Addition reactions of singlet oxygen to olefins have been the subject of inquiry since the discovery of singlet oxygen by Kautsky over a century ago. This report concerns ene reactions yielding allylic hydroperoxides, a process involving addition of singlet oxygen to C=C bonds and simultaneous abstraction of an allylic hydrogen. When there is more than one set of allylic hydrogens in a given olefin, multiple allylic hydroperoxides are produced. Due to the difficulties in controlling small and highly reactive singlet oxygen, it has not been possible to control the regioselectivity or reactions upon unhindered olefins such as methyl cycloalkenes. A few years ago, we disclosed that preferential abstraction of hydrogen from the methyl group of methyl cycloalkenes could be achieved by preorganizing the olefin through cation–π interactions within zeolites, and this has been confirmed by several other groups. In this report, we show that the abstraction of methyl hydrogen by singlet oxygen can be eliminated by encapsulating the methyl cycloalkenes within a water-soluble, deep-cavity cavatand, octa acid (OA, Figure 1). This study was prompted by our realization that the methyl group of these guests can be used to anchor and hence orient the olefin within the cavity of OA, and hence supramolecular steric hindrance could be used to prevent singlet oxygen from approaching the methyl group. We have achieved this goal, and the results are presented in this report.

Since the host–guest complexation behavior and the product selectivity for ene reaction in 1-methyl cyclopentene (1a), 1-methyl cyclohexene (1b), and 1-methyl cycloheptene (1c) (Scheme 1) are identical, we discuss the results using 1b as the model. Addition of 1 equiv of OA to a turbid aqueous borate buffer (pH ~8.9) solution containing 1 mM of the olefin resulted in a clear solution, suggesting it had been solubilized by complexation within OA. A 1H NMR titration study of this complex confirmed a 1:1 ratio of the host and guest (Figure 1), while pulse field gradient spin echo diffusion experiments revealed the complex to be a quaternary, 2:2 capsular complex (Supporting Information). Complexation within the capsule resulted in significant upfield shifting of the guest signals (relative to CDCl3). The most significantly shifted guest signal was from the methyl groups (~4.3 ppm), indicating that they are each anchored at the narrowest part of each cavity. Upfield shifting and 2D 1H NMR experiments (Supporting Information) suggested that, of the three sets of allylic hydrogens in the guest, H3 (Figure 1) would be most accessible and H7 (methyl) would be the least accessible to any reagent entering the capsule at the equator. This model suggested that, whereas in chloroform yields three hydroperoxides (Scheme 1), a single hydroperoxide should predominate with included within the OA capsule.

We believe that space-filling is primarily behind guest orientation, although weak C–H···π interactions between the C–H of the methyl group and the π-electrons of the cavity wall are also likely contributors to this orientational isomerism. To test the above model, oxidation of 1a,b,c included within OA was performed by generating singlet oxygen in aqueous borate buffer by using either water-soluble Rose Bengal (RB) or water-insoluble dimethyl benzil (DMB) as the sensitizer (Scheme 1). In the latter case, DMB was itself encapsulated within a capsule of dimeric OA. Generation of singlet oxygen by RB and OA encapsulated DMB was confirmed by directly monitoring the emission from singlet oxygen upon excitation of
the sensitizers (Supporting Information). Lifetime measurements of singlet oxygen generated by DMB@OA 2 in H 2 O and D 2 O solutions (5 and 41 µs, respectively; Supporting Information) suggested that singlet oxygen spends most of its lifetime in the aqueous medium. 19 The oxidation studies were performed by irradiating (>500 nm) RB in 1 mM D 2 O solution of 1b@OA 2 under oxygen atmosphere for 10 min (conversion 60–70%). In the alternate method, a buffer solution containing equal amounts of DMB@OA 2 (5 mM) and 1b@OA 2 (1 mM) was irradiated (>310 nm, 4 h). NMR analysis revealed that the mixing of these two capsular complexes did not result in the formation of the mixed capsule DMB·1b@OA 2 (Supporting Information). The hydroperoxides formed in the reaction were stable for weeks in aqueous medium as long as they remained within the OA capsule. The hydroperoxides were extracted with CDCl 3 and characterized by 1 H NMR. Product distribution was estimated by GC after reducing the hydroperoxides to alcohols with excess triphenyl phosphine. The mass balance, monitored by an external standard, was above 90% in all cases. Product distributions for OA-encapsulated species and free alkene in acetonitrile are listed in Scheme 1. Clearly the observed product selectivity for the former is consistent with the expectation that the least hindered allylic hydrogen H 3 would be abstracted by singlet oxygen. To ensure that the observed selectivity was not due to selective extraction of 4b, the three peroxides 2b, 3b, and 4b obtained from solution irradiation were included within OA and extracted without any change in the ratio.

While sensitization of oxygen by RB was expected, it is significant that DMB@OA 2 was able to generate singlet oxygen that could regioselectively oxidize the olefin. To probe this further, the following photophysical studies were performed. We estimated the rate constant for oxygen-induced quenching of * 3 DMB@OA 2 by monitoring the phosphorescence and T→T* absorption of * 3 DMB with respect to oxygen concentration. It is important to note that the quenching constants obtained by the two methods were gratifyingly close (7.9 × 10 7 and 8.7 × 10 7 M −1 s −1 , respectively; Supporting Information). In addition, we note that the rate constants are an order of magnitude smaller than the diffusion rate constant in solution (~10 2 M −1 s −1 ) yet are very much higher than the rate of energy transfer between biacetyl/hemicarcerand triplet and oxygen (~1 × 10 6 M −1 s −1 ). 20–22 In the latter case, the energy transfer is believed to occur through the walls of the hemicarcerand.

We suggest that the larger rate constant observed in this study excludes such a “through the host wall” mechanism. Presence of rise time in the singlet oxygen phosphorescence kinetic profile (τ = 30 µs; Supporting Information) shows the quenching to be dynamic rather than static. On the basis of the above arguments, we suggest that the measured quenching rate constant represents the opening and closing of the capsule that controls the rate at which oxygen can access DMB. The ability to generate singlet oxygen by DMB@OA 2 is due to the fact that the rate of capsule opening and closing is able to compete with the decay of * 3 DMB@OA 2 (τ = 596 µs). Consistent with the prediction that *sensitizers@OA 2 with shorter lifetime would be unable to generate singlet oxygen, we find that the fluorescence and S 1 lifetime of pyrene@OA 2 (τ = 340 ns) and phenanthrene (τ = 50 ns) were affected only to a small degree by oxygen. We believe that, in addition to the lifetime, the nature of the guest would play a role in the capsule opening–closing process.

The overall mechanism as we visualize it is illustrated in Scheme 2. This model is based on the observation that DMB@OA 2 and 1b@OA 2 when mixed together do not undergo exchange and remain as independent capsules. The important steps in the oxidation process are (a) generation of * 3 DMB, (b) capsule opening, establishment of contact between oxygen and * 3 DMB, and energy transfer, (c) exit of singlet oxygen from DMB@OA 2 to aqueous medium, and (d) entry of singlet oxygen to 1b@OA 2 and regioselective oxidation. Further explorations underway in our laboratory will help us fine-tune the understanding of this unprecedented regioselective oxidation of olefins in water, as are other investigations into the use of supramolecular protection strategies to control photoreactions. 23,24

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Supporting Information Available: Experimental details, NOESY and TOCSY spectrum of 1b@OA, photophysical plots, and 1 H NMR of heterocapsules. This material is available free of charge via the Internet at http://pubs.acs.org.

References


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