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Highly Efficient Supramolecular Catalysis by Endowing the Reaction Intermediate with Adaptive Reactivity

Yang Jiao, Bohan Tang, Yucheng Zhang, Jiang-Fei Xu, Zhiqiang Wang, and Xi Zhang*

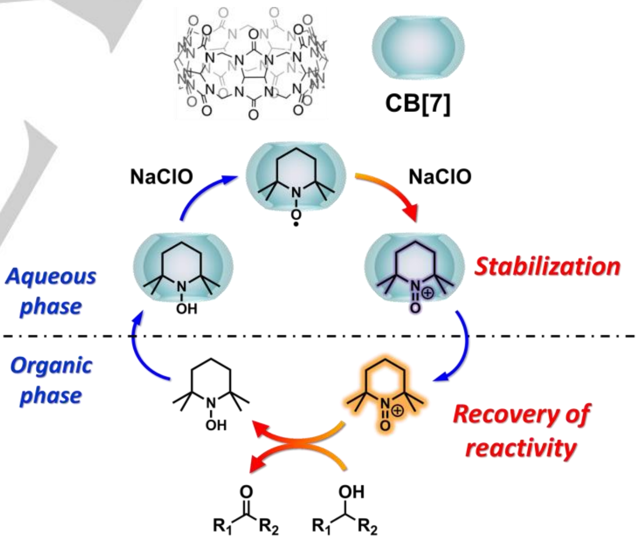
Abstract: A new strategy of highly efficient supramolecular catalysis is developed by endowing the reaction intermediate with adaptive reactivity. The supramolecular catalyst, prepared by the host-guest complexation between 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) and cucurbit[7]uril (CB[7]), was used for biphasic oxidation of alcohols. Cationic TEMPO$^+$, the key intermediate, was stabilized by the electrostatic effect of CB[7] in aqueous phase, thus promoting the formation of TEMPO$^+$ and inhibiting side reactions. Moreover, through the migration into organic phase, TEMPO$^+$ was separated from CB[7] and recovered the high reactivity to drive a fast oxidation of substrates. The adaptive reactivity of TEMPO$^+$ induced an integral optimization of the catalytic cycle and greatly improved the conversion of reaction. This work highlights the unique advantages of dynamic noncovalent interactions on modulating the activity of reaction intermediates, which may open new horizons for supramolecular catalysis.

Supramolecular catalysis is a rapidly expanding discipline aiming to facilitate the chemical reactions by dynamic noncovalent interactions,[1] such as hydrogen bonding, metal-ligand interaction, ion-π interaction and host-guest interactions.[2] During the past decades, various host-guest systems have been designed as supramolecular catalysts to improve the efficiency of reactions in two different ways. On one hand, it is a well-established principle that the host molecule serves as a nanoreactor to encapsulate the substrates in the confined environment and accelerate the reaction.[3] On the other hand, new kinds of host-guest catalysts are developed, which enable the rational modulating on the activity of reaction intermediates by electrostatic effect, steric hindrance and so forth.[4] In spite of the significant advances, there are enormous rooms that deserve to be explored in this line of research.

Reaction intermediates are involved in numerous chemical and biological processes,[5] which mediate the transformation in two steps. The first step is the generation of intermediates from substrates, for which high stability is favorable. The second step is the consumption of intermediates to products, in which high reactivity is desirable. These two steps are in contradiction to some extent, and it is a great challenge for traditional catalysts to balance the stability and the reactivity of intermediates by covalent chemistry.

Supramolecular chemistry could provide a feasible solution owing to the dynamic nature of noncovalent interactions. Herein, we have developed a supramolecular strategy to endow the reaction intermediates with adaptive reactivity for improving the efficiency of reactions. The oxidation of alcohols, a widely employed fundamental reaction in organic synthesis,[6] was chosen as a model system for illustrating this new concept.

A common method for alcohol oxidation[7] employs sodium hypochlorite (NaClO) as the oxidant and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO)[8] as the catalyst to perform the biphasic oxidation of alcohols. As a proposed mechanism, the initial step is the oxidation of TEMPO to the corresponding oxoammonium cation (TEMPO$^+$), which serves as the key intermediate in the catalytic cycle.[6a, 7] Hence, modulating the activity of TEMPO$^+$ is crucial for optimizing the overall process. Since the major drawback is the side reactions of TEMPO$^+$ in aqueous phase,[9] many efforts have been devoted to stabilizing TEMPO$^+$ *via* covalent modification of TEMPO and lowering the operating temperature to 0 °C.[10] Meanwhile, these methods tend to impair the reactivity of TEMPO$^+$ and the subsequent oxidation of alcohol substrates.



Scheme 1. The proposed supramolecular catalytic cycle with TEMPO/CB[7] for promoted biphasic oxidation of alcohols.

To address this issue, we proposed a supramolecular catalytic cycle to endow TEMPO$^+$ with adaptive reactivity by taking advantage of the dynamic property of host-guest interactions and the heterogeneous feature of the oxidation process. As shown in Scheme 1, cucurbit[7]uril (CB[7]),[11] a macrocyclic host with seven carbonyl groups on each portal, was associated with TEMPO to form a supramolecular catalyst. In this way, the redox property of TEMPO could be modulated by the electrostatic effect of the carbonyl groups of CB[7], and thus the oxidation of TEMPO would be faster to generate a more stable TEMPO$^+$ in

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aqueous phase than without the addition of CB[7]. It could accelerate the initial step of the catalytic cycle and avoid the side reactions of $TEMPO^+$. Moreover, owing to the reversible host-guest complexation, $TEMPO^+$ could be dissociated with CB[7] and released into the organic phase as CB[7] is insoluble in the organic solvents. It would lead to the regeneration of free form $TEMPO^+$ and recover its high reactivity to drive a fast oxidation of alcohols. Therefore, the $TEMPO^+$ generated from TEMPO/CB[7] system may possess the combination of the stability in aqueous phase and the reactivity in the organic phase, and thus the adaptive reactivity governed by these two factors would jointly contribute to an promoted catalytic oxidation.

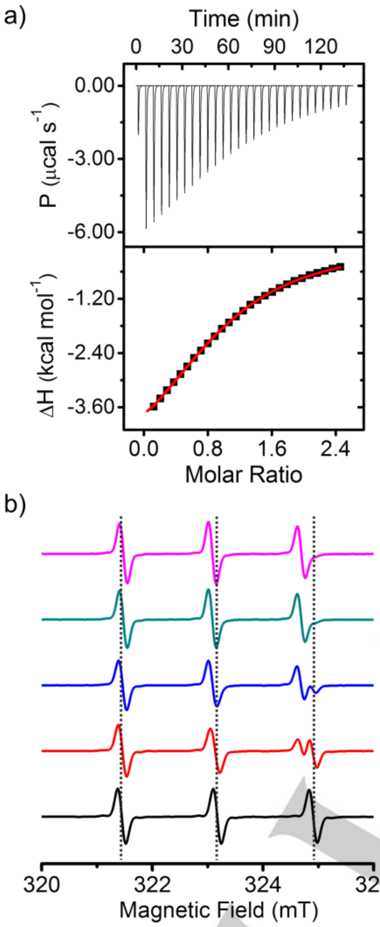

Figure 1. a) ITC data and fitting curves ($NaHCO_3$ buffer, pH = 8.20, T = 25.0 °C) of CB[7] (5.0 mM) into TEMPO (0.5 mM). b) EPR spectra of TEMPO (0.1 mM) with the gradual addition of CB[7] (1:0, 1:0.5, 1:1, 1:2 and 1:3).

The TEMPO/CB[7] supramolecular complex was fabricated conveniently by mixing TEMPO with CB[7] in aqueous solution, as confirmed by isothermal titration calorimetry (ITC) and electron paramagnetic resonance (EPR) spectroscopy. By fitting the ITC data (Figure 1a), the binding stoichiometry between TEMPO and CB[7] was determined to be 1:1, and the binding constant was 3.9×10^3 M^{-1}. In addition, as shown in the EPR spectra (Figure 1b), TEMPO itself displayed a triplet peak at the *g* value of 2.0055 with a hyperfine splitting constant (a_N) of 17.30 G. After the addition of CB[7], the value of a_N had a drastic decrease to 16.07 G, as a consequence of the inclusion of the N-O group of TEMPO by CB[7].[12] It should be noted that more than 1 equiv. CB[7] was needed for the complete formation of the supramolecular complex, corresponding to the moderate affinity between TEMPO and CB[7] as indicated by ITC. This host-guest complexation is driven mainly by the enthalpy effect, that is, the release of high-energy water from the cavity of CB[7]. The moderate affinity is favorable for realizing the adaptive reactivity. Moreover, considering that radicals are sensitive to its microenvironment,[13] the introduction of CB[7] is conceivable to modulate the reactivity of TEMPO radicals.

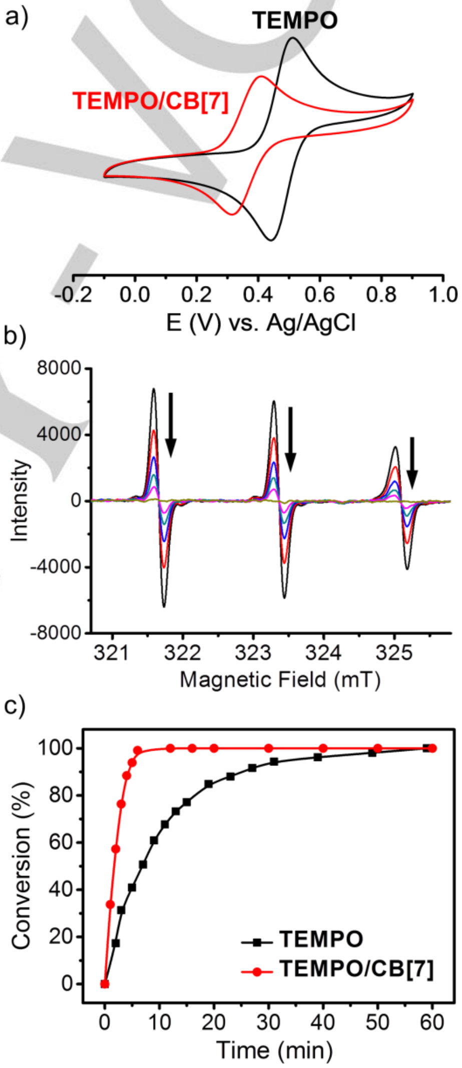

Figure 2. a) Cyclic voltammograms of TEMPO and TEMPO/CB[7] in $NaHCO_3$ buffer. b) The chemical oxidation process of TEMPO/CB[7] in $NaHCO_3$ buffer monitored with EPR spectroscopy. c) Time-conversion curves for the oxidation of TEMPO (■) and TEMPO/CB[7] (●).

Cyclic voltammetry was employed to reveal the effect of CB[7] on the redox property of TEMPO. As shown in Figure 2a, TEMPO underwent a reversible one-electron oxidation to form

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TEMPO$^+$ at a half-wave potential ($E_{1/2}$) of 0.477 V vs. Ag/AgCl. In contrast, the $E_{1/2}$ of TEMPO/CB[7] was 0.362 V, which was 115 mV less positive than TEMPO itself, indicating that TEMPO/CB[7] is easier to be oxidized. The probable mechanism behind this considerable shift of oxidation potential is that CB[7] binds with the oxidized form TEMPO$^+$ more strongly than the reduced form TEMPO (Figure S6), as driven by the additional electrostatic interactions between the cationic TEMPO$^+$ and the carbonyl groups of CB[7].[11b, 11c] It indicates that the electrostatic effect of the carbonyls of CB[7] plays the essential role in lowering the oxidation potential, which may promote the oxidation of TEMPO.

To confirm this assumption, we performed the chemical oxidation of TEMPO and TEMPO/CB[7] with NaClO, and the kinetics was monitored with EPR spectroscopy. In the case of TEMPO, the EPR signals gradually decreased over the time, indicating the consumption of TEMPO radical to form TEMPO$^+$. However, in the case of TEMPO/CB[7], the decrease of the EPR signals was much faster than TEMPO itself (Figure 2b and S2). As shown in Figure 2c, it took 60 min for the complete oxidation of TEMPO, while it took only 6 min for TEMPO/CB[7], 10 times faster than TEMPO itself. Therefore, the introduction of CB[7] can remarkably accelerate the oxidation of TEMPO and the generation of TEMPO$^+$.

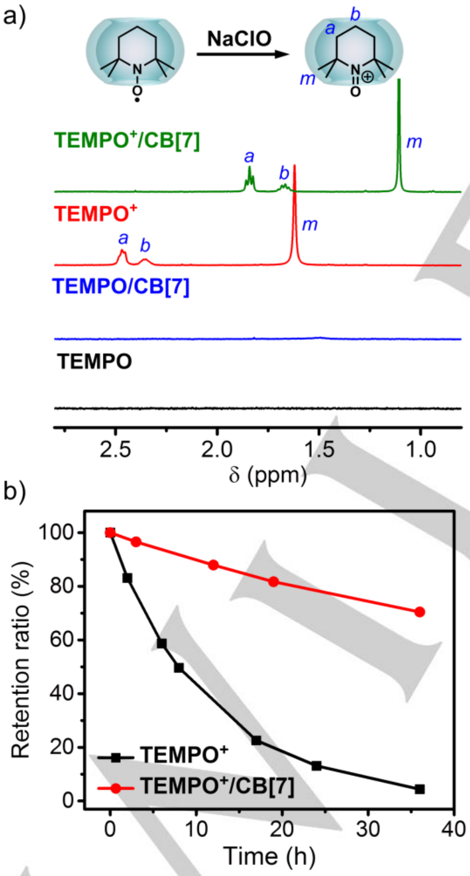

Figure 3. a) Partial ^{1}H NMR spectra (NaHCO$_3$ buffer in D$_2$O, pH = 8.20) of TEMPO, TEMPO/CB[7], TEMPO$^+$ and TEMPO$^+$/CB[7]. The concentrations of the solutions were all 2.0 mM. b) The stability of TEMPO$^+$ (■) and TEMPO$^+$/CB[7] (●) in NaHCO$_3$ buffer monitored by ^{1}H NMR spectroscopy.

^{1}H NMR spectroscopy was used to confirm the formation of TEMPO$^+$ and evaluate its stability in aqueous phase. As shown in Figure 3a, no signals were observed in the ^{1}H NMR spectra of TEMPO or TEMPO/CB[7] because of their paramagnetic properties. After oxidation, three sets of signals appeared as ascribed to the three kinds of protons in TEMPO$^+$. In addition, all the signals shifted upfield in the presence of CB[7], indicating the encapsulation of TEMPO$^+$ by CB[7] to form a host-guest complex. Furthermore, after 2 h, the signals of TEMPO$^+$ completely disappeared, whereas most of TEMPO$^+$/CB[7] remained, suggesting the drastically different stabilities between TEMPO$^+$ and TEMPO$^+$/CB[7] (Figure S3).

To compare the stability of TEMPO$^+$ and TEMPO$^+$/CB[7] at room temperature quantitatively, excess NaClO was added to protect TEMPO$^+$ for monitoring the decrease of NMR signals. As shown in Figure 3b and S4, TEMPO$^+$ was so unstable in aqueous phase that the ^{1}H NMR signals diminished rapidly even with excess NaClO. In this condition, TEMPO$^+$ was consumed in two pathways: the reduction back to TEMPO by water and the side reactions to the products without catalytic activity.[9] Both ways would lower the catalytic efficiency of TEMPO. However, TEMPO$^+$/CB[7] showed a much better stability in aqueous phase, and about 70% of TEMPO$^+$ remained after 36 h at room temperature. It indicates that the life of TEMPO$^+$ is greatly prolonged by the electrostatic effect of CB[7], which is the prerequisite for the subsequent phase transfer and the oxidation of substrates.

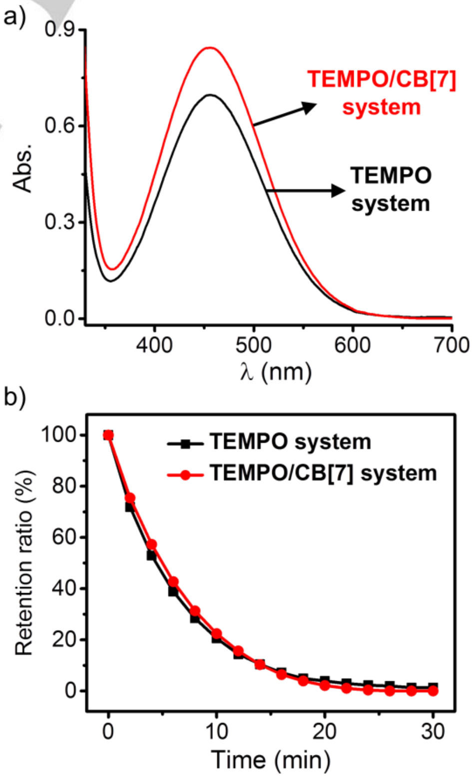

Figure 4. a) UV/Vis spectra of TEMPO$^+$ in CDCl$_3$ solution generated from TEMPO system or TEMPO/CB[7] system. b) The reactivity of TEMPO$^+$ in CDCl$_3$ solution generated from TEMPO system (■) or TEMPO/CB[7] system (●), as indicated by the decrease of absorption peak of TEMPO$^+$ at 455 nm.

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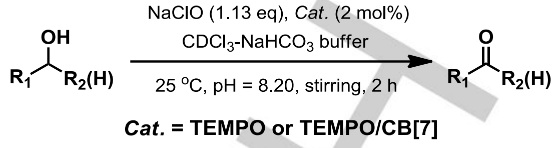
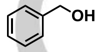
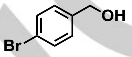
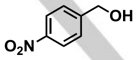
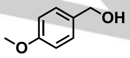
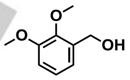
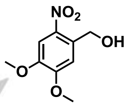
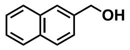
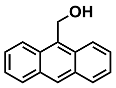
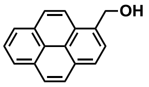
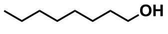
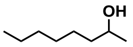
We wondered if TEMPO$^+$ could recover the high reactivity after the migration from aqueous phase to the organic phase. First, to understand whether the encapsulation of TEMPO$^+$ by CB[7] affected the phase transfer behaviors of TEMPO$^+$, the biphasic oxidations of TEMPO and TEMPO/CB[7] were performed in the $CDCl_3$/$NaHCO_3$ buffer system, respectively. After the oxidation, UV/Vis absorption spectroscopy was used to measure the amount of TEMPO$^+$ in the organic phase. As shown in Figure 4a, there existed TEMPO$^+$ in the organic phase for both systems, indicating that CB[7] did not block the phase transfer of TEMPO$^+$. Instead, for the TEMPO/CB[7] system, a more accumulation of TEMPO$^+$ was observed, on account of the faster formation and the higher stability of TEMPO$^+$/CB[7] before the phase transfer. Moreover, as indicated by ^{1}H NMR spectra in Figure S7, TEMPO$^+$ was dissociated with CB[7] during the phase transfer process, since CB[7] is insoluble in the organic solvent.[11a, 14] This event led to the regeneration of free form TEMPO$^+$ and the recovery of its high reactivity. Consequently, these two kinds of TEMPO$^+$ generated from TEMPO system and TEMPO/CB[7] system displayed similar reactivity in the organic phase, both of which could be rapidly consumed to drive the oxidation reaction (Figure 4b). Therefore, benefitting from the dynamic association and dissociation with CB[7], TEMPO$^+$ can be stable enough in aqueous phase and highly reactive in the organic phase. Such adaptive reactivity is likely to promote the overall process of the catalytic oxidation of alcohols.

We explored if a higher catalytic efficiency on the biphasic oxidation of alcohols could be achieved by TEMPO/CB[7] supramolecular catalyst. To this end, the oxidation reactions of a series of alcohols were performed in the $CDCl_3$/$NaHCO_3$ buffer system at room temperature. The conversions of alcohols were determined by ^{1}H NMR analysis of the crude reaction mixture, as summarized in Table 1. Benzyl alcohol as well as benzyl alcohols with different para-substituents (Entry 1-4) could be selectively transformed into the corresponding aldehydes in high efficiencies with TEMPO/CB[7] supramolecular catalyst, while the conversions were just moderate with TEMPO catalyst. We also observed the similar promotion on the oxidation of polysubstituted benzyl alcohols (Entry 5-6). Notably, polycyclic aromatic alcohols, such as 2-naphthalenemethanol, 9-anthracenemethanol and 1-pyrenemethanol (Entry 7-9), displayed a significant improvement of the conversions with TEMPO/CB[7] supramolecular catalyst, from around 30% to more than 90%. TEMPO/CB[7] supramolecular catalyst facilitated the oxidation of aliphatic alcohols as well (Entry 10-11), though the improved conversions were limited. The limitation may result from the inherent low activity of aliphatic alcohols compared with aromatic alcohols.[15]

Therefore, we have achieved a more effective biphasic oxidation of alcohols with TEMPO/CB[7] supramolecular catalyst than traditional TEMPO catalyst. The reaction system is convenient to operate at room temperature and a broad range of alcohols can be transformed in high conversions. This adaptive supramolecular catalytic cycle induced by CB[7] promotes the overall reaction through the following aspects: i) the accelerated generation of TEMPO$^+$, ii) the stabilization of TEMPO$^+$ in aqueous phase, and iii) the recovery of the reactivity of TEMPO$^+$ in the organic phase.

Table 1. Compared biphasic oxidation of alcohols with TEMPO catalyst or TEMPO/CB[7] supramolecular catalyst.



Entry	Substrate	Conversion	
		TEMPO	TEMPO/CB[7]
1		64.8%	91.0%
2		55.6%	94.7%
3		63.9%	94.2%
4		59.0%	97.5%
5		47.4%	93.4%
6		64.4%	92.8%
7		32.4%	96.2%
8		36.7%	90.3%
9		26.5%	99.7%
10		39.9%	64.1%
11		41.2%	73.8%

In conclusion, we have developed a new supramolecular strategy to promote the alcohol oxidation reaction by endowing the reaction intermediate with adaptive reactivity. This facile supramolecular approach is free of the tedious covalent modification of the catalyst. In other words, TEMPO, the commercially available and cheap reagent, can be directly applied to the catalytic reaction at room temperature instead of 0 °C. This line of research represents a demonstration that the dynamic nature of noncovalent interactions is particularly advantageous for the rational modulating on the activity of reaction intermediates and the integral optimization of reaction efficiency. It is anticipated that such a methodology may be extended to other kinds of reactions, thus opening new horizons for highly efficient supramolecular catalysis.

Acknowledgements

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Keywords: supramolecular chemistry • cucurbituril • host-guest systems • TEMPO • supramolecular catalysis

[1] a) P. W. N. M. van Leeuwen, in *Supramolecular Catalysis*, Wiley-VCH Verlag GmbH & Co. KGaA, **2008**; b) J. Meeuwissen, J. N. Reek, *Nat. Chem.* **2010**, *2*, 615-621; c) M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1660-1733; d) M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1734-1787.

[2] a) B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608-6609; b) L. Shi, X. Wang, C. A. Sandoval, M. Li, Q. Qi, Z. Li, K. Ding, *Angew. Chem.* **2006**, *118*, 4214-4218; *Angew. Chem. Int. Ed.* **2006**, *45*, 4108-4112; c) G. Roelfes, B. L. Feringa, *Angew. Chem.* **2005**, *117*, 3294-3296; *Angew. Chem. Int. Ed.* **2005**, *44*, 3230-3232; d) K.-Y. Ye, Q. Cheng, C.-X. Zhuo, L.-X. Dai, S.-L. You, *Angew. Chem.* **2016**, *128*, 8245-8248; *Angew. Chem. Int. Ed.* **2016**, *55*, 8113-8116; e) Y. Liao, Z. Cheng, W. Zuo, A. Thomas, C. F. J. Faul, *ACS Appl. Mater. Interfaces* **2017**, *9*, 38390-38400; f) A. S. Mahadevi, G. N. Sastry, *Chem. Rev.* **2013**, *113*, 2100-2138; g) C. Wang, F. N. Miros, J. Mareda, N. Sakai, S. Matile, *Angew. Chem.* **2016**, *128*, 14634-14638; *Angew. Chem. Int. Ed.* **2016**, *55*, 14422-14426; h) Y. Kang, X. Tang, H. Yu, Z. Cai, Z. Huang, D. Wang, J.-F. Xu, X. Zhang, *Chem. Sci.* **2017**, *8*, 8357-8361; i) P. Zhang, J. Meijide Suarez, T. Driant, E. Derat, Y. Zhang, M. Menand, S. Roland, M. Sollogoub, *Angew. Chem.* **2017**, *129*, 10961-10965; *Angew. Chem. Int. Ed.* **2017**, *56*, 10821-10825.

[3] a) W. L. Mock, T. A. Irra, J. P. Wepsiec, T. L. Manimaran, *J. Org. Chem.* **1983**, *48*, 3619-3620; b) J. Kang, J. Rebek Jr, *Nature* **1997**, *385*, 50; c) C.-H. Tung, L.-Z. Wu, L.-P. Zhang, B. Chen, *Acc. Chem. Res.* **2003**, *36*, 39-47; d) D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem.* **2004**, *116*, 6916-6919; *Angew. Chem. Int. Ed.* **2004**, *43*, 6748-6751; e) M. Yoshizawa, M. Tamura, M. Fujita, *Science* **2006**, *312*, 251.

[4] a) Y. Jiao, W.-L. Li, J.-F. Xu, G. Wang, J. Li, Z. Wang, X. Zhang, *Angew. Chem.* **2016**, *128*, 9079-9083; *Angew. Chem. Int. Ed.* **2016**, *55*, 8933-8937; b) Q. Song, F. Li, Z. Wang, X. Zhang, *Chem. Sci.* **2015**, *6*, 3342-3346; c) Y. Jiao, K. Liu, G. Wang, Y. Wang, X. Zhang, *Chem. Sci.* **2015**, *6*, 3975-3980.

[5] a) C.-X. Zhuo, Q.-F. Wu, Q. Zhao, Q.-L. Xu, S.-L. You, *J. Am. Chem. Soc.* **2013**, *135*, 8169-8172; b) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765-773; c) J. John, J. Thomas, W. Dehaen, *Chem. Commun.* **2015**, *51*, 10797-10806; d) B. Verbelen, S. Boodts, J. Hofkens, N. Boens, W. Dehaen, *Angew. Chem.* **2015**, *127*, 4695-4699; *Angew. Chem. Int. Ed.* **2015**, *54*, 4612-4616; e) Y.-W. Zheng, B. Chen, P. Ye, K. Feng, W. Wang, Q.-Y. Meng, L.-Z. Wu, C.-H. Tung, *J. Am. Chem. Soc.* **2016**, *138*, 10080-10083; f) J. W. Whittaker, *Chem. Rev.* **2003**, *103*, 2347-2364; g) Y. Zhang, X. Zhu, A. T. Torelli, M. Lee, B. Dzikovski, R. M. Koralewski, E. Wang, J. Freed, C. Krebs, S. E. Ealick, H. Lin, *Nature* **2010**, *465*, 891-896.

[6] a) J. M. Bobbitt, C. BrüCkner, N. Merbouh, in *Organic Reactions*, John Wiley & Sons, Inc., **2004**; b) X. Lang, X. Chen, J. Zhao, *Chem. Soc. Rev.* **2014**, *43*, 473-486; c) A. Badalyan, S. S. Stahl, *Nature* **2016**, *535*, 406-410; d) W. R. Leow, W. K. Ng, T. Peng, X. Liu, B. Li, W. Shi, Y. Lum, X. Wang, X. Lang, S. Li, N. Mathews, J. W. Ager, T. C. Sum, H. Hirao, X. Chen, *J. Am. Chem. Soc.* **2017**, *139*, 269-276; e) L.-M. Zhao, Q.-Y. Meng, X.-B. Fan, C. Ye, X.-B. Li, B. Chen, V. Ramamurthy, C.-H. Tung, L.-Z. Wu, *Angew. Chem.* **2017**, *129*, 3066-3070; *Angew. Chem. Int. Ed.* **2017**, *56*, 3020-3024.

[7] P. L. Anelli, C. Biffi, F. Montanari, S. Quici, *J. Org. Chem.* **1987**, *52*, 2559-2562.

[8] a) L. Tebben, A. Studer, *Angew. Chem.* **2011**, *123*, 5138-5174; *Angew. Chem. Int. Ed.* **2011**, *50*, 5034-5068; b) X. Lang, J. Zhao, X. Chen, *Angew. Chem.* **2016**, *128*, 4775-4778; *Angew. Chem. Int. Ed.* **2016**, *55*, 4697-4700.

[9] a) T. Endo, T. Miyazawa, S. Shiihashi, M. Okawara, *J. Am. Chem. Soc.* **1984**, *106*, 3877-3878; b) C. Yang, O. Fontaine, J. M. Tarascon, A. Grimaud, *Angew. Chem.* **2017**, *129*, 8778-8782; *Angew. Chem. Int. Ed.* **2017**, *56*, 8652-8656.

[10] a) M. Shibuya, M. Tomizawa, I. Suzuki, Y. Iwabuchi, *J. Am. Chem. Soc.* **2006**, *128*, 8412-8413; b) S. Hamada, T. Furuta, Y. Wada, T. Kawabata, *Angew. Chem.* **2013**, *125*, 8251-8255; *Angew. Chem. Int. Ed.* **2013**, *52*, 8093-8097; c) M. Rafiee, K. C. Miles, S. S. Stahl, *J. Am. Chem. Soc.* **2015**, *137*, 14751-14757.

[11] a) J. W. Lee, S. Samal, N. Selvapalam, H.-J. Kim, K. Kim, *Acc. Chem. Res.* **2003**, *36*, 621-630; b) J. Lagona, P. Mukhopadhyay, S. Chakrabarti, L. Isaacs, *Angew. Chem.* **2005**, *117*, 4922-4949; *Angew. Chem. Int. Ed.* **2005**, *44*, 4844-4870; c) K. Kim, N. Selvapalam, Y. H. Ko, K. M. Park, D. Kim, J. Kim, *Chem. Soc. Rev.* **2007**, *36*, 267-279; d) K. I. Assaf, W. M. Nau, *Chem. Soc. Rev.* **2015**, *44*, 394-418; e) S. J. Barrow, S. Kasera, M. J. Rowland, J. del Barrio, O. A. Scherman, *Chem. Rev.* **2015**, *115*, 12320-12406; f) J. Li, Y. Zeng, X. Zhang, T. Yu, J. Chen, Y. Li, *Acta Chim. Sin.* **2015**, *73*, 826-834.

[12] a) E. Mezzina, F. Cruciani, G. F. Pedulli, M. Lucarini, *Chem. Eur. J.* **2007**, *13*, 7223-7233; b) D. Bardelang, K. Banaszak, H. Karoui, A. Rockenbauer, M. Waite, K. Udachin, J. A. Ripmeester, C. I. Ratcliffe, O. Ouari, P. Tordo, *J. Am. Chem. Soc.* **2009**, *131*, 5402-5404.

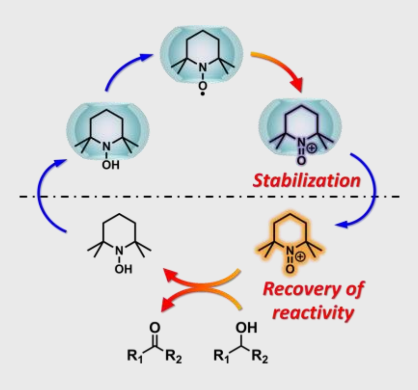
[13] a) S. D. Rychnovsky, R. Vaidyanathan, T. Beauchamp, R. Lin, P. J. Farmer, *J. Org. Chem.* **1999**, *64*, 6745-6749; b) B. M. Mills, N. Fey, T. Marszalek, W. Pisula, P. Rannou, C. F. J. Faul, *Chem. Eur. J.* **2016**, *22*, 16950-16956; c) M. Yan, J. C. Lo, J. T. Edwards, P. S. Baran, *J. Am. Chem. Soc.* **2016**, *138*, 12692-12714.

[14] A. L. Koner, C. Marquez, M. H. Dickman, W. M. Nau, *Angew. Chem.* **2011**, *123*, 567-571; *Angew. Chem. Int. Ed.* **2011**, *50*, 545-548.

[15] a) R. Liu, X. Liang, C. Dong, X. Hu, *J. Am. Chem. Soc.* **2004**, *126*, 4112-4113; b) M. Zhang, C. Chen, W. Ma, J. Zhao, *Angew. Chem.* **2008**, *120*, 9876-9879; *Angew. Chem. Int. Ed.* **2008**, *47*, 9730-9733.

COMMUNICATION

Endowing the intermediate with adaptive reactivity: A highly efficient supramolecular catalysis is developed to promote biphasic alcohol oxidation. Owing to the dynamic host-guest complexation with cucurbit[7]uril, the cationic intermediate is stabilized in aqueous phase and recovers its reactivity in the organic phase. The adaptive reactivity induces an integral optimization of the catalytic cycle and greatly improves the efficiency of reaction.



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