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Light-Driven Catalysis within Dendrimers: Designing Amphiphilic Singlet Oxygen Sensitizers

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In the attempt to mimic nature and design more complex molecular devices, dendrimers[1] represent a unique class of artificial building blocks due to their structural uniformity, multivalency, and large variation of chemical composition.[2] The concept of utilizing dendrimers as nanoreactors has received considerable attention over the past years since advantages of homogeneous and heterogeneous catalysis can be combined, in particular, precise control over the reactive site and catalyst recyclability, respectively. Two opposite approaches have been explored, namely the attachment of catalytic sites at the periphery of a dendrimer[3] as well as the placement of the active site at the core.[4] The latter design traditionally suffered from the increasingly difficult mass transport in higher-generation dendrimers. However, our group has recently overcome this problem by designing an amphiphilic dendritic system capable of efficiently catalyzing an elimination reaction.[5] This catalytic "pump" is based on the slight change in polarity that results from the chemical transformation of an alkyl halide into an alkene. It utilizes the contrasting polar inner and nonpolar outer environments of a dendrimer to preferentially accumulate substrates and stabilize transition states and intermediates in the interior, while simultaneously expelling the product to the exterior, thereby preventing inhibition. Intrigued by these promising findings and in view of our recent success with highly efficient light-harvesting dendrimers,[6] we sought to expand the scope of our approach to photoreactions. Here, we present the first results on light-driven catalysis at the core of the dendrimers, utilizing the concepts of amphiphilic design and photosensitization.

Our system is based on the large polarity difference between substrate and product in the [4 + 2]cycloaddition of singlet oxygen[7] ($^{1}O_2$) to dienes with subsequent reduction to the allylic diol.[8] By encapsulating a $^{1}O_2$-sensitizing core into a globular dendrimer[9] having a hydrophobic interior and hydrophilic surface dissolved in a polar solvent a nanoscale photoreactor is created. To minimize free energy the hydrophobic substrate will be concentrated near the nonpolar core, where the reagent $^{1}O_2$ is photogenerated, while the subsequently formed polar product will migrate to the polar solvent (Figure 1). The high internal substrate concentration and enhanced lifetime of $^{1}O_2$ in the hydrophobic environment[7] of the core constitute a favorable combination for this bimolecular reaction.

An *o,o′,p,p′*-tetraalkoxybenzophenone core was chosen as the sensitizing core because of its multiple points for dendron attachment and availability. In addition, both the quantum yield for generation of $^{1}O_2$ and the wavelength of absorption increase upon introduction of electron-donating groups into the system.[10] An aliphatic polyester backbone based on 2,2-bis(hydroxymethyl) propionic acid[11] was selected due to its oxidative robustness and convenient synthesis via a recently developed divergent route.[12]

The model reaction, involving formation of *cis*-2-cyclopentene-1,4-diol **3** from cyclopentadiene **1** and therefore an extreme polarity change (Scheme 1), was chosen due to (i) the intrinsically fast cycloaddition,[13] that originates from the fixed s-cis configuration of the diene and minimizes competing pathways such as [2 + 2]cycloaddition and ene-reaction, and (ii) the very short lifetime of the initially formed endoperoxide **2**.[14] Furthermore, thiourea has been widely used for the chemoselective reduction of endoperoxides and does not affect ester linkages.[15] Interestingly, **3** is usually synthesized via a similar route using Rose Bengal as the sensitizer[16] and represents an important intermediate in some synthesis of prostaglandins.[17]

To avoid phenolic ester linkages, that might alter the core's photophysical characteristics[18] and give rise to detrimental side reactions such as Photo-Fries rearrangements, 2,2′,4,4′-tetrahydroxybenzophenone was first alkylated using 11-bromo-1-undecanol, a spacer that also provides increased interior hydropho-

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(18) The UV/vis absorption spectra of **6b**, **7b**, **8b**, and **9** are virtually identical with 2,2′,4,4′-tetramethoxybenzophenone.

10.1021/ja016076s CCC: $20.00

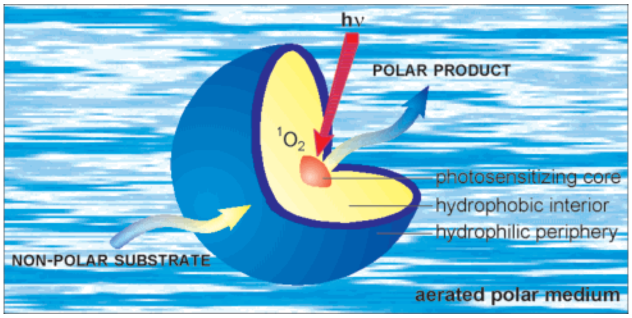
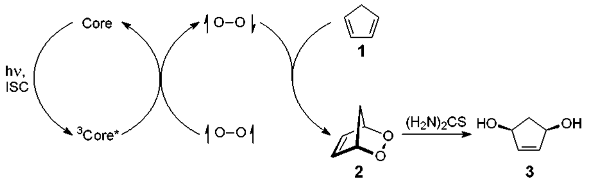
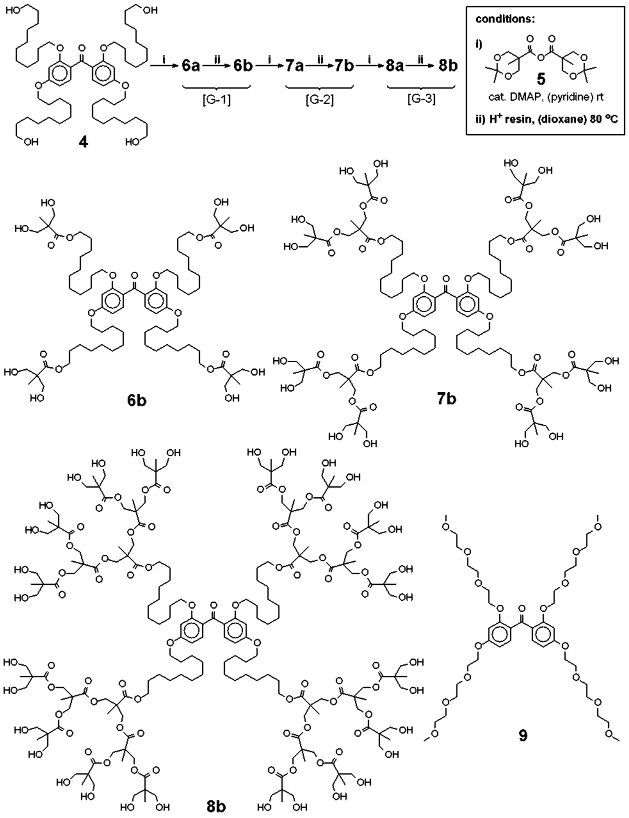


Figure 1. Illustration of the concept of excited-state catalysis using an amphiphilic singlet oxygen sensitizer.

Scheme 1



Scheme 2



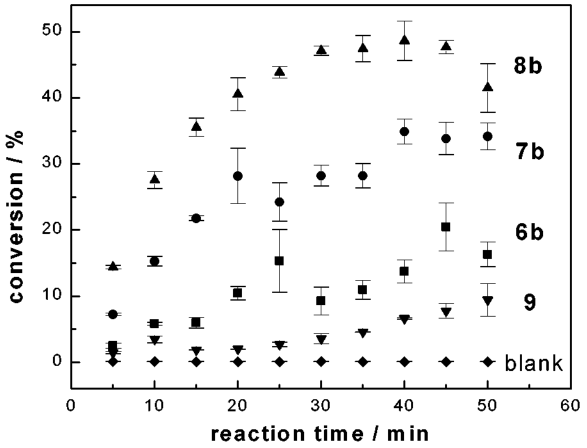


Figure 2. Conversion (formation of **3** normalized over initial concentration of **1**) as a function of reaction time for catalysts **6b**, **7b**, **8b**, model compound **9**, and in the absence of catalyst. Conditions: [**3**]:[thiourea]:[catalyst] = 1:0.7:0.001 in CH$_3$OH.[19]

bicity, to afford **4** (Scheme 2). A slight alteration of the existing dendrimer construction protocol,[12] that utilized benzylidene-protecting groups, was necessary since the benzophenone core was not compatible with the hydrogenolysis deprotection conditions. Hence, anhydride **5** was employed as acylating agent, and deprotection was accomplished using acidic conditions. Repetition of the sequence afforded hydroxyl-terminated first-, second-, and third-generation dendrimers **6b**, **7b**, and **8b**. For comparison purposes we prepared model compound **9** with polar surface etherification of 2,2′,4,4′-tetrahydroxybenzophenone with tri(ethylene glycol) monomethyl ether.

Photocatalysis experiments employing 0.1 mol % of the different generation catalysts **6b**, **7b**, **8b** as well as model compound **9** were performed, and the production of **3** was monitored (Figure 2). Although detailed kinetic analysis is complicated due to the inherent complexity of the system, relative reactivity trends can be deduced, and it can clearly be seen that higher generation dendrimers lead to faster reactions and higher levels of conversion. Model compound **9**, on the contrary, displayed rather low catalytic activity, while control experiments employing no catalyst showed negligible background reactions. Obviously, the size of the hydrophobic container is crucial for improved catalyst performance. We reason that the observed behavior is primarily due to the increased *local* concentrations of substrate as well as $^1O_2$, however solvation and solubility effects might also be operating. Notably, the catalysts exhibited good photostability since less than 10% decomposition occurred during the reaction, based on UV/vis absorbance.

In addition to more detailed studies regarding the actual mechanism, solvent effects,[20] and product selectivity using acyclic dienes,[21] we are currently investigating the incorporation of more efficient photosensitizers and donor chromophores as well as the construction of larger molecular containers by accelerated strategies.[22]

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Supporting Information Available: Experimental details and chemical characterization data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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