

Supplementary information for
Hybrid homogeneous/heterogeneous relay catalysis for efficient synthesis
of 5-aminomethyl-2-furancarboxylic acid from HMF

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1. Experimental Procedures

1.1 Chemicals

5-hydroxymethylfurfural (HMF, 99%), 2,5-furandicarboxylic acid (FDCA, 98%), VOSO₄ (97%), Nb₂O₅ (99.99%), NH₃ in methanol (7M), tetrabutylammonium hydrogen sulfate (TBAHS, 98%), benzyltributylammonium chloride (BTBAC, 98%), and tetramethylammonium hydrogen sulfate (TMAHS, 99%) were supplied by Aladdin Industrial Inc. Tetrabutylammonium chloride (TBAC, 99%) and 5-hydroxymethyl-2-furancarboxylic acid (HMFCFA, 97%) were collected from Shanghai Macklin Biochemical Technology Co., Ltd. 2,5-diformylfuran (DFF, 98%) and 5-formylfuran-2-carboxylic acid (FFCA, 98%) were received from Titan Technology Co., Ltd. Cu(NO₃)₂·3H₂O (99%), acetonitrile (99.8%), methanol (99.7%), nitric acid (65.0%), 1,4-dioxane (99.5%), 1,2-dichloroethane (99.5%), formic acid (99.5%), acetic acid (99%) and cyclohexane (99.7%) were purchased from Sinopharm Chemical Reagent Co., Ltd. Ru(NO)(NO₃)₃ were supplied by Sigma Aldrich (Shanghai) Trading Co., Ltd. All chemicals were of analytical grade and used as received without further purification.

1.2 Characterization

In situ infrared spectroscopy measurements were conducted on a Mettler Toledo's ReactIR 701L instrument equipped with a diamond attenuated total reflectance probe (ATR). The model of the probe is DST series 6.3 mm AgX FiberConduct. The conditions of the solution during scanning are consistent with the reaction conditions.

Inductively coupled plasma-optical emission spectrometry (ICP-OES) was employed to determine the vanadium content in the reaction system using an Agilent 5110 analyzer equipped with a CCD array detector. Sample digestion was carried out in a microwave oven. Subsequently, the vessel was cooled to room temperature and diluted to 50 mL with double-distilled water, prior to the ICP-OES analysis. During the test, the pump rate was 100 r·min⁻¹, the nebulizer flow was 0.70 L·min⁻¹, the auxiliary gas was 1.0 L·min⁻¹, and the sample flush time was 20 s.

Cyclic voltammogram (CV) was recorded on an CHI1140c electrochemical workstation. Using glassy carbon (GC) electrode as the working electrode, platinum wire as the counter electrode, and Ag/AgCl as the reference electrode, CV curves were

determined by three-electrode method. The measurement was conducted in the solution with a scan rate of $50 \text{ mV}\cdot\text{s}^{-1}$. The conditions of the solution during scanning are consistent with the reaction conditions.

Room temperature electron spin resonance (ESR) spectra were acquired at 9.8 GHz (X-band) with a Bruker EMX PLUS spectrometer.

X-ray diffraction (XRD) was operated on a Bruker D8 Advance X-ray diffractometer using the Ni-filtered Cu-K α radiation source at 40 kV and 40 mA.

XPS spectra were recorded on a X-ray Photoelectron Spectrometer (Thermo Scientific Ltd.) using a monochromatized Al K α radiation source. The binding energy was calibrated by the C 1s peak at 284.8 eV.

1.3 HMF-to-FFCA oxidation and analytical method

Oxidation of HMF was investigated in a 10 mL glass reaction tube with an oxygen balloon. Typically, 5 mmol HMF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂ and 0.1 mmol TBAHS were dissolved into 2.5 mL CH₃CN, and then the reaction was carried out for a certain period of time at a suitable temperature. During the reaction, oxygen balloon continuously provides molecular oxygen for the reaction. After the reaction, the products were diluted with pure water and tested.

Analysis of HMF, DFF, FFCA, and FDCA was made on a Agilent 1260 high-performance liquid chromatography (HPLC) system with an Aminex HPX-87H column (7.8 \times 300 mm). Acetonitrile and 0.5 wt% H₂SO₄ with a volume ratio of 20: 80 were used as mobile phase at a flow rate of $0.9 \text{ mL}\cdot\text{min}^{-1}$. The content of HMF, DFF, FFCA and FDCA in the product solution was directly obtained by the calibration curve of external standard constructed by pure substance, and the conversion and selectivity were calculated. HMF conversion, DFF selectivity, FFCA selectivity, FDCA selectivity were defined as follows:

$$\text{Conversion} = \frac{n_{\text{HMF,initial}} - n_{\text{HMF,final}}}{n_{\text{HMF,initial}}} \times 100\% \quad (1)$$

$$\text{Selectivity}_{\text{DFF}} = \frac{n_{\text{DFF,final}}}{n_{\text{DFF,final}} + n_{\text{HMFCa,final}} + n_{\text{FFCA,final}} + n_{\text{FDCA,final}}} \times 100\% \quad (2)$$

$$\text{Selectivity}_{\text{FFCA}} = \frac{n_{\text{FFCA,final}}}{n_{\text{DFF,final}} + n_{\text{HMFCa,final}} + n_{\text{FFCA,final}} + n_{\text{FDCA,final}}} \times 100\% \quad (3)$$

$$\text{Selectivity}_{\text{FDCA}} = \frac{n_{\text{FDCA,final}}}{n_{\text{DFF,final}} + n_{\text{HMFCa,final}} + n_{\text{FFCA,final}} + n_{\text{FDCA,final}}} \times 100\% \quad (4)$$

In a larger-scale reaction, 100 mmol (12.61 g) of HMF were used, with the amounts of VOSO₄, Cu(NO₃)₂, TBAHS, and CH₃CN scaled accordingly. The mixture was thoroughly stirred to ensure the reaction temperature remained below the set point. HPLC was used to quantify the FFCA formed, with experiments replicated in triplicate, yielding a standard deviation of less than 5%. The reaction mixture was then subjected to rotary evaporation to remove the solvent. The resulting residue was dissolved in an aqueous sodium bicarbonate solution (8.4 g NaHCO₃ in 100 mL H₂O) and stirred for 10 minutes to convert FFCA into its sodium salt. The solution was filtered to remove insoluble impurities, and the filtrate was acidified with dilute hydrochloric acid (1 mol/L, 100 mL), resulting in the precipitation of FFCA. The pale yellow FFCA powder was eventually recovered by vacuum filtration, resulting in a 96% isolation yield.

1.4 Preparation of Ru/Nb₂O₅

In the case of the Ru/Nb₂O₅ (Ru: 1 wt%) catalyst, Nb₂O₅ was initially dispersed into aqueous Ru(NO)(NO₃)₃ solution with stirring and kept overnight. The mixed solution was slowly evaporated at 333 K under 0.01 MPa and then dried at 373 K for 1 h under vacuum conditions. The recovered solid powder was pretreated under 5% H₂/Ar flow at 673 K for 2 h, and then passivated under air at room temperature before the catalytic reactions.

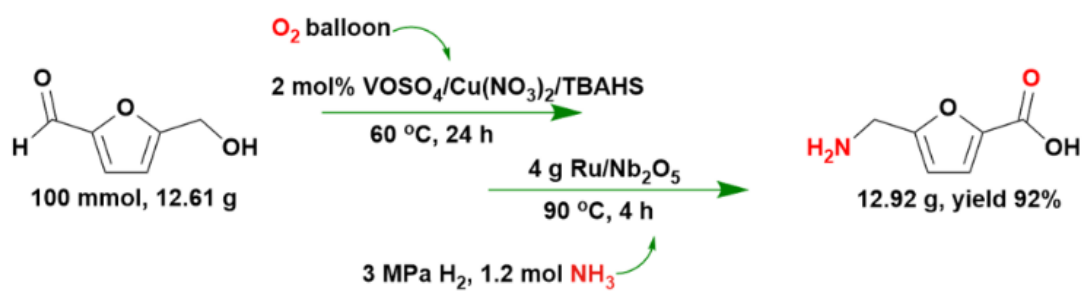
1.5 Reductive amination of FFCA

Catalytic tests for the reductive amination of carbonyl compounds were operated in a 20 mL Hastelloy-C high pressure Parr reactor. Typically, 20 mg Ru/Nb₂O₅ catalyst, 0.5 mmol FFCA, 4.14 mL CH₃OH and 0.86 mL 7 M NH₃/MeOH solution were loaded into the reactor, and 3 MPa H₂ was then introduced. The reactor was set at 363 K under stirring. Analysis of AMFC was also made on the Agilent 1260 HPLC.

In a larger-scale reaction, 13.45 g of previously isolated FFCA were used, with the amounts of Ru/Nb₂O₅ and NH₃/MeOH scaled accordingly. HPLC was used to quantify the AMFC formed, with experiments replicated in triplicate, yielding a standard deviation of less than 5%. After removing the catalyst by filtration, the filtrate was concentrated

using a rotary evaporator to obtain a mixture of AMFC and unreacted FFCA. This mixture was then treated with dilute hydrochloric acid (1 mol/L, 100 mL) to convert AMFC into its ammonium salt. The solution was filtered, and the filtrate was subjected to rotary evaporation to yield pure AMFC. The overall yield of the two-step process was 92%.

Supplementary data (Table S1-S6, Fig. S1-S8)



Scheme S1. Up-scaled synthesis of AMFC from HMF.

Table S1. Dissolution of VOSO₄ at different temperatures with or without TBAHS

Entry	Amount of Additive	Temperature (°C)	Concentration of Vanadium (g·L ⁻¹)
1	/	25	1.053
2	0.1 mmol TBAHS	25	3.592
3	/	60	3.365
4	0.1 mmol TBAHS	60	6.517

Reaction conditions: 0.1 mmol VOSO₄, 0.1 mmol TBAHS, 2.5 mL CH₃CN, concentration of vanadium was measured by ICP-OES.

Table S2. The influence of Cu(NO₃)₂ on the solubilization effect of TBAHS

Entry	Amount of Cu(NO ₃) ₂	Concentration of Vanadium (g·L ⁻¹)
1	/	3.592
2	0.5 equiv.	3.608
3	1 equiv.	3.583
4	2 equiv.	3.579

Reaction conditions: 0.1 mmol VOSO₄, 0.1 mmol TBAHS, 2.5 mL CH₃CN, room temperature, concentration of vanadium was measured by ICP-OES.

Table S3. Oxidation of HMF at different temperatures

Entry	Temperature (°C)	Conv. (%)	Select. (%)		
			DFE	FFCA	FDCA
1	50	100	19	76	5
2	60	100	9	86	5
3	70	100	8	83	9
4	80	100	3	83	14

Reaction conditions: 5 mmol HMF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 0.1 mmol TBAHS, 2.5 mL CH₃CN, O₂ balloon, 24 h.

Table S4. Oxidation of HMF under different pressures

Entry	O ₂ pressure (bar)	Conv. (%)	Select. (%)		
			DFE	FFCA	FDCA
1	1	100	9	86	5
2	3	100	10	86	5
3	5	100	8	84	8
4	10	100	8	83	9
5	20	100	7	82	11

Reaction conditions: 5 mmol HMF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 0.1 mmol TBAHS, 2.5 mL CH₃CN, 60 °C, 24 h.

Table S5. Oxidation of HMF in different mixed solvents

Entry	Solvent	Conv. (%)	Select. (%)		
			DFP	FFCA	FDCA
1	MeCN:Diox=1:1	100	14	84	2
2	MeCN:DCE=1:1	100	9	91	0
3	MeCN:CYH=1:1	100	70	30	0
4	MeCN:HCOOH=1:1	100	20	69	11
5	MeCN:AcOH=1:1	100	49	51	0
6	MeCN:MeOH=1:1	30	68	2	0
7	MeCN:H ₂ O=1:1	87	93	7	0
8	MeCN:DCE=2:1	100	3	97	0
9	MeCN:DCE=1:2	100	33	65	0

Reaction conditions: 5 mmol HMF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 0.1 mmol TBAHS, 2.5 mL solvent, 60 °C, O₂ balloon, 24 h.

Table S6. Comparison of reported FFCA preparation methods

Entry	Catalyst	C _{HMF} (mol/L)	T (°C)	t (h)	p (MPa)	Addition	FFCA Yield (%)
1	VOSO ₄ /Cu(NO ₃) ₂ /TBAHS	2	60	24	0.1	/	97
2 ¹	CuO·CeO ₂	0.2	110	3	0.9	/	90
3 ²	MgO·CeO ₂	0.14	130	9	0.9	/	90
4 ³	AuNP-sPSB	0.06	110	16	0.1	Cs ₂ CO ₃	74
5 ⁴	Na ₃ H ₆ FeMo ₆ O ₂₄	0.2	100	8	0.1	K ₂ CO ₃	75
6 ⁵	Mn ₃ Fe ₇	0.05	140	3	3	Na ₂ CO ₃	36
7 ⁶	(NH ₄) ₃ H ₆ CoMo ₆ O ₂₄	0.02	130	6	0.1	/	60
8 ⁷	CotA-TJ102	0.05	55	12	0.1	CH ₃ COONa, TEMPO	98

Table S7. Effect of temperature on the yield of AMFC over Ru/Nb₂O₅

Entry	Temperature (°C)	AMFC yield (%)
1	60	0
2	90	97
3	120	76

Reaction conditions: 0.02 g catalyst, 0.5 mmol FFCA, 5 mL MeOH, 6 mmol NH₃, 3 MPa H₂, 4 h.

Table S8. Effect of substrate/ammonia ratio on the yield of AMFC over Ru/Nb₂O₅

Entry	Amount of NH ₃ (mmol)	AMFC yield (%)
1	2	61
2	4	77
3	6	97
4	8	96

Reaction conditions: 0.02 g catalyst, 0.5 mmol FFCA, 5 mL MeOH, 3 MPa H₂, 90 °C, 4 h.

Table S9. Comparison of reported AMFC preparation methods

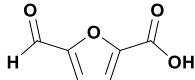
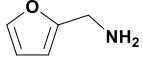
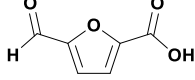

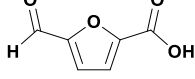
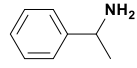
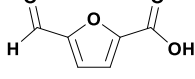
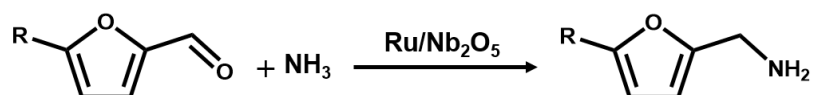
Entry	Substrate	Catalyst	C _{substrate} (mol/L)	Ammonia source	AMFC Yield (%)
1		Ru/Nb ₂ O ₅	0.2	NH ₃	96
2 ⁸		Cs ₂ CO ₃	/	/	62
3 ⁹		TAs	0.01		44-89
4 ¹⁰		Immobilized CvTA	0.01		77
5 ¹¹		<i>E.coli</i> _TAF cells	0.15	HCOONH ₄	81

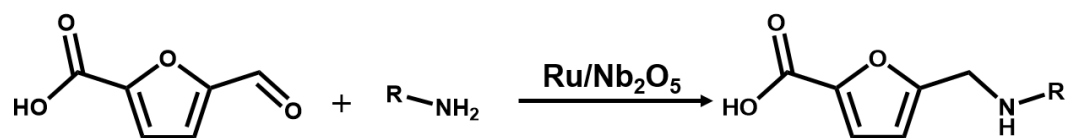
Table S10. Reductive Amination of furan aldehyde with ammonia.



Entry	Substrate	Yield (%)
1		69
2		63
3		78

Reaction conditions: 0.02 g catalyst, 0.5 mmol substrate, 5 mL MeOH, 6 mmol NH₃, 3 MPa H₂, 90 °C, 4 h.

Table S11. Reductive Amination of FFCA with primary amines.



Entry	R-NH ₂	Yield (%)
1		72
2		89
3		88

Reaction conditions: 0.02 g catalyst, 0.5 mmol FFCA, 5 mL MeOH, 6 mmol R-NH₂, 3 MPa H₂, 90 °C, 4 h.

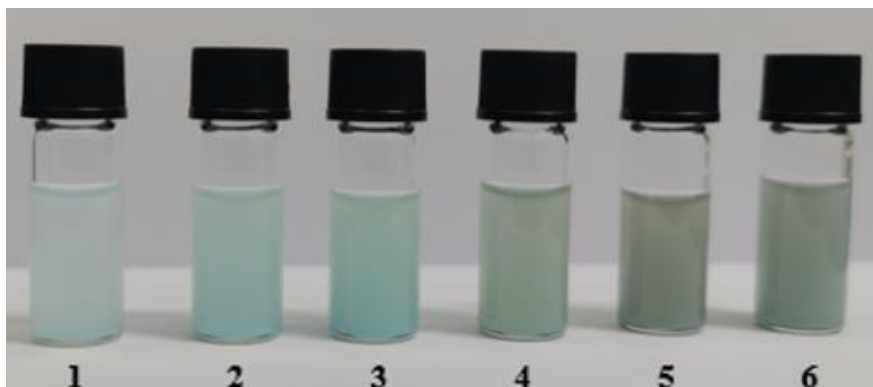


Figure S1. The color of the system changes after adding different amounts of TBAHS.

Reaction conditions: 0.1 mmol VO_2^+ , 2.5 mL CH_3CN , stir for 30 minutes. 1, without addition; 2, 0.02 mmol TBAHS; 3, 0.03 mmol TBAHS; 4, 0.05 mmol TBAHS; 5, 0.1 mmol TBAHS; 6, 0.2 mmol TBAHS.

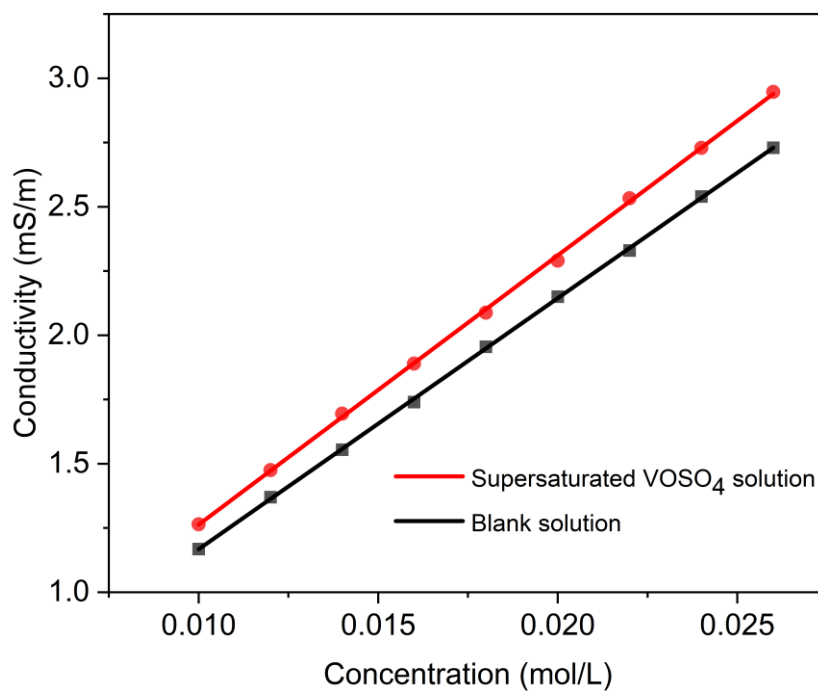


Figure S2. The conductivity test.

Add an equal amount of TBAHS to the supersaturated VOSO₄ solution and acetonitrile and then measure the conductivity of the solution. The discernible rise in conductivity in the supersaturated solution, relative to the blank solution, suggests the solubilization of TBAHS.

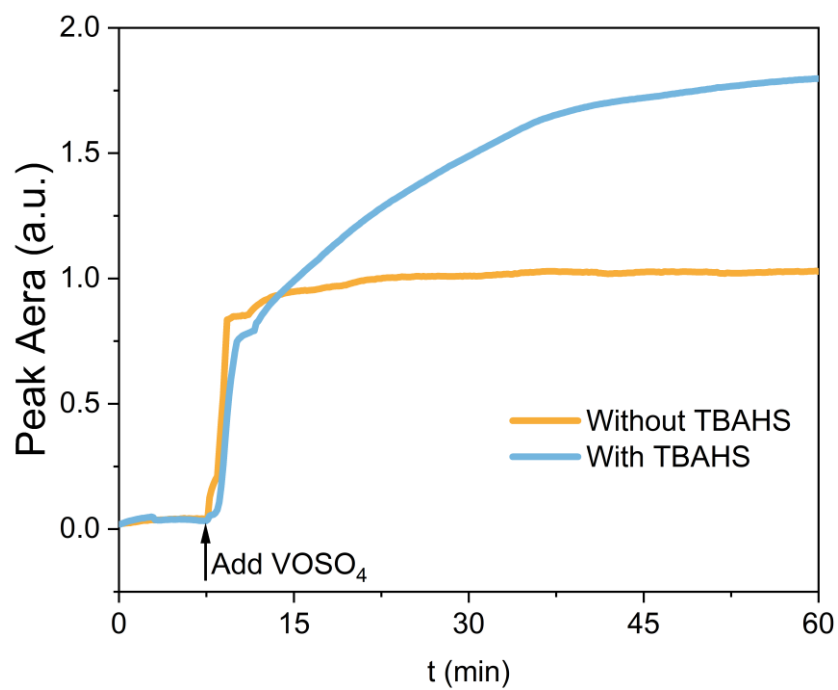


Figure S3. Relationship of peak area and reaction time.

Reaction conditions: 5mmol DFF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 2.5 mL CH₃CN, 60 °C, O₂ balloon.

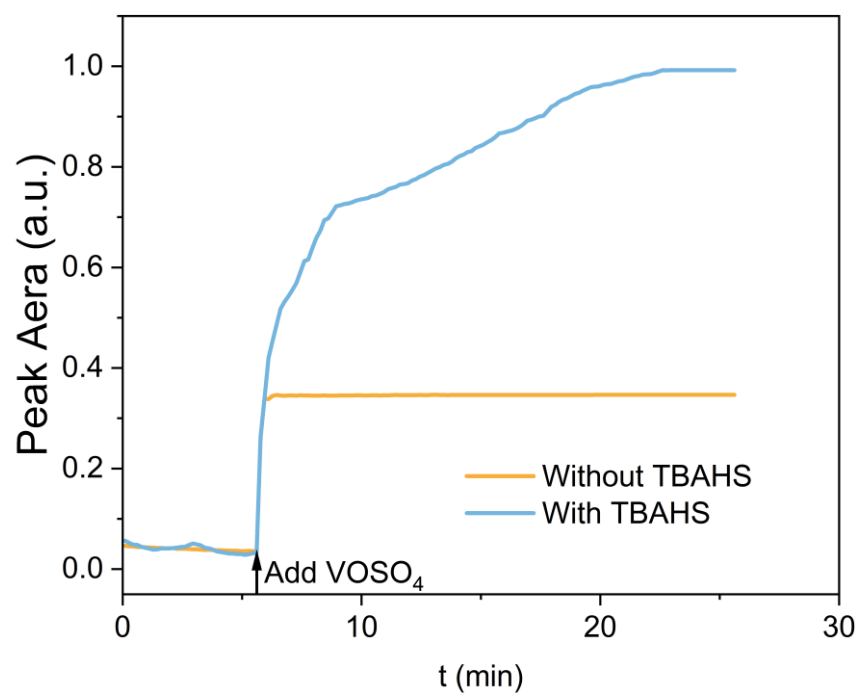


Figure S4. Relationship of peak area and reaction time.

Reaction conditions: 5mmol DFF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 2.5 mL CH₃CN, room temperature, O₂ balloon.

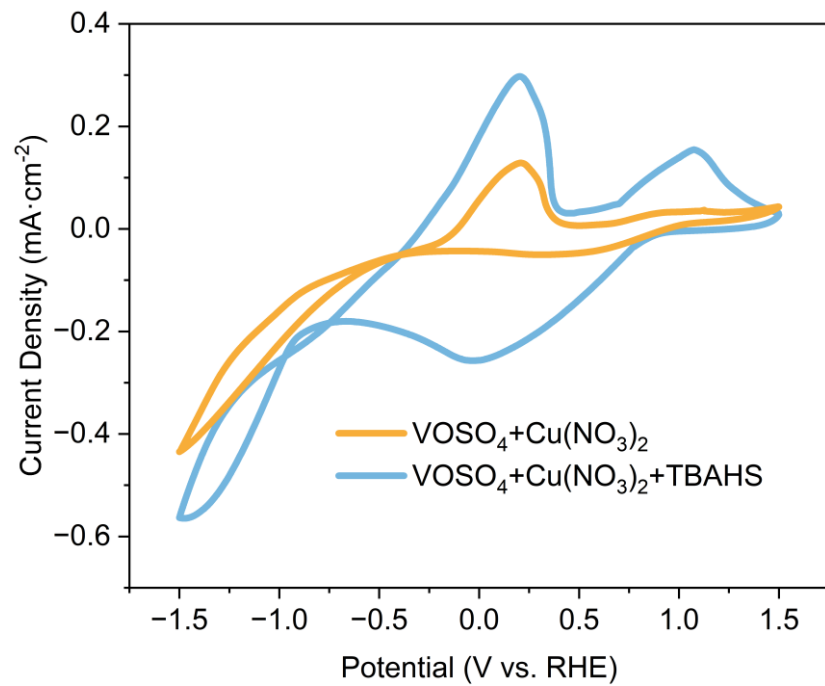


Figure S5. Cyclic voltammetry test.

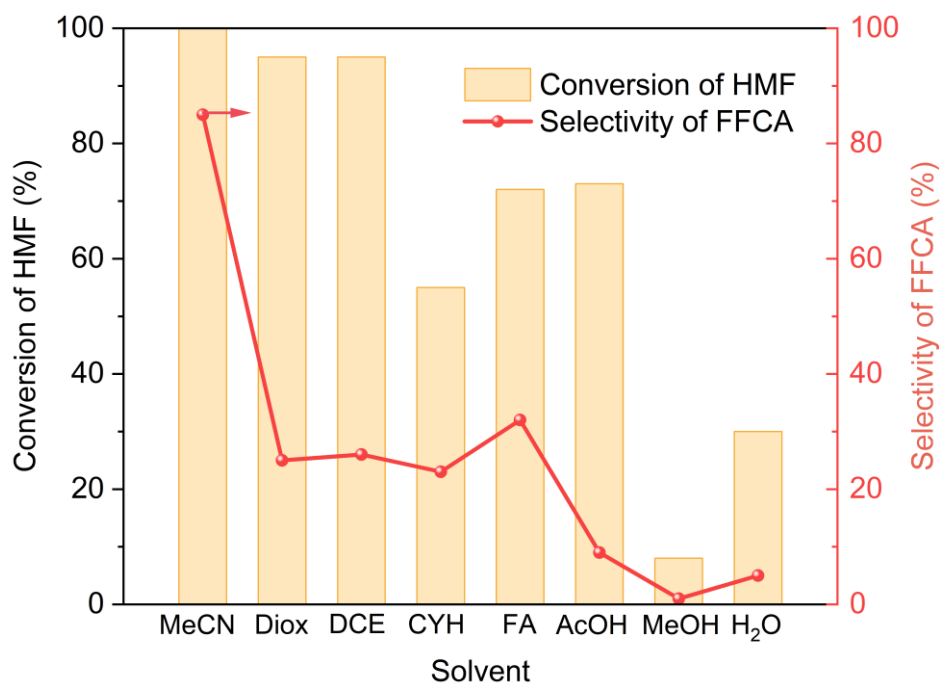


Figure S6. The dependence of HMF conversion or FFCA selectivity on solvent.

Reaction conditions: 5 mmol HMF, 0.1 mmol VOSO₄, 0.1 mmol Cu(NO₃)₂, 2.5 mL CH₃CN, 60 °C, O₂ balloon, 24 h.

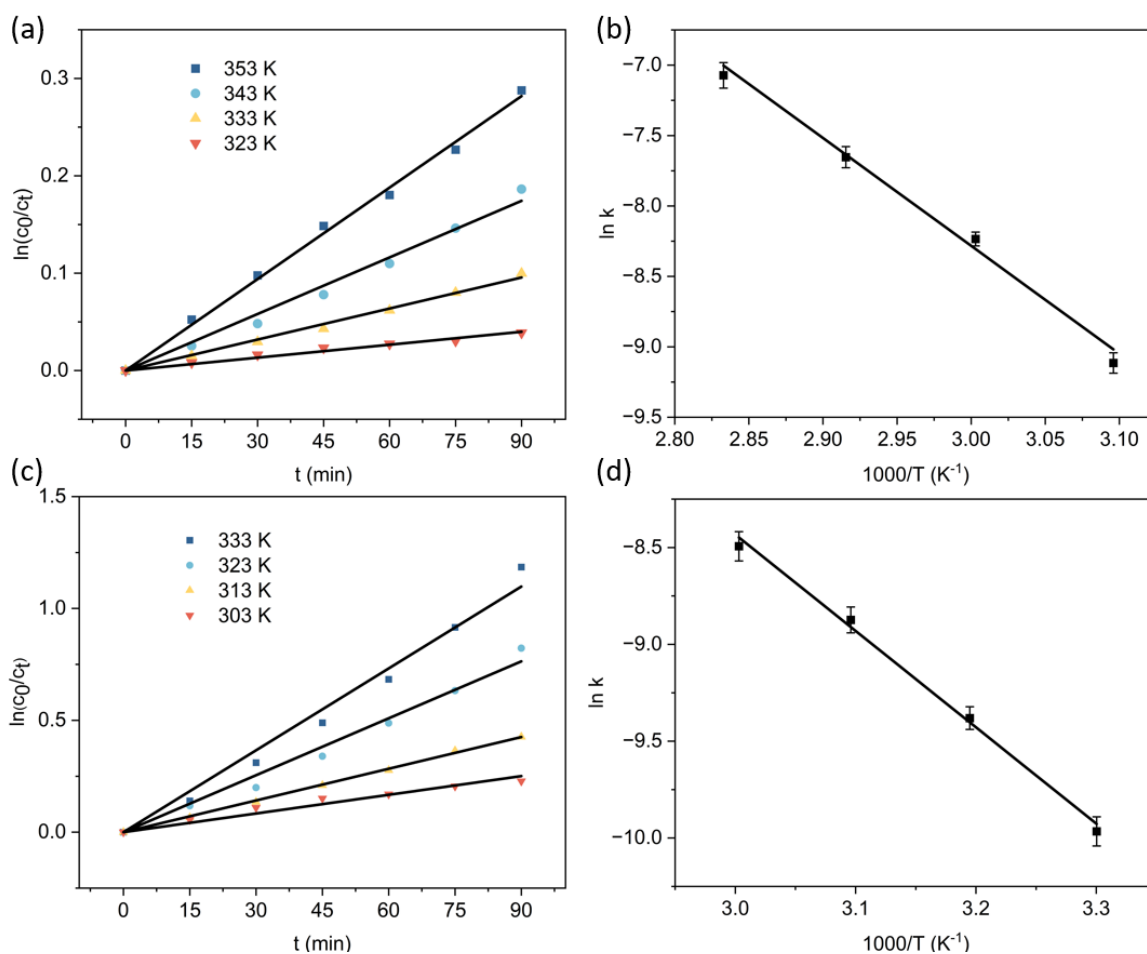
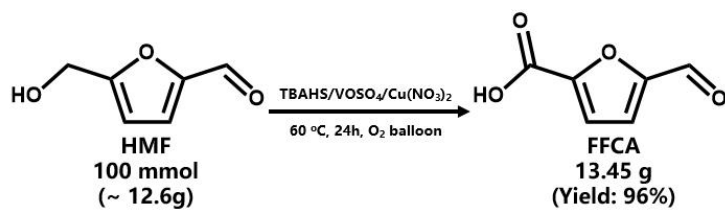
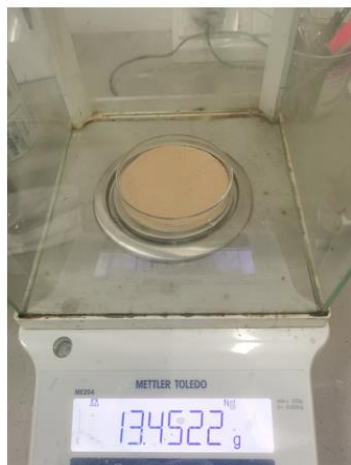


Figure S7. (a) Relationship of $\ln(C_0/C_t)$ and reaction time of DFF oxidation to FFCA. (b) Arrhenius plot for the oxidation of DFF. (c) Relationship of $\ln(C_0/C_t)$ and reaction time of HMF oxidation to DFF. (d) Arrhenius plot for the oxidation of HMF.

Reaction conditions: 5 mmol HMF or DFF, 0.1 mmol $VOSO_4$, 0.1 mmol $Cu(NO_3)_2$, 0.1 mmol TBAHS, 2.5 mL CH_3CN , O_2 balloon.



(a)



(b)

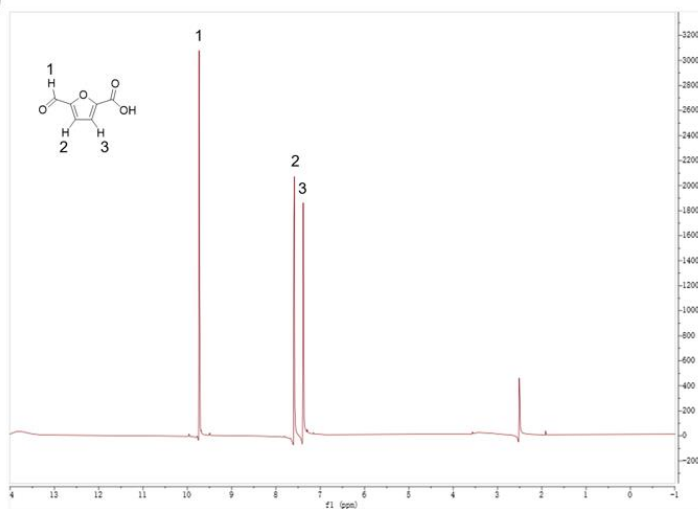


Figure S8. (a) Isolated FFCA product. (b) ^1H NMR spectrum of the isolated FFCA product.

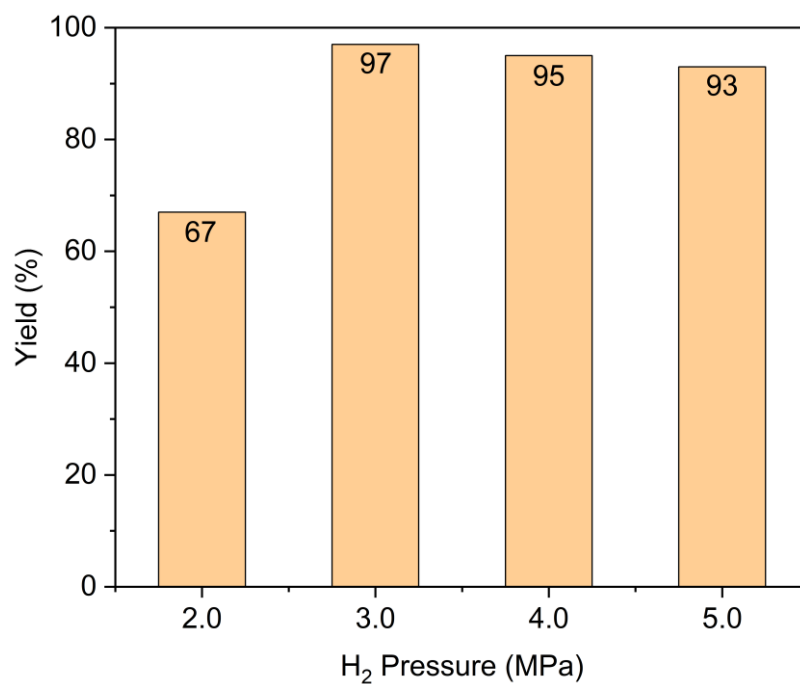


Fig. S9 Effect of hydrogen pressure on the yield of AMFC over Ru/Nb₂O₅

Reaction conditions: 0.02 g catalyst, 0.5 mmol FFCA, 5 mL MeOH, 8 mmol NH₃, specified pressure H₂, 90 °C, 4 h.

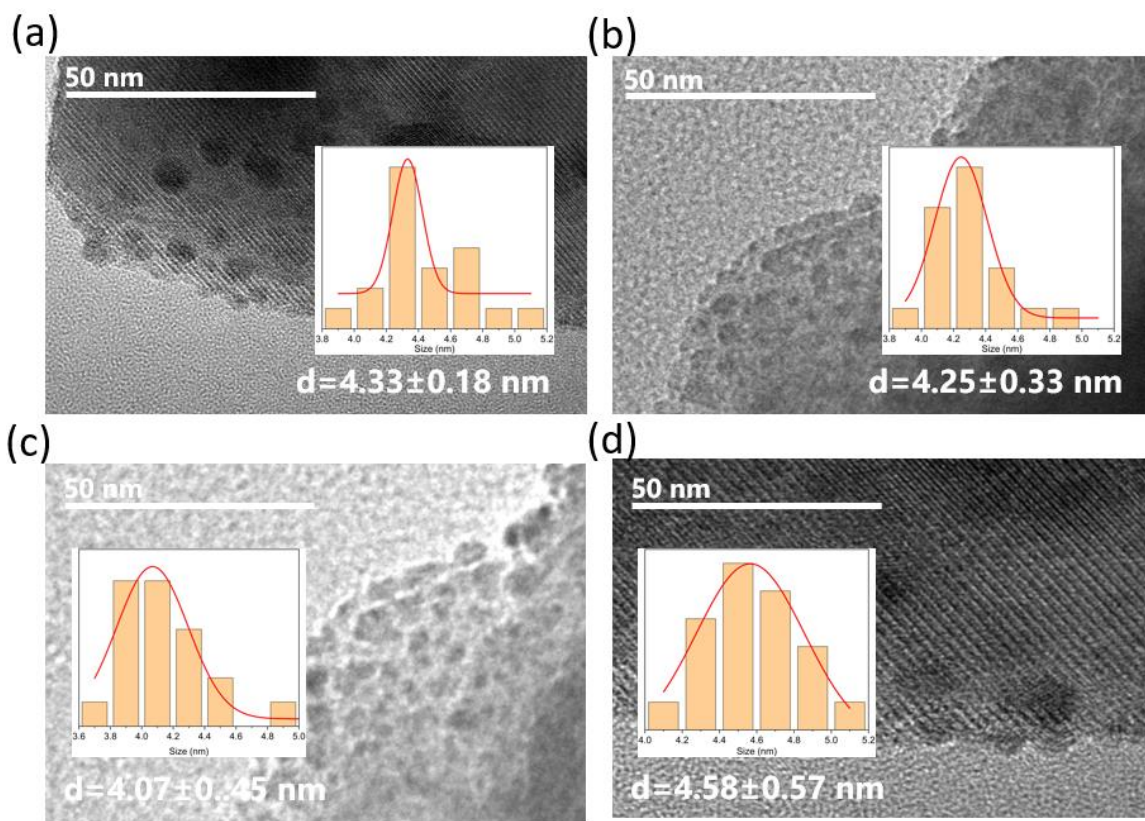


Fig. S10 TEM of (a) Ru/Nb₂O₅, (b) Ru/SiO₂, (c) Ru/Al₂O₃, (d) Ru/ZrO₂

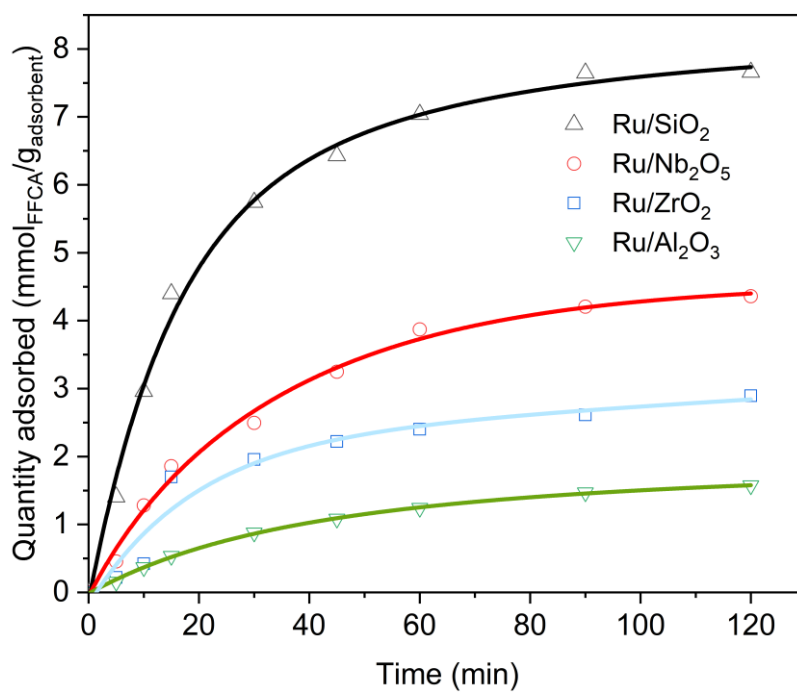
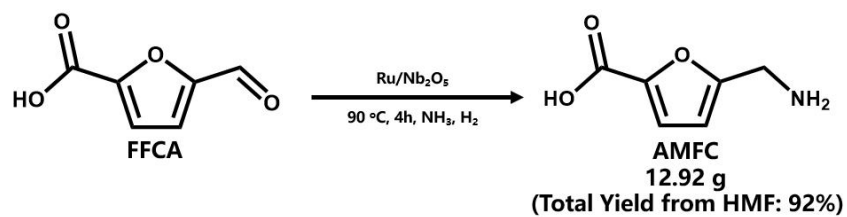


Fig. S11 Adsorption kinetics of FFCA in Ru-based catalysts

Reaction conditions: 0.02 g catalyst, 1 mmol FFCA, 5 mL MeOH.



(a)



(b)

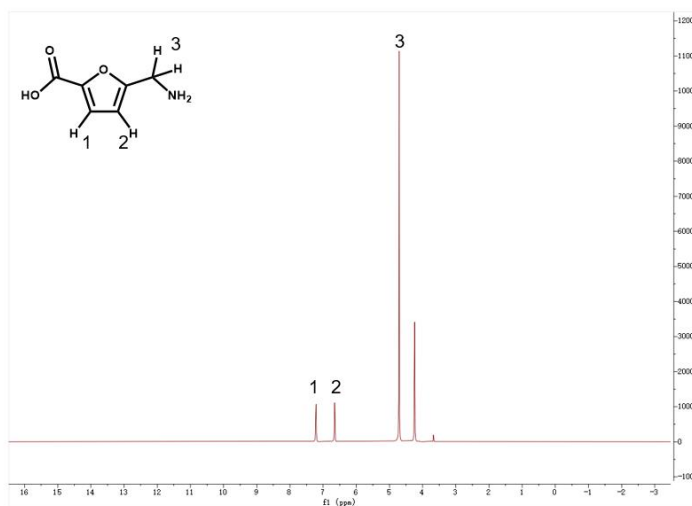


Figure S12. (a) Isolated AMFC product. (b) ^1H NMR spectrum of the isolated AMFC product.

References:

1. M. Ventura, M. Aresta and A. Dibenedetto, *ChemSusChem*, 2016, **9**, 1096-1100.
2. M. Ventura, F. Lobefaro, E. de Giglio, M. Distaso, F. Nocito and A. Dibenedetto, *ChemSusChem*, 2018, **11**, 1305-1315.
3. A. Buonerba, S. Impemba, A. D. Litta, C. Capacchione, S. Milione and A. Grassi, *ChemSusChem*, 2018, **11**, 3139-3149.
4. J. J. Xu, Z. G. Zhu, Z. L. Yuan, T. Su, Y. C. Zhao, W. Z. Ren, Z. H. Zhang and H. Y. Lü, *J. Taiwan Inst. Chem. E.*, 2019, **104**, 8-15.
5. P. Pal, S. Kumar, M. M. Devi and S. Saravanamurugan, *J. Supercrit. Fluids*, 2020, **160**, 104812.
6. Y. B. Sun, K. X. Yang, Z. G. Zhu, T. Su, W. Z. Ren and H. Y. Lu, *Chem. Commun.*, 2022, **58**, 8105-8108.
7. C. Y. Zhang, X. Chang, L. Zhu, Q. G. Xing, S. P. You, W. Qu, R. X. Su and Z. M. He, *Int. J. Biol. Macromol.*, 2019, **128**, 132-139.
8. A. W. Lanckenau and M. W. Kanan, *Chem. Sci.*, 2020, **11**, 248-252.
9. A. Dunbabin, F. Subrizi, J. M. Ward, T. D. Sheppard, H. C. Hailes, *Green Chem.*, 2017, **19**, 397-404.
10. A. Lancien, R. Wojcieszak, E. Cuvelier, M. Duban, P. Dhulster, S. Paul, F. Dumeignil, R. Froidevaux, E. Heuson, *ChemCatChem*, 2021, **13**, 247-259.
11. Z. C. Wu, W. W. Li, M. H. Zong and N. Li, *Chem. Eur. J.*, 2024, **30**, e202400269.