2009

Singlet Oxygen Delivery Through the Porous Cap of a Hollow-Core Fiber Optic Device

Matibur Zamadar
Stephen F Austin State University, zamadarmr@sfasu.edu

David Aebisher

Alexander Greer

Follow this and additional works at: http://scholarworks.sfasu.edu/chemistry_facultypubs

Part of the Analytical, Diagnostic and Therapeutic Techniques and Equipment Commons, and the Chemistry Commons

Tell us how this article helped you.

Recommended Citation
Zamadar, Matibur; Aebisher, David; and Greer, Alexander, "Singlet Oxygen Delivery Through the Porous Cap of a Hollow-Core Fiber Optic Device" (2009). Faculty Publications. Paper 27.
http://scholarworks.sfasu.edu/chemistry_facultypubs/27

This Article is brought to you for free and open access by the Chemistry and Biochemistry at SFA ScholarWorks. It has been accepted for inclusion in Faculty Publications by an authorized administrator of SFA ScholarWorks. For more information, please contact cdsscholarworks@sfasu.edu.
Singlet Oxygen Delivery Through the Porous Cap of a Hollow-Core Fiber Optic Device

Matibur Zamadar, David Aebisher, and Alexander Greer*
Department of Chemistry and Graduate Center, City University of New York, Brooklyn College, Brooklyn, New York 11210

Received: August 17, 2009; Revised Manuscript Received: October 13, 2009

The development of the first photosensitizer/fiber optic device is reported. An oxygen-flowing, fiber-capped configuration is used for the application of heterogeneous, spatially confined singlet oxygen delivery in aqueous media. This is a unique device, unlike other heterogeneous photosensitizers, in which local concentrations of singlet oxygen can be delivered via introduction and withdrawal of the fiber tip.

Introduction

In 2008, we reported a photochemical approach to the clean generation of singlet oxygen in aqueous solution with a porous glass sensitizer [meso-tetra(N-methyl-4-pyridyl)porphine 1] adsorbed onto porous Vycor glass (PVG).1,2 The porous glass sensitizer involved oxygen “collision” onto the matrix for the conversion of ground-state O2 into 1O2, reflecting 1O2 diffusion into the bulk aqueous solution (Scheme 1).2 Singlet oxygen was detected in water by time-resolved methods or reaction with an alkene molecule to give a hydroperoxide.3 Our attention to a porous glass sensitizer stemmed from a desire to fix the photosensitizer to the end of a hollow fiber optic through which O2 flows to “deliver” singlet oxygen site selectively on the microscale. Few reports have appeared on heterogeneous sensitizers coupled to fiber optics4-7 or the production of singlet oxygen by heterogeneous sensitizers in water.8,9 Clearly, at present, methods that generate singlet oxygen are not coupled into maneuverable delivery devices. We report here the first study of a hybrid sensitizer/fiber optic device for singlet oxygen generation at the fiber tip. The prototype device is based on micro-optic technology10 for localizing singlet oxygen in water and has the potential for use in cancer treatment and in water disinfection.

Results and Discussion

The singlet oxygen fiber device consisted of a porous Vycor cap coated with compound 1 (see Scheme 1) as sensitizer placed on the end of a hollow core photonic bandgap fiber. Compressed oxygen was delivered through the core of the fiber to the cap and into water solutions containing N-benzoyl-DL-methionine anion (0.02 M) as an indirect method to analyze singlet oxygen production. Oxygen flowed through the fiber, and irradiation with 532-nm laser light focused into the proximal end of the fiber led to the sulfoxide as the only product at the distal end in water. The same product was observed in D2O and in H2O. The experimental evidence suggesting the viability of the device in Scheme 2 includes the following: A hollow core photonic bandgap fiber HC-580 (capable of transmitting 520-630 nm light, core diameter of 4.9 µm, acrylate coating diameter of 220 µm) was coupled to a green LED or a 10-Hz Nd:YAG laser operating at 532 nm. The equation from Gaussian optics for the focal length with optimum mode matching the single-mode HC-580 fiber accounts for the preferred use of a 10× objective.11

A Newport laser-to-fiber coupler with 0.1-µm x-y-z translation resolution aligned the microscope objective to focus green light into the optical fiber, and a Teflon-lined fiber chuck upon tightening accommodated the 220-µm fiber. The 532-nm beam exiting the distal end of the 30-cm length of fiber was 0.15 mW (LED) and 0.11 mJ/pulse (Nd:YAG). The intensity of the light exiting the fiber is a function of its length. The attenuation is ~1 dB/m, and bending the fiber does not increase the attenuation noticeably.

Previous studies of gas and light passage through hollow optical fibers12,13 suggested that ground-state O2 could be delivered through our HC-580 fiber. A 406-µm channel was mechanically drilled through one side of a polystyrene cuvette (10 mm light path length, 12.5 mm × 45 mm) using a micro diamond-head drill. The fiber was inserted into a ferrule collar glued into the hole in the cuvette with ethyl cyanoacrylate glue, where a 2-mm segment of the fiber protruded into the center of the cuvette (Figure 1A, B). The cuvette was placed into the center of the laser-to-fiber coupler, where the 532-nm beam passes through the opposite (unmodified) side of the quartz cuvette and entered the fiber (Figure 1B). A 3-mm hole was

* E-mail: agreer@brooklyn.cuny.edu.
drilled into the square polytetrafluoroethylene cuvette cover (12.5 mm²) glued to the cuvette. A plastic 200 µL pipet tip was inserted to about 1/4 of its length and glued in place. The top of the cuvette was connected to an oxygen tank, where compressed oxygen flowed at 40 PSI into the cuvette. The flow rate of oxygen through the uncapped hollow fiber was 0.12 mL/hour.

The end of the hollow fiber was capped with the porous glass photosensitizer \(3 \times 10^{-7}\) mol sensitizer \(1\) was adsorbed onto 0.013-g preshaped PVG (dimensions: 3 mm² × 0.8 mm). The fiber acrylate coating was not removed so that the intensity of light was the same at the source and at the fiber-PVG junction.

The colorless PVG cap was converted to deep red or black on adsorption of \(\text{O}_2\). About 0.5% of the cap surface was covered with photosensitizer, and the photosensitizer remained adhered to the cap in contact with water.\(^1\,\,^2\) No desorption of \(1\) from PVG was observed at pH 3, 7, and 10. Photobleaching of the fiber cap with the 5 mW laser was not evident up to 30 h of irradiation. Cap samples could be ground down to 0.6 mm, but any thinner led to cap leaking or cracking.

A hole with the dimensions 2.38 mm × 0.38 mm was drilled length-wise into the sensitizer-coated porous silica cap (Figure 2). The fiber was inserted into the cylinder hole and glued into place at the hole entrance. As desired, water did not fill the cap hole; neither did water fill the hollow fiber by capillary action. Excitation occurred by scattering of the light through the cap and absorption of the radiation by the sensitizer adsorbed to the surface. The sensitizer-coated surface faced the bulk solution, and \(\text{O}_2\)

transport occurred by a pressure gradient, diffusing through the membrane cap; bubbles effused slowly. Parts per million oxygen delivered to a 100-µL water sample via the fiber-compressed oxygen tank system in Figure 2 was determined with a \(p\text{O}_2\) micro-oxygen electrode (Table 1). The capped fiber flowed \(\text{O}_2\) about 20 times slower than the uncapped fiber. Other researchers have also demonstrated the transportation of gases through porous Vycor glass.\(^1^4\)\(^\text{-}^1^7\)

The experimental evidence suggested that singlet oxygen exited the distal end of the cap of the photosensitizer/fiber optic device and was trapped with \(N\)-benzoyl-DL-methionine anion (2, 0.02 M) in the surrounding aqueous solution (Figure 3). Only one product was formed \(\text{N}\)-benzoyl-DL-methionine S-oxide (3) which was monitored by \(^1\)H NMR spectroscopy and is consistent with its literature assignment.\(^1^8\)\(^\text{-}^1^9\) Methionine 2, as the anion, does not adsorb onto the PVG, and no trace of methionine molecules passes through the PVG membrane. The lifetime of \(\text{O}_2\) increases by 20-fold in D\(_2\)O as compared to H\(_2\)O;\(^2^0\) however, the sulfoxidation reaction was found to be about 2 times faster in D\(_2\)O than H\(_2\)O (cf. 11% to 5%) after irradiation with the fiber device for 9 h at pH 8. The 2-fold increase of sulfoxide in D\(_2\)O as compared to H\(_2\)O was less than expected and may relate to a surface effect (some singlet oxygen adsorption or quenching of singlet oxygen by anionic Si–O–

![Figure 1.](image1)

![Figure 2.](image2)

![Figure 3.](image3)

**TABLE 1: Quantities of Oxygen Delivered through a 30-cm Segment of the HC-580 Fiber into 100 µL of H\(_2\)O from an Oxygen Tank at 40 PSI (room temperature)\(^a\)**

<table>
<thead>
<tr>
<th>time (min)</th>
<th>uncapped fiber ppm/O(_2) in H(_2)O</th>
<th>capped fiber ppm/O(_2) in H(_2)O</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>8.59</td>
<td>34.0</td>
</tr>
<tr>
<td>10.0</td>
<td>9.03</td>
<td>64.0</td>
</tr>
<tr>
<td>21.0</td>
<td>9.59</td>
<td>129.0</td>
</tr>
<tr>
<td>30.0</td>
<td>9.99</td>
<td>184.0</td>
</tr>
<tr>
<td>50.0</td>
<td>10.35</td>
<td>214.0</td>
</tr>
</tbody>
</table>

\(^a\)Porous Vycor glass cap (dimensions: 3 mm² × 0.8 mm).
coefficient purchased from Advanced Glass and Ceramics (Holden, MA).

**Experimental Section**

withdrawal of the fiber tip.

of singlet oxygen can be delivered via introduction and

**Conclusion**

Steady-state (i–iv), control (v), and time-resolved experiments (vi) point to a singlet oxygen mechanism for the heterogeneous PVG sensitizer. (i) Quenching studies carried out with the singlet oxygen quencher sodium azide (2 mM) in D$_2$O led to the reduced production of methionine S-oxide 3 (cf. 17% to 5%). (ii) Product yields were identical for the photooxidation of methionine 2 carried out in the presence of the radical scavenger D-mannitol (33 mM). (iii) Cumyl radical-derived products were not observed when using cumene radical scavenger in high concentrations; that is, when cumene was used as solvent. (iv) Previous studies showed the photooxidation of *trans*-2-methyl-2-pentenooante anion 4 afforded one main product, the hydroperoxide 5 from the singlet oxygen "ene" reaction (1H NMR spectra indicate 1~2% byproduct derived from type I reactions with oxygen radicals) (Figure 4). (v) Sulfonation of 2 did not take place in the dark. (vi) O$_2$ molecules were generated in aqueous media; in the absence of oxidizable reagents, O$_2$ was converted to O$_2^-$ physically and was monitored by time-resolved O$_2^-$ (Δ$A_3$) phosphorescence at 1270 nm. 1 From studies of singlet oxygen diffusion, the square of distance ($d$) that an oxygen molecule travels during time ($t$) with the diffusion coefficient ($D_0$) is given by the equation $d^2 = 6D_0t$. 22~24 Thus, singlet oxygen is expected to diffuse a short distance (~150 nm) away from the silica cap into bulk H$_2$O.

**Conclusion**

This manuscript describes the development of a prototype (portable) singlet oxygen delivery device. The above data demonstrate that the oxygen-flowing fiber-capped configuration is suited for the heterogeneous generation of singlet oxygen in aqueous solution. The device is unique. Local concentrations of singlet oxygen can be delivered via introduction and withdrawal of the fiber tip.

**Experimental Section**

**General Aspects.** Porous Vycor glass (Corning 7930) was purchased from Advanced Glass and Ceramics (Holden, MA). N-Benzoyl-DL-methionine sodium salt (Aldrich), sodium azide (Aldrich), cumene (Aldrich), D-mannitol (Aldrich), mesotetra(N-methyl-4-pyridyl)porphine tetratosylate (Frontier Scientific), and adipic acid (Monsanto Chemical Co.) were used as received. Deuterium oxide-d$_2$ (Aldrich), chloroform-d$_3$ (Aldrich), and acetonitrile-d$_3$ (Isotec, Inc.) were of spectroscopic grade. Deionized H$_2$O was from a U.S. Filter Corporation deionization system (Palm Desert, CA). The 532-nm excitation was achieved by soaking the PVG cap in 15 mL of 3.3 M aqueous solution of 1 for 48 h. A plateau was reached when there was 2.5 × 10$^{-7}$ mol 1 adsorbed onto the PVG cap. The amount of 1 adsorbed onto the PVG cap was calculated from the difference in absorbance of the solution before introduction of PVG, and the absorbance of the same solution, after the removal of PVG. The adsorption process was followed by monitoring the largest of the four Q-bands of 1-ads at $\tilde{\lambda} = 525$ nm. The sensitizer-coated caps were rinsed with distilled water prior to use to remove any unbound 1. A 2.38-mm × 0.38-mm core was drilled lengthwise into the sensitizer-coated PVG cap. The 220-μm-o.d. fiber was inserted into the cap hole and glued into place at the hole entrance. Desorption of 1 was not observed when sensitizer-coated PVG (7.5 × 10$^{-7}$ mol 1 onto 1.5 g PVG) was placed into 2 mL of H$_2$O solution at pH = 3, 7, and 10 and stirred for 8 h. No desorption of 1 was observed with Soxhlet extraction, in which acetonitrile and methanol were used as solvents; neither was desorption of 1 observed in a Soxhlet extractor with 2 N NaOH solution for 48 h. Desorption of 1 (≈70%) took place when the PVG cap was in a Soxhlet extractor in 2 N HCl over 48 h.

**Methionine Trapping Studies.** Methionine trapping studies were conducted in 100 μL of H$_2$O and D$_2$O containing 0.02 M methionine 2. The ratio of the void space inside the PVG cap to the 100-μL bulk solvent volume was ~1:300, in which ~0.3% of the solution volume resides in the cap relative to bulk
solution. A sensitizer-coated PVG cap was immersed into H2O and D2O while connected to the fiber optic device. Oxygen flowed through the fiber during the irradiation of samples with the green LED for 9 h. The long irradiation times were due to the low intensity of the radiation through the fiber cap. At <15% conversion, methionine S-oxide 3 was detected as the sole product on the basis of 1H NMR. Sulfone or cleavage products from (S)-hydroperoxysulfinium ylide chemistry were not observed.25,26 The internal standard adipic acid (0.02 M) was added to determine the concentration of the photooxidation samples. The percent yield was determined by comparison of the sulfoxide with the methylene protons of adipic acid (internal standard) by 1H NMR spectroscopy. The structure of N-benzoyl-DL-methionine S-oxide anion was elucidated by 1H NMR (D2O) δ 2.24 (m, 1H), 2.40 (m, 1H), 2.71 (s, 3H), 2.99 (m, 2H), 4.54 (m, 1H), 7.54 (m, 2H), 7.63 (m, 1H), 7.82 (m, 2H).

Further Experiments. Additional experiments included the following: (1) A 1.0-mL D2O solution containing methionine 2 (20 mM) and 2.5 × 10−7 mol I adsorbed onto 0.097 g PVG and was irradiated with the Rayonet reactor for 10 h, in which formation of methionine S-oxide 3 was detected as the sole product with 1H NMR spectroscopy. The structure of N-benzoyl-DL-methionine S-oxide anion was elucidated by 1H NMR (D2O) δ 2.24 (m, 1H), 2.40 (m, 1H), 2.71 (s, 3H), 2.99 (m, 2H), 4.54 (m, 1H), 7.54 (m, 2H), 7.63 (m, 1H), 7.82 (m, 2H).

Acknowledgment. We thank the National Institutes of Health (S06 GM076168-01) and the PSC–CUNY Grants Program for support.