



Synthetic application of photoactive porous monolithic polymers

M. Isabel Burguete, Raquel Gavara, Francisco Galindo *, Santiago V. Luis *

Departamento de Química Inorgánica y Orgánica, Universitat Jaume I, Av. Sos Baynat, s/n, E-12071 Castellón, Spain

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ABSTRACT

The oxidation of 2-furoic acid to 5-hydroxy-5H-furan-2-one has been accomplished in quantitative yield in chloroform using a novel supported photocatalyst. This material comprises Rose Bengal grafted to the surface of a highly crosslinked polystyrene-divinylbenzene polymer, which was synthesized in a porous monolithic format.

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Selective oxygenations are key steps in many organic syntheses, and methods to achieve them in a quantitative, selective, clean, cheap, and sustainable way are continuously under development.¹ Photocatalytic approaches are gaining increasing acceptance provided they use light to trigger the reaction processes and hence allow the possibility to carry out oxidation in a more controllable manner than conventional thermal methods. In this regard, the utilization of molecular oxygen in combination with a photosensitizer is currently in commonplace in many synthetic laboratories.² Among the photocatalytic processes using oxygen, triplet sensitization of ground-state triplet oxygen to produce excited-state singlet oxygen ($^1\text{O}_2$, $^1\Delta_g$) is one of the most popular reactions since $^1\text{O}_2$ has a well-known reactivity as an electrophile.³

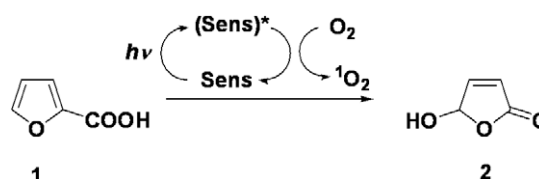
One of the drawbacks of using a photocatalyst is the need for removing it from the reaction medium once the oxidation is finished, which is typically done by means of a chromatographic separation. In order to improve this purification step, several solid-supported photocatalysts for the generation of $^1\text{O}_2$ have been described, which allow the removal of the catalyst by means of a simple filtration or centrifugation.⁴ One of the most employed photocatalysts of this type is Rose Bengal (a well-known $^1\text{O}_2$ generator)⁵ covalently linked to a low crosslinked polystyrene matrix (Merrifield resin),⁶ or other supports.⁷ However, to date, the utilization of the soluble sensitizer (Rose Bengal disodium salt) is preferred in the majority of photooxygenations described in the literature.

We have recently reported a polystyrene-derived photosensitizer that utilizes Rose Bengal as a photoactive agent, which differs

from the gel-type resins in that it has been synthesized in the format of a porous monolithic polymer, which implies higher cross-linking degrees and lower particle sizes than the classical gel-type support. The studies carried out so far showed higher efficiencies for the bleaching of 9,10-diphenylanthracene as well as a positive photodynamic action against melanoma cancer cells.⁸ As continuation of such a project, we were interested in exploring the synthetic photocatalytic potential of this new class of porous polymers for the oxidation of a substrate of synthetic interest, especially in comparison with the classical gel-type photocatalyst.

For such purpose we selected the oxidation of 2-furoic acid **1** to butenolide **2** (5-hydroxy-5H-furan-2-one) as the benchmark reaction (Scheme 1). Butenolide **2** is an important starting substrate for the synthesis of insecticides, prostanoids, alkaloids, etc. A long list of applications of **2** can be found in the literature.⁹ Several strategies for the syntheses of **2** have been reported so far, which demonstrates the importance of this starting material.¹⁰ Moreover, the oxidation of furans to butenolides is the final key step in a great number of described total syntheses,¹¹ but typically using soluble photosensitizers.

The oxidation of **1** to **2** was carried out using four different photosensitizers. The employed photocatalysts were Rose Bengal



Scheme 1.

* Corresponding authors. Tel.: +34 964 728239; fax: +34 964 728214.
E-mail addresses: francisco.galindo@uji.es, luis@uji.es (F. Galindo).

disodium salt (**RB**), a conventional low crosslinking (1%) gel-type polystyrene with attached **RB** (**PGel**), and two porous resins differing in their degree of crosslinking: **P20** and **P80**, with 20% and 80% crosslinking degrees, respectively. All the photosensitive polymers were prepared by reaction of the corresponding chloromethylated matrices with **RB** in dry DMF (see details in the [Supplementary data](#)).¹² They were characterized by means of mercury intrusion porosimetry, Infrared and Raman spectroscopies,¹³ scanning electron and fluorescence microscopies and diffuse reflectance UV–vis spectroscopy. The content of **RB** grafted onto the surface of each polymer was determined by basic hydrolysis of such **RB** moieties and UV–vis measurement of the hydrolysates. [Figures 1 and 2](#) show some selected microscopic and spectroscopic features of photocatalyst **P20**, as an illustrative example. [Table 1](#) collects pertinent characterization data.

For the oxidation of 2-furoic acid **1** to (5-hydroxy-5H-furan-2-one) **2**, each photosensitizer was added to a solution of substrate ($[1] = 3 \times 10^{-2}$ M) in either MeOH or CHCl_3 , equilibrated with air. Such solutions were irradiated with a 125 W medium pressure Hg vapor lamp for 6 h, with continuous agitation (in open reaction tubes). The reactions were monitored by UV–vis following bleaching of the characteristic absorption band of **1** at 247 nm (note that **2** does not absorb at such wavelength). At the end of the irradiation period the solutions were filtered, concentrated, and analyzed by ^1H NMR confirming the formation of **2** in different yields. [Table 2](#) summarizes the reaction yield of **2** for the different reactions.

As can be seen from [Table 1](#), the main differences between the photocatalysts are the degree of crosslinking, the **RB** loading, the pore diameter of the corresponding monolith, and the particle size

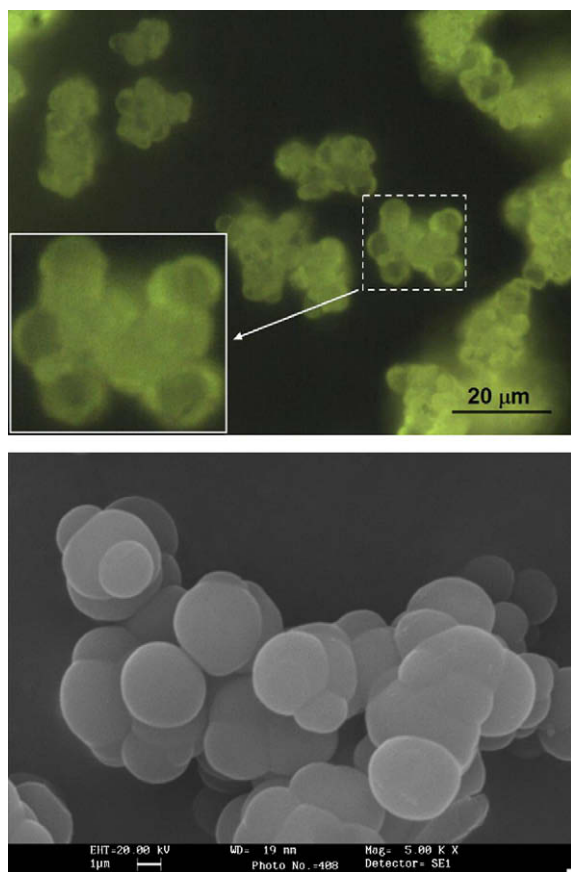


Figure 1. Representative microscopic characterization of photocatalyst **P20**. Top image: optical microscopy (fluorescence). Bottom image: scanning electron microscopy.

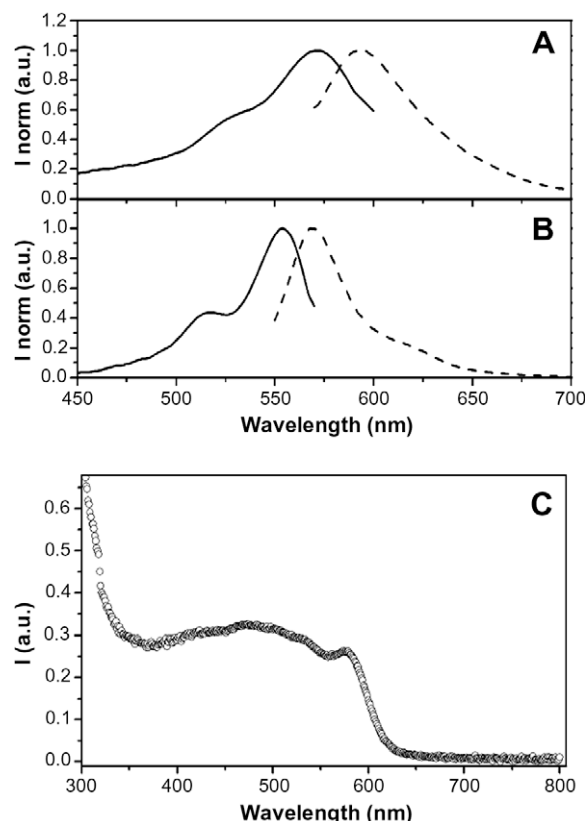


Figure 2. Representative spectroscopic characterization of photocatalyst **P20**. (A) Excitation (left) and emission (right) spectra of solid **P20** with em: 620 nm and exc: 550 nm, respectively. (B) *idem* with Rose Bengal (10 μM) in methanol, for comparative purposes (note the spectral shift between **RB** supported and in solution). (C) Diffuse-reflectance UV–vis spectrum of **P20**.

Table 1
Supported photocatalysts properties

Property	PGel	P80	P20
% Crosslinking	1	80	20
Particle size ^a (μm)	50–110	1–10	5–35
Mean pore diameter ^b (μm)	—	1.16	10.95
Abs. max. ^c (nm)	n.d. ^e	574, 400–550 (broad)	579, 400–550 (broad)
RB loading ^d ($\mu\text{mol/g}$)	150	2–3	2–3

^a Microscopic estimation of the aggregates (in the case of porous polymers each aggregate is composed of several microspheres of 1–2 μm).

^b Determined by mercury intrusion porosimetry from the corresponding monolithic polymer.

^c Diffuse reflectance UV–vis.

^d Hydrolysis and UV–vis determination of **RB**.

^e Not determined due to signal saturation.

of the aggregates. Despite attempts to increase the loading of **RB** above 3 $\mu\text{mol/g}$ (for the porous matrices), it remained elusive. Nevertheless, this feature seems to have a positive effect on the photocatalytic performance of the photosensitizers, especially for **P20**, as it will be shown later. The reason for such difficulty in the attachment of a higher number of photosensitizer molecules onto the surface of **P80** and **P20** can be found in the limited accessibility of solvent and **RB** to the chloromethylated groups in a highly crosslinked resin, in striking contrast to the much more swellable gel-type polymer **PGel**. The morphology of the porous photocatalysts ([Fig. 1](#)) is in accordance with that described for analogous matrices, used mainly for chromatographic¹⁴ or catalytic applications.¹⁵ It is

Table 2
Photooxidation of **1** to **2** (photosensitized oxidation)^a

Entry	Photocatalyst	Solvent	Yield of 2 (%)
1	RB ^b	MeOH	79
2	PGel ^c	MeOH	70
3	P80 ^c	MeOH	68
4	P20 ^c	MeOH	71
5	RB ^b	CHCl ₃	100
6	PGel ^c	CHCl ₃	65
7	P80 ^c	CHCl ₃	67
8	P20 ^c	CHCl ₃	100

^a Irradiation conditions: 125 W medium pressure Hg lamp; light filter: FeCl₃ 0.1 M aqueous solution (450 nm cut-off), air equilibrated, stirred solutions, *t* = 6 h, [1] = 3 × 10⁻² M.

^b [RB] = 6 × 10⁻⁵ M.

^c 4 mg of polymer/ml (this represents formally 1.2 × 10⁻⁵ M of **RB** for **P20** and **P80** and 6 × 10⁻⁴ M of **RB** for **PGel**).

also worth noting that the spectral shift in the excitation and emission bands for attached **RB** (Fig. 2) is evidenced for an important hydrophobic environment of **RB** close to the polystyrenic matrix.⁶

In methanol, the performances of all the four photocatalysts are quite similar, as can be seen in Table 2, with slightly better efficiency for **RB**. But in chloroform **RB** and **P20** are the most effective systems (far better than the classical gel-type photosensitizer), with the additional advantage, in comparison to **RB**, of ease of sensitizer removal after the reaction by means of a simple filtration step. A striking fact that is observed from these irradiations is that despite **P20** and **P80** being 50 times less loaded in **RB** (3 μmol/g) than **PGel** (150 μmol/g), the synthetic efficiency of such porous resins is comparable, or clearly better in the case of **P20** in chloroform, than the Merrifield resin-derived photosensitizer. The reason for such behavior could be due to the absence of aggregation between units of **RB**, a fact already observed by Neckers et al. for other gel-type polymers but not described to date for porous-type (rigid) matrices. Additionally, the low particle size also allows getting more dispersed suspensions in the case of the porous monolithic polymers. As a matter of fact, when **P20** is placed in chloroform or methanolic solutions, a uniform colloidal suspension is readily formed, in clear contrast with **PGel**, which forms visible aggregates separated from the bulk solution. However, the differences between **P20** and **P80** cannot be explained at the moment with the current data in hand, and will be the matter of future research, although the pore diameter of the parent polymeric monoliths probably is playing an important role. On the other hand, it is not expected that the effect of the porous matrix would be an increase in the quantum yield of ¹O₂ production (very high for **RB**: ca. 0.8 in polar protic solvents⁵). Likely, the high specific surface of **P20** creates the appropriate conditions for a high adsorption of substrate, and hence enhances the global yield of the oxidation reaction due to the high local concentration of 2-furoic acid close to the source of singlet oxygen.

In summary, the utilization of photochemically active porous matrices for the synthesis of butenolide **2**, from furoic acid **1**, has been demonstrated. This kind of materials represents a practical alternative to both gel-type resins and soluble **RB**. Current work is in progress in order to know the mechanistic details of the observed enhanced reactivity and to expand the number of porous polymers used as supports.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.065.

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- Summarized preparation of polystyrene matrices: The monomer/porogens mixture (4/6 w/w) with 1 wt % of AIBN (respect to monomers) was purged with N₂ and heated at 80 °C for 24 h. The resulting polymer was washed with THF in a Soxhlet apparatus for 24 h and dried in a vacuum oven. Summarized procedure for the grafting of **RB**: The chloromethylated resin (1.00 g) and Rose Bengal sodium salt (1.07 g) were reacted in DMF (25 ml) at 60 °C for 20 h. Then, the mixture was filtered through a sintered-glass funnel and the resin was washed with 100 ml portions of several solvents and finally with methanol in a Soxhlet apparatus. Finally the polymer was dried in a vacuum oven.

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