Radical Reactions

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A Supramolecularly Activated Radical Cation for Accelerated Catalytic Oxidation

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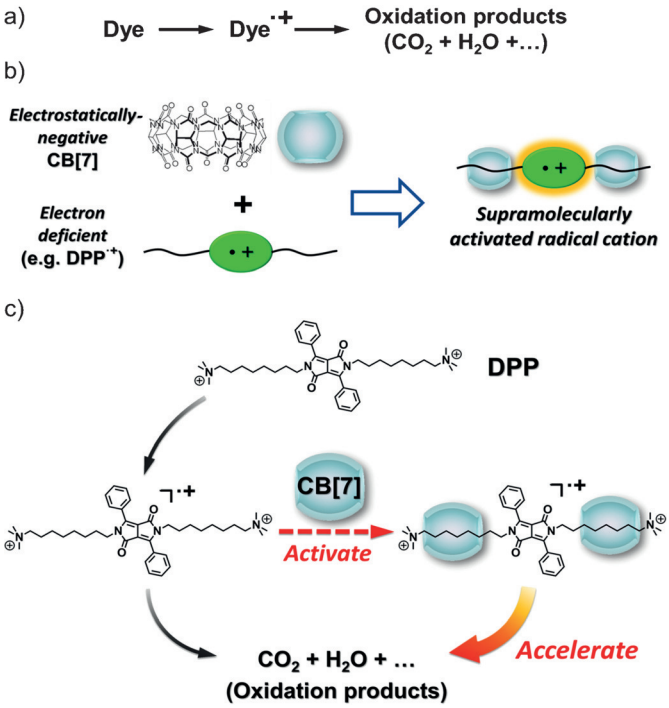
Abstract: *Tuning the activity of radicals is crucial for radical reactions and radical-based materials. Herein, we report a supramolecular strategy to accelerate the Fenton reaction through the construction of supramolecularly activated radical cations. As a proof of the concept, cucurbit[7]uril (CB[7]) was introduced, through host–guest interactions, onto each side of a derivative of 1,4-diketopyrrolo[3,4-c]pyrrole (DPP), a model dye for Fenton oxidation. The DPP radical cation, the key intermediate in the oxidation process, was activated by the electrostatically negative carbonyl groups of CB[7]. The activation induced a drastic decrease in the apparent activation energy and greatly increased the reaction rate. This facile supramolecular strategy is a promising method for promoting radical reactions. It may also open up a new route for the catalytic oxidation of organic pollutants for water purification and widen the realm of supramolecular catalysis.*

Organic radicals, which contain unpaired electrons, are among the most widely studied chemical species. Owing to their open-shell electronic structure, organic radicals are endowed with high reactivity, magnetic properties, and distinctive spectroscopic properties.[1] From this point of view, organic radicals are extremely promising for applications in spin probes[2] and "living" polymerization[3] as well as the development of magnetic materials[4] and optoelectronic materials.[5] Rational tuning and control over the activity of organic radicals is important for their further application. During the past decades, much effort has been devoted to the stabilization of transient radicals[6] for applications in practical material devices. Considering that organic radicals play essential roles in numerous chemical[7] and biological processes,[8] if there is a way to activate radicals, one may find a new route to facilitate reactions and understand the reaction mechanisms.[9] In this regard, additional possibilities of radical reactions may be uncovered and created.

The Fenton reaction refers to the complete oxidation of aromatic compounds by a combination of hydrogen peroxide (H_2O_2) and iron salts, and has found widespread application in the degradation of pollutant dyes in water.[10] As a possible mechanism,[11] the whole oxidation process of dye molecules can be roughly divided into two steps, with the radical cation of the dye acting as the intermediate (Scheme 1 a).[10b,12] Therefore, activation of the radical cation may be a feasible strategy for accelerating the Fenton reaction.



Scheme 1. a) Possible mechanism of the Fenton reaction: a dye radical cation acts as an intermediate. b) Idea behind the design of a supramolecularly activated radical cation. c) Proposed mechanism of an accelerated Fenton reaction.

We wondered if a supramolecular strategy could be employed to activate radical cations, which might further promote radical reactions. As cucurbit[7]uril (CB[7]) is a macrocyclic host bearing seven carbonyl groups on each edge,[13] it is likely that a supramolecularly activated radical cation could be constructed by the association of an electron-deficient radical cation with electrostatically negative CB[7] (Scheme 1 b). This strategy to accelerate the Fenton reaction by improving the activity of radical cations generated during the oxidation process was tested by the use of a derivative of 1,4-diketopyrrolo[3,4-*c*]pyrrole (DPP, a typical kind of fluorescent dye[14]) as a model dye to undergo Fenton oxidation. CB[7] was expected to encapsulate the two alkyl chains of the DPP derivative (referred to simply as "DPP" herein) to form a supramolecular complex through host–guest interactions.[15] Upon the addition of Fenton reagents (a combination of H_2O_2

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and $FeCl_3$ in this study), the generated DPP radical cation should be activated by the electrostatically negative carbonyl groups of CB[7]. Thus, the oxidation rate could be improved by the formation of this more reactive intermediate (Scheme 1c).

The DPP/$(CB[7])_2$ supramolecular complex was fabricated simply by mixing the DPP derivative with CB[7] in water in a molar ratio of 1:2, as confirmed by NMR spectroscopy and isothermal titration calorimetry (ITC). From the ^1H NMR spectra in Figure 1a, we found that upon

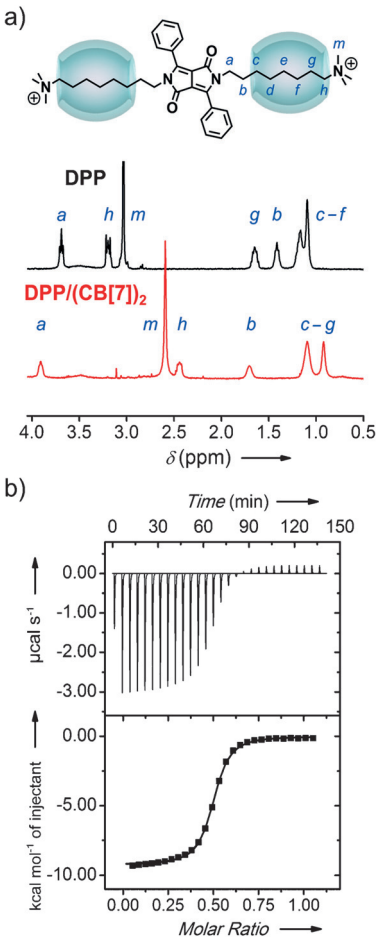

Figure 1. a) Partial ^1H NMR spectra (D_2O) of DPP (1.0 mM) and DPP/$(CB[7])_2$ (1.0 mM). b) ITC data and fitting curve for the titration of DPP (1.0 mM) into CB[7] (0.2 mM).

the addition of 2 equivalents of CB[7], the signals for protons *c–m* near the quaternary ammonium ion underwent upfield shifts as a consequence of inclusion by CB[7]. Meanwhile, the signals for protons *a* and *b* near the amide nitrogen atom underwent downfield shifts, probably as a result of electrostatic interactions with the carbonyl groups of CB[7].[6f,16] We carried out ITC experiments to obtain thermodynamic information about the supramolecular complexation (Figure 1b). A clear and sharp transition appeared at a DPP/CB[7] molar ratio of 1:2, and the binding constant was calculated to be $6.4 \times 10^5\,M^{-1}$ by fitting the data. The combined host–guest interaction and electrostatic interaction between DPP and CB[7] are responsible for the high binding constant, which is strong enough for the formation of a DPP/$(CB[7])_2$ supramolecular complex with a well-defined composition.

To test whether CB[7] could indeed accelerate the Fenton reaction, the kinetics of the Fenton oxidation of DPP and the DPP/$(CB[7])_2$ supramolecular complex were compared. In the case of DPP, the characteristic absorption peak at 460 nm gradually decreased during the oxidation process (Figure 2a). However, in the case of DPP/$(CB[7])_2$, the characteristic

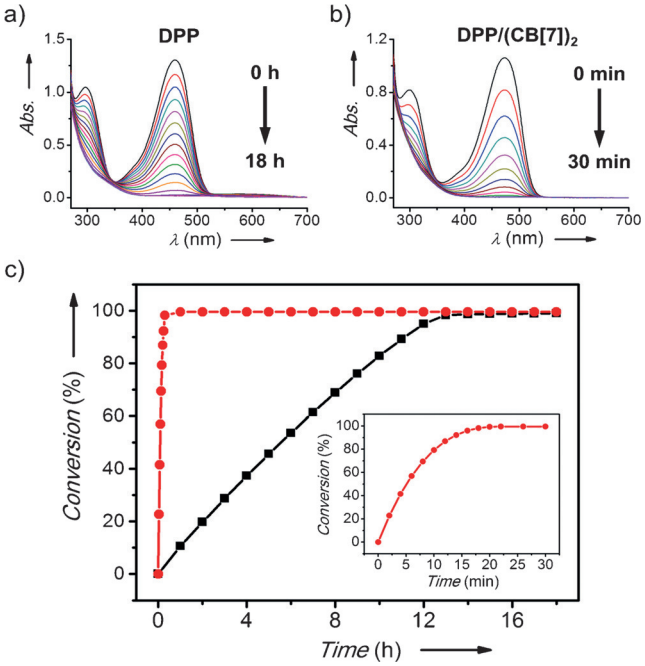

Figure 2. UV/Vis absorption spectroscopy was used to monitor the Fenton oxidation of a) DPP and b) DPP/$(CB[7])_2$ at 25 °C. c) Time–conversion curves of DPP (■) and DPP/$(CB[7])_2$ (●) at 25 °C. Inset: Magnification of the time–conversion curve of DPP/$(CB[7])_2$.

absorption peak at 475 nm decreased much faster (Figure 2b). From the time–conversion relationships in Figure 2c, we found that it took about 14 h for the complete degradation of DPP at 25 °C, whereas it took only 20 min for the DPP/$(CB[7])_2$ supramolecular complex. Therefore, we could conclude that the introduction of CB[7] significantly improved the reaction rate, by a factor as high as 42.

To understand the mechanism behind the accelerated Fenton reaction, we studied the oxidation kinetics of DPP and the DPP/$(CB[7])_2$ supramolecular complex at the same concentration and different temperatures (see Figure S7 in the Supporting Information). The half-life ($t_{1/2}$), obtained from time–conversion curves, was chosen to be the indicator of the reaction rate. The $t_{1/2}$ value for Fenton oxidation is highly dependent on temperature, and thus the apparent activation energy (E_a) can be calculated according to the Arrhenius formula (see the Supporting Information). The E_a value for DPP is 107.8 kJ mol^{-1}, whereas the E_a value for the DPP/$(CB[7])_2$ supramolecular complex is just 84.3 kJ mol^{-1} (Figure 3). This result indicates clearly that supramolecular complexation with CB[7] greatly decreases

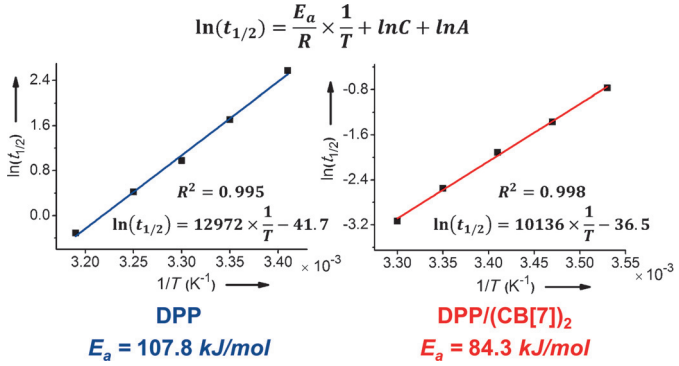

Figure 3. Linear fitting of half-life ($t_{1/2}$) to reaction temperature (T) to give the apparent activation energy (E_a) of the Fenton oxidation of DPP and DPP/(CB[7])$_2$.

the apparent activation energy by 23.5 kJ mol^{-1}, which accounts for the remarkable acceleration of Fenton oxidation.

To confirm the activation effect of CB[7], we investigated the reactivity of the radical cations, the key intermediate, by comparing the concentration evolution of the DPP radical cation and the DPP/(CB[7])$_2$ supramolecular radical cation. For DPP, a broad absorption band ranging from 550 to 700 nm appeared during the oxidation process, along with the decline of the absorption of the DPP chromophore (Figure 4a). This new absorption band corresponding to the absorption of the DPP radical cation (see Figure S12)[17] increased gradually at first and then decayed until the completion of oxidation. The generation of the DPP radical cation was verified by electron paramagnetic resonance (EPR) spectroscopy. A typical EPR signal with $g = 2.0031$ was observed and ascribed to the DPP radical cation (see Figure S10).[18]

Different phenomena were observed during the oxidation of the DPP/(CB[7])$_2$ supramolecular complex. Throughout the oxidation process, the concentration of the DPP/(CB[7])$_2$ supramolecular radical cation remained at a very low level (Figure 4b), never exceeding 2% of the maximum concentration of the DPP radical cation in a normal Fenton oxidation. Moreover, similar behavior was observed in EPR spectra. In contrast to the typical EPR signal of the DPP radical cation, the concentration of the DPP/(CB[7])$_2$ supramolecular radical cation was too low to give an explicit EPR signal with a high enough signal-to-noise ratio (Figure 4c). These results indicate that the DPP/(CB[7])$_2$ supramolecular radical cation is distinctly less accumulated during the oxidation process. This low accumulation may result from: I) slowing down of the radical-generation step, or II) speeding up of the radical-consumption step. Considering the acceleration of the overall reaction, we believe that the latter is the more probable cause, whereby the reactivity of the DPP radical cation is greatly improved by the supramolecular complexation of CB[7].

The above comparisons came from two parallel reaction systems, that is, the oxidation of either DPP or the DPP/(CB[7])$_2$ supramolecular complex. It was important to investigate whether CB[7] could activate the DPP radical cation directly. For this purpose, CB[7] (2 equiv) was added half-way through the Fenton oxidation of DPP. Interestingly, we found that the amount of the accumulated radical cation decreased rapidly as soon as CB[7] was added (Figure 4d). This phenomenon, which we called "in situ activation", is a further and more solid confirmation of the formation of a supramolecularly activated radical cation. Notably, the activated radical cation leads to two opposite effects on the Fenton reaction: The first step leading to the radical cation as

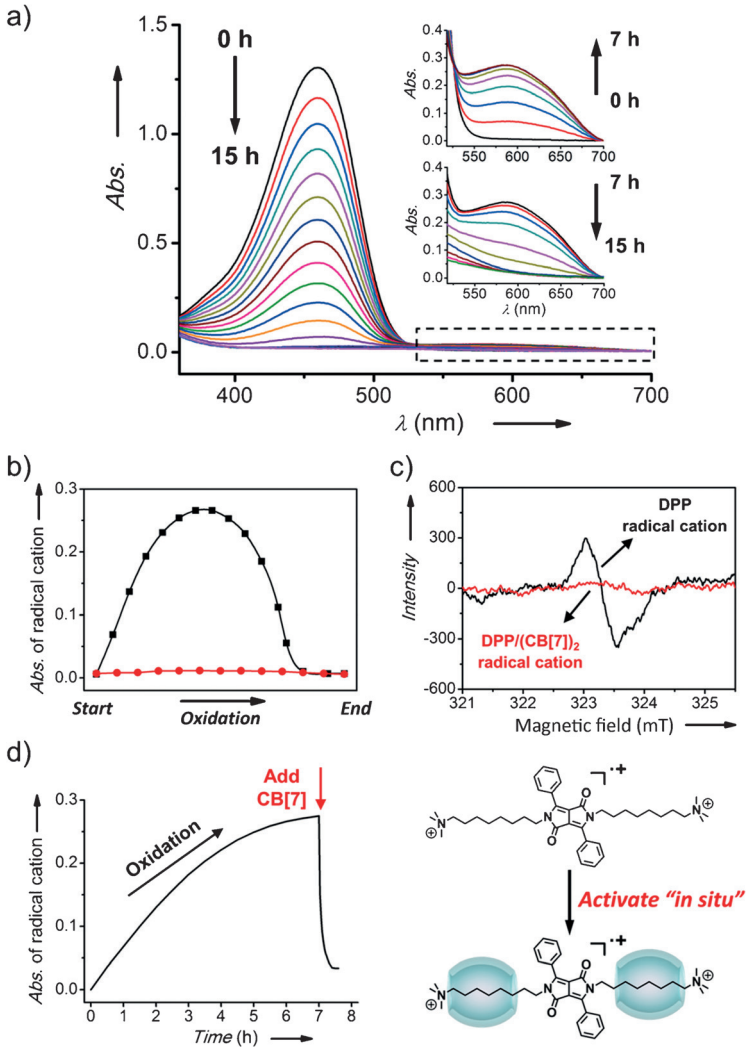

Figure 4. a) UV/Vis absorption spectroscopy was used to monitor the changes in the species present during the Fenton oxidation of DPP. Insets: Magnification of the region marked with a dashed box. b) Evolution of the concentration of the DPP radical cation (■) and the DPP/(CB[7])$_2$ supramolecular radical cation (●) throughout the oxidation process. c) EPR spectra of the DPP radical cation and the DPP/(CB[7])$_2$ supramolecular radical cation after half of the total reaction time of the oxidation process. d) Activation of the DPP radical cation by CB[7] "in situ": CB[7] was added after 7 h during the Fenton oxidation of DPP.

a product would be hindered to some extent, whereas the second step with the radical cation as a reactant would be promoted. Since the overall reaction is greatly accelerated, it is conceivable that the second step is the rate-determining step. Therefore, as a more reactive intermediate, the DPP/$(CB[7])_2$ supramolecular radical cation can lower the activation energy of the second step, thus inducing a drastic decrease in the apparent activation energy of the Fenton reaction.

To elucidate the nature of the supramolecular activation of the DPP radical cation by CB[7], we performed DFT calculations to obtain charge and spin densities (see the Supporting Information for computational details). According to the "free valence" index,[19] a measure of the localization degree of free spins in conjugated systems dictates the reactivity of π radicals. The calculated Mulliken spin-density distributions of the DPP radical cation and the DPP/$(CB[7])_2$ supramolecular radical cation are depicted in Figure 5 (see Table S2 in the Supporting Information for specific spin-

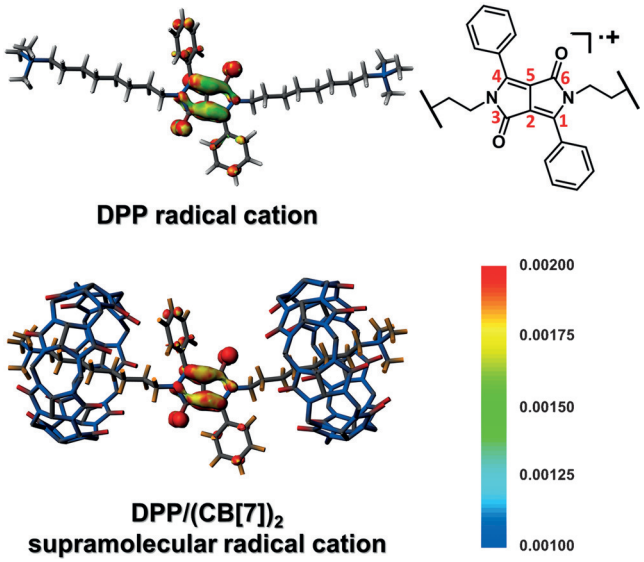

Figure 5. Spin-density distribution of the DPP radical cation (top) and DPP/$(CB[7])_2$ supramolecular radical cation (bottom).

density values for each relevant carbon atom). The DPP radical cation, a typical π radical, tends to delocalize the single electron over a conjugated range, so the spin densities of the six aromatic carbon atoms (C1–C6 as numbered in Figure 5) are averaged relatively. Upon supramolecular complexation by CB[7], spin density localized on C1 and C2 (or C4 and C5) is enhanced, and there is less spin density on C3 (or C6). Consequently, compared with the DPP radical cation, the single electron of the DPP/$(CB[7])_2$ supramolecular radical cation is more localized, and the degree of localization is increased, thus inducing a more reactive radical system.[20] Moreover, as a result of the change in spin distribution, the C=C bond between C1 and C2 (or C4 and C5) has higher electron density, which probably facilitates the oxidative cleavage of the C=C bond and the Fenton degradation of the DPP aromatic system.

In conclusion, we have developed a supramolecular strategy to accelerate the Fenton reaction through the construction of a supramolecularly activated radical cation. Through the host–guest complexation between CB[7] and a derivative of the dye DPP, the activity of the oxidation intermediate, the DPP radical cation, was improved greatly owing to the electrostatically negative carbonyl groups of CB[7], thus inducing a decrease in the apparent activation energy and significant promotion of the reaction rate. This supramolecular approach is facile and highly efficient, and may be extended to other kinds of radical reactions. It is anticipated that this line of research could open up a new route for the catalytic oxidation of organic pollutants for water purification and could widen the realm of supramolecular catalysis.

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Keywords: cucurbiturils · host–guest systems · radical cations · self-assembly · supramolecular chemistry

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