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Autocatalytic-Assisted Photorelease of a Sensitizer Drug Bound to a Silica Support

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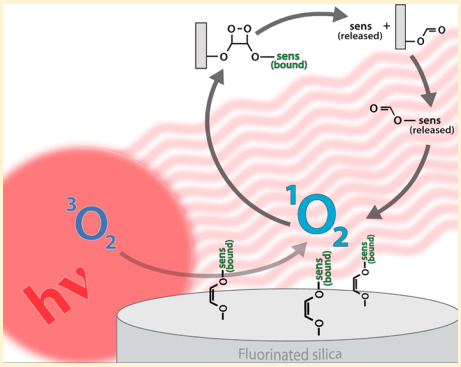
Supporting Information

ABSTRACT: The photorelease of a sensitizer from a fluorinated silica surface occurs by a reaction of singlet oxygen with the vinyl ether bond linker with scission of a dioxetane intermediate. Irradiation of the released sensitizer generates singlet oxygen, which accelerates the release of more sensitizer via an autocatalytic reaction. Sigmoidal behavior of sensitizer release in *n*-butanol and *n*-octanol occurs at an optimal temperature of 20 °C. The photorelease efficiency was reduced at low temperatures, where the sensitizer was retained on the surface due to a long-lived dioxetane with inefficient scission, and also reduced at high temperatures, due to a slower reaction of $^1O_2$ with the vinyl ether bond. Immediate acceleration is a result of released sensitizer being used as a dopant to eliminate the induction step, further implicating an autocatalytic mechanism. However, the sigmoidal sensitizer release was not correlated to solvent viscosity, heat, or light from the dioxetane decomposition or to minor O_2 solubility enhancements caused by the fluorinated silica. The mechanistic information collected here can be used to help control the pace of drug release; however, it remains to be seen whether an autocatalytic-based drug delivery system has an advantage to those with non-sigmoidal kinetics.



INTRODUCTION

The development of autocatalytic reactions could provide a new method for drug photorelease. Although autocatalysis in photorelease processes is rare, in 2011, Kutateladze et al. developed such a process for photoremoving protecting groups, where Ph_2CO was spiked into a UV-irradiated dithiane reaction to unmask further Ph_2CO molecules.[1,2] An example of the role of $^1O_2$ in an autocatalytic process was seen by Rumbles et al. in hexapropyl bis(dimethylamino) zinc porphyrazine where the product seco-zinc porphyrazine was a better photosensitizer, thus increasing the generation of itself.[3]

The Kutateladze[1,2] and Rumbles[3] studies were of interest to us, as we are designing drug photorelease systems based on singlet oxygen chemistry. In this paper, the photorelease of a sensitizer from a fluorinated silica surface is initiated by a reaction with singlet oxygen. Irradiation of the released sensitizer generates singlet oxygen, which accelerates the release of more sensitizer in an autocatalytic fashion.

RESULTS AND DISCUSSION

Scheme 1 shows a fluorinated silica surface [Vycor glass monolith coated with $(CH_3O)_3SiCH_2CH_2CF_2CF_2CF_2CF_3$ = 1.6 mmol/g silica],[4] studied here that photoreleases the sensitizer, 4-formatebenzyl-pyropheophorbide ester (sensU). The photorelease of sensU occurs by a reaction of singlet oxygen with the vinyl ether bond linking the pheophorbide to the silica with the subsequent scission of a dioxetane intermediate.

As is shown below, we find "S-shaped" sigmoidal photorelease behavior with this fluorinated silica sensitizer system, which led us to elucidate the mechanism, and is the topic of this paper. An autocatalytic process has been assumed using Scheme 1 as a reference:

$$\text{sensB}(k) \rightarrow \text{sensU} \tag{1}$$

where sensB is the amount of the sensitizer "bound" to the silica surface and sensU is the amount of sensitizer "unbound" and released into the bulk at time t (h). The reaction with singlet oxygen cleaves the ethene linker via an unstable dioxetane intermediate. The rate law is

$$\text{rate} = k[\text{sensB}][\text{sensU}] \tag{2}$$

in which

$$-\text{d}[\text{sensB}]/\text{d}t = k[\text{sensB}][\text{sensU}] = \text{d}[\text{sensU}]/\text{d}t \tag{3}$$

$$-\text{d}[\text{sensB}]/\text{d}t = k([\text{sensB}]_0 - x)([\text{sensU}]_0 + x) = \text{d}[\text{sensU}]/\text{d}t \tag{4}$$

where x equals the amount of fluorinated silica sensitizer reacted at a given period of time and $[\text{sensB}]_0 - x$ is taken to be $[\text{sensU}]_t$ at time t. The solution of eq 4 gives

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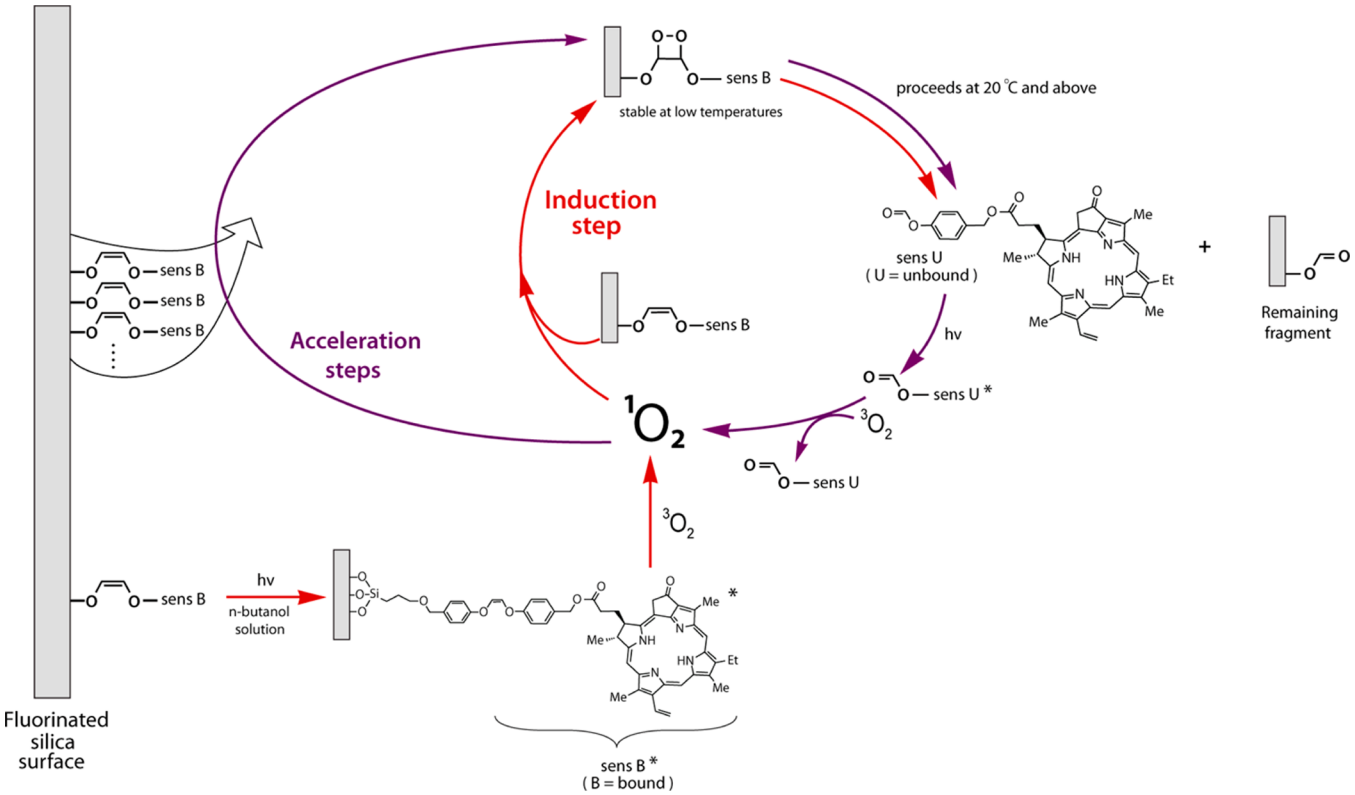
Scheme 1. Proposed Autocatalytic Mechanism



$$\{1/([\text{sensB}]_0 \cdot [\text{sensU}]_0)\} \ln\{([\text{sensU}]_t \cdot [\text{sensB}]_0) / ([\text{sensU}]_0 \cdot [\text{sensB}]_t)\} = k \cdot t \quad (5)$$

A midreaction surge of photoreleased sensitizer from the fluorinated silica surface is expected. This is because the sensitizer detachment by sensB (induction step) would become trumped by sensU (acceleration steps), where the presence of sensU leads to increased amounts of itself. The data provided below are consistent with the mechanism shown in Scheme 1.

A New Sensitizer Drug Photorelease Process (Figure 1). A 0.2 g piece of the fluorinated silica sensitizer in an oxygen-saturated 1 mL *n*-butanol solution was irradiated with a 669 nm diode laser at 20 °C for 2 h. This led to the photorelease of sensU from the fluorinated silica into the *n*-butanol solution.

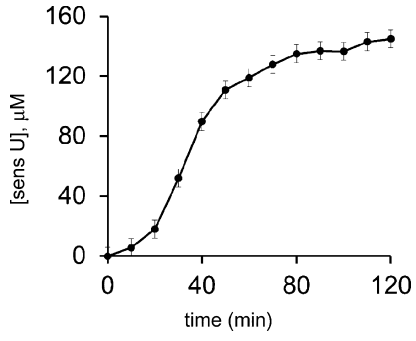


Figure 1. The concentration of sensU photoreleased free from the fluorinated silica sensitizer as a function of time in *n*-butanol at 20 °C. The fluorinated silica was removed, and the concentration of sensU by UV−vis was measured at the indicated times.

The concentration of sensU in solution was determined by UV−vis by monitoring the largest *Q*-band at λ = 663 nm.

Figure 1 shows the sigmoidal photorelease behavior that is observed for the fluorinated silica sensitizer. As we see, there is an ∼20 min induction period, followed by an acceleration, and then deceleration and saturation at 50 min. After 2 h, sensU was nearly quantitatively released (97%), whereas the adsorptive return of sensU to the fluorinated silica surface was ∼3%.

Next, we sought information on whether the sigmoidal release was retained at different temperatures, keeping in mind that dioxetane stability is usually increased at low temperature.[5] Table 1 shows the photorelease results at temperatures ranging from −50 to 100 °C. The results carried out at lower temperatures are discussed next, followed by those at higher temperatures.

The Sigmoidal Behavior Was Not Retained at Lower Temperatures (Table 1). Sigmoids were *not* seen at lower temperatures, which we attribute to increases in the stability of the surface-bound dioxetane, and thus the retention of the sensitizer drug on the fluorinated silica surface. The ethene was first converted to the dioxetane and then on to the final carbonyl products after scission of the dioxetane.

At 10, 0, −25, and −50 °C, the percent yield of photoreleased sensU was progressively diminished in *n*-butanol. Indirect evidence for the surface-bound dioxetane was by GC/MS for O=PPh$_3$ after a reaction with PPh$_3$ in the dark (Scheme 2). (Peroxides are known to be readily trapped by phosphines, often through phosphorane intermediates.[6,7]) Trapping with PPh$_3$ accounted for the surface-bound dioxetane in the amount of ∼70% at −35 °C and ∼20% at 10 °C. The lower percent at 10 °C reflected a lower quantity of the dioxetane on the silica surface. The mass balances of the

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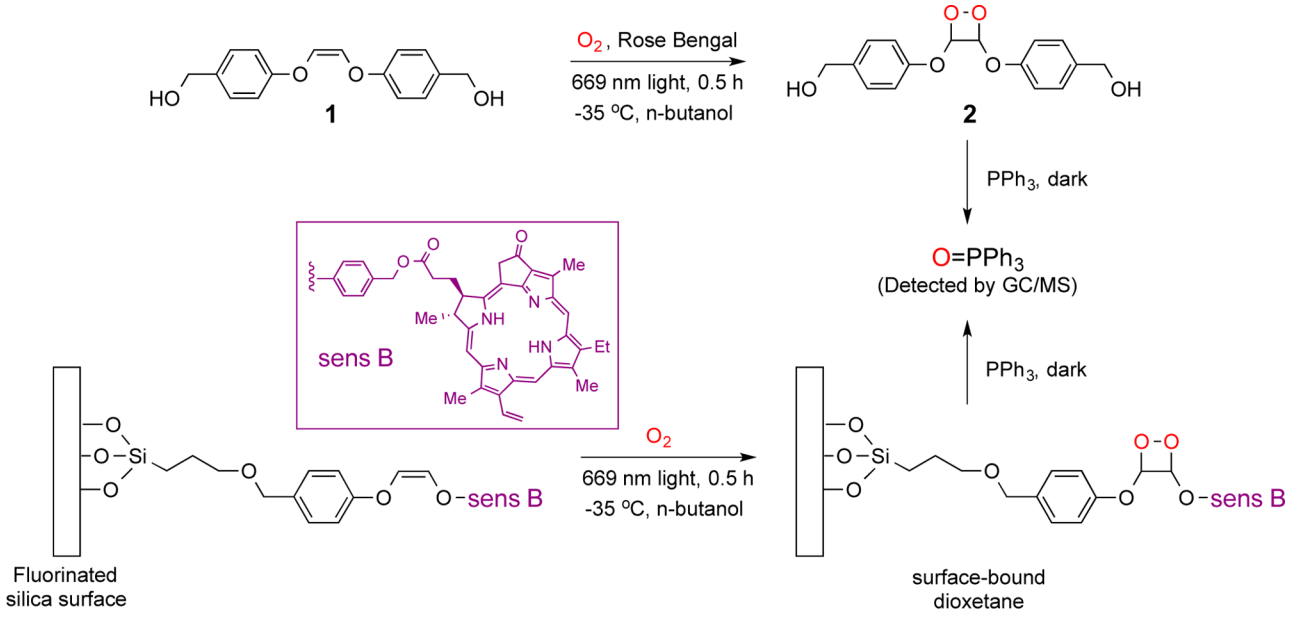
Table 1. Temperature Dependence of the Photorelease of Sensitizer (SensU) from the Fluorinated Silica Sensitizer into *n*-Butanol

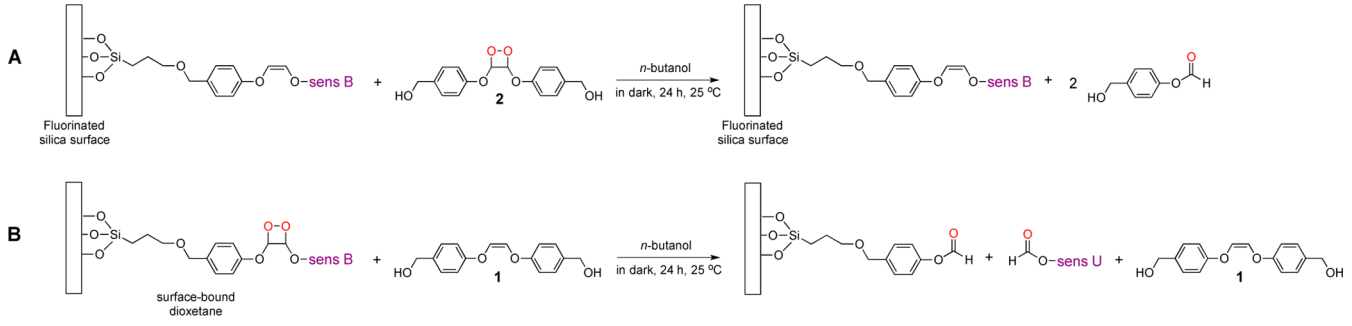
entry	temp (°C)	viscosity (mcp)	% yield of sensU after irradiation for 40 min	ratio of sensU yield relative to the experiment at 20 °C	% yield of sensU after irradiation for 2 h[a]	adsorptive return of sensU (nmol) after 2 h[b]
1[b]	100	1.0	58 ± 5	0.85	99 ± 1	3.0 ± 0.8
2[b]	50	1.2	60 ± 5	0.88	96 ± 3	3.6 ± 0.7
3[b]	25	1.7	67 ± 5	0.99	92.8 ± 4.3	4.4 ± 0.4
4[b]	20	3.1	68 ± 5	1.0	97 ± 7	4.0 ± 0.3
5[c]	10	1.5	52 ± 5	0.76	89 ± 5	3.7 ± 0.5
6[c]	0	4.9	45 ± 6	0.66	66 ± 8	2.7 ± 0.5
7[c]	−25	11	22 ± 1	0.32	36 ± 6	1.3 ± 0.2
8[c]	−50	34	7.9 ± 0.3	0.12	26 ± 7	0.4 ± 0.2
9[d]	20 (or 100)	3.1 (or 1.0)	0	0	0	0

[a]After 2 h, the percent conversion of the ethene linker was ∼100%. [b]The ethene linker bonds were fully converted to the carbonyl fragments. [c]The ethene linker bonds were converted to the dioxetane with partial decomposition and conversion to the carbonyl fragments. [d]Solution was degassed with argon.

Scheme 2



Scheme 3



remaining ∼30 and ∼80%, respectively, were the carbonyl products, one of which was sensU, detected by UV−vis. That the ethene bonds were consumed was based on matching the amount of photoreleased sensitizer to sensitizer liberated from a glass piece of identical weight after dipping it into a hydrofluoric acid solution.

The above results were anticipated, since dioxetane stability was expected to increase at lower temperatures. Small molecule di- and tetra-*O*-vinyl ethers are known to react with $^1O_2$ to form dioxetanes, which can be detected by low-temperature NMR at −78 °C.[8,9] These vinyl ether dioxetanes decompose cleanly to formate compounds on warming or in the presence of a sensitizer or silica.[8,9] In our case, the dioxetane is residing on a solid surface and the release of sensU into solution comes as a phase transition. Table 1 also shows that the adsorptive capacity of the sensitizer decreased slightly at lower temperature, which

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is reminiscent of the temperature-dependent adsorption behavior of dyes on chitosan and montmorillonite surfaces.[10]

Since dioxetanes are high-energy intermediates,[11−13] ethene cleavage of the fluorinated silica sensitizer may be caused in part by the decomposition of dioxetane molecules *in the dark*. Therefore, we conducted control reactions as depicted in Scheme 3 which show that dioxetane diol **2** (∼9.2 mM), prepared by Rose Bengal photosensitization at −35 °C in *n*-butanol, when added to 0.2 g of fluorinated silica sensitizer in the dark and warmed to room temperature, did not release sensU after 24 h. Similarly, surface-bound dioxetane generated at −35 °C was incapable of cleaving ethene **1** in the dark. As might have been anticipated, the amount of light emitted by the surface-bound dioxetane during decomposition was far too small to have any significant effect. The thermal decomposition of the adamantylideneadamantane 1,2-dioxetanes[14] only yields $\sim 6 \times 10^{19}$ photons/mol which is insufficient as a light source in our case. Ten or a hundred million times more photons were produced by the diode laser per mole of reagent in our experiments. Furthermore, the heat generated by the decomposition of dioxetane was too small to account for any significant release of sensitizer, because the ethene bonds of the fluorinated silica sensitizer are stable to boiling methanol and toluene over many hours. The results of photorelease experiments carried out at higher temperatures are discussed next.

Sigmoidal Photorelease Behavior Is Observed at Higher Temperatures. Upon irradiation of the fluorinated silica sensitizer at 20−100 °C, sigmoidal release plots were observed (Figures S1−S5, Supporting Information). At these temperatures, the surface-bound dioxetane was short-lived as all sensitizer molecules were photoreleased from the fluorinated silica after 2 h, and the postreaction "spent" fluorinated silica did not oxidize PPh_3 in *n*-butanol.

Table 1 and Figure 2 show that the optimal temperature for the photorelease was 20 °C. The half-lives of the photorelease

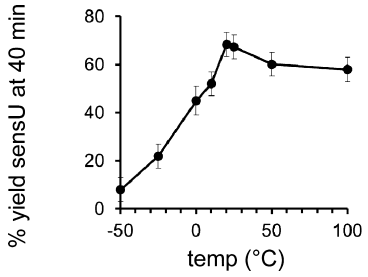

Figure 2. The percent yield of sensU photoreleased from the fluorinated silica sensitizer after irradiation for 40 min in *n*-butanol at various temperatures.

of sensitizer in Figure 3 show that the photooxidation of the ethene bond is slightly reduced at higher temperature. This led us to seek a kinetic model of the photocleavage process in the 20−100 °C regime where S-shape sigmoidal plots were observed.

Kinetic Model of the Photocleavage Process. Sigmoids were seen, and Table 2 shows good correlations of 0.989−0.932 from plots of the data with eq 5 to obtain *k* (autocatalytic fitting). The *k* values (autocatalytic fitting) for photorelease of sensU in *n*-butanol and *n*-octanol were identical to within experimental error (entries 3 and 4, Table 2). The data do not fit well to linear first-order (−ln[sensU] vs time) or second-

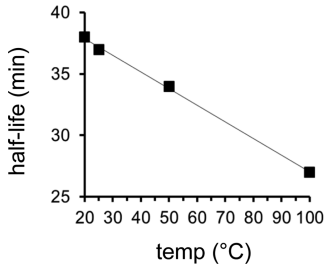

Figure 3. A plot of half-lives for sensitizer photorelease vs temperature. These points were taken from the halfway point between the bottom and top of the sigmoids.

order (1/[sensU] vs time) plots based on poor R^2 values of 0.899−0.703. An Arrhenius plot of ln *k* (autocatalytic fitting) vs $1/T$ is curved, which is reminiscent of Arrhenius plots of enzymes displaying autocatalytic behavior,[15] which are also curved. In our experiments, as the temperature increased from 20 to 100 °C, *k* decreased by 31% from 6.5×10^3 to 4.5×10^3 M^{-1} min^{-1}, and the negative activation energy decreased from −6.46 to −6.35 kJ/mol. Our result can be understood in terms of reduced product formation from lower ethene reactivity with $^1O_2$ at higher temperatures. Reaction efficiency can be decreased at higher temperatures, which is a behavior of an entropy-controlled reaction of $^1O_2$ with the ethene, which has been noted in vinyl ether,[16,17] ene,[18] sulfide,[19] organometallic,[20] and hydrazone compounds.[21] Furthermore, the lifetime of $^1O_2$ is also known to decrease slightly at higher temperatures.[22]

In our experiments, the rate-determining step may be the diffusion of $^1O_2$ to the ethene site. Although the residence time of sensU in the adsorbed state is brief, it might also correspond to a rate-determining step in the sensitizer release. Viscous friction was expected between the solvent molecules and the departing sensitizer, but Table 1 shows that the yields of sensitizer photorelease were not correlated to solvent viscosity. Viscosity-dependent processes are known to slow the O_2 quenching of triplet porphyrin photosensitizers,[23,24] but this quenching process is a much shorter time-scale event compared to sensitizer departure from the silica surface. We should note that a semisigmoidal plot results at 10 °C and is probably a mixture between autocatalysis and sensitizer retention stemming from some dioxetane stability. The steepest sigmoid observed was at 20 °C (which indicates an amplified surge of sensU), compared to higher temperatures.

Origin of the "Surge" in Photoreleased Sensitizer Off of the Silica Surface (Figure 4). Here, we sought to understand why there is an accelerated release of sensitizer molecules. The data point to a mechanism where *unbound* sensU photocatalyzes the release of sensitizer molecules *bound* on the fluorinated silica surface at temperatures at or above 20 °C in *n*-butanol. Figure 4B infers that, at the induction step, ^{3}sensB* sensitizes triplet oxygen to release sensU. At this stage of the reaction, the concentration of sensU is low, and the rapid photorelease process is forestalled until higher concentrations of sensU become available. During the acceleration, there was a surge in the concentration of sensU. Cleavage of the ethene linker bond is due to a higher proportion of $^1O_2$ generated by *unbound* ^{3}sensU* than from *bound* ^{3}sensB*.

However, the fact that we see relatively smooth sigmoids in the photocleavage in the 20−100 °C range does not guarantee that the process is autocatalytic. Thus, experiments were conducted to pinpoint the likely cause of this sigmoidal

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Table 2. Rate Constants for Sensitizer Photoreleased from Heterogeneous Sensitizers by Autocatalytic, First-Order, and Second-Order Fittings[a]

			autocatalysis		first order		second order	
entry	medium	temp (°C)	k ($\times 10^3$ M^{-1} min^{-1})	R^2	k (min^{-1})	R^2	k ($\times 10^2$ M^{-1} min^{-1})	R^2
1	*n*-butanol	100	4.5 ± 0.5	0.988	0.026 ± 0.005	0.899	5.0 ± 0.4	0.735
2	*n*-butanol	50	4.5 ± 0.5	0.983	0.053 ± 0.003	0.784	1.3 ± 0.4	0.787
3	*n*-butanol	25	6.6 ± 0.5	0.944	0.058 ± 0.005	0.848	5.2 ± 0.6	0.703
4	*n*-octanol	25	6.7 ± 0.5	0.932	0.015 ± 0.003	0.823	2.4 ± 0.5	0.810
5	*n*-butanol	20	6.5 ± 0.5	0.989	0.021 ± 0.003	0.744	6.2 ± 0.4	0.882
6[b]	*n*-butanol	20	4.8 ± 0.5	0.974	0.027 ± 0.004	0.850	5.1 ± 0.3	0.830
7[b]	*n*-octanol	25	4.3 ± 0.4	0.975	0.020 ± 0.004	0.893	4.2 ± 0.4	0.861
8[c]	*n*-octanol	25			0.022 ± 0.004	0.989	5.0 ± 0.4	0.740

[a]The fluorinated silica sensitizer (0.2 g) was placed into a 1 mL solution in a Pyrex test tube, where oxygen was sparged into solution with a Pasteur pipet. The sample was then irradiated with 669 nm laser light, and the yield of photoreleased sensU was measured by UV−vis (largest of the four *Q*-band peaks of sensU at λ = 663 nm). [b]30 nmol of sensU (concentration = 30 μM) was spiked into the solution at time = 0. [c]The native non-fluorinated silica sensitizer was used (ref 5).

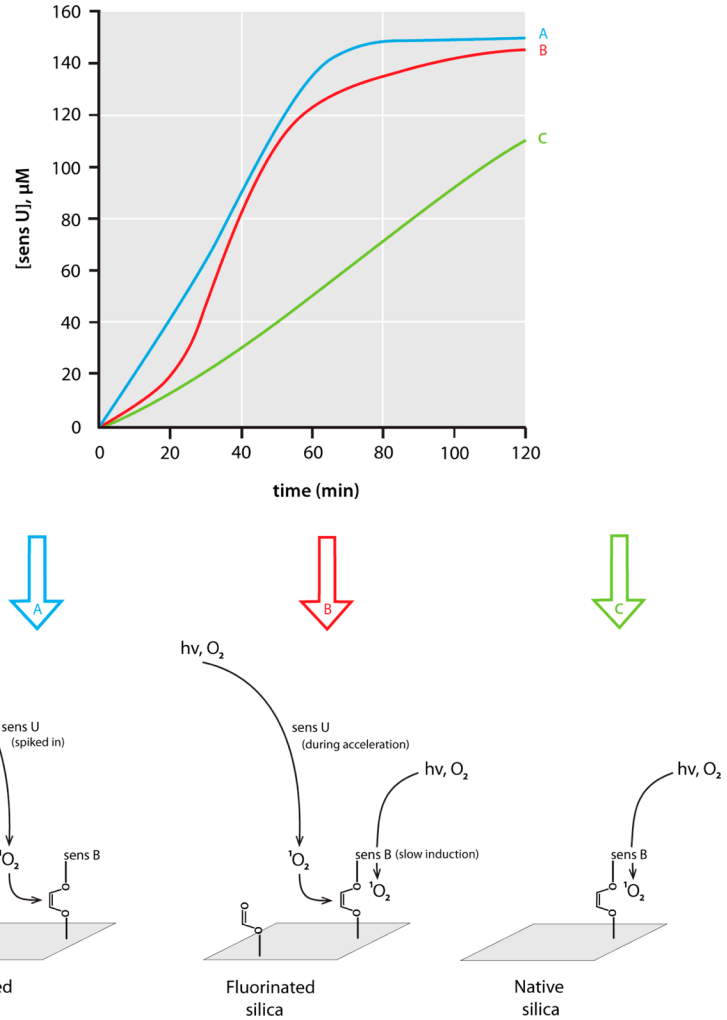

Figure 4. Modes of photorelease of the pheophorbide sensitizer bound to the fluorinated silica surface. (A) The induction period is absent in the sample spiked with sensU at t = 0 min. (B) The sigmoidal behavior of sensitizer release from the fluorinated silica sensitizer with cooperative production of sensU. (C) The linear behavior of sensitizer release from the native silica sensitizer with noncooperative production of sensU.

photorelease behavior, which was not seen with the native silica sensitizer reported earlier.[25] This led us to study the effect of spiking concentrations of sensU into the reaction at time = 0.

Rapid Photorelease Is Caused by the Presence of Cleaved Sensitizer. When sensU was spiked into *n*-butanol and *n*-octanol solution (concentration = 30 μM), the induction step for the photocleavage of sensU from the fluorinated silica sensitizer disappeared and there is an immediate acceleration stage (Table 2, entries 6 and 7). Figures 4A and S6 (Supporting Information) show this absence of the induction step when sensU was spiked into solution. Compare parts A and B of Figure 4 where there is an induction step in the latter. That the

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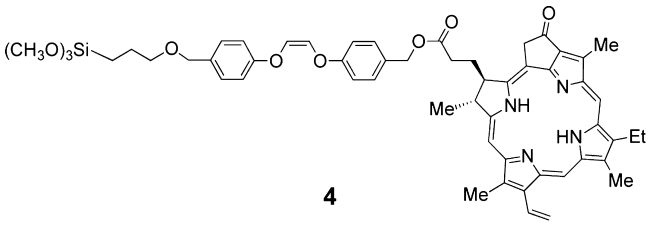
induction period could be bypassed was quite informative. It not only indicated a dependence on sensU concentration, but it also pointed to the role of sensU as a key promoter of ethene photooxidation in the release of more sensU.

Thus, a rhetorical, Hamlet-like question came to mind: *To rinse or not to rinse*? Our synthesis involves the covalent bonding of the sensitizersilane **4** to the fluorinated silica surface and postreaction rinsing with solvent to remove residual unattached sensitizersilane **4**. To bypass the induction step (red-colored line, Figure 4B), the fluorinated silica sensitizer was synthesized, but without rinsing residual adsorbed sensitizer, which would leave the surface more susceptible to photodetachment. On the other hand, if high amounts of non-covalently bound sensitizer remained, the effects could be the opposite; sensitizer release may be slowed by a self-quenching reaction and be subject to aggregation and solvent effects, although this type of concentration effect on release has not been fully explored.



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We should emphasize that there is much we know about this sensitizer, but there is also much we still do not know. Regarding the aggregation of sensU, we expect that aggregated sensU will have difficulty in entering the autocatalytic cycle due to low $^1O_2$ photosensitization efficiency, for example, due to shorter excited-state lifetimes.[26] Experimental conditions were met so that the photorelease into *n*-butanol and *n*-octanol was not due to a breakdown of Beer's law in the UV−vis detection of sensU or to aggregation. We felt that measuring quenching rates of $^3O_2$ with excited surface-bound vs homogeneous sensitizer was out of the scope of the present study, since an uncleavable sensitizer solid would need to be developed. Although in 2008,[27] we did begin to study triplet *meso*-tetra(*N*-methyl-4-pyridyl)porphine lifetimes in aqueous solution (τ_0 = 49 μs) and adsorbed onto native porous Vycor glass (τ_0 = 57 μs); the lifetimes were similar, but the $^3O_2$ quenching rates were reduced by 4-fold in the latter, which was attributed to reduced numbers of trajectories of triplet oxygen to the triplet sensitizer on the native silica surface.

Tuning of Photorelease Process through Silica Fluorination. There are key differences between the sensitizer photorelease from fluorinated silica reported here to that previously reported for native silica.[25] Fluorinated and native silica sensitizers are both capable of producing $^1O_2$. Interestingly, the fluorinated silica sensitizer is different with enhanced reactivity of $^1O_2$ mainly from cleaved sensU generating additional quantities of sensU.

Figure 4B shows the sigmoidal shape of the fluorinated silica sensitizer with sensU release via induction, acceleration, and deceleration stages. Compare this plot to Figure 4C, which shows a linear release of sensU in the native silica sample. Clearly, very different kinetics arises from the SiOH and nonafluorosilane coated surfaces.

Organic photochemistry literature points us to O−H, O−D, and C−X vibrational deactivation (e.g., X = H, D, and F) for an understanding of $^1O_2$ physical quenching[28] and how solids such as silica and zeolites can participate in quenching.[29,30] Thus, a reasonable notion for the contrasting photorelease from native silica is its SiO−H bonds that can physically quench $^1O_2$ to suppress external attack of $^1O_2$ on the ethene linker, whereby $^1O_2$ is only delivered when photogenerated nearby by sensB. Studies of stereoselectivities for $^1O_2$ attack[31,32] and solvent $^1O_2$ quenching data support this notion.[33]

As for the solubility of O_2, based on measurements with a pO_2 electrode, we established that oxygen solubility levels rise by addition of the fluorinated silica sensitizer into solution. In *n*-butanol, the saturation of the solution with O_2 produces 15 ppm (0.47 mM), but when 0.2 g of fluorinated silica is added, the O_2 solubility was 17.5 ppm (0.55 mM). This increase in O_2-carrying capacity was due to enhanced molecular interactions of O_2 with fluorosilanes anchored to the silica and relates to a number of examples of O_2 concentration increases in fluorinated media, such as artificial bloods[34] and ionic liquids.[35] It can also be noted that, under an argon atmosphere, sensitizer molecules did not cleave from the fluorinated silica sensitizer after irradiating at 20 or 100 °C for 2 h, which further supported the notion that the reaction occurs by the sensitized formation of singlet oxygen.

In summary, irradiation of the fluorinated silica sensitizer caused the release of the sensitizer drug (sensU) under certain conditions. Sigmoidal release behavior was observed at temperatures of ≥20 °C but not ≤10 °C. The surface-bound dioxetane was found to cleave to the carbonyl fragments at ≥20 °C. We now know there are opposing effects: the photorelease efficiency was low at low temperatures, where the sensitizer was retained on the surface due to a long-lived dioxetane, and also at high temperatures, due to lower reactivity of $^1O_2$ with the ethene group. A medium temperature of 20 °C seemed to be just right. Immediate acceleration is a result of sensU being used as a dopant to eliminate the induction step, but there was no correlation between the sigmoidal release profile to solvent viscosity effects, to heat and light given off by the surface-bound dioxetane during its decomposition, or to the small O_2 solubility enhancements caused by the fluorinated silica. We believe the above information can be used as a guide in the design of more elaborate $^1O_2$-based photoreleasable systems.

■ CONCLUSION

The fluorinated silica sensitizer was synthesized by loading silica with a fluorosilane and an ethene-conjugated sensitizersilane **4**. This heterogeneous sensitizer showed an acceleration in sensitizer payload release after irradiating for 20 min. Rapid release characteristics were seen where the sensitizer photorelease occurred by an autocatalytic reaction.

Future experiments could take advantage of $^1O_2$-based autocatalysis to control the pace of drug release from systematically designed materials. It remains to be seen whether the autocatalysis of this reaction has an advantage to those with non-sigmoidal kinetics. As the field of PDT advances, autocatalysis might be exploited for a controlled surge of sensitizer and $^1O_2$ molecules. The ability to control the delivery of sensitizer and $^1O_2$ based on an understanding of the present autocatalytic system could inspire the design of an *oscillating* "on−off" system for controlling biological responses in a manner somewhat like acute vs metronomic PDT.

■ EXPERIMENTAL SECTION

Materials and Instrumentation. 3,3,4,4,5,5,6,6,6-Nonafluorohexyltrimethoxysilane, pyropheophorbide-*a*, triphenylphosphine, biphenyl, Rose Bengal, *n*-butanol, *n*-octanol, toluene, THF, dichloromethane,

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chloroform, ethanol, ethylene glycol, and hydrofluoric acid were obtained commercially. Porous Vycor glass (pore size = 40 Å) was dried in a muffle furnace at 500 °C. A UV−visible spectrometer was used for quantitative purposes. Mass spectrometry data were obtained with a GC/MS instrument and a time-of-flight MS instrument coupled with an LC. Oxygen concentrations in *n*-butanol were measured with a pO_2 electrode.

Preparation of the Fluorinated Sensitizer Silica. Using a known method,[4] pieces of porous Vycor glass (ea. 0.2 g) reacted with 0.32 mmol of $(CH_3O)_3SiCH_2CH_2CF_2CF_2CF_2CF_3$ in refluxing toluene (coverage: 99% of the SiOH groups). Fluorinated glass pieces were then covalently bound to the sensitizer by loading with sensitizersilane **4** (studded to most of the remaining 0.99% of the SiOH groups).[25] To remove any unreacted sensitizersilane **4**, the glass was rinsed with THF, dichloromethane, and methanol, and placed into a Soxhlet extractor with methanol at 68−70 °C for 24 h.[36] Each 0.2 g piece of fluorinated silica was coated with 0.154 μmol of sensitizer (accurate to ±2%), as determined by liberating the sensitizer from the surface by immersing it into a 30% (v/w) HF solution at 25 °C for 1 day. After the solution was neutralized with 0.2 M NaOH, followed by chloroform extraction, the concentration of the liberated sensitizer was determined by UV−vis using previously constructed calibration curves.

Typical Photocleavage Procedure. The fluorinated silica sensitizer (0.2 g) was placed into a 1 mL *n*-butanol or *n*-octanol solution in a Pyrex test tube (10 × 100 mm), where oxygen was spared through a Pasteur pipet for 5−15 min. A diode laser (669 nm) was used as the light source. The light was passed through an SMA port, which delivered 232 mW out of the end of a 3.0 m borosilicate bundled optical fiber. The stainless steel head of the optical fiber was positioned in the inner body of the test tube, and dangled 3 cm above the heterogeneous sensitizer in a horizontal position. The light was not focused and was homogeneous over the top part of the sample. Over the 2 h irradiation period, the heterogeneous sensitizer was rotated several times so that nearly the same amount of light was delivered to all faces of the sample. Concentrations of O_2 were kept higher than that of the covalently bound sensitizer molecules (sensB). Temperatures were controlled by use of an oil bath for heated samples, and ice water, blue ice refrigerant packs, or dry ice/ethanol/ethylene glycol mixtures for cooled samples. The concentration of solution-dissolved sensU was monitored by UV−vis, although the instrument cuvette holder was not temperature controlled so that sample temperatures changed by as much as ∼5 °C up or down depending on whether the sample was cool or hot prior to replacing it back in the temperature controlled environment. LCMS was also used to identify sensU. Even though photostabilities of porphyrin sensitizer vary in different solvents,[37] we saw no significant photobleaching in the photorelease experiments up to 2 h. The mass balance is sensU and the remaining formate fragment, in which sensU was recovered from the *n*-butanol and *n*-octanol solutions.

Photolysis under an Argon Atmosphere. We placed 0.2 g of fluorinated silica sensitizer into 1 mL of *n*-butanol in a Pyrex test tube. The solution was bubbled with argon for 20 min and then irradiated at 25 °C for 2 h. There was no release of sensU based on UV−vis spectroscopy. The fluorinated silica sensitizer was recovered and remained charged with 100% of the covalently bound sensitizer molecules.

Phosphine Trapping of Surface-Bound Dioxetane. We placed 0.2 g of fluorinated silica sensitizer into 1 mL of *n*-butanol in a Pyrex test tube. The solution was bubbled with oxygen for 5−15 min and irradiated at different temperatures for 2 h. In the dark, 0.055 mmol of PPh_3 was added to the solution containing the photooxidized fluorinated silica sensitizer. The yield of the dioxetane was estimated by the GC/MS detection of $O{=}PPh_3$ via calibration plots that had been previously constructed with biphenyl as an internal standard.

Photooxidation of (*Z*)-(4,4′-(Ethene-1,2-diylbis(oxy))bis(1,4-phenylene))dimethanol (1). A 1 mL oxygen-saturated *n*-butanol solution of 0.055 mmol of ethene **1** and 5×10^{-5} M Rose Bengal was irradiated for 2 h at −35 °C. In the dark, an equimolar amount of PPh_3 (0.055 mmol) was added to the solution of ethene **1** that had been irradiated. The yield of dioxetane **2** (75 ± 5%) was estimated by the reaction of PPh_3 which gave $O{=}PPh_3$.

Reaction of Surface-Bound Dioxetane with Ethene 1. We placed 0.2 g of fluorinated silica sensitizer into 1 mL of *n*-butanol in a Pyrex test tube. The solution was bubbled with oxygen for 15 min and irradiated at −35 °C for 2 h. In the dark, 0.15 mmol of ethene **1** was added to the solution containing the photooxidized fluorinated silica sensitizer. The surface-bound dioxetane decomposes cleanly to formate compounds on warming or in the presence of ethene **1** but did not lead to cleavage of ethene **1** itself. The surface-bound dioxetane did not absorb the 669 nm diode laser light and did not contribute to its scission, since UV light is required.[38]

Addition of (*Z*)-3,4-Bis(4-hydroxmethylphenoxy)-1,2-dioxetane (2) with the Fluorinated Silica Sensitizer. A 1 mL oxygen-saturated *n*-butanol solution of 0.009 mmol of ethene **1** and 5×10^{-5} M Rose Bengal was irradiated for 15 min and 2 h at −35 °C. In the dark, 0.2 g of fluorinated silica sensitizer was added and the solution warmed to room temperature for 24 h. There was no evidence for the presence of sensU in the solution based on UV−vis.

Photooxidation of the Heterogeneous Sensitizer in the Presence of Cleaved Sensitizer. One mL oxygen-saturated *n*-butanol and *n*-octanol solutions of sensU (30 nmol, final concentration = 30 μM) and 0.2 g of fluorinated silica sensitizer were irradiated at 25 °C for 2 h. The concentration of sensU in solution was determined by UV−vis.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Eight plots of sensitizer photorelease from the fluorinated and native silica sensitizer are provided with data fitted to first-order, second-order, and autocatalytic kinetic reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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