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Computer-assisted design of metal-free catalysts for highly efficient hydration of epoxides at mild temperatures and atmospheric pressure *via* multiple hydrogen bonding interactions†

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Through computer-assisted design, a multiple hydrogen bonding catalyst was developed to achieve efficient hydration of epoxides under mild temperatures and atmospheric pressure, eliminating the use of metals. Through the introduction of multiple hydrogen bonds and the prediction of optimal bond strength, guanidine-functionalized and hydroxyl-bridged IL with four hydrogen bonds exhibited the highest activity, leading to an excellent yield of 97% at 50 °C and 1 bar CO_2. A combination of control experiments, isotope labeling experiments and quantum-chemical calculations were carried out to reveal the mechanism, which indicated that the interactions of multiple hydrogen bonds could promote the reaction effectively. We believe this strategy using multiple hydrogen bonding interactions provides a novel idea for developing metal-free catalysts.

1,2-Diols are commonly used as coolants and as the basic material of polyester fiber and resin.[1] At present, the industrial synthesis of ethylene glycol (EG) mainly depends on the thermal hydration of ethylene oxide (EO). However, due to the limitation of side reactions,[2a] a large amount of water (20–25 mol/mol EO) is needed to obtain high selectivity. The distillation of EG from excess water usually leads to huge energy consumption. Some metal catalysts, like Co and Sn, were initially used for the hydration of EO under low H_2O/EO ratio and mild conditions (Table S1†), however, these catalysts are harmful to humans and the environment owing to their toxicity.[3] Therefore, developing metal-free catalysts to achieve highly efficient and selective hydration is desired.

Ionic liquids (ILs) could provide a valuable alternative that avoids the usage of metals.[4] However, due to the high energy barrier in the process of direct hydration, the reaction needs high temperature and pressure, like 120 °C and 2 MPa N_2.[2a] Two-step transformations from epoxy to intermediates such as cyclic carbonate (EC) have been found to be suitable for the production of EG. For example, Gao's group achieved high selectivity with a lower H_2O/EO ratio (<1.5),[2b] although the reaction still required a high temperature (100 °C) and high-pressure CO_2 (1.5 MPa). Therefore, developing a novel strategy for efficient hydration under mild temperatures and atmospheric pressure using a metal-free is still challenging.

Although the two-step process was considered to effectively reduce the energy barrier, the formation of four main transition states in the reaction still required high energy, leading to the need for high temperatures and pressure. It has been reported that hydrogen bonding can effectively stabilize the transition state,[5] however, it is not able to achieve the same strong activation ability as a coordination bond induced by a metal because of the weak interaction of a single hydrogen bond. Recently, due to their strong nucleophilicity and high selectivity, multiple hydrogen bonds have been widely used in some fields such as supramolecular self-assembly,[6] healable polymers,[7] molecular recognition[8] and hydrogen bond cross-linked polymer materials.[9] Inspired by this, we attempted to introduce multiple hydrogen bonds into the structure of a catalyst in order to effectively reduce the energy barrier of the hydration (Fig. 1).

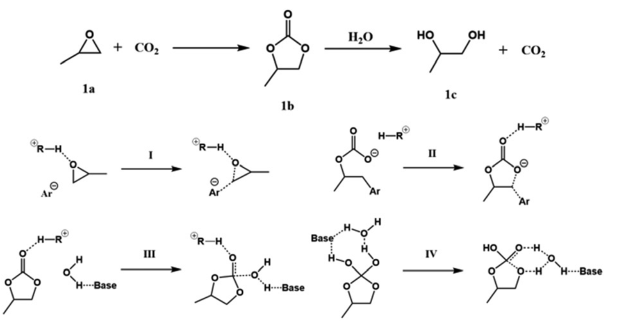

Fig. 1 The two-step reaction process and four main transition states in the two-step process.

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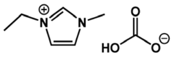
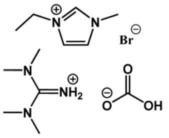
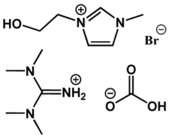
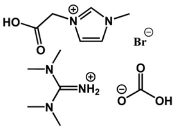
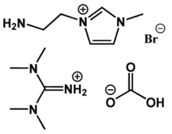
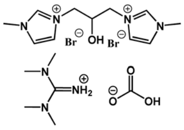
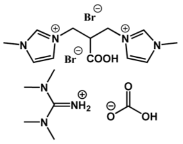
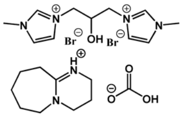
Considering that hydrogen bonds play different roles in the four main transition states, which require different hydrogen bond strengths, it is necessary to design the structure of multiple hydrogen bonding catalysts. The strategy of computer-aided design could help us to filter and predict the optimal structure before experiment.[10] This method of calculating the reaction energy barrier directly, which is not based on experimental trial and error, will have great significance in the screening of these catalysts with multiple hydrogen bonds.

Herein, we reported the design of multiple hydrogen bonding catalysts for hydration, through the strategy of a computer-aided method, eliminating the use of a metal catalyst. By comparing the reaction energy barriers through quantum-chemical calculations, a series of hydrogen bonds such as two hydrogen bonds, three hydrogen bonds and four hydrogen bonds were introduced, and the optimal hydrogen bond strengths were predicted. An ideal metal-free catalyst with multiple hydrogen bonds guanidine-functionalized and hydroxyl-bridged IL was selected, which was further verified to be highly effective in the hydration of epoxides at mild temperatures and atmospheric pressure. Through control experiments, isotope labeling experiments, and density functional theory (DFT), the roles of multiple hydrogen bonds and CO_2 were investigated in detail, indicating the importance of multiple hydrogen bonding interactions.

The hydration of propylene oxide (PO) was chosen as the model reaction. During the two-step process, the first step process had a higher energy barrier, which was considered to be the rate-determining step. For the two main transition states in the first step process (I, II), various common cations with bromine anions were firstly used to calculate the reaction barrier (Table S2, entries 1–11†). The results showed that when the cations could provide hydrogen bonding, the reaction energy barrier would be reduced to a certain extent (Table S2, entries 9–11†). Among these, C-2 H in [Emim] had the better hydrogen bond strength and achieved the lowest reaction energy barrier compared to the other cations (Table S2, entry 11†). Secondly, [Emim] with different common anions was

Table 1 Prediction of the effect of different catalysts on the reaction energy barrier

Entry	Catalyst	Hydrogen bond number	I	II	III	IV
1		1	25.1	27.2	23.7	13.6
2		2	25.1	22.7	21.1	13.7
3		3	21.7	24.3	17.6	13.7
4		3	16.5	28.9	20.6	13.7
5		3	26.2	22.7	19.1	13.7
6		4	11.5	10.1	13.2	13.7
7		4	15.0	11.2	15.0	13.7
8		4	11.5	2.01	10.2	15.1

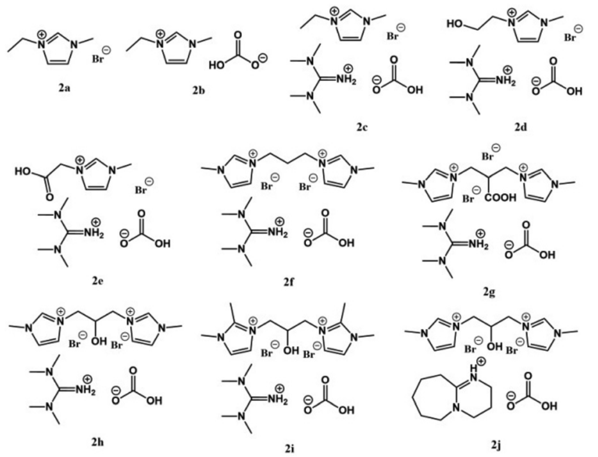
also substituted into the reaction process for calculation (Table S2, entries 11–18†). It was seen that [Emim][HCO_3] showed the best catalytic activity (Table S2, entry 18†).

On the basis of [Emim][HCO_3], we further added hydrogen bonds into the structure of the ILs. At first, because it was difficult for [HCO_3] to leave, the cyclization process of cyclic carbonate (II) had a high energy barrier. Based on this, we added [TMGH][Br] to the original structure (Table 1, entry 2), which could form hydrogen bonds with [HCO_3] to help it leave. As expected, the reaction energy barrier of II with two hydrogen bonds reduced to some extent. In order to further reduce the energy of ring opening of epoxides, some groups with other hydrogen bonds such as hydroxyl, amino and carboxyl groups were added to the original structure for the calculation (Table 1, entries 3–5). The results showed that the decrease of the open-ring energy barrier of epoxy (I) was often accompanied by an increase of the ring-closing barrier of cyclic carbonate (II). Among these, guanidine-functionalized and hydroxyl-functionalized IL with three hydrogen bonds had the optimal hydrogen bond strength (Table 1, entry 3). Although the reaction energy barrier had been further reduced, the reaction still required a lot of energy.

On the basis of the original structure, we further added a fourth hydrogen bond to optimize the configuration of the catalysts. To our delight, the reaction energy barrier of each step by guanidine-functionalized and hydroxyl-bridged IL with four hydrogen bonds was further reduced, and the energy barrier of the rate-determining step was only 13.7 kcal mol^{-1} (Table 1, entry 6). Besides, carboxyl functional groups and organic bases DBU were also added to the structure for calculation (Table 1, entries 7 and 8). Based on the literature,[12] we also considered the effect of cations with different hydrogen bonds on the state of anions and further explained the role of the hydrogen bonds (Fig. S4†).

Based on the above calculated results, it appeared that the addition of multiple hydrogen bonds could reduce the energy barrier effectively and different transition states needed the corresponding optimal hydrogen bond strength. Among these, ILs including [HCO_3], [TMGH] and bis-C-2 H with hydroxyl groups were the best match, which could reduce the reaction energy barrier most effectively (Table 1, entry 6). Did this

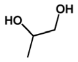
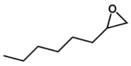
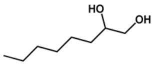
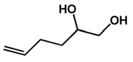
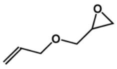
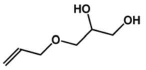
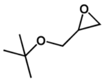
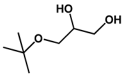
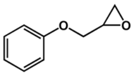
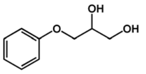
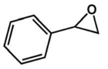
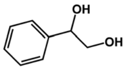
Table 2 The effect of different metal-free catalysts on the hydration of PO



Entry[a]	Catalyst	Amount (mol%)	T (°C)	Yield[b] (%)
1	**2a**	15	50	25
2	**2b**	15	50	30
3[d]	**2c**	15	50	68
4[d]	**2d**	15	50	76
5[d]	**2e**	15	50	65
6[d]	TMG	15	50	30
7[e]	**2f**	10	50	80
8[e]	**2g**	10	50	88
9[e]	**2h**	10	50	97
10[c,e]	**2h**	10	50	71
11[e]	**2i**	10	50	91
12[f]	**2j**	10	50	88
13[e,g]	**2h**	10	50	87
14[e,h]	**2h**	10	50	94
15	NaOAc	10	50	15
16	Et_3N	10	50	20

[a] Reaction conditions: PO (5 mmol), H_2O (25 mmol), catalyst, 24 h, and CO_2 (~1 bar). [b] Determined by GC. [c] Without CO_2. [d] With extra 15 mol% TMG. [e] With extra 20 mol% TMG. [f] With extra 20 mol% DBU. [g] 1 bar 15%CO_2. [h] Catalyst was used fifth time.

Table 3 Scope of internal epoxides and epoxides with different terminal groups

Entry[a]	Substrate	Product	Yield[b] (%)
1[c]			97
2			>99
3			>99
4			>99
5			98
6			>99
7			>99

[a] Reaction conditions: epoxide (5 mmol), H_2O (25 mmol), catalyst **2h** (0.5 mmol), TMG (1 mmol), 70 °C, 24 h and CO_2 (~1 bar). [b] Determined by ^1H NMR. [c] 50 °C.

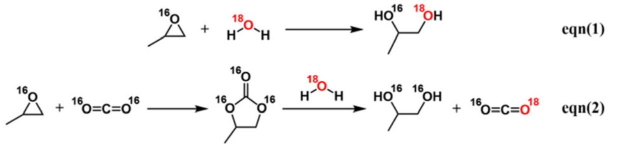


Fig. 2 Isotope labeling experiments for the mechanism.

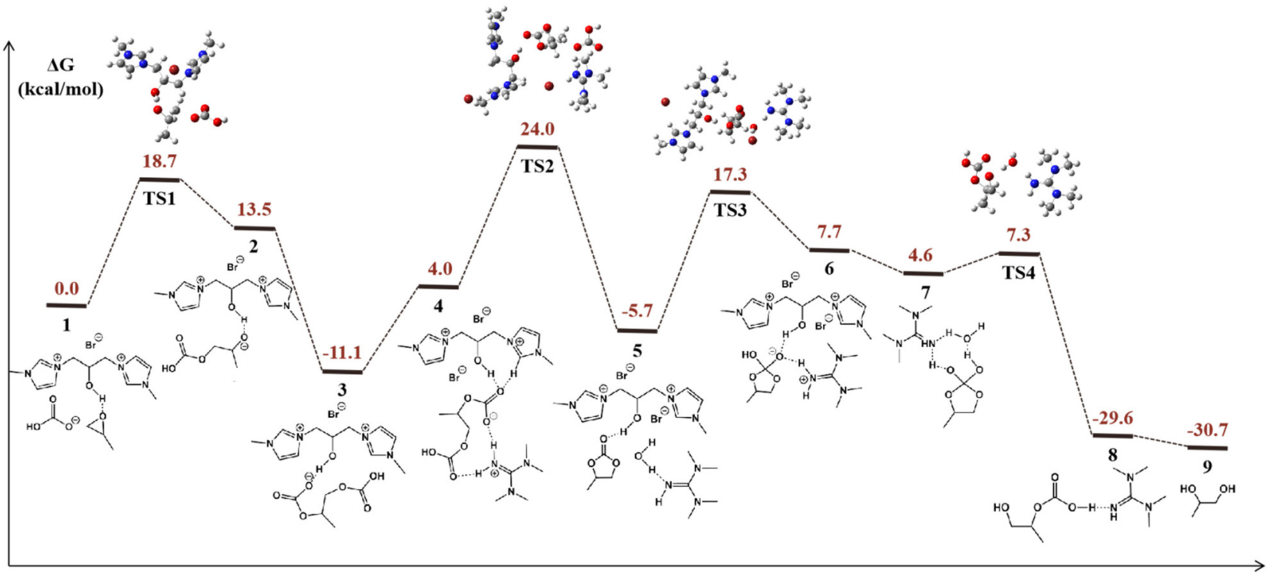


Fig. 3 Computational studies of the reaction mechanism.

mean that this multiple hydrogen bonding catalyst would exhibit a higher catalytic activity than the others?

To verify this hypothesis, corresponding catalysts with multiple hydrogen bonds were synthesized and the structures were determined by NMR spectra (Fig. S1†). Then, hydration of PO was carried out at 50 °C under 1 bar CO_2.

After optimizing the H_2O/PO ratios and the amounts of catalyst (Table S3†), a yield of 97% was obtained when guanidine-functionalized and hydroxyl-bridged IL with four hydrogen bonds (**2h**) was used as the catalyst (Table 2, entry 9). Under the same conditions, some common bases such as NaOAc and Et_3N only had 15% and 20% yield (Table 2, entries 15 and 16). As far as we know, this was the first work that could effectively achieve hydration of epoxides under mild conditions and atmospheric pressure using a metal-free catalyst (Table S1†). We also tested the recycling of catalyst **2h** and its performance at a flue gas concentration of CO_2 (Table 2, entries 13 and 14). Furthermore, other catalysts were also tested and the results are summarized in Table 2. Consistent with the data of the prediction, the yield was highly related to hydrogen bond number. With the increase of hydrogen bond multiplicity, the yield increased accordingly (Table S4†).

Using the ideal metal-free catalyst with four hydrogen bonds **2h**, we further explored the substrate scope under mild temperatures and atmospheric pressure. The catalytic performance of **2h** for different types of epoxides was investigated and the results are listed in Table 3. It was seen that the yield of most of diols was excellent, where the yield was higher than 97%. The hydration reaction of the epoxides was more difficult with the increase of steric hindrance, where higher temperatures were required to obtain satisfactory conversion.

In order to further explore the reaction process, isotope labeling experiments were carried out by using isotope-labeled water. In contrast to the direct hydration reaction (Fig. 2, eqn (1)), unlabeled PG (*m*/*z* 76) and labeled $C^{18}OO$ (*m*/*z* 46) were detected, indicating that CO_2 participated and changed the reaction path (Fig. 2, eqn (2)). The process of CO_2 and H_2O participation in the reaction can be seen in Fig. 3. Detected PG (*m*/*z* 78) and $C^{18}O^{18}O$ (*m*/*z* 48) also proved that CO_2 worked as the cocatalyst (Fig. S3†).

Based on the experimental results and literature reports, a possible reaction mechanism was proposed.[2] DFT calculations were further carried out at the B3LYP/6-311++G (d,p) level to explain the role of multiple hydrogen bonding catalysts and clarify the mechanism (Fig. 3), where the solvation effect of water was also included by using solvation model density (SMD).

At first, $[HCO_3]$ in **1** nucleophilically attacked the epoxy carbon of the reactant PO, overcoming an energy barrier of 18.7 kcal mol^{-1}. The closing of the five-membered-ring and formation of propylene carbonate (PC) required an activation free energy of 20.0 kcal mol^{-1}. Then, the PC in **5** was hydrolyzed with an energy barrier of 23.0 kcal mol^{-1}, making it the rate-determining step in the reaction. Finally, **8** was produced through the opening of the penta-ring in **7** with TMG, requiring an energy barrier of 2.7 kcal mol^{-1}. After the release of CO_2, product **9** was formed. The role of the multiple hydrogen bonds was also determined in the DFT calculations.

Conclusions

In conclusion, a multiple hydrogen bonding catalyst was developed through the strategy of computer-aided design. Through the addition of hydrogen bonds and the prediction of the optimal hydrogen bond strength, the ideal metal-free catalyst with four hydrogen bonds **2h** was designed, which could effectively catalyze the hydration of epoxides under mild temperatures and atmospheric pressure. Through a combination of control experiments, isotope labeling experiments and quantum-chemical calculations, we found that the synergy of the multiple hydrogen bonds was the main reason for such a high catalytic activity. Finally, we believe this strategy using multiple hydrogen bonding interactions provides a novel idea for developing metal-free catalysts, which has potential in other metal-catalyzed reactions such as the synthesis of alkylidene cyclic carbonates.[11]

Conflicts of interest

The authors declare no competing financial interests.

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References

1 J. Zheng, L. Huang, C. Cui, Z. Chen, X. Liu, X. Duan, X. Cao, T. Yang, H. Zhu, K. Shi, P. Du, S. Ying, C. Zhu, Y. Yao, G. Guo, Y. Yuan, S. Xie and L. Zheng, *Science*, 2022, **376**, 288–292.

2 (*a*) Q. Su, X. Tan, X. Yao, T. Ying, L. Dong, M. Fu, W. Cheng and S. Zhang, *Green Chem.*, 2021, **23**(8), 2992–3000; (*b*) T. Ding, J. Zha, D. Zhang, J. Zhang, H. Yuan, F. Xia and G. Gao, *Green Chem.*, 2021, **23**(9), 3386–3391.

3 (*a*) B. Li, S. Bai, X. Wang, M. Zhong, Q. Yang and C. Li, *Angew. Chem., Int. Ed.*, 2012, **51**(46), 11517–11521; (*b*) M. Zhong, H. Li, J. Chen, L. Tao, C. Li and Q. Yang, *Chem. – Eur. J.*, 2017, **23**(48), 11504–11508; (*c*) Z. Dai, Q. Sun, F. Chen, S. Pan, L. Wang, X. Meng, J. Li and F.-S. Xiao, *ChemCatChem*, 2016, **8**(4), 812–817; (*d*) M. Zhong, Y. Zhao, Q. Yang and C. Li, *J. Catal.*, 2016, **338**, 184–191; (*e*) H. Li, J. Chen, J. Liu, C. Li, L. Liu and Q. Yang, *ChemNanoMat*, 2021, **7**, 1–8; (*f*) Z.-J. Yang, Y.-F. Li, Q.-B. Wu, N. Ren, Y.-H. Zhang, Z.-P. Liu and Y. Tang, *J. Catal.*, 2011, **280**(2), 247–254; (*g*) B. Tang, W. Dai, G. Wu, N. Guan, L. Li and M. Hunger, *ACS Catal.*, 2014, **4**(8), 2801–2810; (*h*) W. Dai, C. Wang, B. Tang, G. Wu, N. Guan, Z. Xie, M. Hunger and L. Li, *ACS Catal.*, 2016, **6**(5), 2955–2964; (*i*) D. Wang, Y. Yang, F. Zhang, P. Jiang, W. Gao, R. Cong and T. Yang, *J. Phys. Chem. C*, 2021, **125**(24), 13291–13303; (*j*) H. Li, M. Zhong, C. Li, Y. Ren, J. Chen and Q. Yang, *ChemCatChem*, 2019, **11**(16), 3952–3958; (*k*) X. Liu, W. Mao, J. Jiang, X. Lu, M. Peng, H. Xu, L. Han, S. Che and P. Wu, *Chem. – Eur. J.*, 2019, **25**(17), 4520–4529.

4 (*a*) T. Zhao, X. Hu, D. Wu, R. Li, G. Yang and Y. Wu, *ChemSusChem*, 2017, **10**, 2046–2052; (*b*) G. Shi, K. Chen, Y. Wang, H. Li and C. Wang, *ACS Sustainable Chem. Eng.*, 2018, **6**(5), 5760–5765; (*c*) Y. Zhao, B. Yu, Z. Yang, H. Zhang, L. Hao, X. Gao and Z. Liu, *Angew. Chem., Int. Ed.*, 2014, **53**(23), 5922–5925; (*d*) Y. Zhao, Z. Yang, B. Yu, H. Zhang, H. Xu, L. Hao, B. Han and Z. Liu, *ChemSci.*, 2015, **6**(4), 2297–2301; (*e*) J. Hu, J. Ma, Q. Zhu, Z. Zhang, C. Wu and B. Han, *Angew. Chem., Int. Ed.*, 2015, **54**(18), 5399–5403.

5 (*a*) T. Wang, D. Zheng, J. Zhang, B. Fan, Y. Ma, T. Ren, L. Wang and J. Zhang, *ACS Sustainable Chem. Eng.*, 2017, **6**(2), 2574–2582; (*b*) Y. Kumatabara, M. Okada and S. Shirakawa, *ACS Sustainable Chem. Eng.*, 2017, **5**(8), 7295–7301; (*c*) Z. Zhang, F. Fan, H. Xing, Q. Yang, Z. Bao and Q. Ren, *ACS Sustainable Chem. Eng.*, 2017, **5**(4), 2841–2846; (*d*) J. Hu, J. Ma, H. Liu, Q. Qian, C. Xie and B. Han, *Green Chem.*, 2018, **20**(13), 2990–2994; (*e*) X. Yang, Q. Zou, T. Zhao, P. Chen, Z. Liu, F. Liu and Q. Lin, *ACS Sustainable Chem. Eng.*, 2021, **9**(31), 10437–10443; (*f*) J. Liu, G. Yang, Y. Liu, D. Zhang, X. Hu and Z. Zhang, *Green Chem.*, 2020, **22**(14), 4509–4515.

6 (*a*) L. R. MacGillivray, *Angew. Chem., Int. Ed.*, 2012, **51**(5), 1110–1112; (*b*) M. C. Young, L. R. Holloway, A. M. Johnson and R. J. Hooley, *Angew. Chem., Int. Ed.*, 2014, **53**(37), 9832–9836; (*c*) D. E. Fagnani, M. J. Meese, K. A. Abboud and R. K. Castellano, *Angew. Chem., Int. Ed.*, 2016, **55**, 1–7; (*d*) P. Teng, G. M. Gray, M. Zheng, S. Singh, X. Li, L. Wojtas, A. V. Vaart and J. Cai, *Angew. Chem., Int. Ed.*, 2019, **58**(23), 7778–7782.

7 (*a*) G. A. Williams, R. Ishige, O. R. Cromwell, J. Chung, A. Takahara and Z. Guan, *Adv. Mater.*, 2015, **27**(26), 3934–3941; (*b*) X. Dai, Y. Zhang, L. Gao, T. Bai, W. Wang, Y. Cui and W. Liu, *Adv. Mater.*, 2015, **27**(23), 3566–3571; (*c*) Y. Song, Y. Liu, T. Qi and G. Li, *Angew. Chem., Int. Ed.*, 2018, **57**, 13838–13842; (*d*) L. Su, J. Mosquera, M. F. Mabesoone, S. M. Schoenmakers, C. Muller, M. E. Vleugels, S. Dhiman, S. Wijker, A. R. Palmans and E. W. Meijer, *Science*, 2022, **337**, 213–218.

8 (*a*) V. Ganesh, K. Bodewits, S. J. Bartholdson, D. Natale, D. J. Campopiano and J. C. Mareque-Rivas, *Angew. Chem., Int. Ed.*, 2009, **48**(2), 356–360; (*b*) J. Dong and A. P. Davis, *Angew. Chem., Int. Ed.*, 2021, **60**(15), 8035–8048; (*c*) S. Takahashi, T. Katagiri and K. Uneyama, *Chem. Commun.*, 2005, **29**, 3658–3660; (*d*) S. Tashiro, K. Nakata, R. Hayashi and M. Shionoya, *Small*, 2021, **17**(22), e2005803.

9 (*a*) Y. Wu, X. Mao, M. Zhang, X. Zhao, R. Xue, S. Di, W. Huang, L. Wang, Y. Li and Y. Li, *Adv. Mater.*, 2021, **33**(51), e2106079; (*b*) P. Song and H. Wang, *Adv. Mater.*, 2020, **32**(18), e1901244; (*c*) B. Wang, R. B. Lin, Z. Zhang, S. Xiang and B. Chen, *J. Am. Chem. Soc.*, 2020, **142**(34), 14399–14416; (*d*) S. Feng, Y. Shang, Z. Wang, Z. Kang, R. Wang, J. Jiang, L. Fan, W. Fan, Z. Liu, G. Kong, Y. Feng, S. Hu, H. Guo and D. Sun, *Angew. Chem., Int. Ed.*, 2020, **59**, 3840–3845.

10 (*a*) K. Chen, G. Shi, W. Zhang, H. Li and C. Wang, *J. Am. Chem. Soc.*, 2016, **138**(43), 14198–14201; (*b*) V. K. Singh, C. Yu, S. Badgujar, Y. Kim, Y. Kwon, D. Kim, J. Lee, T. Akhter, G. Thangavel, L. S. Park, J. Lee, P. C. Nandajan, R. Wannemacher, B. Milián-Medina, L. Lüer, K. S. Kim,

J. Gierschner and M. S. Kwon, *Nat. Catal.*, 2018, **1**(10), 794–804; (*c*) W. Yan, Z. Guo, X. Jia, V. Kariwala, T. Chen and Y. Yang, *Chem. Eng. Sci.*, 2012, **76**, 26–36; (*d*) Y. Yao, Z. Liu, P. Xie, Z. Huang, T. Li, D. Morris, Z. Finfrock, J. Zhou, M. Jiao, J. Gao, Y. Mao, J. Miao, P. Zhang, R. Shahbazian-Yassar, C. Wang, G. Wang and L. Hu, *Sci. Adv.*, 2020, **6**, eaaz0510; (*e*) L. Falivene, Z. Cao, A. Petta, L. Serra, A. Poater, R. Oliva, V. Scarano and L. Cavallo, *Nat. Chem.*, 2019, **11**, 872–879.

11 (*a*) C. Seo, S. E. Kim, H. Kim and H.-Y. Jang, *ACS Sustainable Chem. Eng.*, 2022, **10**(17), 5643–5650; (*b*) A. Cervantes-Reyes, K. Farshadfar, M. Rudolph, F. Rominger, T. Schaub, A. Ariafard and A. S. K. Hashmi, *Green Chem.*, 2021, **23**(2), 889–897; (*c*) G. Shi, R. Zhai, H. Li and C. Wang, *Green Chem.*, 2021, **23**(1), 592–596; (*d*) H.-R. Tian, Z. Zhang, S.-M. Liu, T.-Y. Dang, Z. Li, Y. Lu and S.-X. Liu, *Green Chem.*, 2020, **22**(21), 7513–7520.

12 (*a*) J. Li, D. Jia, Z. Guo, Y. Liu, Y. Lyu, Y. Zhou and J. Wang, *Green Chem.*, 2017, **19**, 2675–2686; (*b*) Z. Guo, Y. Hu, S. Dong, L. Chen, L. Ma, Y. Zhou, L. Wang and J. Wang, *Chem. Catal.*, 2022, **2**, 519–530; (*c*) Z. Guo, Q. Jiang, Y. Shi, J. Li, X. Yang, W. Hou, Y. Zhou and J. Wang, *ACS Catal.*, 2017, **7**, 6770–6780.