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Efficient Sensitized Photooxygenation in Water by a Porphyrin–Cyclodextrin Supramolecular Complex

Marcella Bonchio,* Tommaso Carofiglio,* Mauro Carraro, Roberto Fornasier, and Umberto Tonellato

ITM CNR-sezione di Padova, Dipartimento di Chimica Organica,
Università di Padova, via Marzolo 1, I-35131 Padova, Italy

marcella.bonchio@unipd.it

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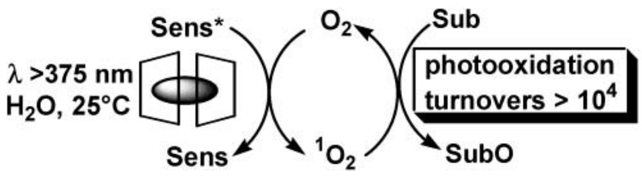
ABSTRACT



The 2:1 inclusion complex between (2,3,6-tri-*O*-methyl)-*β*-cyclodextrin (TM*β*CD) and 5,10,15,20-tetrakis(4-sulfonatophenyl)-porphyrin (TPPS$_4$) behaves as a supramolecular sensitizer in water providing photooxygenation with turnover numbers up to 30 000 with a very minor sensitizer bleaching (<10%). The protocol, which employs only 4 equiv of the cyclodextrin additive with respect to the porphyrin sensitizer (5×10^{-7} M), leads to high yield oxidation of model biomolecules such as L-methionine methyl ester and uracil and is also effective for phenol degradation in aqueous solution.

Dioxygen activation for efficient aerobic oxidations remains a current research challenge.[1] Among photochemical methods, the porphyrin-sensitized production of singlet oxygen ($^1O_2$)[2] in water has a major appeal considering the environmental advantages of low impact photooxygenations[3,4] or photoassisted degradation of organic pollutants[5,6,7] and its application within photodynamic therapy.[8] Two main factors dictate the photoactivity of a porphyrin sensitizer:[9] (i) quantum yields of the excited triplet states and its singlet oxygen production from ground state $^3O_2$ and (ii) stability toward oxidative degradation (photobleaching).[2,8,9] Both properties are badly impaired in water, and this implies severe limitations in the case of chemical and biomedical procedures.[9,10] Although porphyrins are generally characterized by excellent singlet oxygen quantum yields, in aqueous media, their hydrophobic aggregation causes a porphyrin−porphyrin self-quenching and, consequently, a marked reduction of the triplet lifetime.[9,10] At pH = 7, the water-soluble 5,10,15,20-tetrakis(4-sulfonatophenyl)-porphyrin, (TPPS$_4$), with a dimerization constant of ca. 10^5 M^{-1}, is extensively aggregated at concentrations above 10^{-6} M, even in low ionic strength solutions.[10] Moreover, irreversible photobleaching caused by $^1O_2$ itself or other oxygenated reactive intermediates is pH dependent and occurs readily in aqueous media under basic conditions.[8b] As a result, light irradiation of a TPPS$_4$ in water produces a rapid bleaching of the porphyrin.

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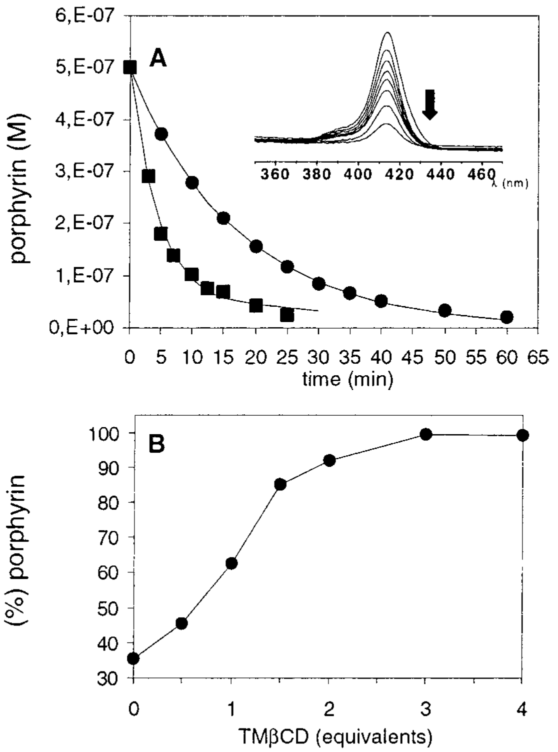
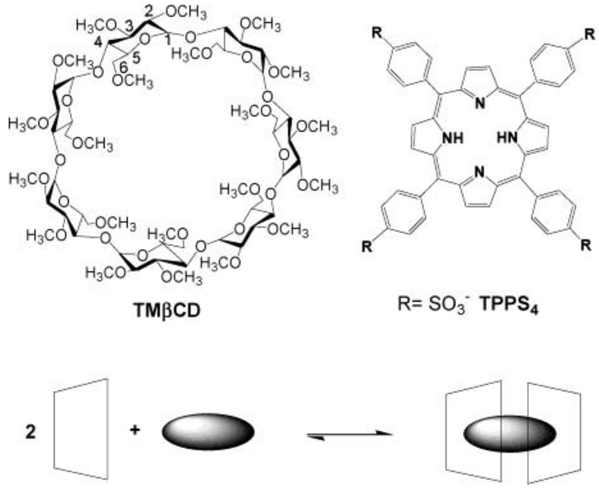


Figure 1. (A) Bleaching of $TPPS_4$ (5×10^{-7} M) upon irradiation at $\lambda > 375$ nm in carbonate buffer (20 mM, pH = 10.5) at 25 °C in H_2O (●) and D_2O (■). (Inset) UV−vis spectrum evolution over time. (B) Effect of added TMβCD (0−4 equiv) on the bleaching inhibition of $TPPS_4$ after 15 min of irradiation in H_2O.

Yet $TPPS_4$ represents one of the most promising hydrophilic sensitizers, and the search for a convenient way to improve its photoactivity is a basic issue for its usage in aqueous media.[8−10] To this end, we exploited the strong affinity of the porphyrin core toward the (2,3,6-tri-*O*-methyl)-β-cyclodextrin (TMβCD) guest to form exceptionally stable inclusion complexes.[11,12] We found that in water, a $TPPS_4$−(TMβCD) inclusion complex behaves as a highly efficient and resistant supramolecular sensitizer with photooxygenation turnover numbers ([substrate]/[porphyrin]) up to 30 000, while the sensitizer bleaching occurs only to a very minor extent (<10%). Our approach delineates an efficient protocol for the photooxygenation of model biomolecules, i.e., L-methionine methyl ester (L-Met-OMe) and uracil, as well for the aerobic oxidative degradation of phenol in aqueous solution under photoirradiation with visible light.

As anticipated, irradiation of an oxygen-saturated aqueous solution of $TPPS_4$ (5×10^{-7} M, 20 mM carbonate buffer, pH = 10.5) using a 500 W Hg/Xe lamp ($\lambda > 375$ nm) gives rise to a rapid bleaching of the porphyrin itself. The degradation of the sensitizer was monitored by UV−vis spectroscopy following the fading of the porphyrin Soret band (413 nm) during irradiation (Figure 1A). At 25 °C, in either H_2O (circles) or D_2O (squares), a first-order decay of the sensitizer absorbance is registered. The fact that porphyrin photodegradation is faster in D_2O ($k_D = (2.8 \pm 0.2) \times 10^{-3}$ s^{-1}, $k_H = (9.7 \pm 0.1) \times 10^{-4}$ s^{-1}), where singlet oxygen has a longer lifetime (20 μs instead of 2 μs in H_2O), confirms the role of $^1O_2$ in the porphyrin bleaching.[8b] Then, we studied the effect of an increasing amount of TMβCD on the photostability of $TPPS_4$ upon 15 min of irradiation in H_2O. Plotting the percent of residual sensitizer versus TMβCD equivalents registers a saturation curve (Figure 1B). Use of 3−4 equiv of TMβCD is sufficient for inhibition of photobleaching.

Scheme 1. Formation of Host−Guest Inclusion Complex between the Hydrosoluble Porphyrin $TPPS_4$ and the Permethylated Cyclodextrin TMβCD



This finding suggests the existence of host−guest inclusion equilibria characterized by extremely high binding constants.[11,12] A detailed structural study, performed for $TPPS_4$ and related hydrosoluble porphyrins,[11,12] indicated the formation of a termolecular complex where two "trans" phenyls of the porphyrin moiety are included in two TMβCD units. In this way, the two TMβCD molecules penetrate deeply to cover the center of the porphyrin ring and $TPPS_4$ remains effectively shielded from the bulk solution (Scheme 1).[11,12]

As further evidence, under the conditions adopted, the use of solution mass spectrometry with negative mode electrospray ionization (ESI-MS) allowed the direct characterization of the 2:1 inclusion complex revealed as the tetracharged molecular ion ($m/z = 946$) and ascribable to the $[TPPS_4-2TM\beta CD]^{4-}$ anionic adduct.[13] The photoactivity of this supramolecular sensitizer toward representative substrates is summarized in Table 1. For comparison purposes, Table 1 includes data concerning the photostability of the porphyrin with and without the cyclodextrin additive in D_2O.

Remarkably, in the presence of TMβCD (4 equiv), the porphyrin bleaching is completely inhibited even under basic conditions (pD = 10), which extends the method's potential.

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(13) The 2:1 complex has been also characterized by MALDI-TOF MS.[12]

Table 1. Photoactivity of the Supramolecular Sensitizer[a]

substrate	TMβCD (equiv)[b]	time (min)[c]	pD	conversion (%)[d]	TPPS$_4$ (%)[e]
		15	6		33
	4	15	6		97
		15	10		14
	4	15	10		97
L-Met-OMe		15	6	83	36
L-Met-OMe	4	15	6	94	93
uracil[f]		30	10	35	18
uracil	4	90	10	93	92
phenol[g]	4	150	10	100	nd[h]

[a] In all reactions: substrate (15×10^{-3} M), TPPS$_4$ (5×10^{-7} M), and TMβCD (20×10^{-7} M) in D_2O with irradiation at $\lambda > 375$ nm ($P(O_2)$ =1 atm; T = 25 °C; Xe–Hg 500 W lamp). [b] Equivalents with respect to TPPS$_4$. [c] Irradiation time. [d] Percent of substrate conversion determined by ^{1}H NMR or HPLC (RP-C18 Phenomenex). Product analysis showed the selective formation of L-methionine methyl ester sulfoxide (diastereomeric mixture). ^{1}H NMR (250 MHz, D_2O) δ: 2.39 (m, 2H), 2.70 (s, 3H), 3.00 (m, 2H), 3.83 (s, 3H), 4.28 (m, 1H) and the occurrence of 1,4-benzoquinone intermediate respectively in L-Met-OMe and phenol photooxidations. In the case of uracil, a complicated mixture of yet unidentified products was obtained. [e] Percent of residual nondegraded sensitizer present in solution as revealed by UV–vis analysis (λ = 413–418 nm). [f] Reaction does not proceed further. [g] Performed in H_2O with phenol (4×10^{-3}M), TPPS$_4$ (1.3×10^{-7} M), and TMβCD (5.3×10^{-7} M). [h] Not determined due to interfering photoproduct absorbance.

During photooxygenation, the self-sensitized degradation of the isolated porphyrin occurs as a parallel process, thus interfering with substrate conversion. This fact has a minor impact with highly reactive substrates such as L-methionine methyl ester (L-Met-OMe) but becomes detrimental in the case of poorly reactive molecules such as uracil. In the latter case, the sensitizer deactivates before reaction completion. Addition of TMβCD guarantees the sensitizer integrity even upon prolonged irradiation (>100 min), thus leading to high substrate conversion. Figure 2 reports the kinetic trace of L-methionine methyl ester (L-Met-OMe) photooxygenation to the corresponding sulfoxide[14] by the supramolecular system (TPPS$_4$–TMβCD). The well-behaved first-order plot (($k_{SO} = (2.2 \pm 0.3) \times 10^{-3}$ s^{-1}) is indicative of an uncomplicated photocatalytic process where (i) the sensitizer remains stable under the turnover regime[15] and (ii) the substrate is not competing with the porphyrin toward the cyclodextrin binding. According to these results, the supramolecular inclusion complex is also effective in protecting the porphyrin moiety toward the reactive persulfoxide intermediate, eventually formed from the thioeter functional group of the amino acid in the presence of singlet oxygen.[8,16]

To investigate the potential of the method for oxidative degradation of organic pollutants in water,[5–7] we performed the photooxygenation of an aqueous phenol solution (pH = 10). Under the conditions adopted (Table 1), phenol oxidation occurs in 120 min with a decrease in the chemical oxygen demand (COD) content of 45% after 4 h irradiation. This latter result is of interest in the field of wastewater treatment with sensitized solar photooxidation.[7]

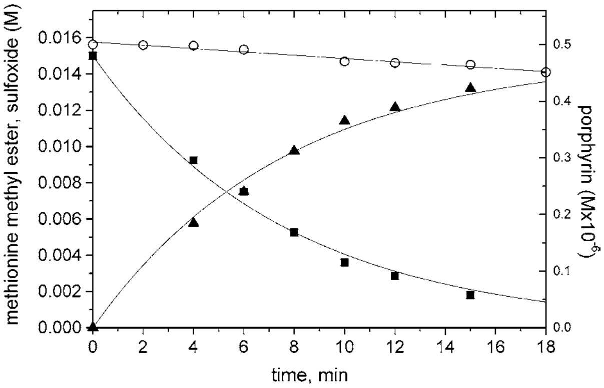

Figure 2. Photooxygenation of L-methionine methyl ester (15×10^{-3} M) by TPPS$_4$ (5×10^{-7} M) and TMβCD (20×10^{-7} M) upon irradiation at $\lambda > 375$ nm ($P(O_2) = 1$ atm; $T = 25$ °C; Xe–Hg 500 W lamp) in D_2O (pD = 6). Concentration vs time of TPPS$_4$ (○); L-methionine methyl ester (■) and L-methionine methyl ester sulfoxide (▲).

The role played by the cyclodextrin additive in enhancing the photocatalytic activity of TPPS$_4$ in water can be further addressed considering the study of Mosinger et al. on the photophysical properties of the title porphyrin as such and as a 1:1 supramolecular complex with 2-hydroxypropyl cyclodextrin (100 equiv).[17] According to their results, the supramolecular sensitizer displays an enhanced lifetime of the porphyrin triplet state but a reduced rate constant of oxygen quenching to produce $^1O_2$.[17] Such a compensation effect leaves unaltered the quantum yields of singlet oxygen formation with or without cyclodextrin. The major effect upon complexation with TMβCD is therefore the protection of the porphyrin moiety against irreversible photobleaching.[11,12,17]

Our results open the way to the exploitation of the strong inclusion properties that the TMβCD manifests with respect to anionic porphyrins in the field of supramolecular catalysis.[18,19] In this light, the self-organized supramolecular sensitizer, obtained by interaction of TPPS$_4$ with TMβCD in water, represents an appealing approach to dimeric binding and therefore implements the elegant synthetic strategies adopted to build covalent CD-based dimeric receptors.[19,20]

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