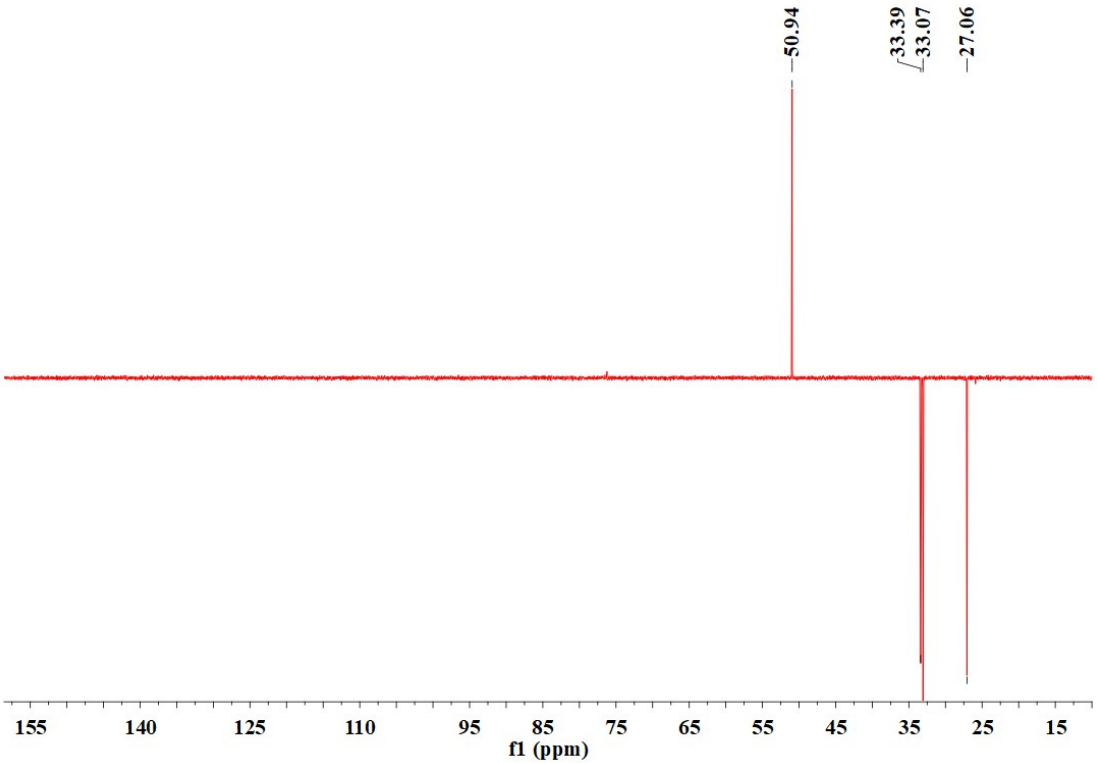

Fig. S8 DETP135 NMR spectrum of M5B. DETP 135 NMR (600 MHz, $CDCl_3$): δ (ppm): 50.94, 33.39, 33.07, 27.06.

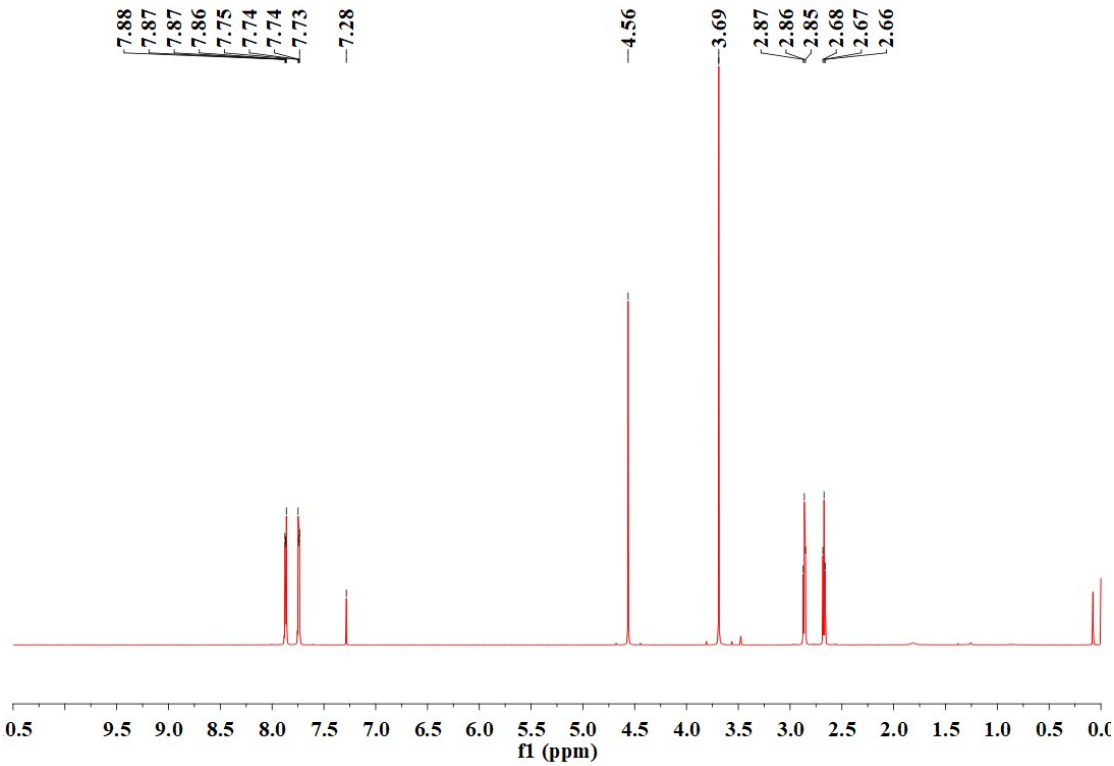

Fig. S9 ^1H NMR spectrum of M5P. ^1H NMR (600 MHz, $CDCl_3$): δ (ppm): 7.87(s, 2H), 7.73(s, 2H), 4.56 (s, 2H), 3.69, (s, 3H). 2.87, 2.86, 2.85 (s, 2H, J=6.5Hz), 2.68, 2.67, 2.66 (s, 2H, J=6.5Hz).

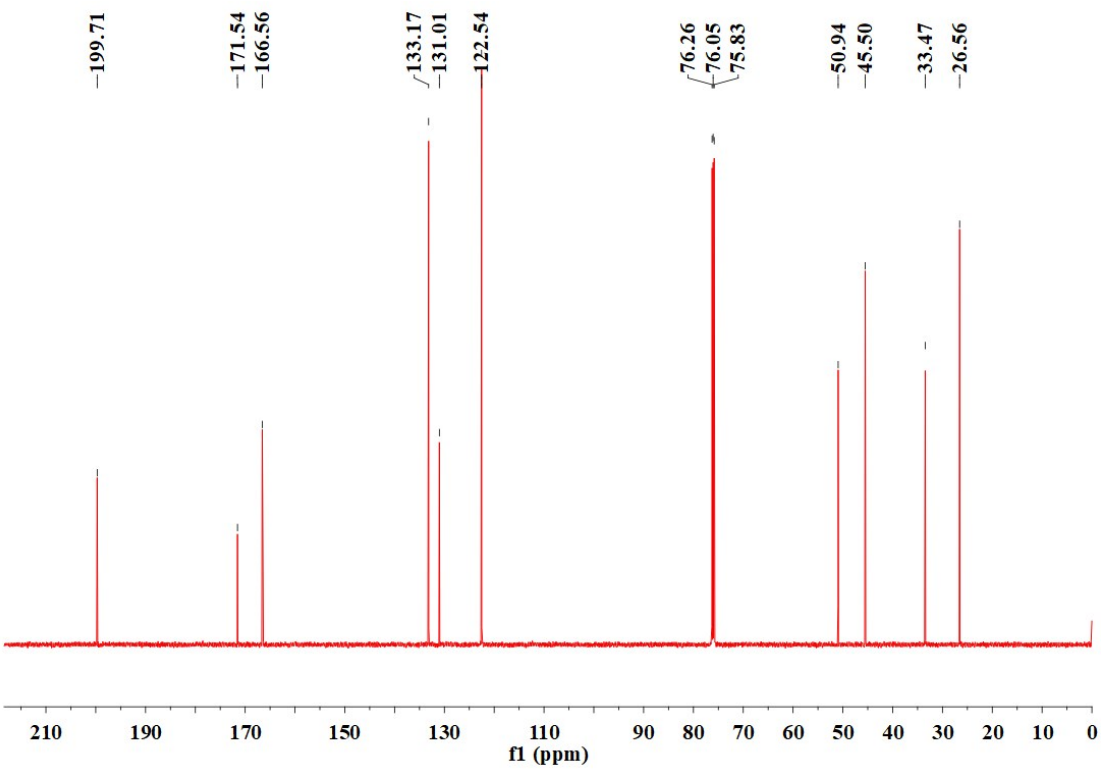

Fig. S10 ^{13}C NMR spectrum of M5P. ^{13}C NMR (600 MHz, $CDCl_3$): δ (ppm): 199.71, 171.54, 166.56, 133.17, 131.01, 122.54, 50.94, 45.50, 33.47, 26.56.

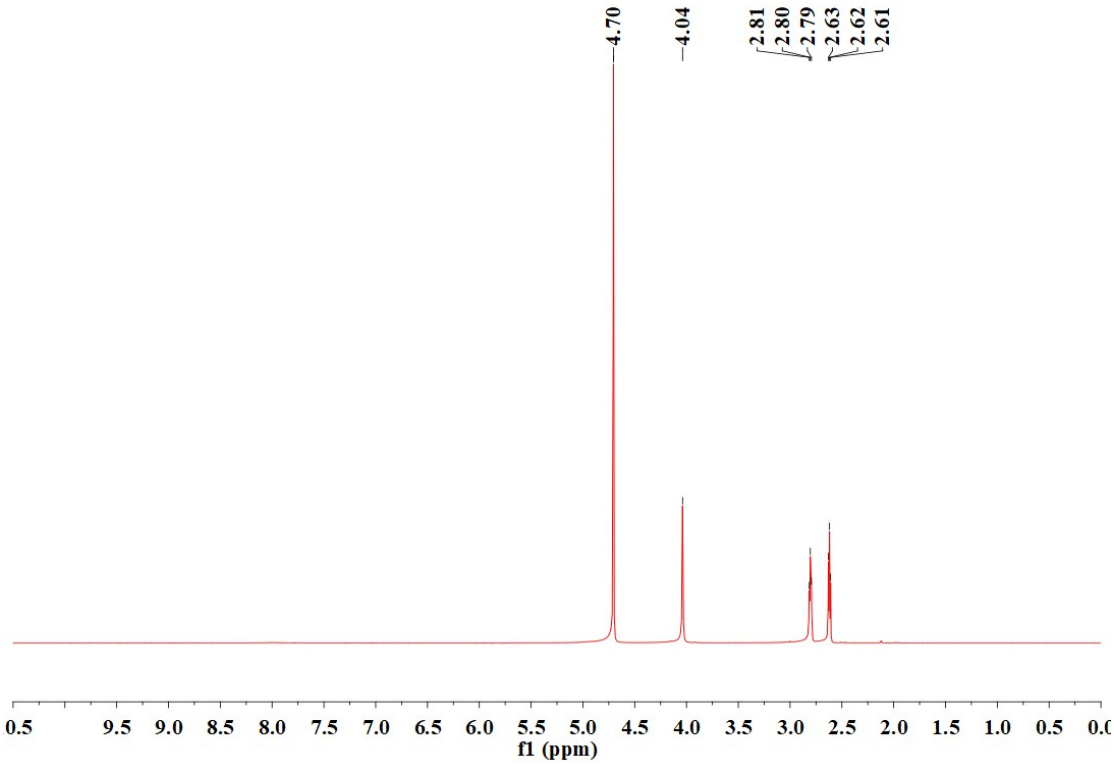

Fig. S11 ^{1}H NMR spectrum of 5-ALA. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm): 4.04 (s, 2H), 2.81, 2.80, 2.79 (s, 2H, J=6.5Hz), 2.63, 2.62, 2.61 (s, 2H, J=6.5Hz).

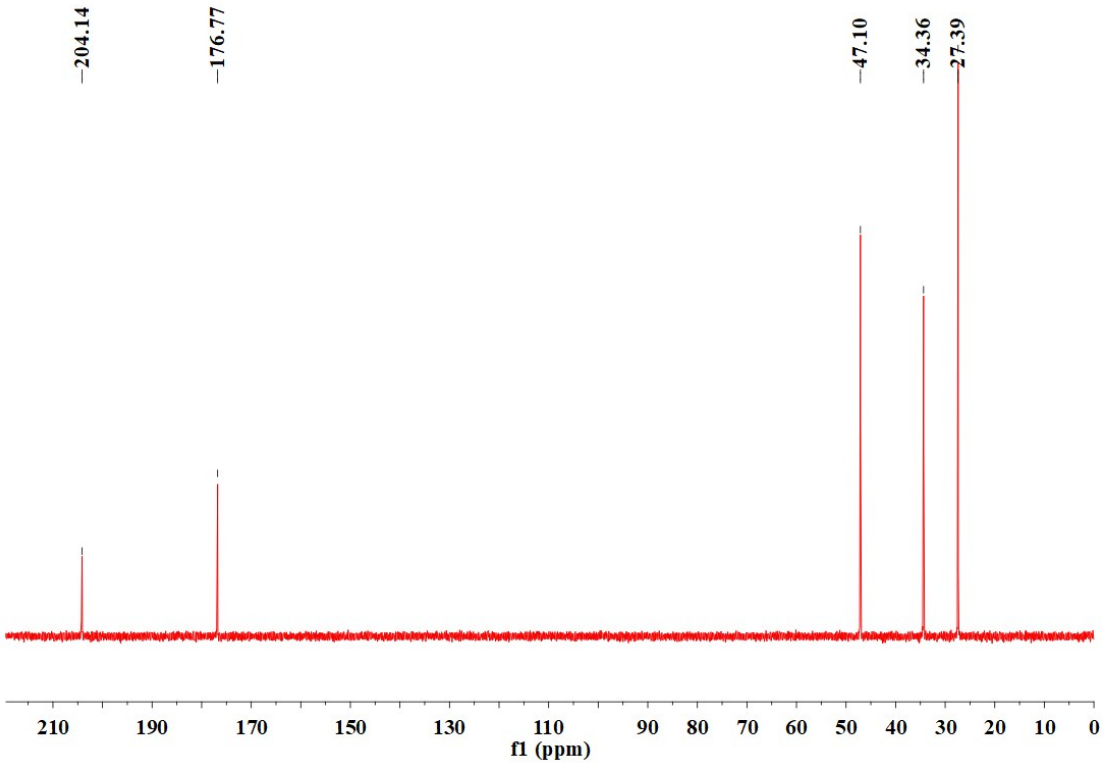

Fig. S12 ^{13}C NMR spectrum of 5-ALA. ^{13}C NMR (600 MHz, D_2O): δ (ppm): 204.14, 176.77, 47.10, 34.36, 27.39.