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Synergistic Porosity and Charge Effects in a Supramolecular Porphyrin Cage Promote Efficient Photocatalytic CO₂ Reduction**

 Lun An⁺, Patricia De La Torre⁺, Peter T. Smith, Mina R. Narouz, and Christopher J. Chang*

Abstract: We present a supramolecular approach to catalyzing photochemical CO₂ reduction through second-sphere porosity and charge effects. An iron porphyrin box (**PB**) bearing 24 cationic groups, **FePB-2(P)**, was made via post-synthetic modification of an alkyne-functionalized supramolecular synthon. **FePB-2(P)** promotes the photochemical CO₂ reduction reaction (CO₂RR) with 97% selectivity for CO product, achieving turnover numbers (TON) exceeding 7000 and initial turnover frequencies (TOF_{max}) reaching 1400 min⁻¹. The cooperativity between porosity and charge results in a 41-fold increase in activity relative to the parent Fe tetraphenylporphyrin (**FeTPP**) catalyst, which is far greater than analogs that augment catalysis through porosity (**FePB-3(N)**, 4-fold increase) or charge (Fe *p*-tetramethylanilinium porphyrin (**Fe-p-TMA**), 6-fold increase) alone. This work establishes that synergistic pendants in the secondary coordination sphere can be leveraged as a design element to augment catalysis at primary active sites within confined spaces.

Introduction

Conversion of carbon dioxide (CO₂) into value-added chemical feedstocks using renewable energy inputs represents a sustainable solution to simultaneously mitigate growing global energy demands and reduce greenhouse gas concentrations.^[1] These challenges continue to motivate widespread efforts in the development of new catalyst systems for the electrochemical and photochemical CO₂ reduction reaction (CO₂RR).^[2] In this regard, homogeneous

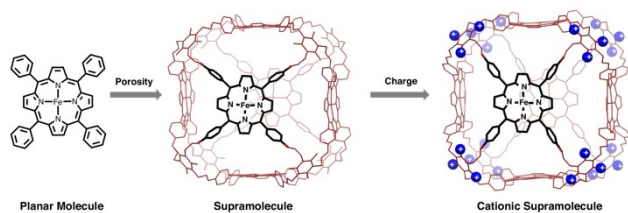
catalysts featuring well-defined metal active sites and ligand scaffolds are valuable in elucidating structure/activity relationships and mechanisms with molecular-level control.^[2b-d,i-k] To date, two main strategies have been adopted to advance the field of molecular CO₂RR catalysis: (1) primary coordination sphere chemistry with ligand modifications to tune redox properties of metal centers,^[3] and (2) secondary coordination sphere chemistry to introduce functionalities beyond the primary active site, including charged^[4] or hydrogen-bonding groups,^[4h,5] to promote capture and transformation of CO₂ and its reduced intermediates. For the latter strategy, we have initiated a program to explore a supramolecular second-sphere approach to enhance CO₂RR^[6] and related small-molecule activation reactions^[7] by integrating planar molecular catalysts into three-dimensional confined space architectures. In particular, porous molecular cages, such as metal-organic coordination cages (MOCs)^[8] and porous organic cages (POCs),^[9] offer the ability to organize reaction substrates^[10] and intermediates,^[11] as well as tune reaction kinetics,^[12] thus capturing the functional essence of enzyme-substrate binding processes.^[13] As discrete molecular analogs of extended covalent organic framework (COF)^[14] and metal organic framework (MOF)^[15] materials used for CO₂RR, porous molecular cages offer comparable advantages of permanent porosity in confined spaces with higher solution processibility and homogeneous molecular control.^[16]

However, despite early advances in the development of molecular cages for energy conversion reactions, these structures largely utilize only one second-sphere feature to augment catalysis—porosity. As such, we sought to incorporate additional second-sphere functionalities into such scaffolds, reasoning that synergy between multiple types of interactions could achieve higher cooperative gains in activity and/or selectivity compared to a single type of interaction. We now report the design, synthesis, and evaluation of a modular porphyrin-based organic cage platform that incorporates dual features of porosity and charge; these multiple second-sphere effects coordinate to amplify photochemical CO₂RR catalysis beyond incorporation of individual second-sphere elements alone (Scheme 1). An alkyne-functionalized iron porphyrin box (**FePB-1(A)**) synthon enables addition of 24 positively-charged ammonium groups via click chemistry to afford **FePB-2(P)**. CO₂RR activity comparisons across a systematic series of analogs that feature only porosity (**FePB-3(N)**) or charge (**Fe-p-TMA**) reveal that the dual-functionalized **FePB-2(P)** catalyst enhances CO₂RR catalysis by over 40-fold over the parent **FeTPP** compound. In contrast, porosity-only or

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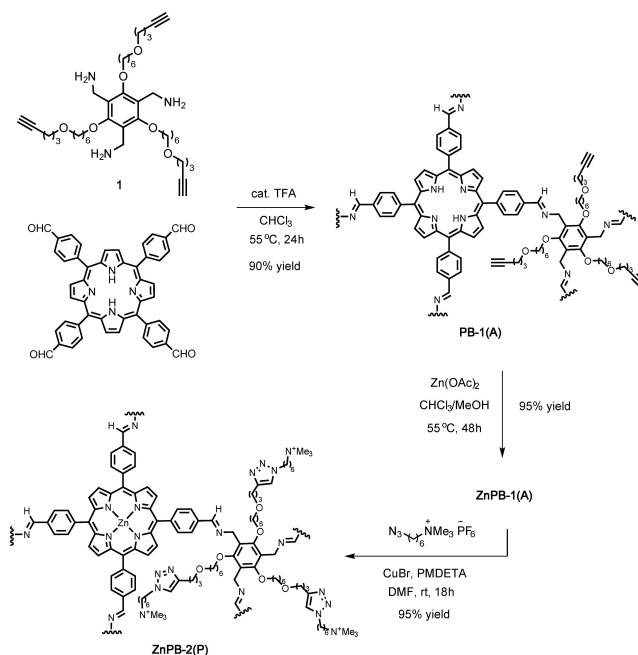
Scheme 1. The design of supramolecular CO₂ reduction reaction (CO₂RR) catalysts based on iron porphyrin organic cages that incorporate cooperative second-sphere porosity and charge effects.

charge-only interactions give more modest 4-fold or 6-fold increases, respectively. **FePB-2(P)** promotes efficient CO₂RR with 97% selectivity for CO product, achieving TON exceeding 1100 and initial TOF_{max} reaching 160 min⁻¹ per Fe center. These results provide a starting point for the broader incorporation of multiple, synergistic second-sphere functionalities as a design element to enhance catalysis in confined molecular spaces.

Results and Discussion

Synthesis and Characterization of a Modular Porous Porphyrin Cage Platform Bearing Peripheral Positive Charges

To start, motivated by broader interest in the development of methods for modular post-synthetic modifications of molecular cages,^[17] we designed and prepared the alkyne-containing clickable porphyrin box **PB-1(A)** starting from an alkyne functionalized triamine linker **1** (Scheme S1). The reported procedure for the unfunctionalized **PB** linker 1,3,5-tris(aminomethyl)-2,4,6-trialkylbenzene features a bromomethylation/azidation/reduction sequence to introduce the three aminomethyl groups.^[18] However, the harsh conditions required in the bromomethylation step (HOAc/HBr, 70 °C, 18 h) prevented us from introducing the alkynyl functionality in the early stage of the synthesis. Instead, three 1-chloro-hexyl groups were selectively introduced by substitution of phloroglucinol and 1-bromo-6-chlorohexane, which were well tolerated in the bromomethylation step and provided accessible chloric handles for late-stage alkylation. The chloride groups were successfully converted to terminal aldehyde groups by a bromination/hydrolysis/oxidation sequence. However, neither the Seyferth–Gilbert homologation nor the Corey–Fuchs reaction was successful in transforming these aldehydes into terminal alkyne functionalities.^[19] After screening several reaction conditions, the alkynyl groups were introduced via an iron-catalyzed reductive etherification reaction of carbonyl with triethylsilane and trimethyl(pent-4-yn-1-yloxy)silane in 93% yield.^[20] Upon deprotection with hydrazine, alkyl functionalized triamine linker (**1**) was obtained. The alkyne functionalized **PB-1(A)** was then assembled in 90% yield by condensing eight triamine linkers (**1**) and six tetraformylphenylporphyrin building blocks in CHCl₃ solution with a catalytic amount of TFA (Scheme 2).^[18] **PB-1(A)** was



Scheme 2. Synthesis of the alkyne-functionalized porphyrin cage **PB-1(A)** and the Zn-metalated, charged porphyrin cage **ZnPB-2(P)**.

thoroughly characterized by NMR, FT-IR, and UV/Vis spectroscopies as well as MALDI mass spectrometry and elemental analysis; the presence of 24 terminal alkynes was confirmed by the observation of a triplet at 1.94 ppm in the ¹H NMR spectrum (Figure S13) and a sharp peak at 3293 cm⁻¹ corresponding to the C–H stretch of the terminal alkynes detected by FT-IR (Figure S17). Notably, this **PB-1(A)** cage serves as a versatile synthon for further functionalization by copper-catalyzed azide-alkyne cycloaddition (CuAAC) click chemistry, after its metalation with zinc acetate to prevent copper insertion into the porphyrin during the click reaction. Initial pilot screening reactions between **ZnPB-1(A)** and N₃-(CH₂)₆-NMe₃⁺PF₆⁻ using typical conditions:^[21] CuSO₄ (1.0 equiv, 4.2 mol % per alkyne) and sodium ascorbate (2.0 equiv, 8.4 mol % per alkyne) in a *t*BuOH/H₂O solvent mixture at room temperature resulted in no product isolated after 24 hours (Table S1, entry 1). Further optimization attempts involving changes in catalyst loading, solvent, and reaction temperature failed to yield the desired product (Table S1, Entries 2–4). To simplify the reaction system, we turned to Cu^I as a catalyst in anhydrous DMF solution. Unfortunately, neither catalytic nor stoichiometric quantities of CuI or Cu(PPh₃)₃Br were successful, even after raising the temperature to 60 °C (Table S1, Entries 5–8). Finally, we were able to obtain the desired product using click-type polymerization conditions^[22] consisting of Cu^IBr (24.0 equiv) with pentamethyldiethylenetriamine (PMDETA) (24.0 equiv). The positively charged **ZnPB-2(P)** organic cage was prepared in 95% isolated yield as confirmed by ¹H- and ¹⁹F NMR, UV/Vis, FT-IR, and elemental analysis (Scheme 2). ¹H NMR analysis of **ZnPB-2(P)** in CD₃CN showed a new peak at 6.70 ppm with an integral of 24 protons (Figure S24), which

was assigned as the triazole signal. Moreover, the singlet at 2.68 ppm corresponding to the trimethylammonium group and the multiple at 0.60–1.70 ppm assigned to alkyl chains further demonstrated the successful addition of $N_3-(CH_2)_6-NMe_3^+$ to **ZnPB-1(A)**. The presence of PF_6^- counter anions was confirmed by observation of a doublet at -72.6 ppm by ^{19}F NMR (Figure S25). Elemental analysis revealed a nitrogen percentage increase from 6.66 % (6.72 % calculated) to 10.89 % (11.25 % calculated) as a consequence of the formed triazole rings and added quaternary ammonium groups, while carbon percentage decreased from 74.53 % (74.91 % calculated) to 53.90 % (56.27 % calculated). Moreover, we were able to characterize **ZnPB-2(P)** using electrospray ionization mass spectrometry (ESI-MS). The multiply charged ions distribution from +13 to +20 were observed as **ZnPB-2(P)** losing the corresponding number of counterions (PF_6^-) ions (Table S2, Figures S28–S36). Taken together, these data further confirm successful **PB** modification through a modular post-synthetic click chemistry method.

Synthesis, Redox Behavior, and Electrochemical CO_2 Reduction Activity of Porous Iron Porphyrin Cage Analogs With or Without Additional Charged Functionalities

To systematically evaluate the effects of second-sphere porosity and charge within these confined space CO_2RR catalysts, we synthesized the Fe analogs of the alkyne-functionalized, neutral, and highly positively charged porphyrin boxes, **FePB-1(A)**, **FePB-3(N)**, and **FePB-2(P)**, respectively (Figure 1a). It is noteworthy that the charged **FePB-2(P)** organic cage is soluble in both DMF and CH_3CN solvents at up to 1 mM concentrations, which is uncommon in **PB** supramolecules.^[23] The newly-synthesized **FePB** cages, as well as the mononuclear **FeTPP** and the tetracationic **Fe-p-TMA**, which provide control compounds for electrostatic effects in planar mononuclear catalysts, were first compared by cyclic voltammetry (CV) using a glassy carbon electrode. The CV of **FePB-1(A)** under an Ar atmosphere shows three redox waves at $E_{1/2} = -0.62$, -1.52 , and -2.11 V vs. ferrocene/ferrocenium (Fc/Fc^+), which we assigned as the formal Fe^{III}/Fe^{II} , Fe^{II}/Fe^I , and Fe^I/Fe^0 redox couples, respectively (Figure 1b). The slight positive shift of Fe^I/Fe^0 couple in **FePB-1(A)** compared to **FeTPP** ($E_{1/2} = -2.15$ V) is likely the result of the electron-withdrawing effect of the imine linkages in the porphyrin box. However, these data show that supramolecular encapsulation has modest effects on intrinsic redox properties of molecular porphyrin building blocks. **FePB-3(N)** displays a similar Fe^I/Fe^0 couple ($E_{1/2} = -2.10$ V) to **FePB-1(A)**, indicating the triazole formed after the click reaction also has little effect on the redox potential of the iron centers, while the broadening of the Fe^{III}/Fe^{II} and Fe^{II}/Fe^I redox couples may be due to increased molecular complexity or varied metal ligation by solvent or counteranion. Interestingly, a 150-mV positive shift of the Fe^I/Fe^0 wave was observed in **FePB-2(P)** ($E_{1/2} = -1.95$ V) compared with **FePB-1(A)** (Figure 1b). The electrostatic effect of introducing twenty-four trimethylammonium groups onto

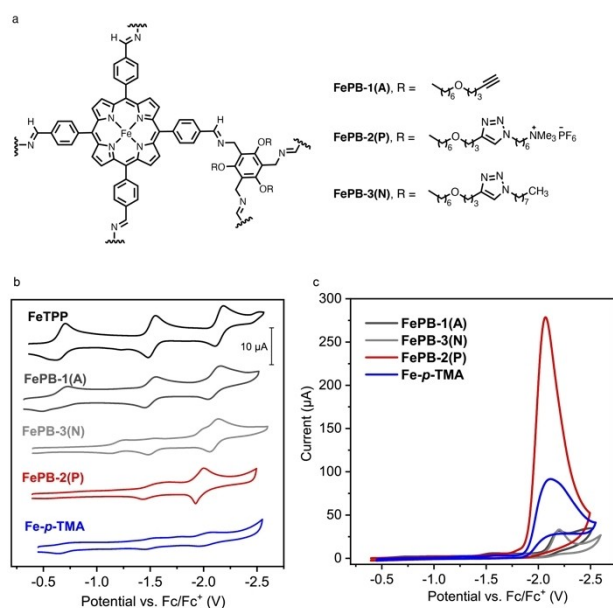


Figure 1. a) Structures of the alkyne porous cage synthon **FePB-1(A)**, the neutral porous cage **FePB-3(N)**, and the charged porous cage **FePB-2(P)**. Electrochemical characterization in 0.1 M Bu_4NPF_6/DMF of 0.1 mM **FePB-1(A)** (dark grey), **-2(P)** (red), **-3(N)** (light grey), 0.6 mM **FeTPP** (black) and **Fe-p-TMA** (blue) under b) Argon atmosphere and c) CO_2 atmosphere with 1 M TFE as a proton source.

the periphery of a porous porphyrin cage scaffold is similar to what was reported for the inductive effect of adding four trimethylanilinium groups to a planar **FeTPP** compound in **Fe-p-TMA** ($E_{1/2} = -2.00$ V).^[24] This charge effect is also responsible for a significant shift of E_{cat0} toward positive potentials (see below). Upon the addition of CO_2 and 1.0 M 2,2,2-trifluoroethanol (TFE) as a proton source, a large current increase is observed for **FePB-2(P)**, indicating fast CO_2 reduction catalysis (Figure 1c). The peak catalytic current under CO_2 for **FePB-2(P)** is substantially higher than that for each of the non-porous or non-cationic catalysts studied. In order to quantify product selectivity and evaluate the electrochemical stability of **FePB-2(P)**, controlled potential electrolysis (CPE) experiments at various applied potentials were conducted in CO_2 -saturated acetonitrile solutions with 1.0 M TFE as the proton source and 1.67 μM of catalyst (10 μM Fe). Carbon monoxide (CO) was detected as the major product with a Faradaic efficiency (FE) of ca. 80 %. The low catalyst loading demonstrated the high activity of **FePB-2(P)** for electrochemical CO_2RR , which gave a high total TON of 2656 within one hour (Figure S53).

Photochemical CO_2 Reduction Activity of Porous Iron Porphyrin Cage Analogs With or Without Additional Charged Functionalities

Encouraged that **FePB-2(P)** is capable of electrochemical CO_2RR activity, we turned our attention to light-driven CO_2 reduction catalysis. In a typical experiment, 2 μM **FePB-**

2(P) catalyst was added to a CO₂-saturated CH₃CN solution containing 200 μM Tris[2-phenylpyridinato-C²,N]iridium (III) (Ir(ppy)₃) as a photosensitizer, 100 mM 1,3-dimethyl-2-phenyl-2,3-dihydro-1*H*-benzo[*d*]imidazole (BIH) as a sacrificial electron donor, and 1 M TFE as a proton source; the

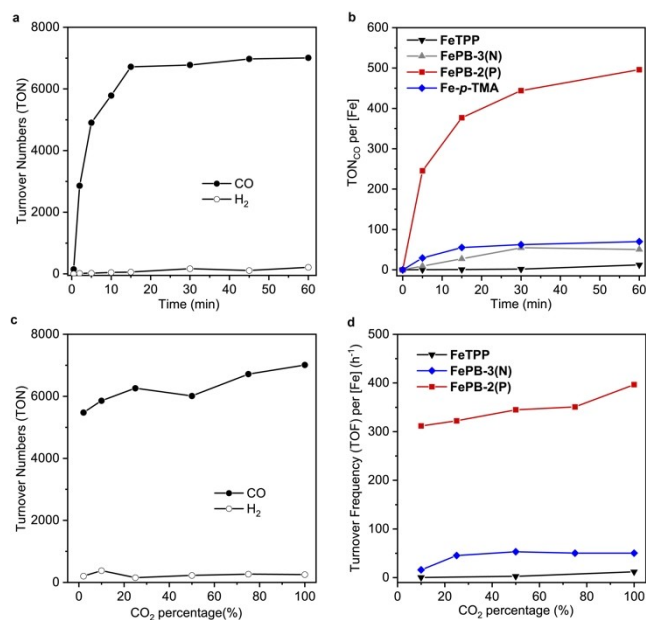


Figure 2. a) Photocatalytic CO₂RR activity of **FePB-2(P)** in CO₂-saturated CH₃CN. b) Photocatalytic CO₂RR activity of **FePB-2(P)** in CO₂-saturated DMF, comparing TON per [Fe] to **FePB-3(N)**, **FeTPP**, and **Fe-p-TMA**. c) Photochemical CO₂RR reduction activity of **FePB-2(P)** in CH₃CN under varying CO₂ concentrations, showing activity down to 2% CO₂. d) Photochemical CO₂RR activity of **FePB-2(P)** in DMF under varying CO₂ concentrations, showing a comparison per [Fe] between **FePB-2(P)**, **FePB-3(N)**, and **FeTPP**. **FePB-2(P)** is active down to 5% CO₂ concentrations. Conditions: 2 μM **FePB** or 12 μM mononuclear catalyst, 200 μM Ir(ppy)₃, 100 mM BIH, and 1 M TFE.

Table 1: Photocatalytic activity of [Fe] under various conditions.

Entry	Catalyst	TON Per [Fe]		TOF _[Fe] ^{max} [min ⁻¹] ^[h]	Selectivity CO [%]
		CO	H ₂		
1 ^[a]	FePB-2(P)	1168	42	164	97
2	FePB-2(P)	496	7	49	98
3	FePB-3(N)	50	7	1.9	88
4	FeTPP	12	5	0.08	70
5	Fe-p-TMA	70	10	5.8	88
6 ^[b]	None	0	1	–	–
7 ^[c]	FePB-2(P)	0	182	–	–
8 ^[d]	FePB-2(P)	40	143	–	22
9 ^[e]	FePB-2(P)	0	0	–	–
10 ^[f]	FePB-2(P)	0	0	–	–
11 ^[g]	FePB-2(P)	33	0	–	100

Reaction Conditions: 200 μM Ir(ppy)₃, 100 mM BIH, 1 M TFE after 1 hour irradiation in a CO₂ saturated DMF solution unless otherwise noted; control experiment data collected after 30-minute irradiation in entries 6–11. [a] In CH₃CN. [b] Without **FePB-2(P)** catalyst. [c] Under Ar atmosphere. [d] Without TFE. [e] Without BIH. [f] Without light irradiation. [g] Without Ir(ppy)₃. [h] Within the first 5 minutes of the reaction, per [Fe].

reactions were irradiated using a 440 nm blue LED light source. Figure 2a shows the catalytic activity of **FePB-2(P)** over a 1-hour period. Within the first two minutes of the reaction, a TOF_{max} of 1429 min⁻¹ is reached; rates of this magnitude are unprecedented for homogeneous Fe porphyrin photocatalysts.^[25] After a 1-hour photolysis period, we obtained a TON of 7006 per box (1168 per Fe center) with 97% selectivity for CO. Control experiments performed show that the catalyst, CO₂, proton source, sacrificial electron donor, light, and photosensitizer, are all required for activity (Table 1, Entries 6–11). Stern–Volmer analysis of the Ir(ppy)₃ excited state was used in order to determine a bimolecular quenching rate constant (*k_q*) of 1.79 × 10¹¹ M⁻¹ s⁻¹ in CH₃CN between Ir(ppy)₃ and **FePB-2(P)** with no emission quenching observed using BIH (Figure S54), indicative of an oxidative quenching mechanism. All other catalysts gave similar quenching rate constants when measured in DMF (Figure S55). The quantum yield for CO production was determined to be Φ = 5.75% by ferrioxalate actinometry (see Supporting Information for details).

To disentangle contributions of second-sphere porosity and charge in **FePB-2(P)**, we evaluated the photocatalytic activity of **FeTPP**, **Fe-p-TMA**, and **FePB-3(N)**. To achieve a fair comparison and to ensure homogeneous conditions for all the catalysts, we used DMF as the solvent, increased catalyst concentration to 12 μM for mononuclear Fe porphyrins and corrected turnover number per iron center (TON_[Fe]) to reflect activity per Fe center, assuming there are 6 active iron centers per molecule of **FePB** catalyst. Figure 2b shows the photocatalytic activity of **FeTPP**, **Fe-p-TMA**, **FePB-3(N)**, and **FePB-2(P)** after 1-hour irradiation in CO₂-saturated DMF using the same standard conditions. We observe that the neutral porous cage catalyst **FePB-3(N)** outperforms **FeTPP**, which we attribute to enhanced substrate confinement effects in porous catalyst structures,^[6] giving **FePB-3(N)** a 4-fold higher TON_[Fe] and superior CO selectivity of 88% (Figure 2b). The previously reported^[25b,c] incorporation of four trimethylanilinium groups into an **FeTPP** framework is reproduced under these conditions, showing higher selectivity and 6-fold higher TON value for CO₂RR with **Fe-p-TMA** (FE_{CO} = 88%, TON_[Fe] = 70) compared to **FeTPP** (FE_{CO} = 70%, TON_[Fe] = 12).

Interestingly, the data reveal that **FePB-2(P)**, which is endowed with both electrostatic and porosity functionalities, achieves a TON_[Fe] of 496 after 1 h irradiation, representing a 41-fold increase in CO₂RR activity over the parent **FeTPP** catalyst. This enhancement is larger than what is observed for porosity-only **FePB-(N)** (4-fold) and charge-only **Fe-p-TMA** (6-fold) congeners, suggesting that integrating dual porosity and electrostatic interactions onto a single platform can work together to enhance photocatalytic CO₂RR activity in synergistic manner (Figure 2b, Table 1, Entries 1–5). Moreover, the high activity of **FePB-2(P)** enables photochemical CO₂RR to proceed under low CO₂ concentrations.^[26] Indeed, Figure 2c shows **FePB-2(P)** achieves a CO TON of 5476 with as little as 2% CO₂ in CH₃CN, maintaining 78% of its activity compared to saturated CO₂ conditions. We speculate that the ability of

FePB-2(P) to maintain high relative CO₂RR rates even at low CO₂ concentrations may be attributed to the propensity of the porous organic cage to promote both carbon capture and conversion.^[6,18] We then compared the CO₂RR activity per [Fe] of **FePB-2(P)** with **FeTPP** and **FePB-3(N)** in DMF (Figure 2d). Going from the planar **FeTPP** catalyst to three-dimensional porous **FePB-3(N)** cage results in an 18-fold increase in TOF under 50 % CO₂ concentrations, suggesting that porosity can play a critical role in facilitating substrate capture and conversion. Moreover, combining second-sphere porosity and charge in **FePB-2(P)** further augments the system, resulting in a 15-fold increase in TOF compared to **FePB-3(N)** at 2 % CO₂ levels.

Conclusion

To close, we have presented a supramolecular approach to enhancing photochemical CO₂RR in confined spaces through synergistic second-sphere porosity and charge effects. We enabled this strategy through the modular post-synthetic modification of porous porphyrin organic cages, where the incorporation of 24 alkyne groups provides a versatile platform for further functionalization via click chemistry. Using this synthon, addition of neutral carbon chain and cationic trimethylammonium groups onto the periphery of the cage scaffold affords **FePB-3(N)** and **FePB-2(P)** supramolecules featuring porosity-only and dual porosity/charge effects, respectively. Comparison of these catalysts with a planar **Fe-p-TMA** catalyst with charge-only effects establishes that dual second-sphere porosity and charge interactions can augment CO₂RR activity in a cooperative manner, exceeding the additive performance of introducing porosity or charge alone. **FePB-2(P)** achieves efficient CO₂RR with 97 % selectivity for CO, TON of 7006, and initial TOF rate of 1429 min⁻¹. Moreover, these combined effects enable retention of efficient photochemical CO₂RR activity at concentrations of CO₂ down to 2 %. This work highlights the use of multiple synergistic second-sphere interactions as an effective design strategy to enhance CO₂ capture and conversion activity, a concept that can be applied to a broader array of small-molecule activation reactions.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the Supporting Information of this article.

Keywords: Carbon Dioxide Reduction • Electrocatalysis • Photocatalysis • Porous Cage • Second-Sphere

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