Supporting Information

Preparation of methyl ethyl ketone from biomass-derived levulinic acid using a metal-free photocatalytic system and life cycle assessment study

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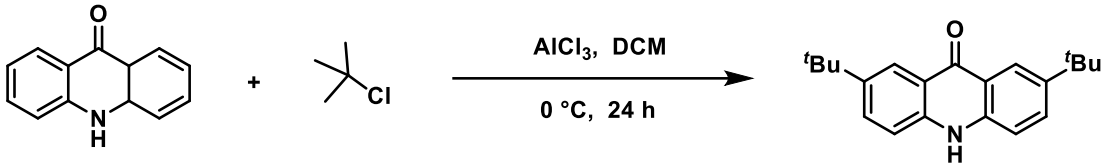
1. General information

All reactions were conducted in a Schlenk tube under an argon atmosphere unless otherwise specifically stated. All commercially available reagents were used without further purification. Anhydrous solvents were purchased from Energy Chemical Co., Ltd. and Adamas Reagent Co., Ltd. Deuterated reagents were purchased from Adamas Reagent Co., Ltd. Levulinic acid was purchased from Adamas Reagent Co., Ltd. The 0.3 mmol scale photoreactor equipped with three 400 nm LEDs (20 W) was purchased from Anhui Kemi Machinery Technology Co., Ltd. All reactions were performed using LED KL-400 nm (20 W) as light source. The 20 W LED KL-400 nm was purchased from Anhui Kemi Machinery Technology Co., Ltd. The continuous-flow photoreactor equipped with a microchannel reaction plate and 400 nm LEDs (600 $mW \cdot cm^{-2}$) was provided by Anhui Kexin Microflow Chemical Technology Co., Ltd.

^1H spectra was recorded on Bruker Avance 400 (400 MHz) spectrometer at ambient temperature with TMS as the internal standard. ^1H NMR data was reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broadt), coupling constant (Hz), integrated. High-resolution mass spectrometry (HRMS) was acquired on a Thermo Scientific LTQ-Orbitrap XL. GC analysis was performed using the Shimadzu 2014C instrument. Column chromatography was performed using silica gel (200-300 mesh). Thin layer chromatography was performed using TLC plates pre-coated with 250 μm thickness silica gel 60 F254 plates.

2. Synthesis of acridine catalyst

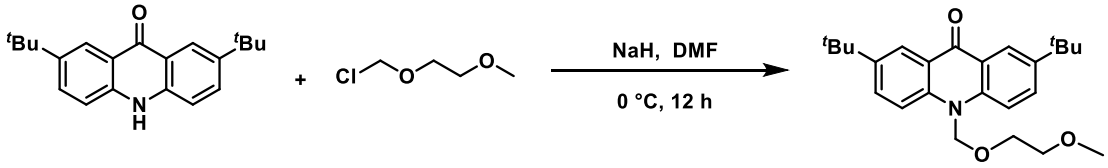
2,7-di-tert-butyl-9(10H)-acridone[1]



At 0°C and argon atmosphere, 9(10H)-acridone (10.00 g, 51.2 mmol) and $AlCl_3$ (13.66 g, 102.4 mmol) were added into a round-bottomed flask, then added CH_2Cl_2 (250 mL) as the solvent. After dissolution, 2-chloro-2-methylpropane (45.6 mL, 410 mmol) was added. The reaction solution was stirred at 0 °C for 24 h. The reaction was quenched with water and extracted with CH_2Cl_2 (100 mL×3). The organic layer was dried over anhydrous Na_2SO_4, filtered through Na_2CO_3 and diatomite, and removed the solvent via vacuum distillation. The resulting solid was suspended in hot MeOH (200 mL) and cooled to 0°C. The precipitate was filtered to afford 2,7-di-tert-butyl-9(10H)-acridone as a yellow solid. The filtrate was suspended in hot MeOH (180 mL) and H_2O (40 mL) was added. After cooling to 0°C, the precipitate was filtered again to obtain 2,7-di-tert-butyl-9(10H)-acridone as a yellow solid. The yield was quantitative.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 2.3 Hz, 2H), 7.72 (dd, J = 8.7, 2.3 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 1.37 (s, 18H).

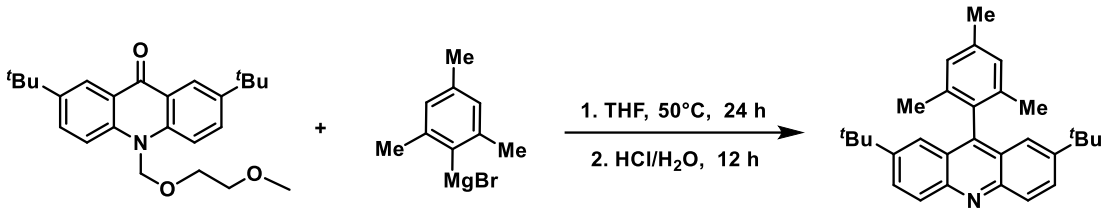
2,7-di-tert-butyl-10-((2-methoxyethoxy)methyl)acridin-9(10H)-one[2]



Under an argon atmosphere, 2,7-di-tert-butyl-9(10H)-acridone (2.20 g, 7.14 mmol) and NaH (0.36 g, 15.2 mmol) were added into a round-bottomed flask, then added DMF (100 ml) as the solvent. The solution was stirred until the solid was completely dissolved. After the mixture was cooled to 0°C, 2-methoxyethoxymethyl chloride (1.5 mL, 13.1 mmol) was slowly added, and the mixture was stirred for 12 hours. The mixture was quenched with water and extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, and then the solvent was removed via vacuum distillation. The crude product was purified by column chromatography on silica gel eluting with diethyl ether/n-hexane (v/v, 1:3) to afford 2,7-di-tert-butyl-10-((2-methoxyethoxy)methyl)acridin-9(10H)-one as yellow powder (1.41 g, 3.57 mmol, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, J = 2.5 Hz, 2H), 7.78 (ddd, J = 9.0, 2.5, 0.8 Hz, 2H), 7.66 (d, J = 9.1 Hz, 2H), 5.82 (d, J = 1.6 Hz, 2H), 3.84 (ddd, J = 5.5, 3.2, 0.8 Hz, 2H), 3.64 – 3.60 (m, 2H), 3.44 (d, J = 1.2 Hz, 3H), 1.41 (d, J = 0.6 Hz, 18H).

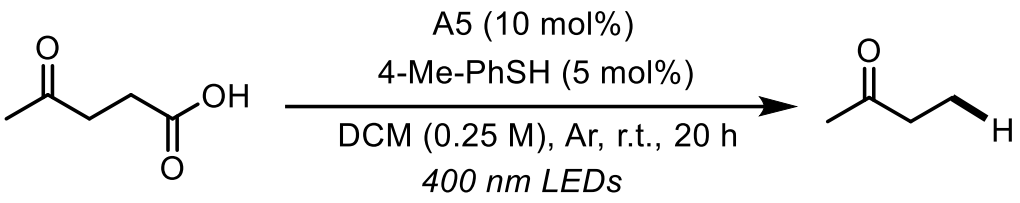
2,7-di-tert-butyl-9-mesitylacridine[3]



At 0 °C and an argon atmosphere, 2,7-di-tert-butyl-10-((2-methoxyethoxy)methyl)acridin-9(10H)-one (651 mg, 2.0 mmol) was added to a round-bottom flask with anhydrous THF (60 mL) as the solvent. Then, a solution of mesitylmagnesium bromide 1 M in THF (6 mL, 3 equiv.) was added slowly. The mixture was stirred at 50 °C for 24 hours. Afterward, concentrated hydrochloric acid (70 mL) and water (50 mL) were added to the reaction mixture and stirred at 50 °C for 12 hours. The mixture was treated with saturated Na_2CO_3 solution to adjust the pH to 8-9 and then extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous Na_2SO_4, and then the solvent was removed via vacuum distillation. The crude product was purified by column chromatography on silica gel eluting with hexane/EtOAc (v/v, 30:1) to afford 2,7-di-tert-butyl-9-mesitylacridine as a yellow solid (0.51 g, 1.24 mmol, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 8.7 Hz, 2H), 7.87 – 7.71 (m, 2H), 7.29 (d, J = 2.2 Hz, 2H), 7.01 (s, 2H), 2.39 (s, 3H), 1.64 (s, 6H), 1.23 (s, 18H).

3. General procedure for protodecarboxylation of levulinic acid



In an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar, levulinic acid (58.06 mg, 0.50 mmol), 10 mol% 2,7-di-tert-butyl-9-mesitylacridine **(A5)** (20.50 mg, 0.05 mmol, unless otherwise stated), and 5 mol% 4-Me-PhSH (3.11 mg, 0.025 mmol, unless otherwise stated) was added followed by 2.0 ml CH_2Cl_2 (0.25 M) as the solvent. The tube was then tightly sealed and stirred under irradiation with 400 nm LEDs (20 W) for 20 h at room temperature. After the reaction, n-dodecane was added to the reaction mixture as the internal standard and then gas chromatography (GC) was used for qualitative and quantitative detection.

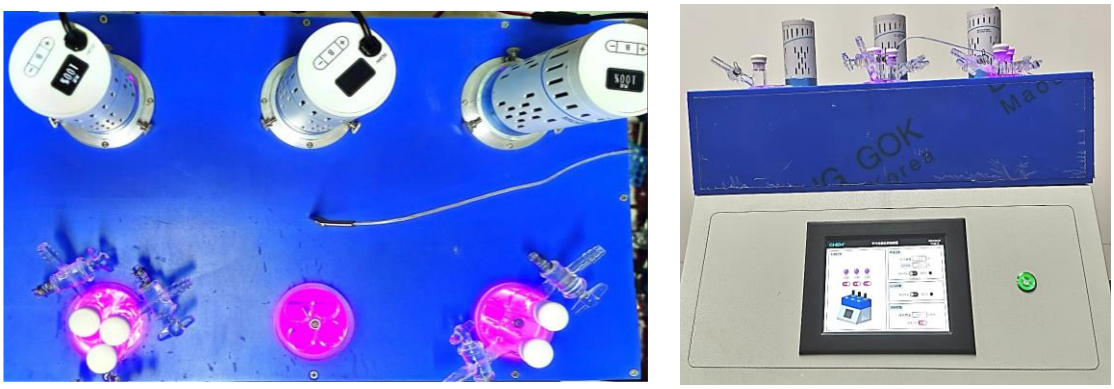
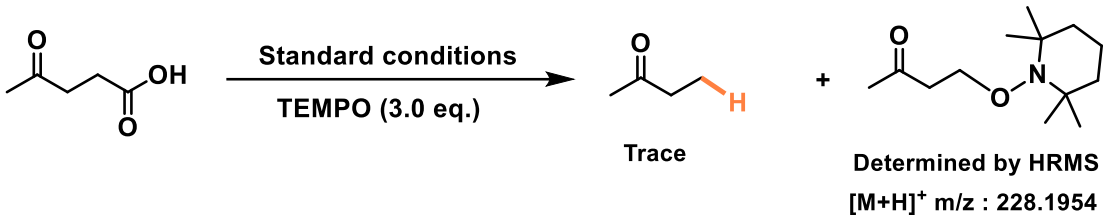


Figure S1. Experimental setup of 0.5 mmol scale reaction.

4. TEMPO trapping experiment



In an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar, levulinic acid (58.06 mg, 0.50 mmol), 2,2,6,6-tetramethylpiperidinooxy (234.4 mg, 1.50 mmol), 10 mol% 2,7-di-tert-butyl-9-mesitylacridine (**A5**) (20.50 mg, 0.05 mmol), and 5 mol% 4-Cl-PhSH (3.62 mg, 0.025 mmol) were added followed by 2.0 mL of CH_2Cl_2 (0.25 M) as the solvent. The tube was then tightly sealed and stirred under irradiation with 400 nm LEDs (20 W) for 20 hours at room temperature. After the reaction, the solution was analyzed by gas chromatography (GC) and high-resolution mass spectrometry (HRMS). It was found that the reaction was completely inhibited, and only a trace amount of the desired product was observed. The TEMPO-adduct was detected by HRMS. HRMS (ESI) for TEMPO-adduct: m/z calculated for [$C_{13}H_{25}NO_2$] [$M+H^+$]: 228.1963, found: 228.1954.

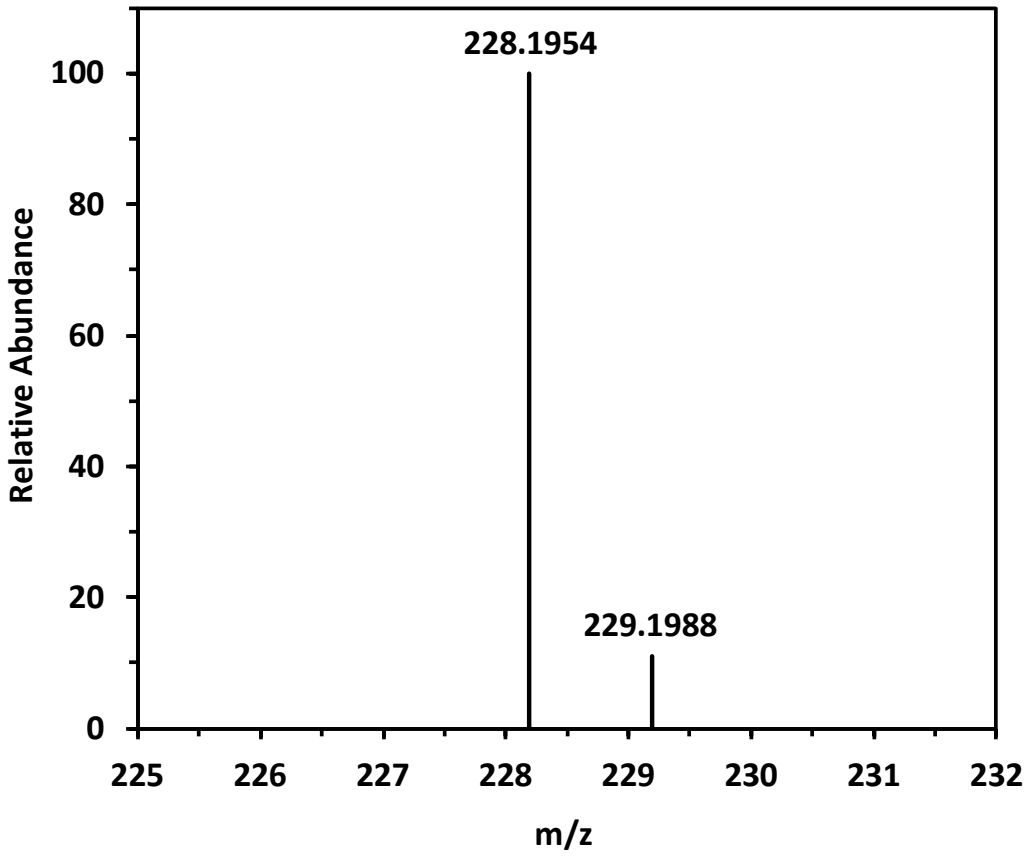


Figure S2. HRMS analysis of the reaction mixtures

5. Scale-up reaction using microchannel continuous flow photoreactor

Levulinic acid (5.81 g, 50.0 mmol), 10 mol% **A5** (2.05 g, 5.0 mmol), and 5 mol% 4-Cl-PhSH (0.36 g, 2.5 mmol) were added to a 250 mL reagent bottle, followed by the addition of 200 mL of methyl ethyl ketone (MEK) as the solvent. The total mass of the reaction solution was accurately weighed, and the bottle was purged with an argon balloon for 15 minutes. The reaction mixture was then pumped into a 3 mL microchannel reaction plate using a peristaltic pump at a flow rate of 10 mL/min. The reaction mixture was retained in the microchannel reaction plate for 45 minutes under the irradiation of 400 nm LEDs (600 $mW \cdot cm^{-2}$). After the reaction was completed, the mass of the reaction solution was accurately weighed, and the yield of MEK was calculated based on the change in mass of the solution before and after the reaction. Dodecane was then added as the internal standard, and the conversion of levulinic acid was measured by gas chromatography (GC).

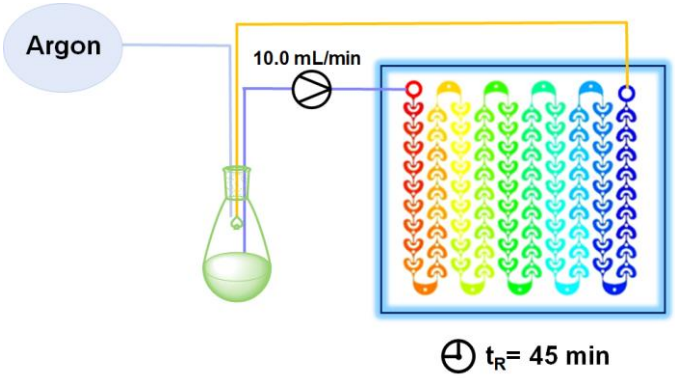


Figure S3. The scale-up reaction of decarboxylative protonation of levulinic acid via a microchannel continuous flow photoreactor

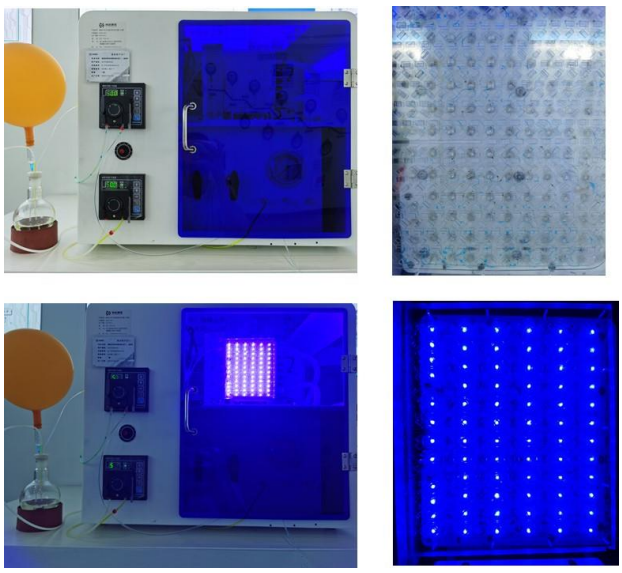


Figure S4. Continuous-flow photoreactor equipped with microchannel reaction plate.

6. Life cycle assessment

Materials and Methods

The life cycle analysis adopted the methodology described in the International Organization for Standardization (ISO) 14040/44, which was divided into four stages: (1) goal and scope definition, (2) life cycle inventory, (3) life cycle impact assessment, and (4) interpretation (ISO 14040, 2006). LCA modeling was performed using openLCA software.

Goal and Scope definition

This LCA model aimed to compare the global warming potential (GWP) data of different methods of producing MEK from LA. The functional unit of the study was the production of 1 kg of MEK. The system boundary of this LCA was "gate-to-gate," including all processes from the factory receiving LA to the factory gate where MEK was synthesized (Figure S5). In this case, the applied catalysts were modeled from cradle to gate to demonstrate the impact of their use in this reaction on global warming potential.

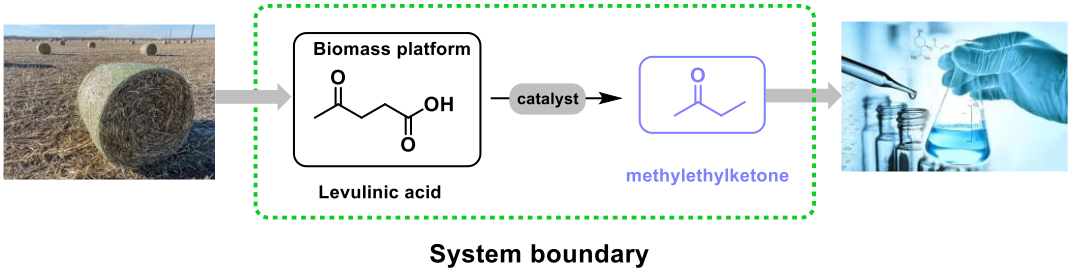


Figure S5. System boundary of LCA study on MEK production from LA.

Life cycle inventory

The life cycle inventory (LCI) included four different methods for the decarboxylation of LA to MEK, which were Scenario (1) Copper mediated decarboxylative protonation of LA,[4] Scenario (2) Silver mediated decarboxylative protonation of LA,[5] Scenario (3) Pd-TiO_2 catalyzed decarboxylative protonation of LA,[6] Scenario (4) Photoinduced metal-free catalyzed protodecarboxylation of LA. Herein, detailed inventory data came from experimental data (foreground system), the ecoinvent v3.8 database (background system), and some published literature.[7] The entire procedure of the decarboxylation reaction and catalyst synthesis route was modeled in openLCA software, and the global warming potential was calculated using the CML-IA baseline method.

Life cycle impact assessment

The global warming potential (GWP) was selected for evaluation to show the carbon footprint of different MEK production approaches through LA. The impact assessment method used was CML-IA baseline. Table S1 was the summary of the GWP data for the substances used in this LCA study.

Table S1. Summary of the GWP data for the substances used in this LCA study

Name	GWP (kg CO_2 eq)	functional unit
aluminium chloride	5.36	1 kg
aniline	3.28	1 kg
benzoic acid	1.91	1 kg
sodium hydroxide	1.27	1 kg
toluene	1.56	1 kg
monochlorobenzene	2.42	1 kg
sodium sulfide	3.03	1 kg
palladium	3880	1 kg
titanium dioxide	2.26	1 kg
copper oxide	5.64	1 kg
potassium hydroxide	2.61	1 kg
phosphoric acid	1.37	1 kg
silver	196	1 kg
methyl ethyl ketone	1.88	1 kg
electricity	1.25	1 kWh

Interpretation

Here, the catalysts used in the synthesis of MEK from LA were modeled as a “cradle-to-gate” process to demonstrate the environmental impact of their synthesis and use in this reaction. The following was the carbon emissions data for the synthesis process of four different catalysts. The functional unit was still the production of 1 kg of MEK.

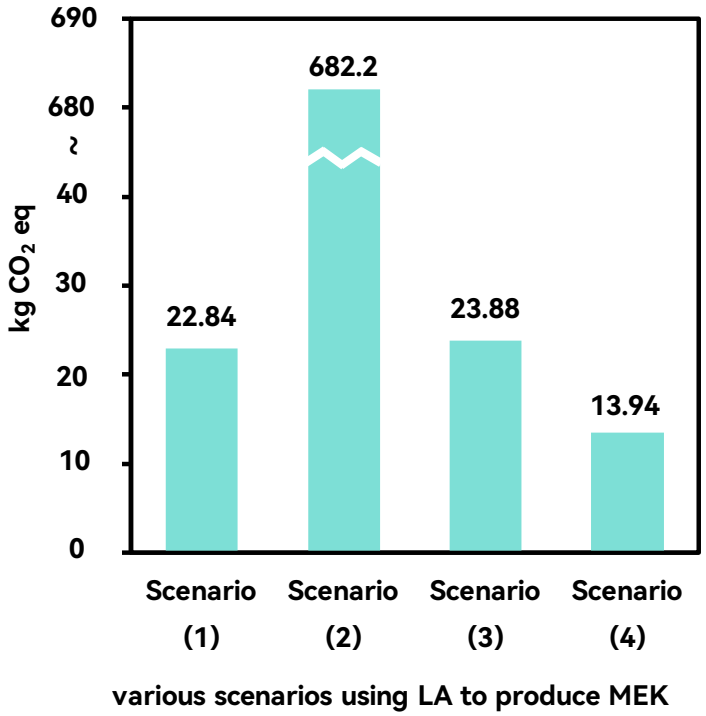
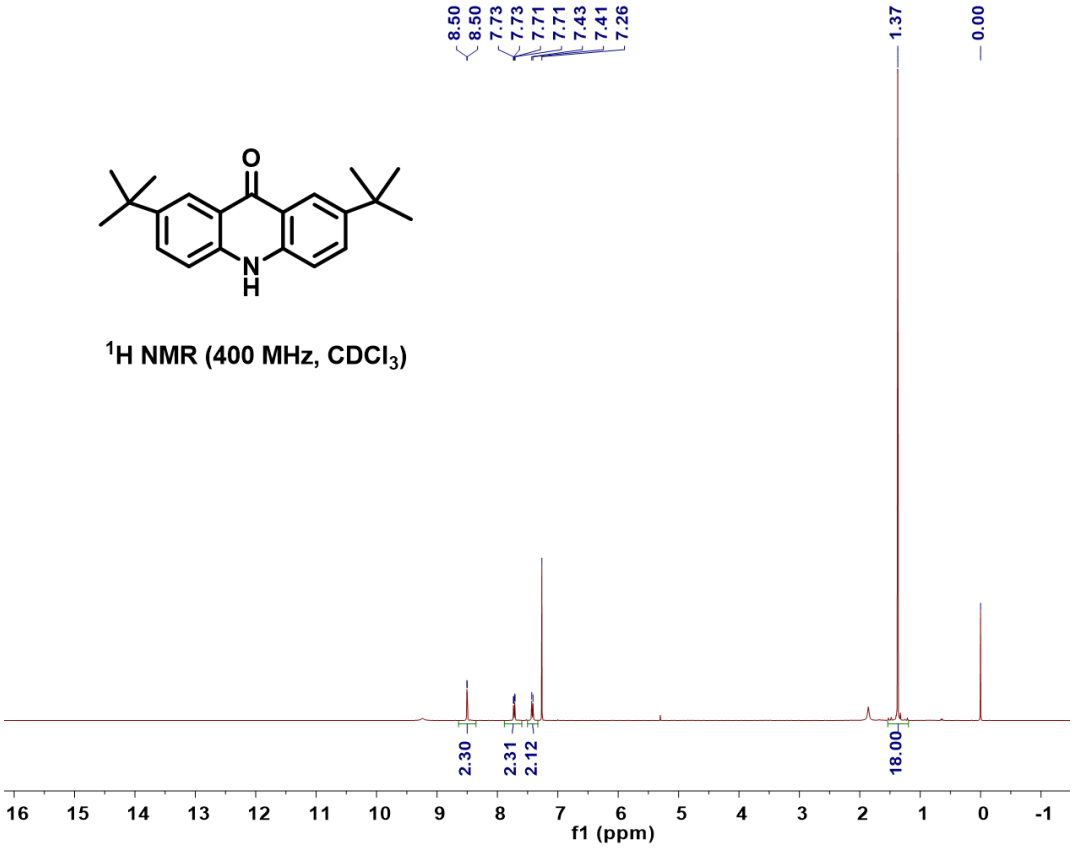
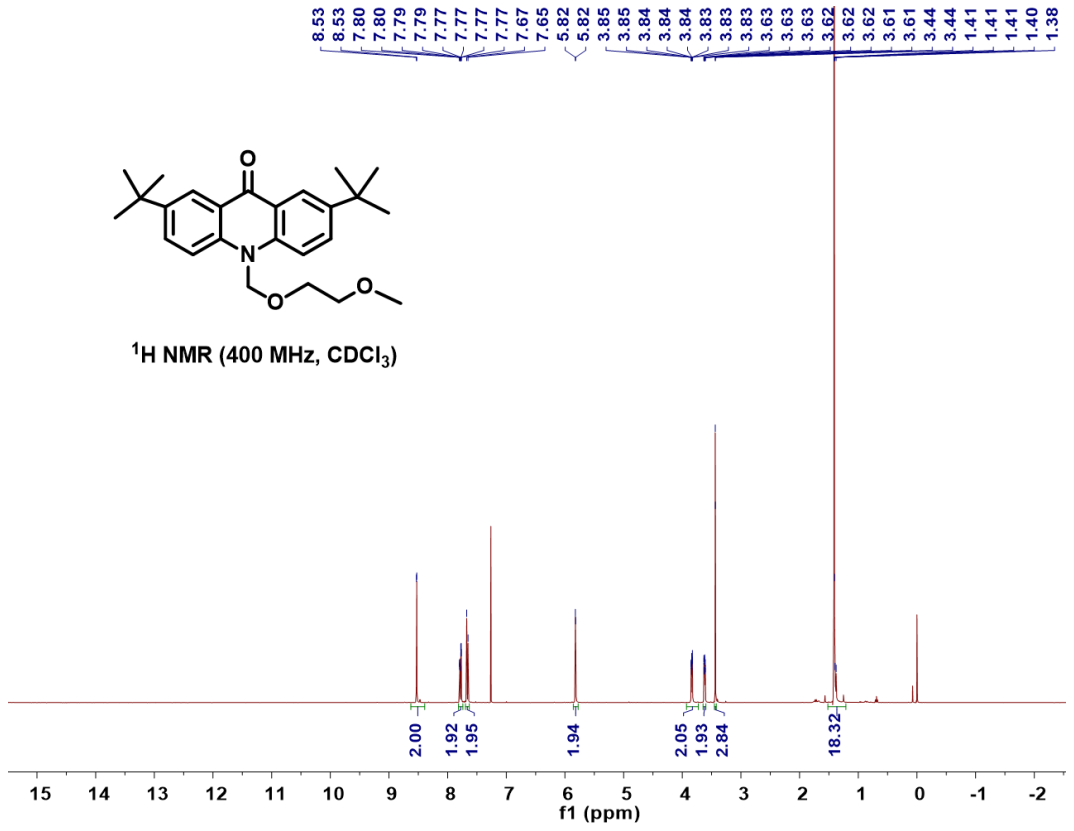


Figure S6. GWP results for catalyst synthesis in four different MEK production scenarios.

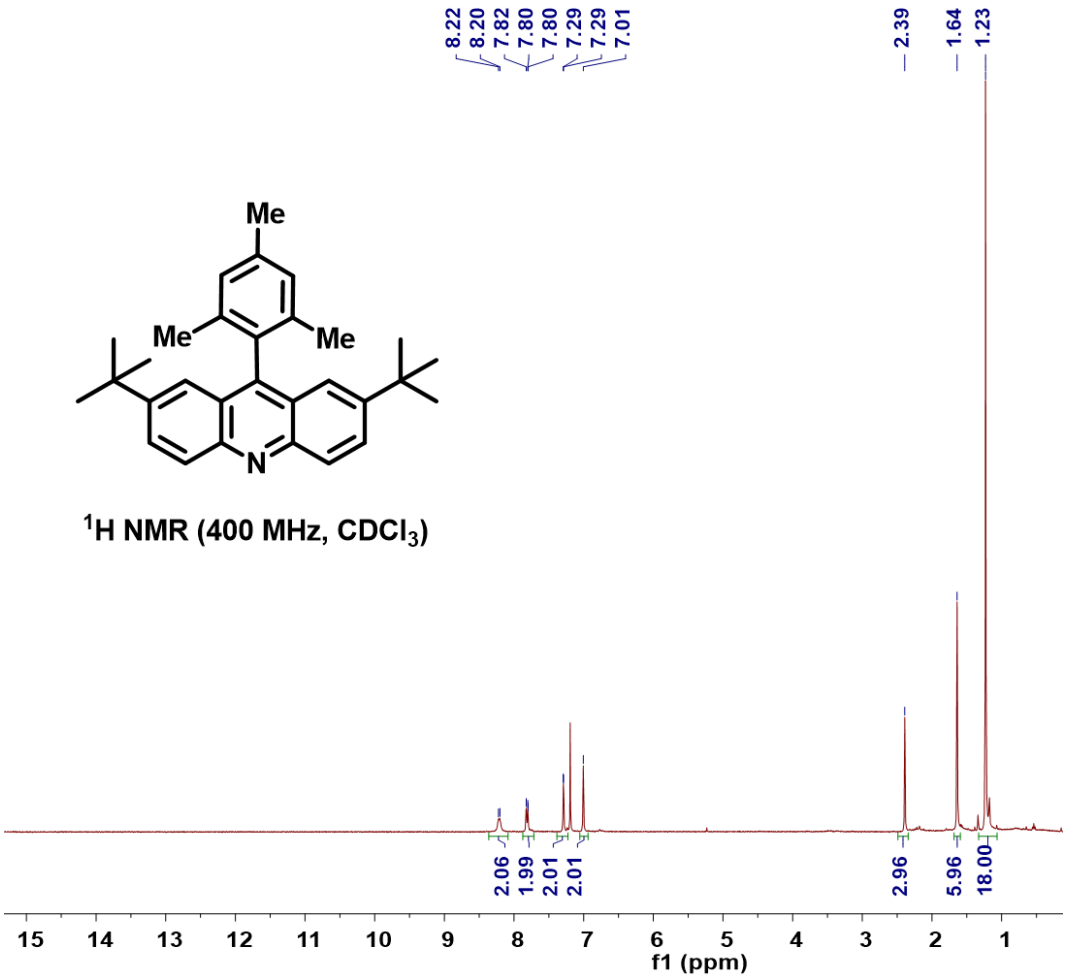
7. NMR spectra



^{1}H NMR (400 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

8. References

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