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Title

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Permalink

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Journal

Nature Synthesis

ISSN

2731-0582

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Publication Date

2026

DOI

10.1038/s44160-025-00961-x

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Peer reviewed

Artificial Synthesis of Carbohydrates from Electrochemically Fixed Carbon Dioxide

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Abstract

Sustainable synthesis of C₅₊ carbohydrates from CO₂ remains challenging due to the complexity of controlled CO₂ reduction and carbon-carbon coupling. Biochemical approaches can convert primary CO₂ reduction products into C₅₊ carbohydrates, but are often constrained by lengthy reaction periods, low production rates, and system complexity. Here, we present a two-step electrochemical reduction–formose reaction method that uses hydroxymethanesulfonate (HMS) as a more stable surrogate for formaldehyde to facilitate the direct synthesis of C₅₊ carbohydrates from electrochemically fixed CO₂. Using cobalt tetraaminophthalocyanine molecules supported on multiwalled carbon nanotubes as an electrocatalyst, we achieve an HMS Faradaic efficiency of ~12% at a total current density of 150 mA cm⁻². Employing direct CO reduction increases the Faradaic efficiency to ~25% with over 63% carbon efficiency. The produced HMS enables an efficient formose reaction under mild conditions reaching a yield of 20.4% for C₅₊ carbohydrates. The CO₂-derived HMS also demonstrates its versatility as a formaldehyde surrogate in other reactions for synthesizing various valuable chemical products, promising a new approach of feeding advanced chemical synthesis with electrochemically fixed CO₂ via the intercepted formaldehyde intermediate.

Introduction

Converting CO₂ into fuels and feedstock chemicals using renewable energy offers a promising solution to mitigating greenhouse gas emissions and achieving a circular carbon economy.¹⁻⁴ While substantial progress has been made in the development of electro- and photocatalytic systems that can produce various C₁ and C₂ products such as CO, formate, methanol, methane, ethylene, and ethanol,⁵⁻¹⁰ new chemistry is still needed for generating more complex and valuable products. Long-chain (C₅₊) carbohydrates are an important target because they are the molecular building blocks of life and have a wide range of applications in food, pharmaceutical, and biotechnology industries.¹¹⁻¹⁴ Upgrading CO₂ to C₅₊ carbohydrates via a single electro- or photocatalytic step, requiring extensive C–C coupling and delicate control in reduction degree, is extremely difficult.^{15,16} Consequently, reported synthesis of C₅₊ carbohydrates from CO₂ usually comprises at least two steps, beginning with either thermochemical or electrochemical reduction of CO₂ to C₁ or C₂ acids or alcohols, followed by multiple biochemical steps incorporating fermentation or enzyme catalysis to yield carbohydrates (Fig. 1a).¹⁷⁻¹⁹ Thermochemical CO₂ hydrogenation as the first step is highly efficient but requires harsh high-temperature and high-pressure reaction conditions and an additional pre-step to generate H₂. The subsequent biochemical process is effective but falls short in production rate, yield, and post-reaction separation, due to the days-long reaction period and the multiple necessary reaction steps. Therefore, efficient and fast synthesis of C₅₊ carbohydrates from electrochemically fixed CO₂ through simple processes is highly desirable.

The formose reaction, which uses formaldehyde as the reactant, is the only known abiotic system capable of producing C₅₊ carbohydrates from a C₁ feedstock in a single step.^{15,20,21} This reaction can achieve high formaldehyde-to-carbohydrate conversion within a short duration of just a few hours, suitable for large-scale production. From the perspective of energy consumption, it makes sense to couple the formose reaction with electrochemical reduction of CO₂ to formaldehyde for sustainable carbohydrate production (Fig. 1b), because the free energy cost of converting CO₂ to carbohydrates all falls in the CO₂-to-formaldehyde step (Fig. 1c), which can be nicely overcome with renewable electricity.²² However, effective formaldehyde production from CO₂ electroreduction has not yet been realized, likely because few electrocatalysts can reduce CO₂ by more than two electrons and formaldehyde is prone to further reduction or disproportionation

under electrochemical conditions in aqueous media. Cobalt phthalocyanine (CoPc)-based materials are perhaps the only effective electrocatalyst for reducing CO₂ via formaldehyde, but the reduction does not stop at formaldehyde due to the low thermodynamic and kinetic barrier for its further reduction to methanol.²³⁻²⁵ Although formaldehyde has been occasionally observed among the products of CoPc-catalyzed CO₂ or CO electroreduction, its yield is very low.^{26,27} It remains a major obstacle to stabilize formaldehyde in electrochemical CO₂ reduction and utilize it for synthesis of more valuable products.

In this work, we develop a strategy which uses hydroxymethanesulfonate (HMS) as a more stable surrogate for formaldehyde to enable the direct synthesis of C₅₊ carbohydrates from electrochemically fixed CO₂. Leveraging the known chemical reaction between formaldehyde and sulfite to form HMS, we manage to intercept the formaldehyde intermediate generated during CO₂ electroreduction catalyzed by cobalt tetraaminophthalocyanine (CoPc-NH₂) molecules supported on multiwalled carbon nanotubes (CNTs). A Faradaic efficiency (FE) of ~12% is achieved for HMS at a total current density of 150 mA cm⁻², improving the state-of-the-art CO₂-to-HMS conversion rate by one order of magnitude. The FE can be further improved to ~25% with an appreciable carbon efficiency of over 60% when employing direct CO reduction. We then use an HMS solution generated from CO₂ electrolysis for the formose reaction, resulting in a yield of 20.4% for C₅₊ carbohydrates. We show that CO₂-derived HMS can serve as a formaldehyde surrogate to go through reactions of symmetric C-C coupling, asymmetric C-C coupling, and C-N coupling for synthesizing various valuable chemicals such as ethylene glycol, sulphonated acetone formaldehyde (SAF) polycondensate, and formaldoxime.

Results and discussion

Intercepting formaldehyde using sulfite

We first sought to verify the feasibility of the concept of intercepting formaldehyde with sulfite during CO₂ electrolysis catalyzed by CoPc-NH₂/CNT, which is one of the few electrocatalysts with stable activity towards reducing CO₂ to methanol.^{24,28} We employed our recently reported three-compartment flow electrolyzer system with a gas diffusion electrode,²⁹ which can achieve a high current density for CO₂ reduction into methanol, to ensure sufficient formaldehyde generation

for capture. Galvanostatic electrolysis was performed in a CO₂-saturated aqueous KHCO₃ electrolyte containing Na₂SO₃ at a moderate total current density of 150 mA cm⁻². In addition to typical products such as H₂, CO, and methanol, HMS was identified in the electrolyte by singlet peaks at ~4.33 ppm in ¹H NMR and ~74.25 ppm in ¹³C NMR (Fig. 2a and Supplementary Fig. 1). This confirms successful interception of CO₂-derived formaldehyde with sulfite via a known reaction involving nucleophilic attack of the sulfur in sulfite on the carbonyl of formaldehyde. We then varied the sulfite concentration (including bisulfite unless otherwise stated) from 0.2 M to 0.8 M to examine its effect on HMS production. The measured FE of HMS increased from 4.6% at 0.2 M to 11.8% at 0.4 M (Supplementary Fig. 2). However, increasing the sulfite concentration further to 0.6 and 0.8 M reduced the rate and selectivity of both HMS and methanol while enhancing CO production, likely because the electrode potential became increasingly positive with higher electrolyte concentrations. To gain mechanistic information, we compared HMS and methanol formation rates in electrolyte with and without sulfite under otherwise identical conditions (Supplementary Fig. 3). The methanol formation rate in the sulfite-containing electrolyte was found to be ~60% of that in the sulfite-free electrolyte, suggesting a partial interception of the methanol formation pathway. The total formation rate of methanol and HMS with sulfite was found to be comparable to the methanol formation rate without sulfite, indicating that both methanol and HMS are formed through a common formaldehyde intermediate. This result supports that HMS formation follows the CO₂-to-formaldehyde pathway.

Based on the optimized electrolyte condition, we conducted current-dependent electrolysis investigations. HMS began to form at 50 mA cm⁻² with an FE of 2.1%, accompanied by a small amount of methanol detected with an FE of 0.7% (Fig. 2b,c and Supplementary Fig. 4). The high formaldehyde interception efficiency of 82% is a clear indication that the C-S coupling reaction between sulfite and formaldehyde outcompetes the electroreduction of formaldehyde to methanol at this electrode potential. As the total current density was increased stepwise from 50 mA cm⁻² to 150 mA cm⁻², both FEs of HMS and methanol gradually increased, reaching the highest FE of 12% for HMS with a partial current density of 17.8 mA cm⁻² (Fig. 2b,c). This is the best performance reported to date for CO₂ electroreduction to HMS, with nearly a three-fold improvement in selectivity and a thirteen-fold increase in rate compared to the previous report using a Cu catalyst

(4% FE and 1.3 mA cm^{-2} for HMS production).³⁰ Further increasing the total current density resulted in lower rate and selectivity for HMS production. Across the entire current density range explored, the total production rate of methanol and HMS combined follows a volcano shape, as commonly seen for CO_2 or CO electroreduction, whereas the HMS/methanol ratio monotonically decreased with increasing total current density (that is, increasingly negative electrode potential), which is due to the fact that the C-S coupling reaction is a chemical step while its competing reaction, namely the reduction of formaldehyde to methanol, is electrochemically driven. At the optimal current density of 150 mA cm^{-2} , the catalyst was able to operate continuously for 5 hours with a stable potential profile and an overall methanol FE of $\sim 10\%$, affording a 17.5 mM HMS solution (Fig. 2d and Supplementary Fig. 5). The slight decrease of HMS FE over time can be attributed to consumption of HCO_3^- which is known to be a secondary proton source for the rate-determining $^*\text{CO}$ -to- $^*\text{CHO}$ step in formaldehyde formation.²³

Since HMS formation via formaldehyde-sulfite coupling is ultimately dependent on formaldehyde production, we sought to further improve the synthesis efficiency by conducting direct CO electrolysis as our recent work reported a high CO-to-methanol FE of 66% catalyzed by CoPc-NH₂/CNT.²³ Conducting CO reduction in an H-cell containing 0.1 M aqueous KHCO_3 with 0.4 M Na_2SO_3 ($\text{pH} = 8.6$), we observed an FE of 20% for HMS at the optimal potential of -0.83 V vs the reversible hydrogen electrode (RHE) (Supplementary Fig. 6). We then varied the electrolyte pH from 7.2 to 11.0 using KOH or H_2SO_4 . Measured at the potential of -1.35 V vs the standard hydrogen electrode (SHE), HMS and methanol FEs as well as the ratio of $\text{FE}_{\text{HMS}}/\text{FE}_{\text{methanol}}$ exhibited a volcano-shaped trend across the pH range (Fig. 2e and Supplementary Fig. 7). This is a result of the interplay among several factors: 1) the competition between CO reduction and H_2 evolution is affected by both pH and HCO_3^- concentration;²³ 2) pH controls the partition between sulfite and bisulfite, which may affect the C-S coupling reaction rate; 3) formaldehyde reduction to methanol, the competing reaction to HMS formation, is affected by pH; and 4) higher pH (> 9) favors the dissociation of HMS. At the optimal pH of 9.0, we achieved an FE of 25% and a notable overall carbon efficiency of 63% for HMS production, with great improvement over direct CO_2 reduction (Fig. 2f). Since CO_2 can be electrochemically reduced to CO with near-unity FE,^{9,31} a tandem process to produce HMS from CO_2 via CO is of potential.

Coupling electrochemical CO₂ reduction with formose reaction

With the success in capturing the unstable formaldehyde intermediate from CO₂ electroreduction catalyzed by CoPc-NH₂/CNT in the form of HMS, we proceeded to the synthesis of carbohydrates utilizing the formose reaction. While numerous studies have reported the formose reaction can convert formaldehyde into a spectrum of C₂ to C₅₊ carbohydrates under mild heating and alkaline conditions,³²⁻³⁴ a similar reaction using HMS as the starting reactant has not yet been reported. We first investigated the stability of HMS against pH at room temperature and found that HMS (50 mM, aqueous) is stable at pH of 8.8 or lower (Supplementary Fig. 8) with negligible decomposition into formaldehyde. This stability allows us to intercept the formaldehyde intermediate in the form of HMS under electrochemical conditions, preventing its further reduction to methanol. At a high pH of 12.5, over 99% of HMS decomposed within 6 hours to release formaldehyde (Supplementary Fig. 8). This result clearly reveals the feasibility of using HMS as an effective formaldehyde surrogate for the formose reaction in alkaline solutions. We then employed the aforementioned CO₂ electrolysis solution containing 17.5 mM HMS for the formose reaction. Prior to reaction, an excess of 10 mM Ca²⁺ was added as the catalyst to the solution after precipitating CO₃²⁻ and SO₃²⁻. To expedite the formose reaction, glycolaldehyde was also added as the initiator to reach a concentration of 10 μM. The reaction was conducted at a mild temperature of 70 °C and a pH of 12.5 for 6 hours (Fig. 3a).

We first performed ¹H NMR spectroscopy to analyze the reaction products. As shown in Fig. 3b and Supplementary Fig. 9, HMS was fully converted, with ~20% of it disproportioning to formate and methanol. We also observed lactic acid (27.2% yield) and acetic acid (1.4% yield), which are formed from retro-aldol breakdown of carbohydrates,^{21,35} as well as glycolaldehyde (0.8% yield) and dihydroxyacetone (3.2% yield) (Supplementary Fig. 10), which are important intermediates leading to the formation of C₅₊ carbohydrates.³² The NMR peaks in the 3.5 to 4.2 ppm region are corresponding to the C-bonded protons in carbohydrate-like species and their derivatives (for example, sugar acids). To quantify these higher-order carbohydrate products, we employed the phenol-sulfuric acid assay, a well-established colorimetric method for determining total C₅₊ monosaccharides.³⁶ The total yield of C₅₊ carbohydrates was determined to be 20.4% comprising 18.8% hexoses and 1.6% pentoses (Fig. 3b). Identification and quantification of each specific

carbohydrate in this complex mixture remains a big challenge in the field,^{21,37} due to the lack of standard analytical techniques to effectively separate carbohydrate isomers and factors like the dynamic Lobry de Bruyn–Van Ekenstein transformation in formose reaction products which facilitates structural interconversion via aldose-ketose isomerization or epimerization.³⁸

To separate the carbohydrate products from the reaction medium, we acidified the post-reaction solution using HCl, evaporated all the liquid, and used ethanol to redissolve the products (Supplementary Fig. 11). After evaporating the ethanol solvent, pure carbohydrate powder was obtained with a crude yield of 45% (Fig. 3d inset). This value is roughly consistent with the yield estimated from the carbohydrate fingerprint region in the NMR spectrum but substantially exceeds the yield determined by the phenol-sulfuric acid assay. This is likely due to the presence of unseparated byproducts, such as sugar acids and C₄ or branched carbohydrates, which have relatively high boiling points and similar physicochemical properties as the target carbohydrates. The sugar acids are generated primarily from the Cannizzaro reaction and degradation of carbohydrates formed during the formose reaction,³⁵ whereas the branched carbohydrates form in the formose reaction through carbon–carbon bond formation at secondary carbon atoms.³⁹ These byproducts give NMR signals in the fingerprint region but are not detectable by the colorimetric method as they cannot form the requisite furfural derivatives. Based on the conservative carbohydrate yield of 20.4%, the overall energy efficiency of the CO₂-to-C₅₊ carbohydrates process is calculated to be approximately 0.8% (see Methods), which is higher than the previously reported electrochemical-biochemical CO₂-to-glucose process (0.65%).¹⁸ Although this is lower than the recently reported CO₂-to-sorbose conversion via a cascade of five enzyme-catalyzed steps (3.5%),¹⁷ our electrochemical-formose route still holds promise because it avoids delicate biosystems, delivers considerably higher reaction rates (Supplementary Table 1), and retains the possibility for further improvement in both HMS production from CO₂ and formose sugar production. However, we should note that the carbohydrates obtained in this work are not food or feed grade, and will likely require downstream purification to comply with food-grade specifications. Our techno-economic analysis (TEA) demonstrates economic profitability for this process when capital, operating, and materials expenses are considered (see Supplementary Note 1 and Supplementary Tables 2-4) (Fig. 3e). Our cradle-to-gate life cycle assessment (LCA)

estimates that the global warming potential of this process is lower than that reported for conventional agriculture (Supplementary Fig. 12 and Supplementary Note 2),¹⁶ reflecting the possibility for reducing environmental impact. Combined TEA and LCA results highlight the plausibility of the electrochemical-formose route as a sustainable approach for producing valuable C₅₊ carbohydrates.

It should be mentioned that Na₂SO₃ only functions as a mediator for the capture-and-release of formaldehyde rather than a co-reactant in carbohydrate formation. It captures formaldehyde as HMS during CO₂ electrolysis, and ends up as CaSO₃ precipitate prior to the formose reaction. The formose reaction thus consumes only the formaldehyde released from HMS and sulfite does not enter the carbohydrate product stream. No additional cost is imposed on downstream separations. If desired, cost can be further reduced by recycling sulfite. A simple recycling loop can be applied to recover Na₂SO₃ from CaSO₃ via acidification or thermal treatment to release SO₂ followed by chemical absorption (Supplementary Fig. 13). Additionally, the close match between the ¹H NMR spectra of carbohydrates derived from HMS and from commercial formaldehyde suggests that sulfite present as CaSO₃ does not participate in or alter the formose chemistry (Supplementary Fig. 14). Therefore, the use of Na₂SO₃ does not impact the economic feasibility of carbohydrate production or interfere with the formose reaction.

Extended applications of HMS in chemical synthesis

Given the success of using HMS for carbohydrate synthesis via the formose reaction, we sought to expand the scope of utilizing HMS as a formaldehyde surrogate in chemical synthesis. All reactions explored in this section were carried out with HMS concentrations of 20 mM or lower, which are readily achievable from our electrochemical CO₂ reduction reactions. We began with electroreductive synthesis of ethylene glycol, which is widely used as an antifreeze agent and a building block in the production of plastics.⁴⁰ An early study demonstrated that graphitic carbon can catalyze the electroreduction of formaldehyde to ethylene glycol in aqueous media.⁴¹ We followed a recent study and employed a commercial carbon black electrocatalyst in 0.1 M aqueous KOH at 60 °C in an H-cell to reduce HMS,⁴² achieving a maximum FE of ~20% at a partial current density of 2.2 mA cm⁻² for ethylene glycol production at -0.65 V vs RHE (Fig. 4a and Supplementary Fig. 15). We observed that the reduction of formaldehyde to methanol dominated

with an FE of 74%, which is likely due to the low concentration of HMS favoring single-molecule reduction over reductive dimerization of formaldehyde. Although the selectivity and rate are too low for practical application, this result successfully demonstrates the feasibility of using HMS to produce ethylene glycol via symmetric C–C coupling and stands as a new example of ethylene glycol electrosynthesis from CO₂.

Beyond electrochemical C–C coupling, we also explored chemical reactions between HMS and other reagents. As a surrogate for electrophilic formaldehyde, HMS is expected to be susceptible to nucleophilic attack, thus applicable to methylation and hydroxymethylation reactions. We first demonstrated the asymmetric C–C coupling reaction between HMS and other aldehydes or ketones that can be transformed into nucleophilic enols. For example, reacting HMS with acetone in aqueous KOH at 60 °C produced a sulphonated acetone formaldehyde polycondensate with a yield of 67% (Fig. 4b). This product has widespread applications in construction and materials industries as a superplasticizer, water reducer, or dispersant.⁴³ Additionally, we explored C–heteroatom coupling reactions for the use of HMS. As an example, formaldoxime was synthesized with a high yield of 99% by reacting HMS with hydroxylamine at room temperature in aqueous KHCO₃ to form C–N bonds (Fig. 4c). Formaldoxime is widely used as an intermediate in organic/pharmaceutical synthesis and as a ligand in analytical chemistry.⁴⁴ These reaction examples collectively demonstrate the potential of using HMS as a reactive yet stable form of electrochemically fixed CO₂ for chemical synthesis.

Conclusions

In summary, we have demonstrated that formaldehyde captured in the form of HMS can enable a two-step electrochemical-formose process for synthesizing valuable carbohydrates, such as pentoses and hexoses, using CO₂ as the carbon source. The successful extension of HMS as a formaldehyde surrogate to symmetric C–C, asymmetric C–C, and C–N coupling reactions suggests a promising approach to bridging CO₂ electrochemical reduction with more advanced chemical and electrochemical reactions through capturing and stabilizing its active intermediates. Future work will focus on enhancing the rate and selectivity of HMS production from CO₂, optimizing

carbohydrate selectivity in the HMS-based formose reaction, and improving the separation of post-reaction products.

Methods

Materials. Materials used in this work were directly purchased from the following suppliers unless otherwise specified. Potassium hydroxide (99.98%) and acetone (>99.5%) were purchased from Fisher Chemical. Sodium sulfite (>98.0%), potassium bicarbonate (99%), and *N,N*-dimethylformamide (DMF, 99.8%) were purchased from Alfa Aesar. Calcium chloride (96%), hydroxylamine hydrochloride (99+%), D-glucose (ACS reagent) and D-galactose (99+%) were purchased from Acros Organics. Glycolaldehyde (crystalline), and Nafion solution (5 wt.%) were purchased from Sigma-Aldrich. 1,3-dihydroxyacetone (97%), D-ribose (98%), D-fructose (99%), D-xylose (99+%) and D-mannose (99+%) were purchased from Thermo Fisher Scientific. Sodium hydroxymethanesulfonate (>97.0%) and D-arabinose (>99.0%) were purchased from Tokyo Chemical Industry. Carbon monoxide (99.3%), carbon dioxide (99.99%), argon (99.999%), and nitrogen (99.999%) gases were purchased from Airgas. Multiwalled CNTs were purchased from C-Nano (product number FT9100). The carbon paper support (Freudenberg, catalogue no. H23C6) with microporous layer coating was purchased from the Fuel Cell Store. The electrolyte solutions were prepared using Milli-Q water (18.2 MΩ cm at 25 °C).

Preparation of CoPc-NH₂/CNT electrode. The synthesis of CoPc-NH₂, purification of CNTs, and preparation of CoPc-NH₂/CNT can be found in our previous work.²³ Briefly, CoPc-NH₂ was synthesized in a solid state reaction from 4-nitrophthalonitrile, CoCl₂·6H₂O, and urea, catalyzed by (NH₄)₆Mo₇O₂₄·4H₂O; CNTs were purified via calcination and HCl treatment; CoPc-NH₂ molecules were assembled on CNTs from their DMF solutions with the assistance of sonication and stirring. CoPc-NH₂/CNT with optimized molecular loadings of 15 wt.% and 10 wt.% were used for CO₂ and CO reduction, respectively.^{23,29} Optimized mass loadings of 1.2 and 0.4 mg cm⁻² for CoPc-NH₂/CNT on carbon paper were used for measurements in the flow cell and H-cell, respectively.^{24,29} To prepare CoPc-NH₂/CNT electrodes, 5 mg of CoPc-NH₂/CNT was mixed with 15 μL of the Nafion solution and 5 mL of ethanol, followed by 30 min of sonication. The resulting ink was drop-casted onto carbon paper support to achieve the desired catalyst loading, covering an

area of approximately 1.0 cm^2 . The electrode was then thoroughly dried using an infrared lamp for subsequent measurements.

Preparation of carbon catalyst electrode. The carbon catalyst electrode for ethylene glycol synthesis was prepared according to a reported method.⁴² To prepare the carbon catalyst, 100 mg of carbon black (Vulcan XC-72 R, Fuel Cell Store) was first purified using 100 mL of 5 wt.% HCl under sonication for 30 min. The Vulcan carbon was then collected by filtration and washed with Milli-Q water until the supernatant reached pH 7. After freeze-drying, the purified Vulcan carbon was annealed at $500\text{ }^\circ\text{C}$ for 3 h under a 5/95 H_2/Ar atmosphere to eliminate oxygen-containing functional groups. A total of 10 mg of the pre-treated Vulcan carbon was mixed with 30 μL of the Nafion solution and 10 mL of ethanol, followed by 30 min of sonication to create an ink, which was drop-casted onto carbon paper to achieve a mass loading of $0.5\text{ mg}\cdot\text{cm}^{-2}$.

Electrochemical reactions. CO_2 electrolysis was performed in a three-channel flow electrolyzer (Gaoss Union, Inc.) with channel dimensions of $2\text{ cm} \times 0.5\text{ cm} \times 0.5\text{ cm}$. The cathode and anode channels were separated by a piece of anion-conducting membrane (Selemion DSV, AGC, Inc.). A platinum foil was used as the counter electrode, and a Ag/AgCl (0.199 V vs. SHE, 4.0 M KCl, Pine Research Instrumentation, Inc.) was used as the reference electrode. The electrolyte was 0.3 M CO_2 -saturated aqueous KHCO_3 containing Na_2SO_3 with varied concentrations. CO_2 gas was delivered into the cathode gas channel at a flow rate of $10.0\text{ cm}^3\text{ min}^{-1}$ using a mass flow controller (Alicat Scientific, Inc.). The catholyte and anolyte flow rates were set to be 1.2 and 50 mL min^{-1} via a peristaltic pump, respectively. CO electrolysis was performed in a home-made two-compartment H-cell separated by an anion-conducting membrane. A graphite rod (Sigma-Aldrich, 99.999%) and a Ag/AgCl were used as the counter electrode and the reference electrode, respectively. The electrolyte was 0.1 M aqueous KHCO_3 containing 0.4 M Na_2SO_3 . Prior to electrolysis, the catholyte was purged for 5 min by delivering CO gas at a flow rate of $50.0\text{ cm}^3\text{ min}^{-1}$. Then, CO gas was continuously supplied to the cathode compartment at a flow rate of $20.0\text{ cm}^3\text{ min}^{-1}$ for CO electrolysis. The symmetric C-C coupling reaction for ethylene glycol synthesis was carried out in the same H-cell. The electrolyte was 0.1 M aqueous KOH containing 20 mM HMS, and the reaction was performed under Ar at $60\text{ }^\circ\text{C}$. All electrochemical experiments were performed using a Bio-Logic VMP3 Multichannel Potentiostat. Chronopotentiometry and chronoamperometry were used for the measurements in the flow cell and H-cell, respectively. The

resistance between the working and reference electrodes was determined by potentiostatic electrochemical impedance spectroscopy and was automatically compensated during measurements.

Thermochemical reactions. Thermochemical reactions including the formose reactions, asymmetric C-C coupling, and C-N coupling were conducted under controlled temperature and stirring conditions. For the formose reaction, the electrolyte containing ~17.5 mM HMS after CO₂ electrolysis was directly used. Prior to reaction, CaCl₂ powder in an equimolar amount to SO₃²⁻ + CO₃²⁻ was gradually added to the electrolyte solution to precipitate CaSO₃ and CaCO₃. The pH of the solution was adjusted to 12.5 by adding 1.0 M aqueous KOH. Additional CaCl₂ and glycolaldehyde were then added to the solution to reach concentrations of 10 mM and 10 μM, respectively. The reaction was maintained at 70 °C for 6 h. Product separation, wherever applicable, was performed following the procedure illustrated in Supplementary Fig. 11. To prepare the aqueous formaldehyde solution for the formose reaction, paraformaldehyde was dissolved and hydrolysed in the Milli-Q water at 60 °C for 1 h. For the asymmetric C-C coupling reaction to synthesize sulphonated acetone formaldehyde polycondensate, commercial HMS and acetone were added in 20 mL 0.1 M aqueous KOH at final concentrations of 10 mM and 50 mM, respectively. This reaction was maintained at 60 °C for 2 h. For the C-N coupling reaction to synthesize formaldoxime, commercial HMS and hydroxylamine hydrochloride were added to 20 mL 0.1 M aqueous KHCO₃ to reach concentrations of 10 mM and 100 mM, respectively. This reaction was conducted at room temperature for 30 min.

Product quantification. Gas-phase products were analyzed using a gas chromatograph (SRI 8610C) equipped with a flame ionization detector for CO quantification and a thermal conductivity detector for H₂ quantification. Liquid products were quantified by a Bruker AVIII 400 MHz NMR spectrometer with water suppression. NMR samples were prepared by mixing 450 μL of the resulting solution of each reaction with 50 μL of 10 mM dimethyl sulfoxide (Alfa Aesar, ≥99.9%) in D₂O (Sigma-Aldrich, 99.9%) as the internal standard. The C₅+ formose reaction products were quantified by the phenol-sulfuric acid assay. Calibration curves were obtained using aqueous solutions of 12–60 mg L⁻¹ glucose and 10–50 mg L⁻¹ ribose as representative standards for hexoses and pentoses, respectively (Supplementary Fig. 16). Typically, 2 mL of a carbohydrate standard or four-fold diluted formose reaction sample was mixed with 50 μL of 80 wt.% phenol aqueous

solution, immediately followed by the addition of 5 mL of concentrated sulfuric acid to produce furfural derivatives for colorimetric assay. Absorption spectra were recorded at 479 and 487 nm for pentoses and hexoses, respectively, using a Shimadzu UV-2600 UV-vis spectrophotometer.

Calculation of energy efficiency (EE). For the CO₂-to-HMS process, the $EE_{\text{electrochemical}}$ can be calculated as follows:

$$EE_{\text{electrochemical}} = \frac{1.23 + (-E_0)}{E_{\text{applied}}} \times FE = \frac{1.23 + 0.07}{3.24} \times 12\% = 4.8\%$$

where E_{applied} is the cell voltage applied in the electrolysis, FE is the Faradaic efficiency of HMS, and $E_0 = -0.07 \text{ V}_{\text{RHE}}$ is the equilibrium potential for CO₂-to-formaldehyde conversion.

To determine the energy efficiency for the HMS-to-carbohydrates process in the formose reaction, we compare the enthalpy of combustion of the resulting carbohydrates to that of formaldehyde. Because carbohydrates containing the same number of carbon atoms have nearly identical enthalpies of combustion, ribose and glucose were selected as representatives. According to data from the National Institute of Standards and Technology and the CRC Handbook of Chemistry and Physics (95th edition), the enthalpies of combustion are as follows: formaldehyde, -566 kJ mol⁻¹; ribose, -2349 kJ mol⁻¹; glucose, -2840 kJ mol⁻¹.

The EE_{Formose} can be calculated as follows:

$$EE_{\text{Formse}} = \left(-2349 \text{ kJ mol} \times \frac{1.6\% \text{ yield}}{5} - 2840 \text{ kJ mol} \times \frac{18.8\% \text{ yield}}{6} \right) / -566 \text{ kJ mol} \\ = 17.1\%$$

Thus, the global energy efficiency for the C₅₊ carbohydrates produced from the two-step electrochemical-formose method can be estimated as:

$$EE_{\text{global}} = EE_{\text{electrochemical}} \times EE_{\text{Formse}} = 4.8\% \times 17.1\% = 0.82\%$$

Data availability

Source data are provided with this paper. All experimental data supporting the findings of this study are available in Supplementary Information.

Acknowledgements

This work was supported by the National Brown Investigator Award (H.W.) and US National Science Foundation (grant number CHE-2154724, H.W.). The flow cell work was supported by the Yale Center for Natural Carbon Capture (H.W.).

Author contributions

J.L. and H.W. conceived this project and designed the experiments. J.L. and K.C. synthesized the catalyst materials, performed the TEA and LCA, and conducted the electrochemical and chemical reactions. Y.S. assisted in some of these experiments. J.Y. carried out the post-reaction separation of carbohydrates. J.L., K.C. and H.W. wrote the manuscript with input from N.E.S. and P.Y.. Y.G. and S.C. contributed to data analysis and edited the manuscript. H.W. supervised the project.

Competing interests

The authors declare no competing interests.

Figure legends and captions

Fig. 1. Comparing different pathways from CO₂ to carbohydrates. (a) Previously reported thermochemical-biochemical and electrochemical-biochemical processes. (b) This work: a two-step electrochemical-formose process. (c) Free energy change for the two-step carbohydrate synthesis involving electrochemical CO₂ reduction followed by the formose reaction.

Fig. 2. HMS production from CO₂ or CO electroreduction in the presence of sulfite. (a) Detection of hydroxymethanesulfonate (HMS) by ¹H NMR and ¹³C NMR. (b) Faradaic efficiencies (FEs) of HMS and methanol and their ratio for CO₂ reduction catalyzed by 15 wt.% CoPc-NH₂/CNT in an aqueous electrolyte containing 0.3 M KHCO₃ + 0.4 M Na₂SO₃ at varied current densities. (c) Partial current densities of HMS and methanol vs electrode potential for reactions in b. (d) FE and concentration of HMS during 5 h CO₂ reduction electrolysis at 150 mA cm⁻². (e) FEs of HMS and methanol and their ratio vs electrolyte pH for CO reduction catalyzed by 10 wt.% CoPc-NH₂/CNT

at -1.35 V vs SHE in an aqueous electrolyte containing 0.1 M KHCO_3 + 0.4 M Na_2SO_3 with its pH adjusted to different values. (f) Comparison of FE and carbon efficiency between CO_2 -to-HMS and CO-to-HMS processes, corresponding to the maximum HMS FE conditions in b and e, respectively. Data are presented as mean values and error bars represent standard deviations ($n = 3$ replicates).

Fig. 3. Carbohydrate synthesis via the formose reaction of a 17.5 mM hydroxymethanesulfonate (HMS) solution from CO_2 electrolysis. (a) Scheme of the formose reaction using HMS as the reactant. (b) ^1H NMR analysis of products from the formose reaction. (c) UV-vis absorption analysis of products from the formose reaction compared with hexose and pentose standards using the phenol-sulfuric acid method. (d) Yield of pentoses and hexoses from the formose reaction. The inset shows the separated carbohydrate solid. (e) Techno-economic assessment of the profit of producing 1 t of C_{5+} carbohydrates from CO_2 as a function of the overpotential and Faradaic efficiency for HMS formation.

Fig. 4. Extended application of hydroxymethanesulfonate in various chemical syntheses. (a) Electrochemical synthesis of ethylene glycol via symmetric C–C coupling. (b) Chemical synthesis of sulphonated acetone formaldehyde polycondensate via asymmetric C–C coupling. (c) Chemical synthesis of formaldoxime via C–N coupling.

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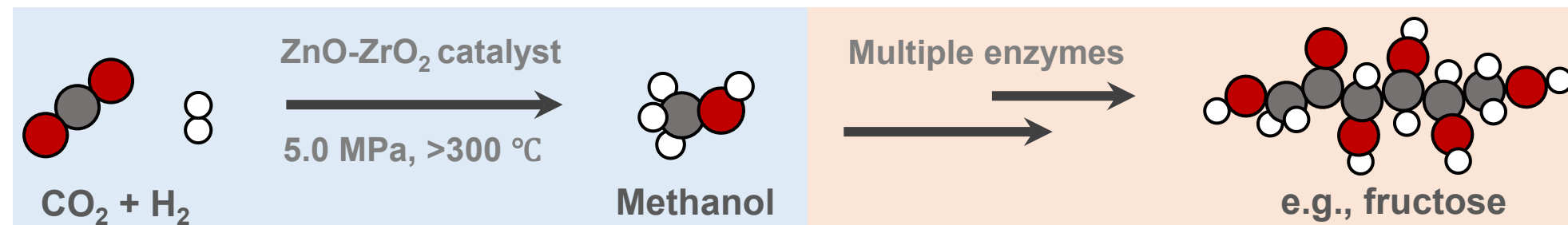
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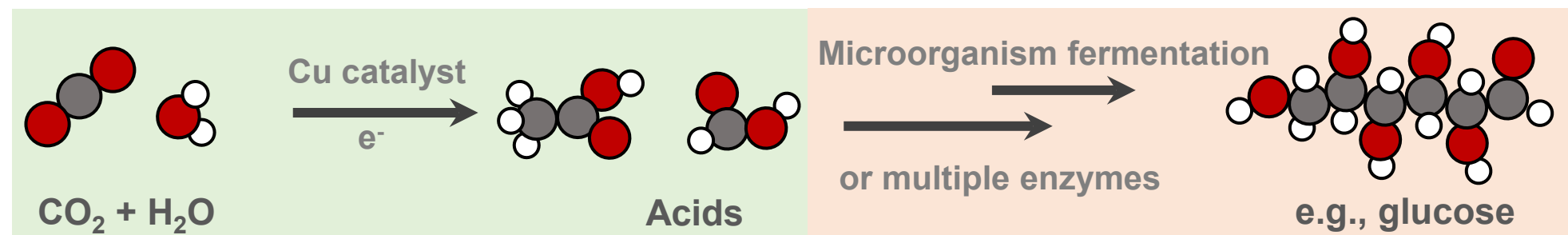
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a Current process

The thermochemical-biochemical process

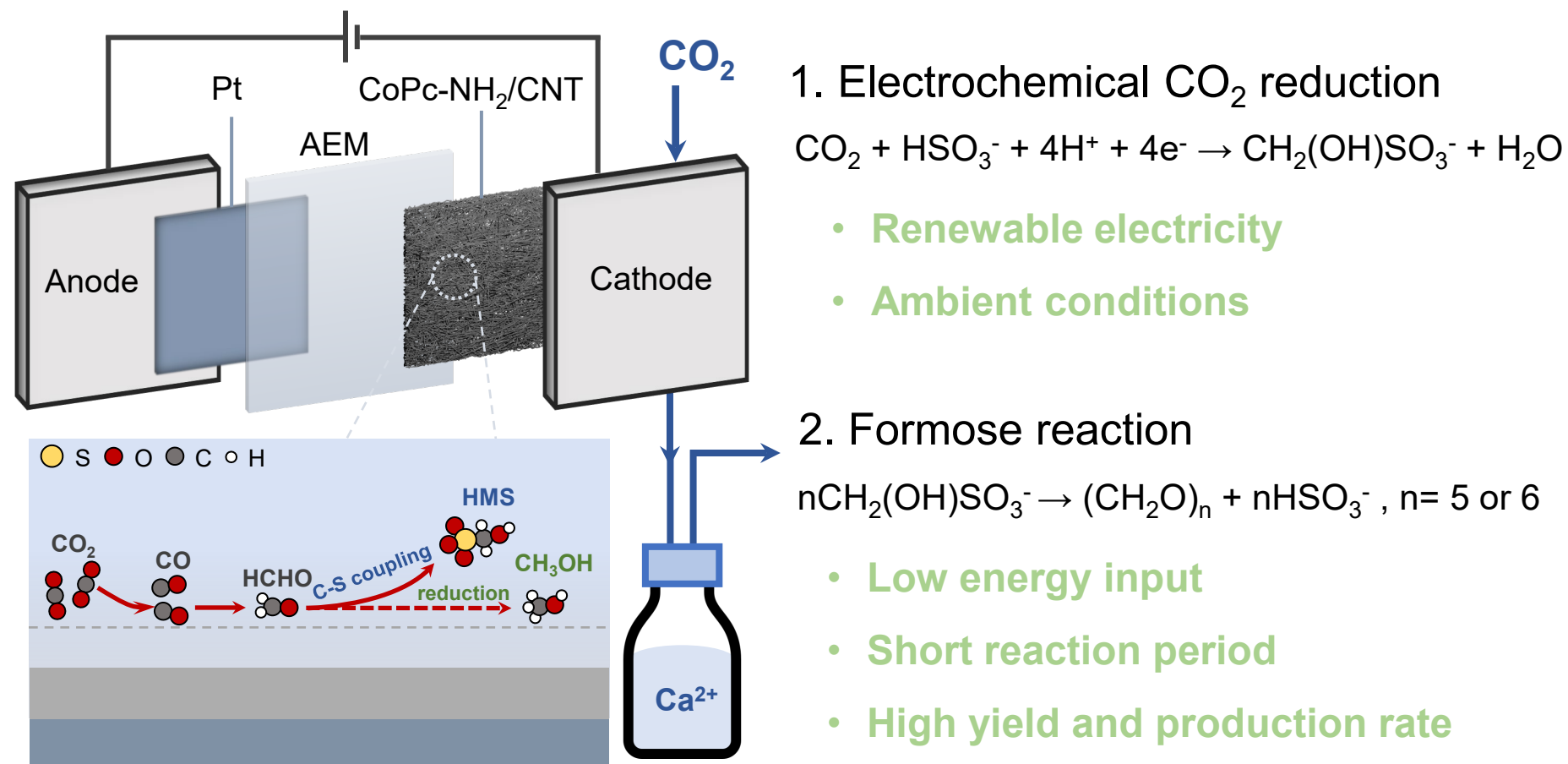


The electrochemical-biochemical process

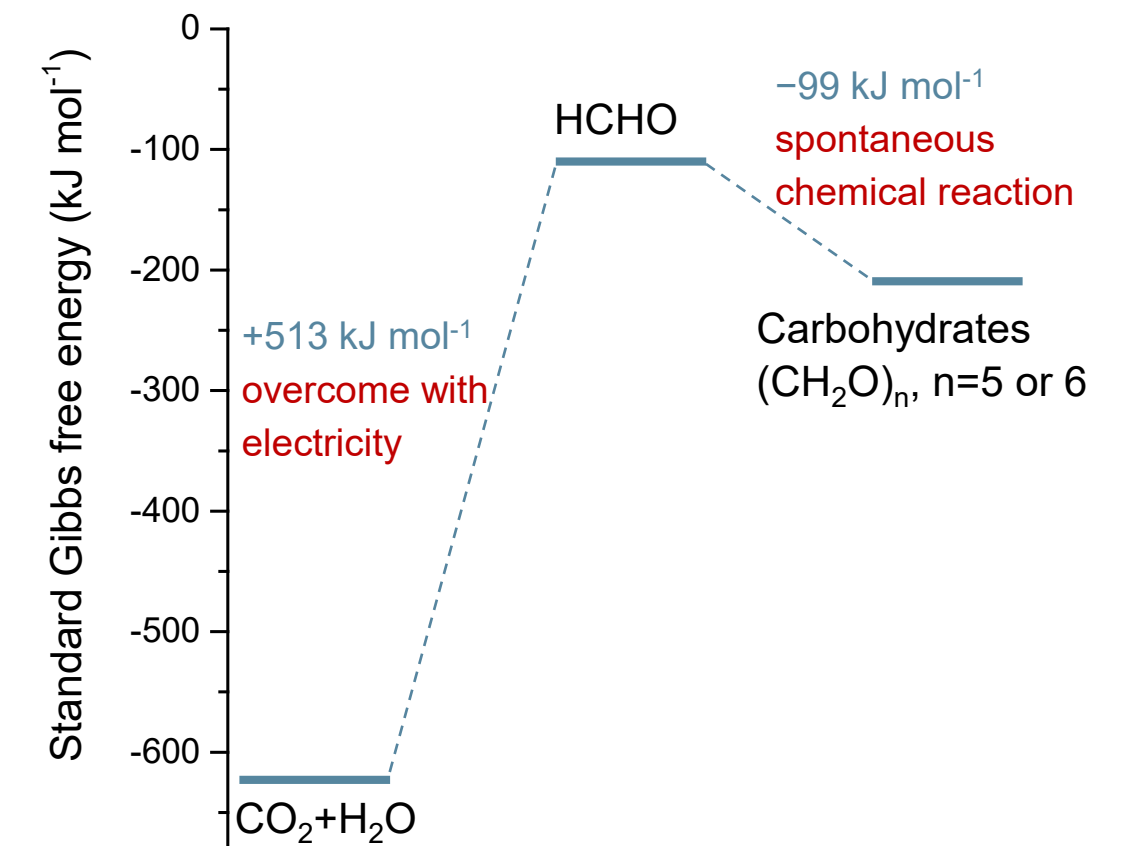


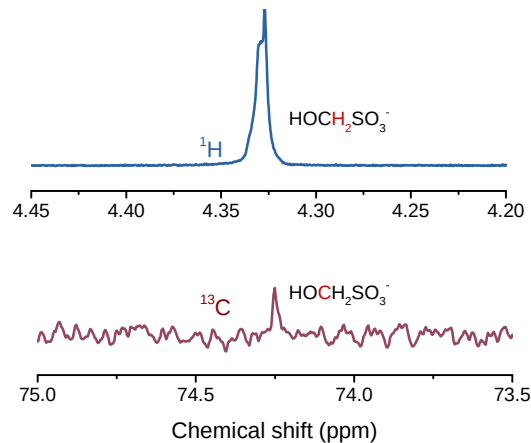
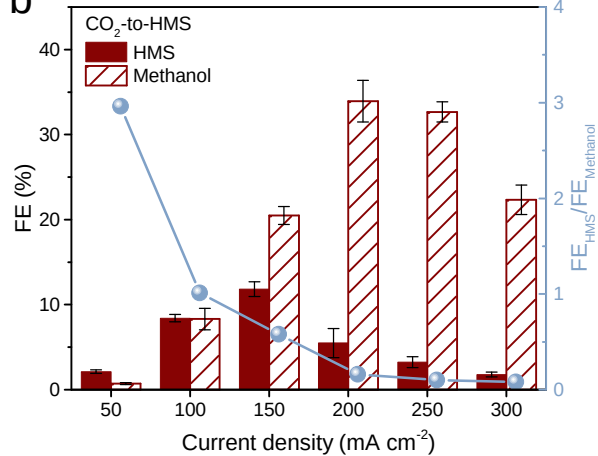
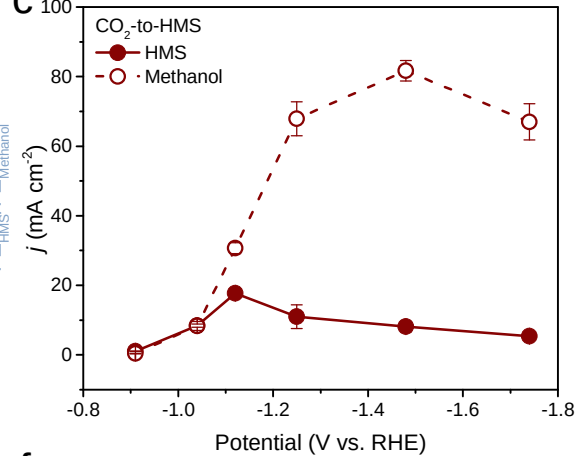
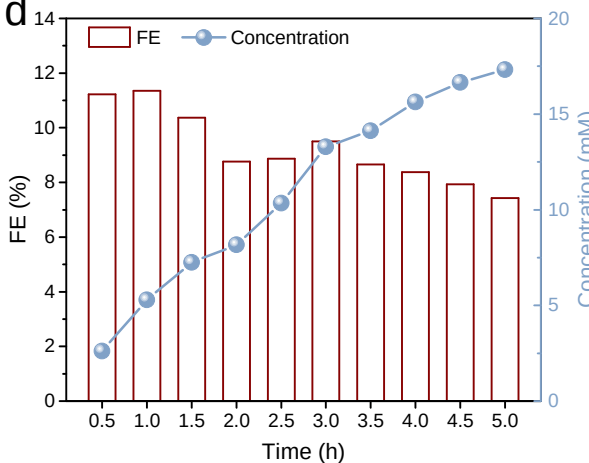
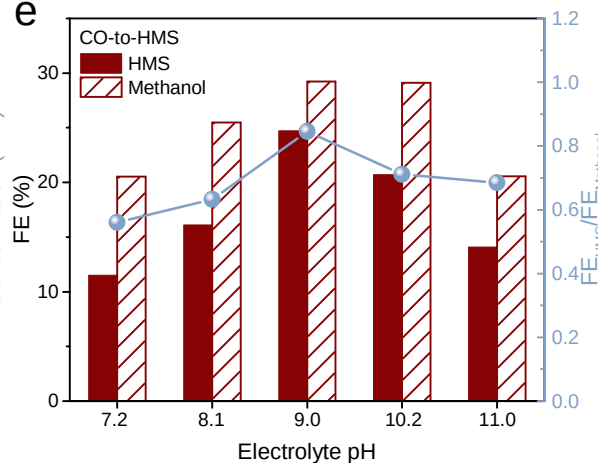
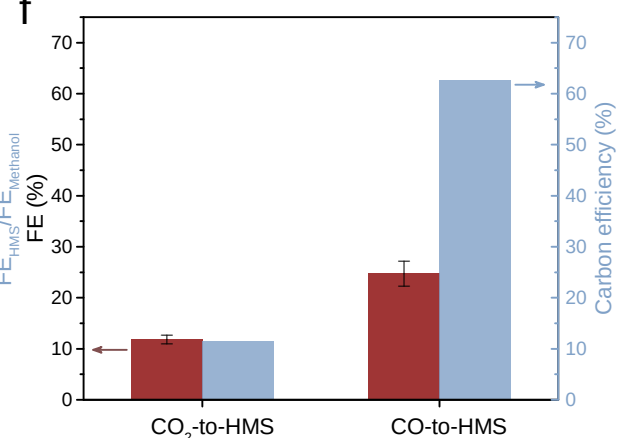
- High energy input
- Harsh conditions
- Complexity of biosystem
- Lengthy reaction period
- Low production rate
- Multiple steps

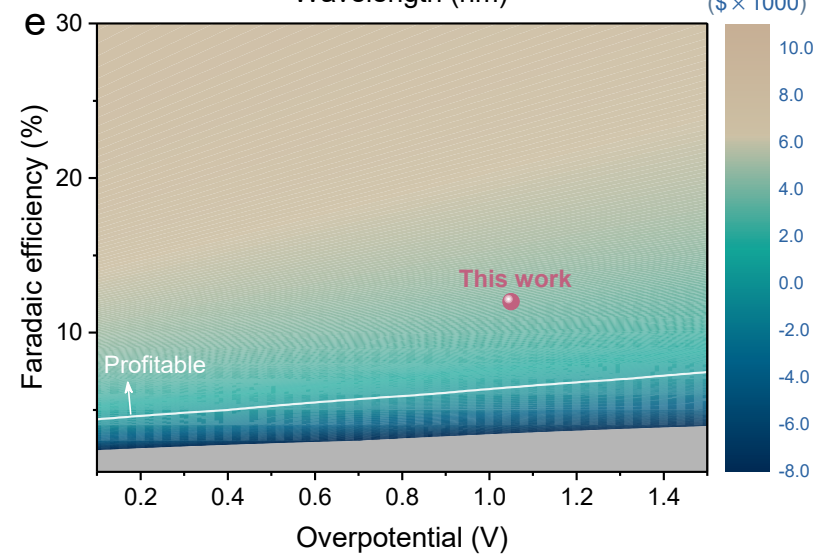
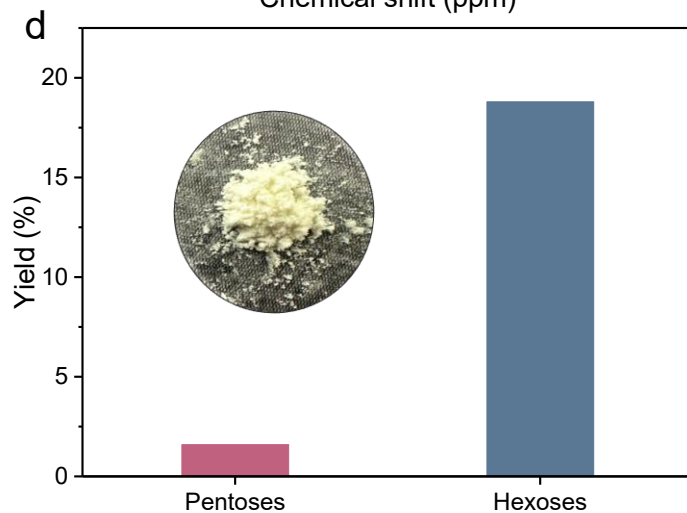
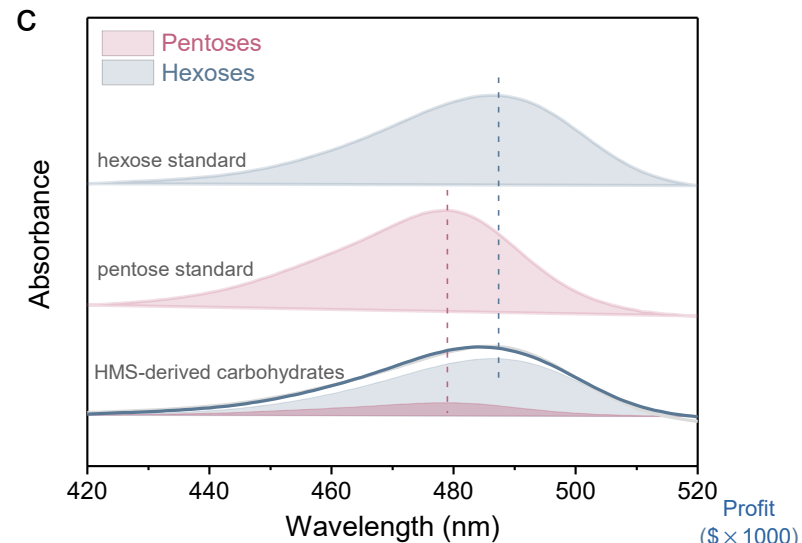
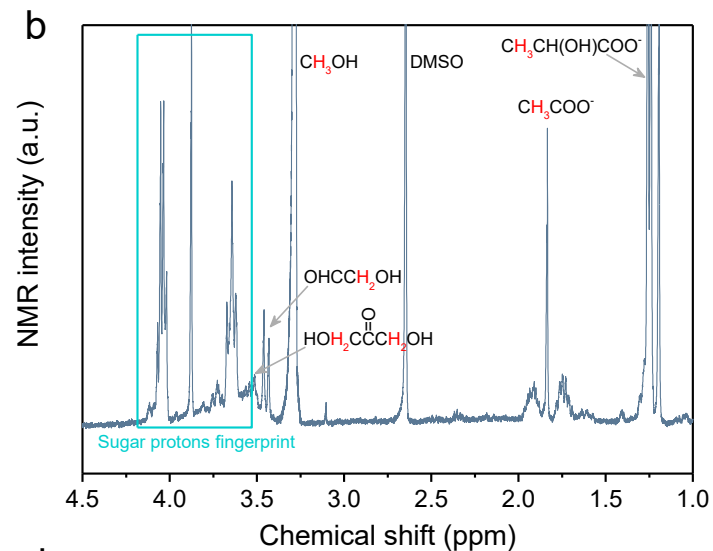
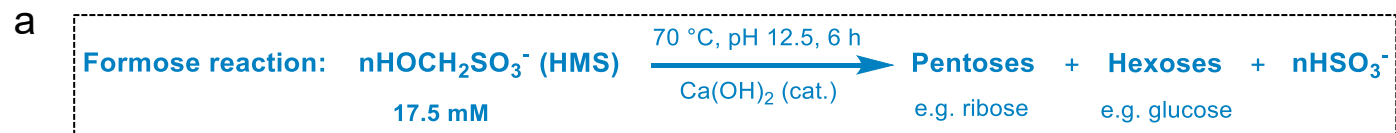
b This work: two-step electrochemical-formose process



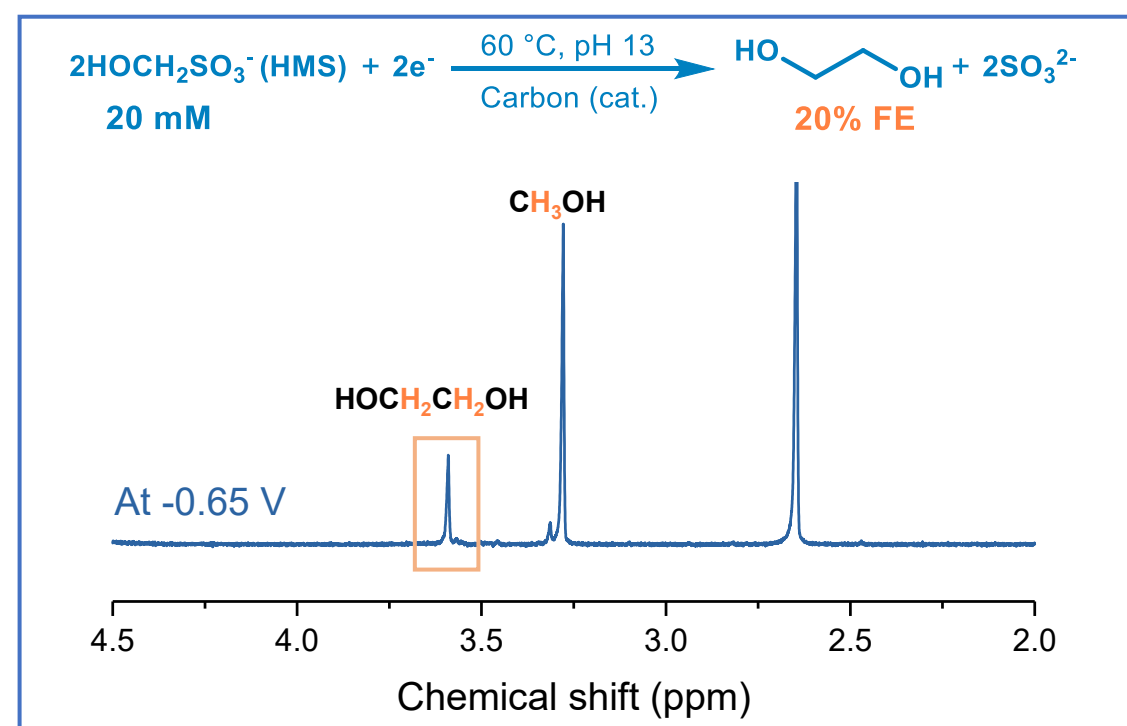
c



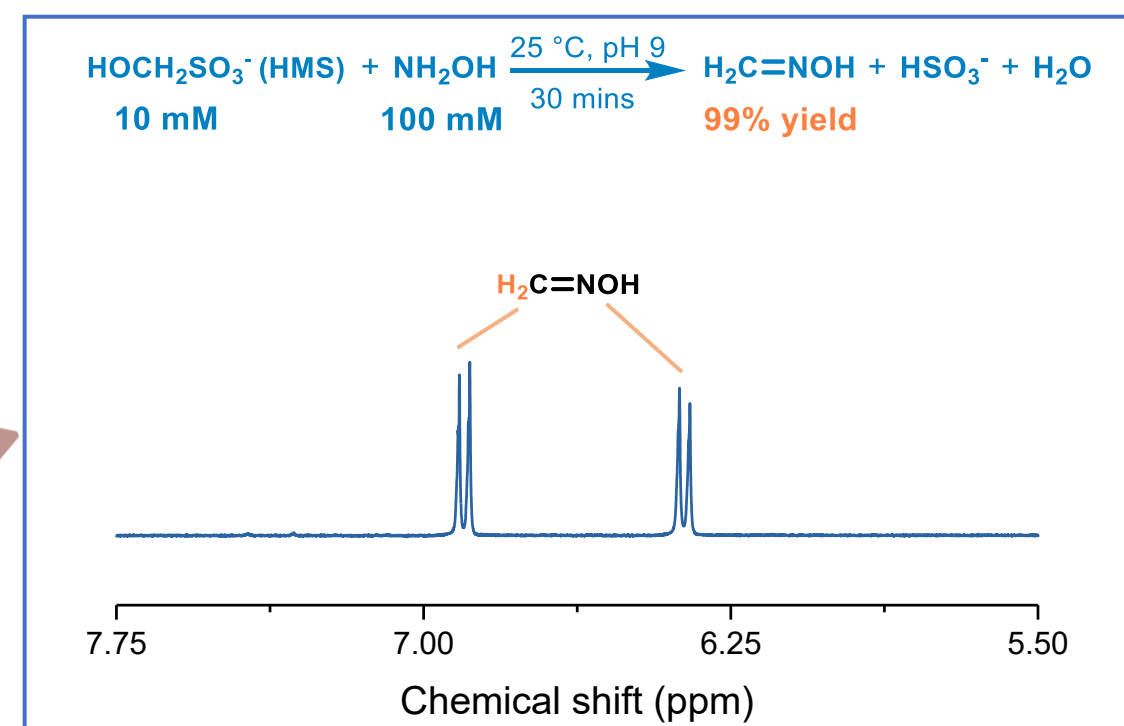
a**b****c****d****e****f**



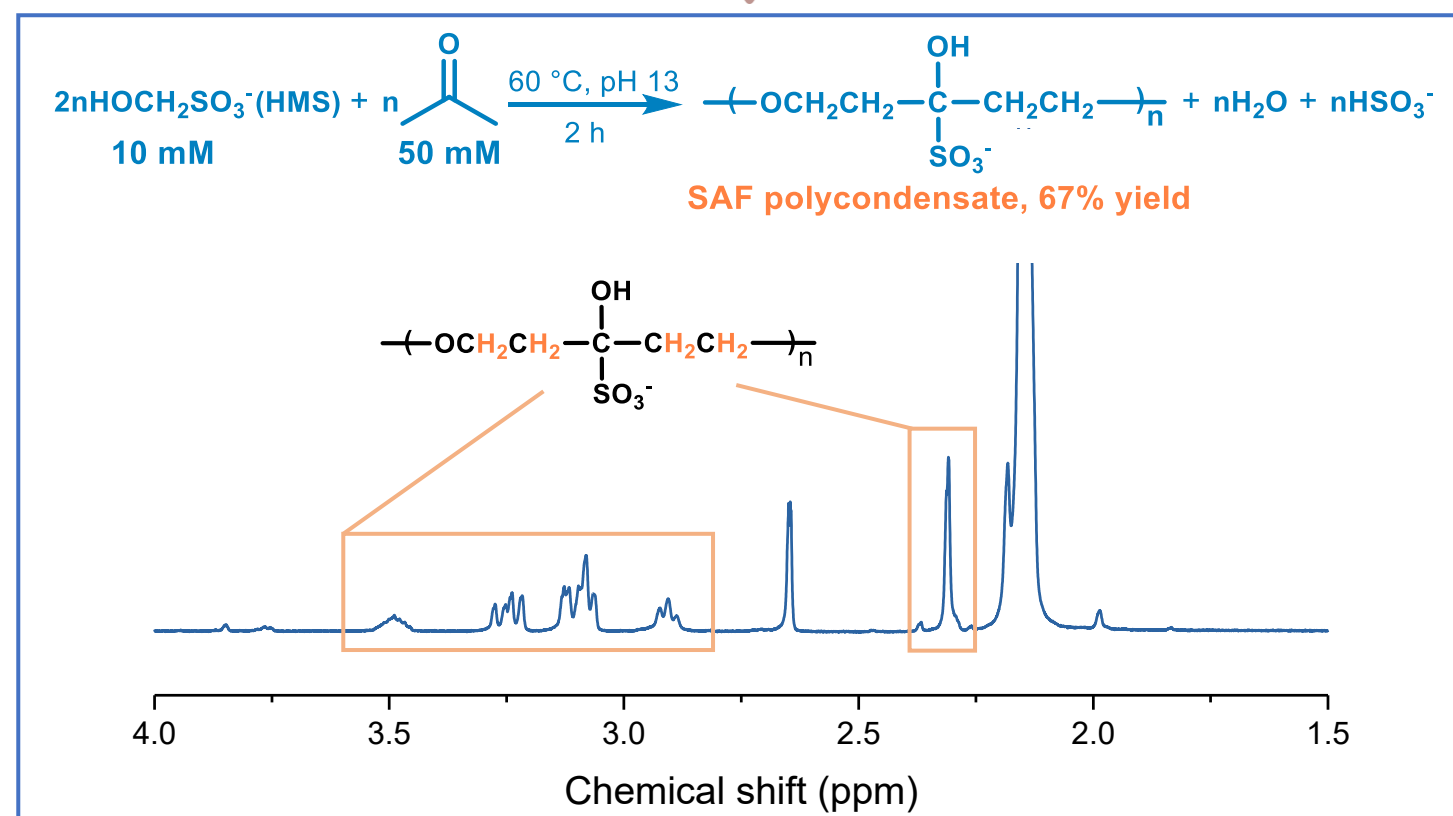
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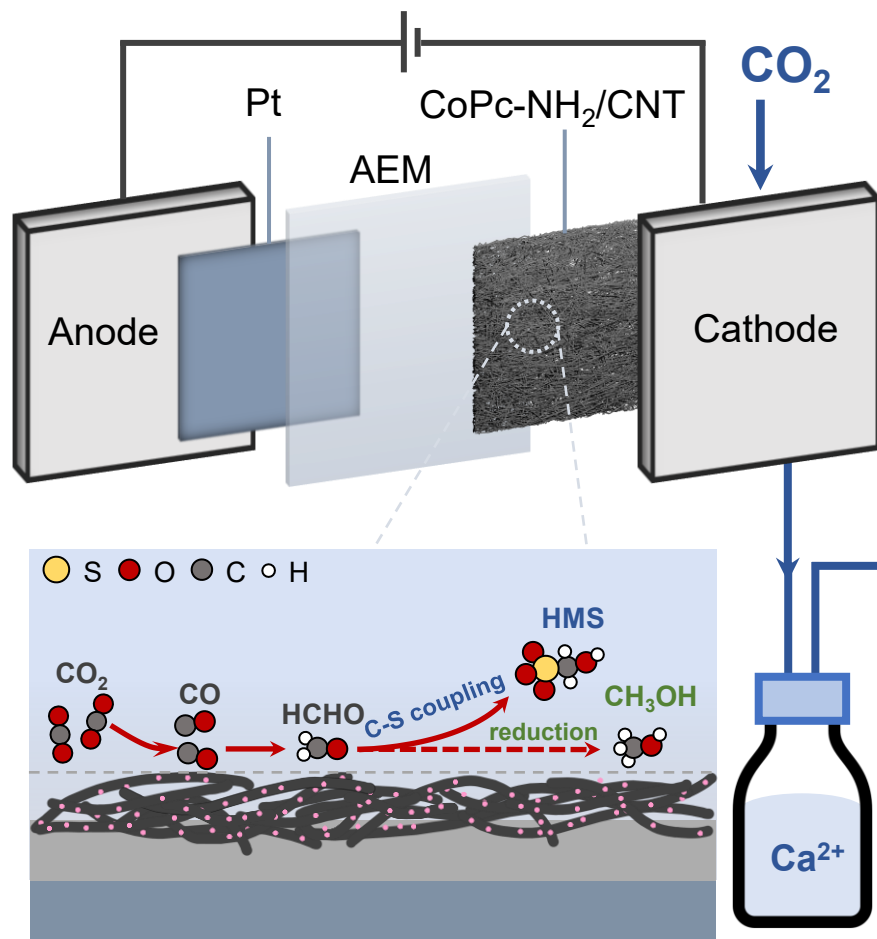


c



b





Two-step electrochemical-formose process

1. Electrochemical CO₂ reduction



- Renewable electricity
- Ambient conditions

2. Formose reaction



- Low energy input
- Short reaction period
- High yield and production rate