

Supporting Information for

**Chemistry in confined space: A strategy for
selective oxidation of hydrocarbons with
high catalytic efficiencies and conversion
yields under ambient conditions**

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Materials and Methods:

All solvents and chemicals used were of commercially available analytical grade, if not mentioned otherwise. Solvents for air-sensitive reactions were distilled under argon.

Synthesis of ligands and preparation of tricopper complexes

Preparation of 3,3'-[1,4-diazepane-1,4-diyl]bis(1-chloropropan-2-ol) (1). A solution of epichlorohydrin (1.85 g, 20 mmol) dissolved in methanol (15.0 ml) was added drop-wise to a solution of homopiperazine (1.02 g, 10 mmol) dissolved in methanol (30.0 ml) and stirred at 5 °C. After stirring for 72 h at 5 °C, the resulting mixture was purified by column chromatography on silica gel using a mixed solvent (8% CH₃OH in CH₂Cl₂) as the eluent. Compound **1** was obtained in 88% yield (2.50 g).

Synthesis of the ligand (3,3'-(1,4-diazepane-1,4-diyl)bis[1-(4-ethylpiperazine-1-yl)propan-2-ol]) (7-N-Etppz). K₂CO₃ (4.15 g, 30 mmol) was added to a CH₃CN (15.0 ml) solution containing compound **1** (4.28 g, 15 mmol), and 1-ethylpiperazine (3.46 g, 30 mmol). The mixture was then heated to 70-80 °C for 48 h under a N₂ atmosphere. After cooling to room temperature, the solution was filtered, and upon evaporation of the filtrate to dryness, the ligand **7-N-Etppz** was obtained. ¹H NMR (CDCl₃, 300 MHz): 1.8 (t, 2H, CH₃); 2.05-2.93 (m, CH₂); 3.6 (s, 2H, CH), 4.4 (s 2H, CH). ¹³C NMR (300 MHz, CDCl₃): the major peaks appeared at 11.74, 11.82, 27.10, 52.0, 52.5, 53.2, 54.4, 55.3, 62.2, 62.4, and 64.7. The ESI-MS (positive ion): m/z 441.

Synthesis of the ligand (3,3'-(1,4-diazepane-1,4-diyl)bis[1-(4-ethylhomopiperazine-1-yl)propan-2-ol]) (7-N-Ethppz). Following the same procedure as above, **7-N-Ethppz** was prepared by mixing compound **1** (4.29 g, 15 mmol) with

1-ethylhomopiperazine (3.80 g, 30 mmol). Yield: 80% (5.6 g). ^1H NMR (CDCl_3 , 300 MHz): 1.11 (s, 4H, CH_3), 1.14 (m, 4H CH_2), 1.15 (d, 6H, CH_2), (m, 16H, CH_2), 2.41-2.88 (m, 8H, CH_2), 3.13 (d, 2H, CH). ^{13}C NMR (300 MHz, CDCl_3): 12.2, 25.4, 46.2, 52.3, 52.5, 52.7, 54.2, 62.0 and 65.5. The ESI-MS (positive ion): m/z 469.

Preparation of the tricopper complex Cu_3Etppz . A anhydrous CH_3CN solution (25 ml) containing **7-N-Etppz** (2.205 g, 5.0 mmol) and three equivalents of $\text{Cu}^{\text{II}}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (5.49 g, 15.1 mmol) were mixed and stirred for 1 h to give a deep green solution, which was filtered, washed with CH_2Cl_2 , and dried in vacuum to give a green powder. The calculated yield was 4.00 g (95%). The elemental analysis of $\text{C}_{23}\text{H}_{46}\text{O}_{11}\text{N}_6\text{Cl}_2\text{Cu}_3$ gave C, 32.77; H, 5.50; N, 9.94%, which were the same as the calculated values within experimental uncertainty: C, 32.72; H, 5.49; N, 9.96%. The ESI-MS (positive ion): m/z 844.02.

Preparation of the tricopper complex Cu_3Ethppz . A anhydrous CH_3CN solution (25 ml) containing **7-N-Ethppz** (2.345 g, 5.0 mmol) and three equivalents of $\text{Cu}^{\text{II}}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (5.49 g, 15.1 mmol) were mixed and stirred for 1 h to give a blue solution, which was filtered, washed with CH_2Cl_2 , and dried in vacuum to give a blue powder. The calculated yield was 4.23 g (97%). The elemental analysis of $\text{C}_{25}\text{H}_{50}\text{O}_{11}\text{N}_6\text{Cl}_2\text{Cu}_3$ gave C, 34.48; H, 5.82; N, 9.60%, which were the same as the calculated values within experimental uncertainty: C, 34.42; H, 5.78; N, 9.63%. The ESI-MS (positive ion): m/z 872.09.

Supporting Figures

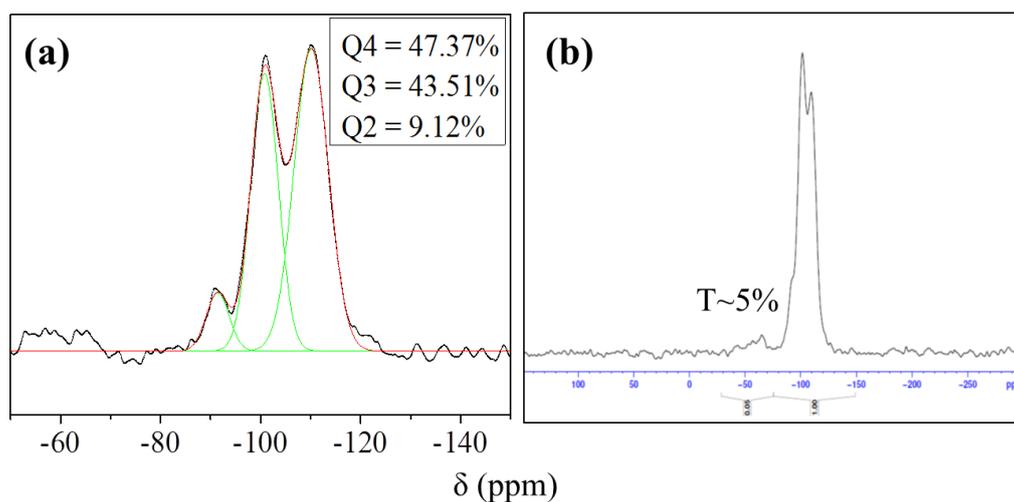


Figure S1. (a) ^{29}Si solid-state NMR spectra of the MSN-TP sample. Each spectrum displays a set of signals Q2, Q3, and Q4, attributed to the $\text{Si}(\text{OH})_2(\text{OSi})_2$, $\text{Si}(\text{OH})(\text{OSi})_3$, and $\text{Si}(\text{OSi})_4$ substructures, respectively. The peak percentages are obtained by de-convoluting each spectrum into their components and fitting the full-width at half-maximum of each component spectrum. (b) ^{29}Si NMR spectrum of the MSN-TP sample, comparing the T signals ($[\text{C}-\text{Si}(\text{OH})(\text{OSi})_2]$ or $[\text{C}-\text{Si}(\text{OSi})_3]$) to the Q signals. The ratio of the areas of the T and Q signals indicates that 5% of the silica surface is conjugated to the functionalizing TP group.

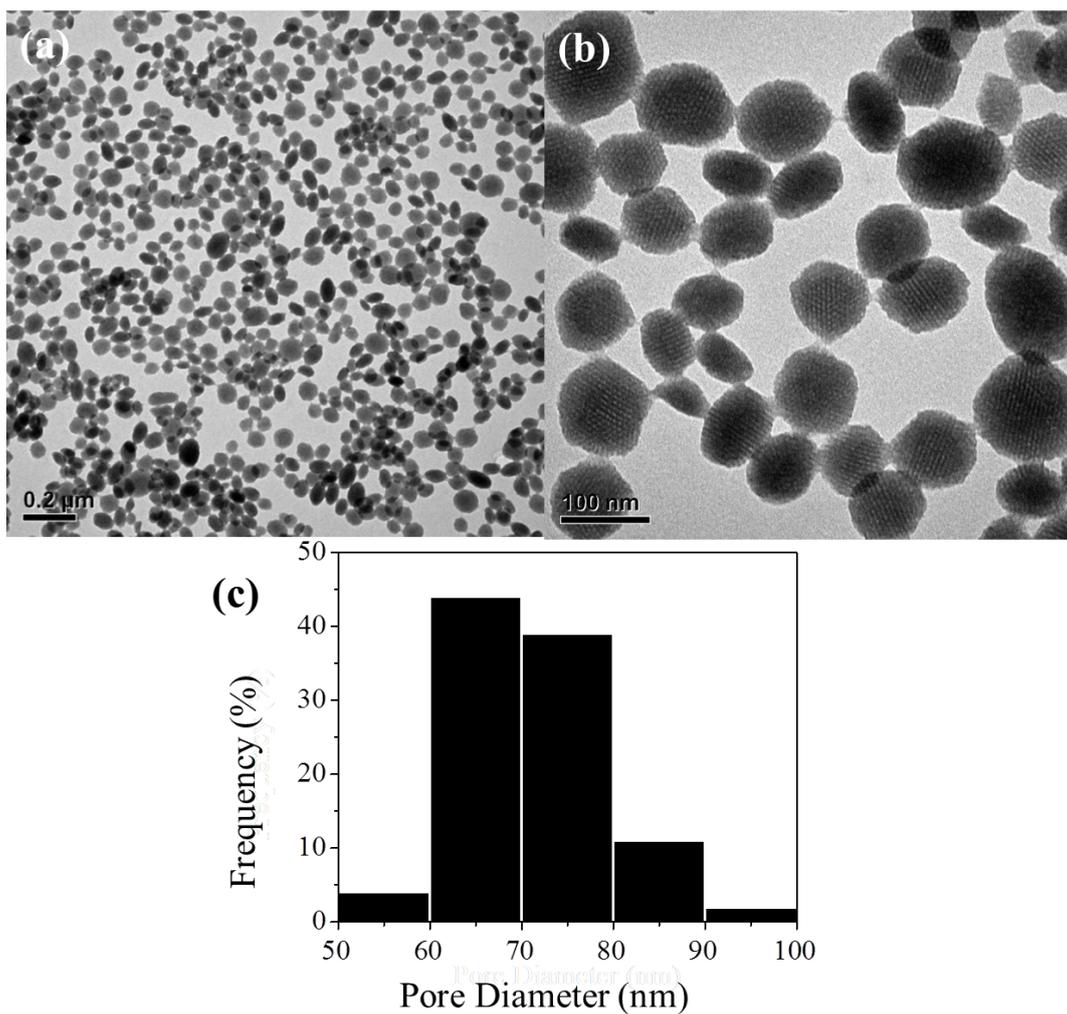


Figure S2. Transmission electron microscopy (TEM) images of the functionalized MSN-TP with different scale bars: **(a)** left: 0.2 μm; **(b)** right: 100 nm. **(c)** The statistical analysis of the TEM image **(a)** gives a particle size distribution of 71.4 ± 7.8 nm for the MSN-TP sample (based on a patch size of 100 particles).

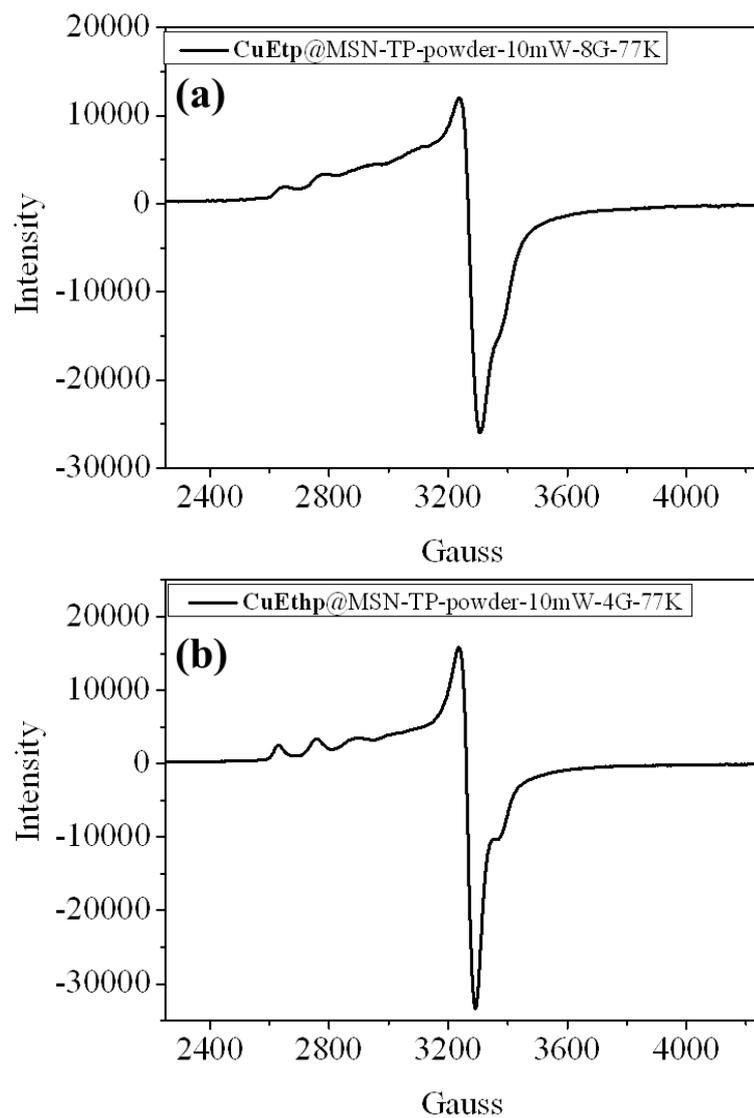


Figure S3. X-band EPR spectra of MSN samples at 77 K: (a) **CuEtp@MSN-TP**; and (b) **CuEthp@MSN-TP**. Conditions: Microwave frequency: 9.45 GHz; microwave power: 10 mW; and modulation amplitude: 4 or 8 G.

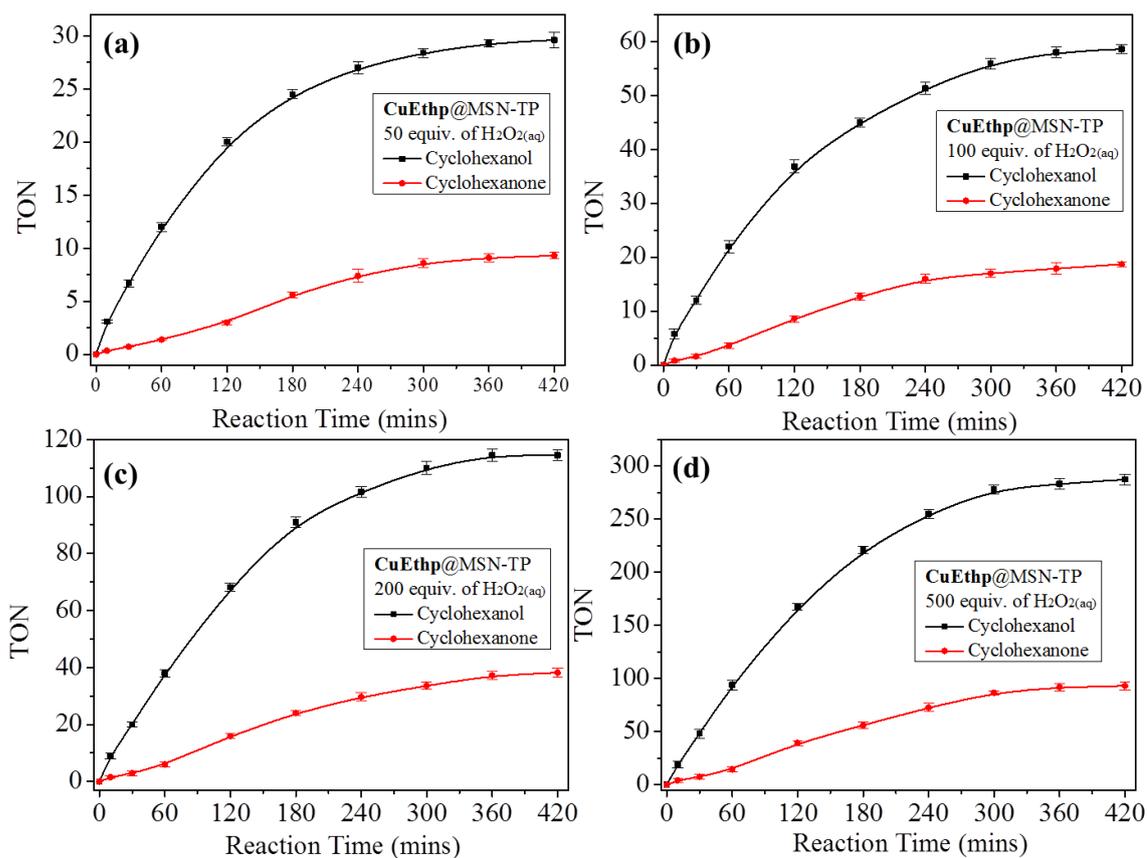


Figure S4. Time course of the TONs in the cyclohexane oxidation catalyzed by CuEthp@MSN-TP catalyst with (a) 50 equiv., (b) 100 equiv., (c) 200 equiv., and (d) 500 equiv. of $H_2O_2(aq)$, used to drive the catalytic turnover.

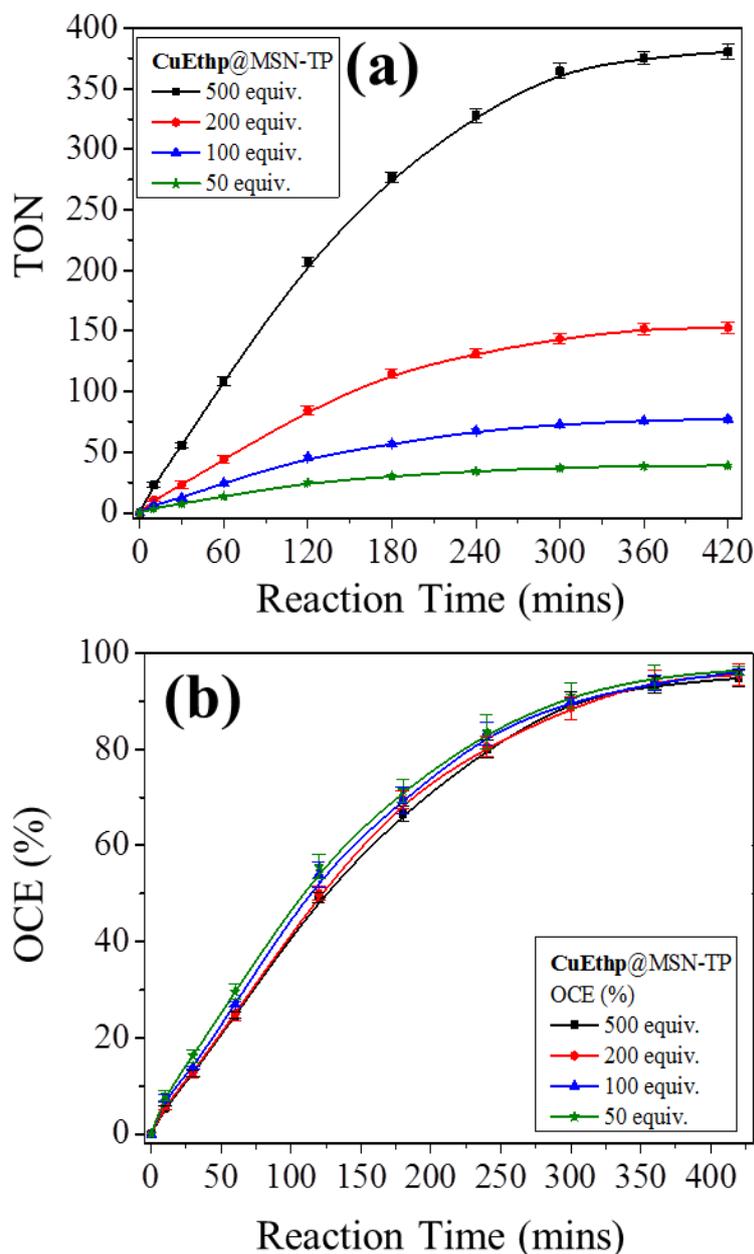


Figure S5. Time course of (a) the total product TONs ($\text{TON}_{\text{-ol}} + \text{TON}_{\text{-one}}$) and (b) the overall catalytic efficiency (OCE) for the cyclohexane oxidation reaction catalyzed by the best performing catalyst, **CuEthp@MSN-TP** catalyst, at room temperature using different amounts of H₂O₂ (equiv.) to drive the catalytic turnover. The OCE is given by the ratio of the numbers of productive catalytic turnover of the catalyst to the amounts of H₂O₂ added to initiate the catalysis: $(\text{TON}_{\text{-ol}} + 2 \text{TON}_{\text{-one}}) / [\text{H}_2\text{O}_2]_0$. $\text{TON}_{\text{-ol}}$ and $\text{TON}_{\text{-one}}$ denote the TONs of cyclohexanol and cyclohexanone, respectively.

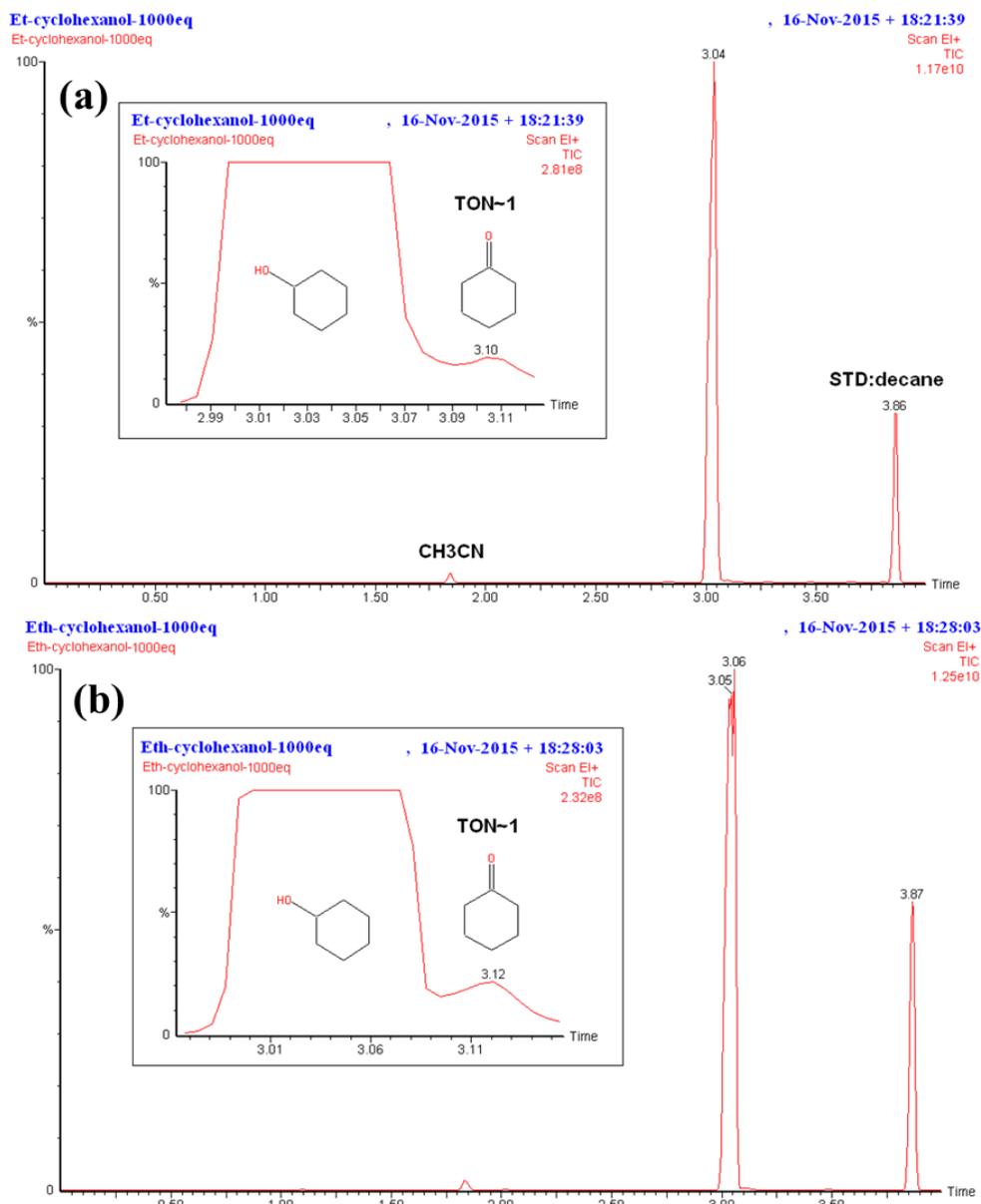


Figure S6. The GC-MS spectra of the products observed in the cyclohexanol oxidation reaction catalyzed by (a) **CuEtp@MSN-TP** and (b) **CuEthp@MSN-TP** samples for 6 h at room temperature without adding any H_2O_2 to drive the catalytic turnover. These control experiments were performed according to the same procedures used in the cyclohexane oxidation reaction, but without adding any H_2O_2 . Only a single turnover of cyclohexanone was observed in the two experiments, indicating that the oxidation of cyclohexanol to cyclohexanone was mediated by the O_2 -activated tricopper complexes. There was no H_2O_2 in the medium to drive the catalytic turnover of the catalyst so that no further catalytic activity was detected for the MSNs.

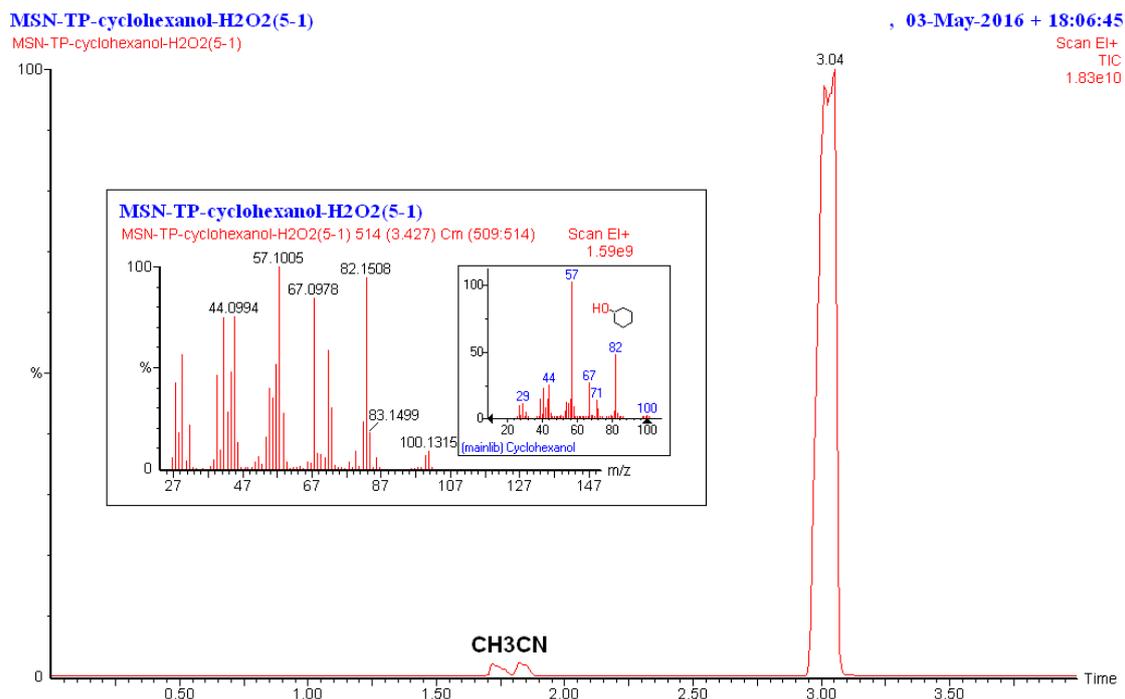


Figure S7. The GC-MS spectra of cyclohexanol oxidation reaction catalyzed by bare MSN-TP sample (20 mg) for 6 h at room temperature in the presence of H₂O₂. The mole ratio of cyclohexane:H₂O₂ used in this control experiment was 5:1, which was the same amount used in the cyclohexane oxidation reaction mediated by the tricopper complex. No catalytic activity was detected with the bare MSN-TP sample, indicating that the conversion of cyclohexanol to cyclohexanone was intrinsic to the active tricopper complex immobilized in MSN-TP by H₂O₂ to drive the catalytic turnover.

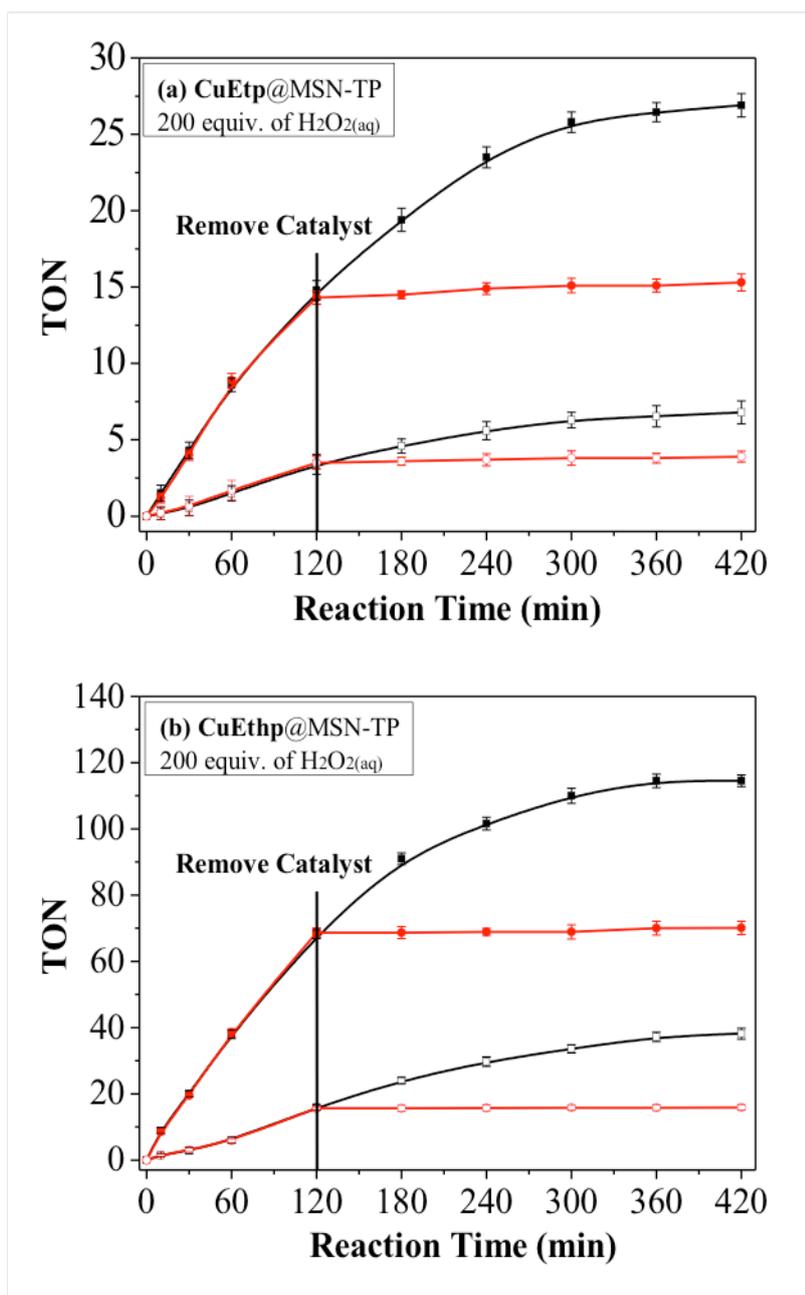


Figure S8. Time course of the TONs for the cyclohexane oxidation reaction catalyzed by (a) **CuEtp@MSN-TP**, and (b) **CuEthp@MSN-TP** samples at room temperature with 200 eq. of H₂O₂ (black line). In each case, a parallel experiment was also conducted under the same conditions, except that the catalytic turnover was interrupted 2 hours into the experiment to quickly separate and remove the MSNs from the liquid phase by centrifugation. Measurement of the catalytic activity was then continued on the supernatant until the end of the 7-h experiment (red line). No catalytic activity was observed for the supernatant.

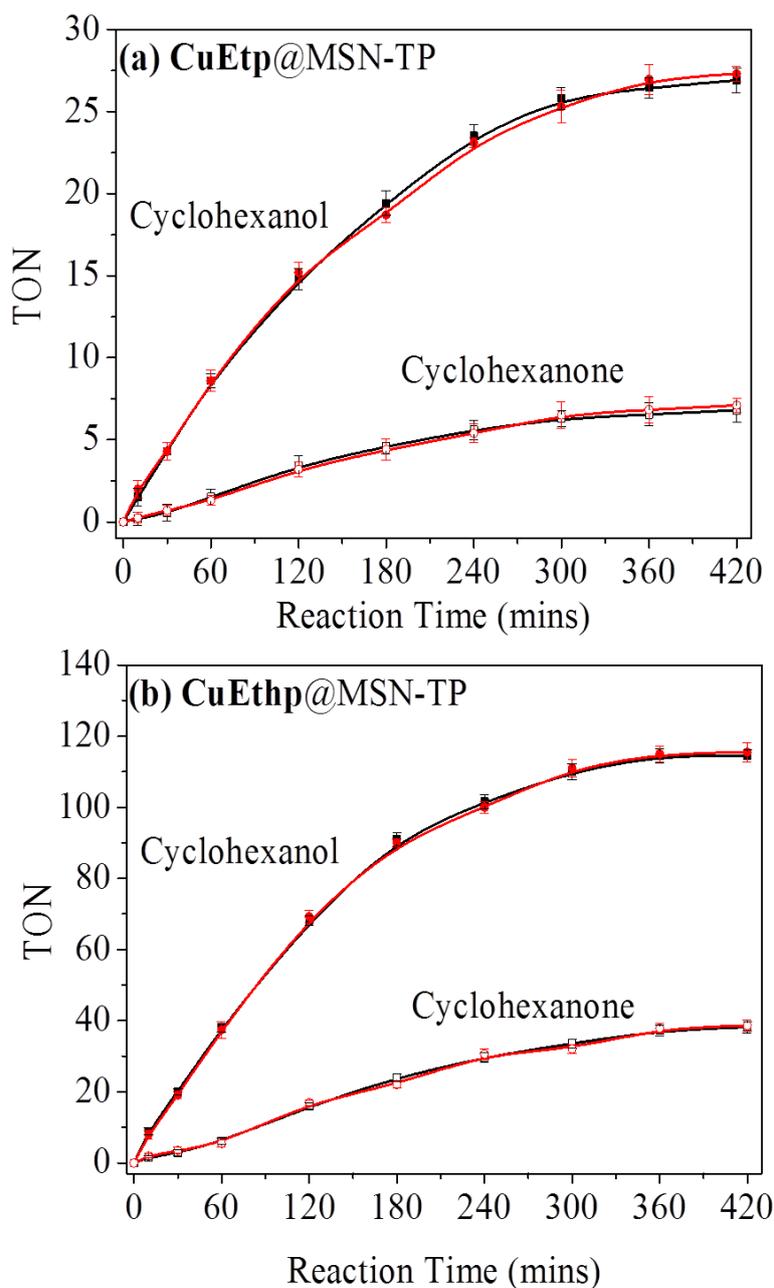


Figure S9. Comparison of the time courses of the cyclohexane oxidation reaction mediated by (a) **CuEtp@MSN-TP**, and (b) **CuEthp@MSN-TP** at room temperature in the absence (black line) and presence (red line) of the radical trapping agent 2,6-di-tert-butyl-p-cresol (1 equiv., based on the amounts of the immobilized tricopper complexes in the MSN-TP samples). The TONs of the products are expressed in terms of the moles of product formed per mole of the tricopper complex in each case.

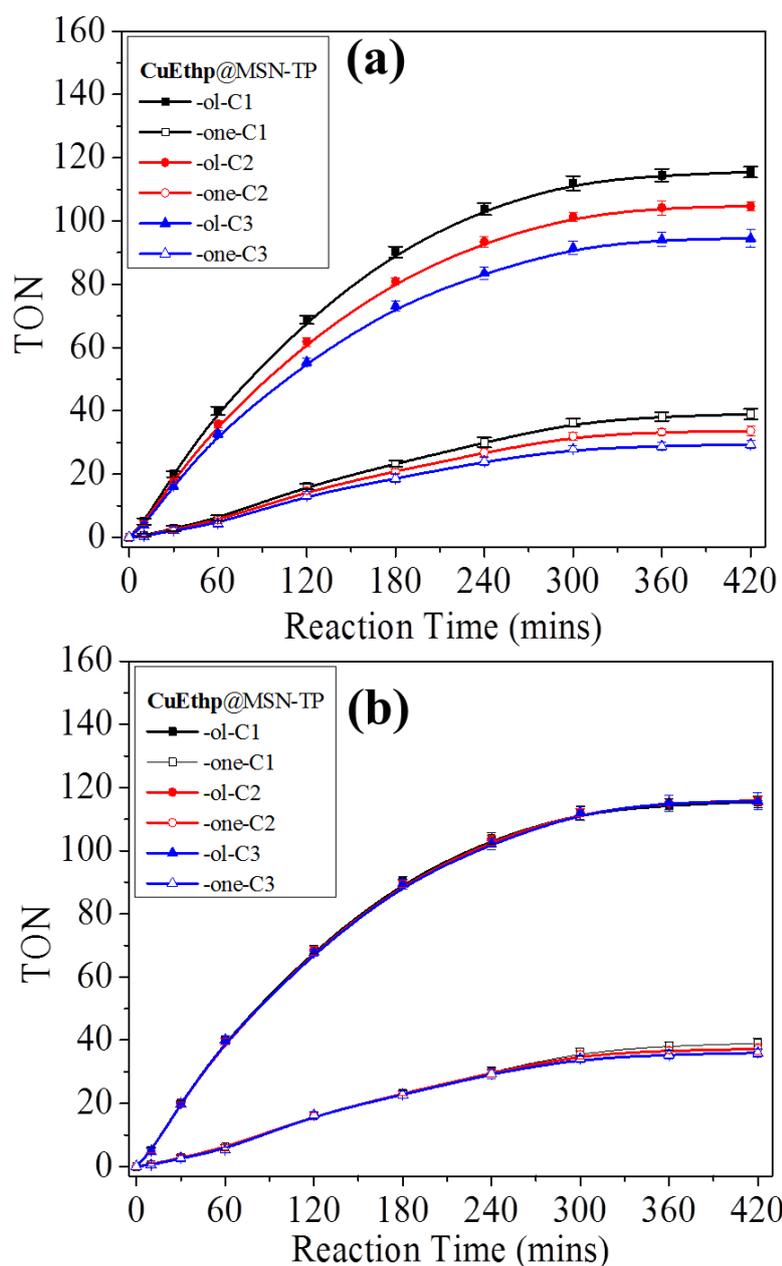


Figure S10. (a) TONs of cyclohexanol (-ol) and cyclohexanone (-one) obtained from the cyclohexane oxidation reaction catalyzed by the **CuEthp@MSN-TP** catalyst at room temperature with 200 equiv. of H_2O_2 for three cycles at varying times. (b) The TONs of -ol and -one of the three cycles were re-calculated based on the amounts of the tricopper complex determined by ICP-MS and C/N elemental analysis before the reaction.

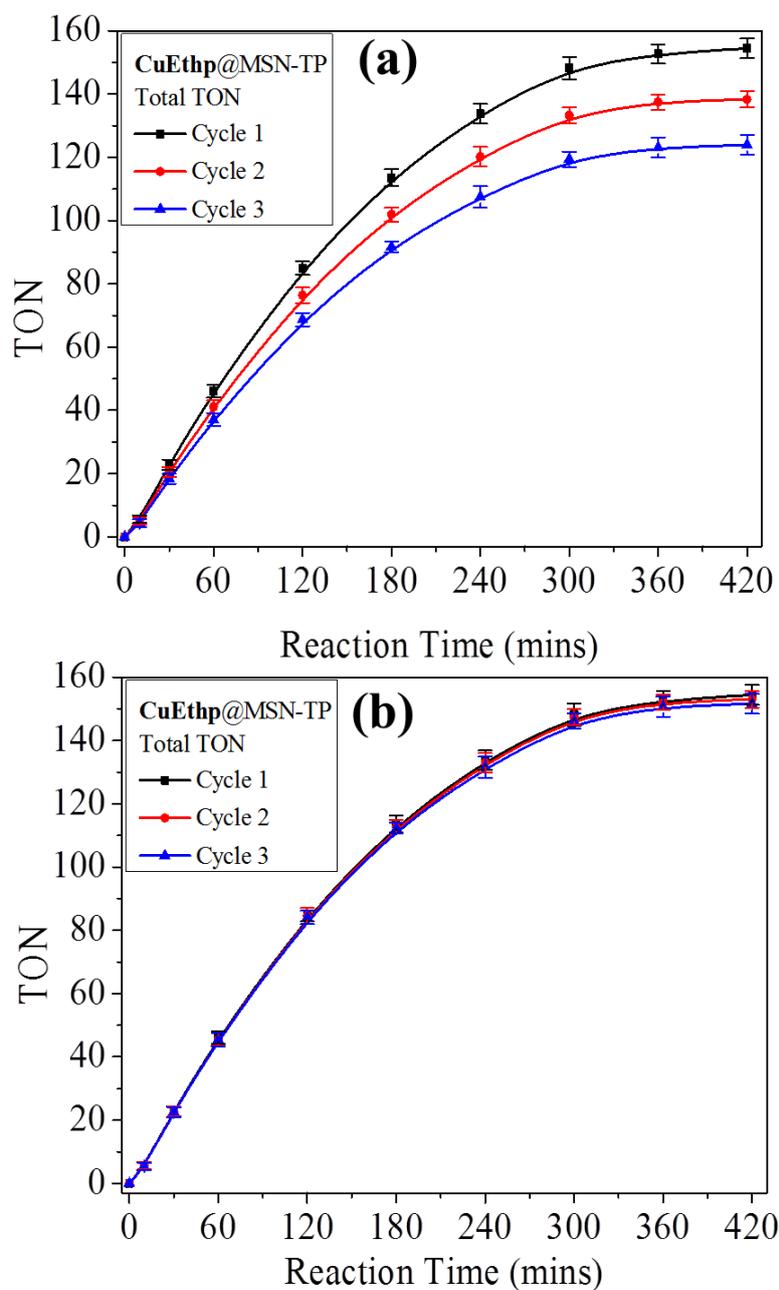


Figure S11. (a) The total product TONs (TON_{ol} + TON_{one}) obtained from the cyclohexane oxidation reaction catalyzed by the CuEthp@MSN-TP catalyst at room temperature with 200 equiv. of H₂O₂ for three cycles at varying times. (b) The total product TONs of the three cycles were re-calculated based on the amounts of the tricopper complex determined by ICP-MS and C/N elemental analysis before the reaction. TON_{ol} and TON_{one} denote the TONs of cyclohexanol and cyclohexanone, respectively.

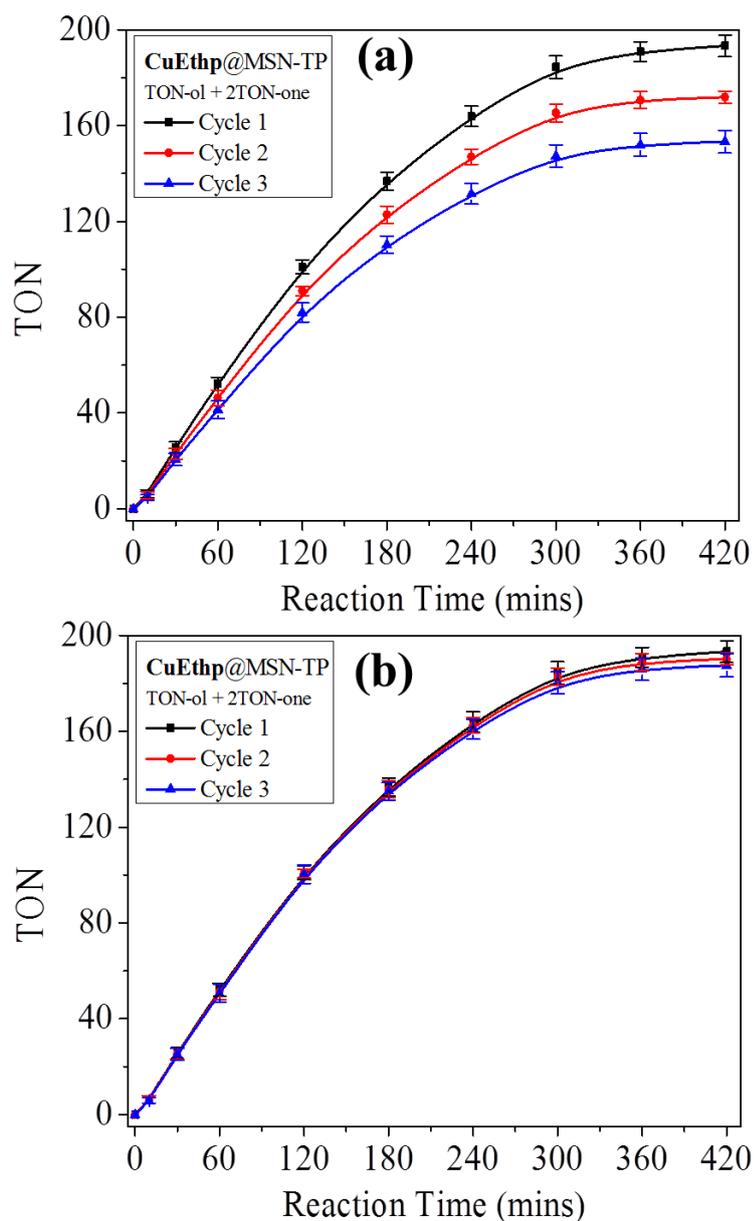


Figure S12. (a) TONs of the productive catalytic turnovers ($\text{TON}_{\text{ol}} + 2 \text{TON}_{\text{one}}$) obtained from the cyclohexane oxidation reaction catalyzed by the **CuEthp@MSN-TP** catalyst at room temperature with 200 equiv. of H_2O_2 for three cycles at varying times. (b) The productive catalytic turnovers of the three cycles were re-calculated based on the amounts of the tricopper complex determined by ICP-MS and C/N elemental analysis before the reaction.

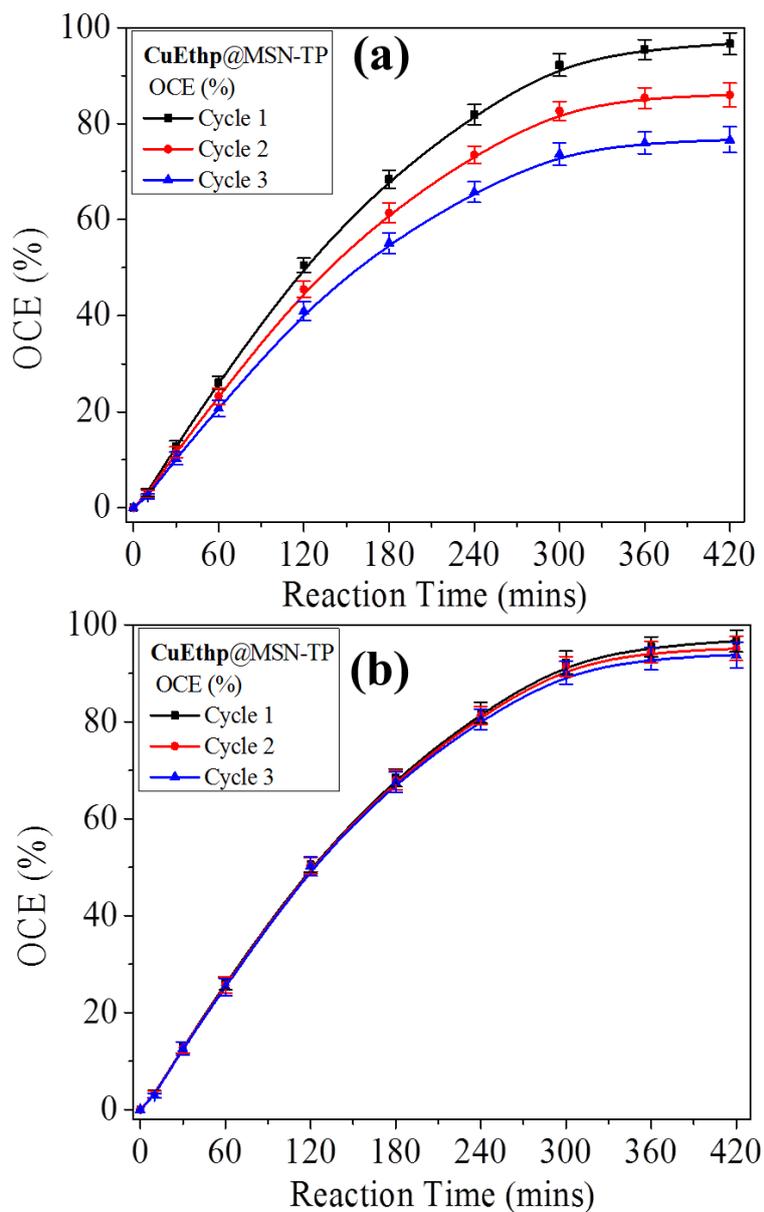


Figure S13. (a) The overall catalytic efficiency (OCE) of the cyclohexane oxidation reaction catalyzed by the **CuEthp@MSN-TP** catalyst at room temperature with 200 equiv. of H_2O_2 for three cycles at varying times. (b) The OCE of the three cycles were re-calculated based on the amounts of the tricopper complex determined by ICP-MS and C/N elemental analysis before the reaction.

Supporting Tables

Table S1. Summary of the TONs, selectivity, and OCE in the cyclohexane oxidation catalyzed by tricopper complexes with different amounts of H₂O₂ to drive the catalytic turnover with and without purging of the MSNs by O₂.

Entry	Catalyst	Substrate (eq.)	O ₂ (ml) ^a	H ₂ O ₂ (eq.)	TON of Products ^b		Selectivity (-ol, %) ^c	OCE (%) ^d
					-ol	-one		
1	CuEtp@MSN-TP	1000	-	200	27.0	6.5	80.6	20.0
2	CuEtp@MSN-TP	1000	-	500	63.5	15.8	80.1	19.0
3	CuEtp@MSN-TP	1000	10	200	27.3	6.6	80.5	20.3
4	CuEtp@MSN-TP	1000	10	500	63.8	15.7	80.2	19.0
5	CuEthp@MSN-TP	1000	-	200	114.5	38.2	75.0	95.5
6	CuEthp@MSN-TP	1000	-	500	287.3	93.1	75.5	94.7
7	CuEthp@MSN-TP	1000	10	200	115.1	38.7	74.8	96.2
8	CuEthp@MSN-TP	1000	10	500	289.0	93.5	75.6	95.2

^a The oxygen was injected in the catalytic system under NTP condition. ^b **-ol**: C₆H₁₂O; **-one**: C₆H₁₀O. ^c Selectivity of C₆H₁₂O. ^d OCE = (TON_{-ol} + 2 TON_{-one})/[H₂O₂]₀

Table S2. Summary of the maximum TONs in the cyclohexane oxidation catalyzed by **CuEtp@MSN-TP** catalyst at room temperature with 200 equiv. of H₂O₂ for three cycles.

CuEtp@MSN-TP						
Cycle	TON -ol ^a	TON -one ^b	TON ^c -ol + -one	Selectivity (-ol , %)	Activity loss (%) ^d	OCE (%) ^e
1	27.0	6.5	33.5	80.6	-	20.0
2	23.6	5.0	28.6	82.5	14.6	16.8
3	20.7	3.6	24.3	85.2	27.5	14.0

CuEthp@MSN-TP						
Cycle	TON -ol ^a	TON -one ^b	TON ^c -ol + -one	Selectivity (-ol , %)	Activity loss (%) ^d	OCE (%) ^e
1	114.5	38.2	152.7	75.0	-	95.5
2	104.7	33.6	138.3	75.7	9.4	86.0
3	94.5	29.4	123.9	76.3	18.9	76.7

^a The TON of C₆H₁₂O, (**-ol** = C₆H₁₂O). ^b The TON of C₆H₁₀O, (**-one** = C₆H₁₀O). ^c The total TON of products. ^d The loss of activity as determined by the decrease in the total TONs. ^e OCE = (TON_{-ol} + 2 TON_{-one})/[H₂O₂]₀