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Fullerene-Promoted Singlet-Oxygen Photochemical Oxygenations in Glass-Polymer Microstructured Reactors

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Abstract: In this paper we report the fabrication of thiolene-based microstructured reactors (MRs) that have been specifically designed to include solid-supported reagents within the microchannels network. We propose a convenient solution to realize reversible press-fit, leak-proof interconnects that greatly simplify the MR coupling to the external environment such as capillary tubing, sample reservoirs and pumps. The MRs have been used to carry out the oxidation of α-terpinene and methionine using [60]fullerene, covalently linked to Tentagel® and silica gel matrices, as a singlet oxygen sensitizer. High conversions have been observed for both substrates although, in the case of α-terpinene, a partial photodegradation of the *endo*-peroxide product was detected. Interestingly, in the case of methionine, a quantitative conversion to the corresponding sulfoxides was achieved in about 40 seconds, using low-power, white LED illumination. The reaction time is considerably shorter when compared to the batch procedure that requires, for the same process, about one hour illumination and the use of a 300-W tungsten halogen lamp.

Keywords: fullerene; microreactors; photooxidation; singlet oxygen

Introduction

Organic photochemistry is playing an important role in organic synthesis as a green chemical processing technology.[1,2] In this connection, microstructured reactors (MRs)[3] represent an interesting alternative to conventional photoreactors because the small size of the fluidic channels leads to higher spatial illumination homogeneity and better light penetration through the entire reactor depth. Also, the elevated surface-to-volume ratio features of MRs allow an effective reagent mixing, enhanced heat- and mass-transfer rates and safer processing of toxic or highly reactive compounds. As an additional benefit, the chemical process under investigation can be scaled up either by running the MR for an extended time, or by replicating the MR unit.

Despite the mentioned advantages, only a few reports on photochemical reactions in MRs have been recorded in the literature. Jensen[4] described the application of MRs to synthesize pinacole from benzophenone and isopropyl alcohol. De Mello[5] reported the singlet oxygen homogeneous photooxidation of α-terpinene in an MR, with Rose Bengal as a photosensitizer. A cycloaddition of singlet oxygen to cyclopentadiene was studied by Jähnisch[6] and co-workers in a falling-film MR. Fukuyama[7] described the [2+2] photocycloaddition of various cyclohexenones with vinyl acetates in a glass microflow system. Meyer[8] reported the photosensitized oxidation of citronellol in an MR with light-emitting diodes (LED) as a source of light.

In this paper we report the fabrication of polymer MRs and their application for heterogeneous singlet oxygen photooxidations of model substrates, such as α-terpinene and methionine. The MRs have been properly designed to host, within the microchannels network, the photosensitizer [60]fullerene that has been immobilized on polystyrene beads or silica gel microparticles. The fabrication of MRs was achieved through a rapid prototyping technique that makes use of a thiolene polymer matrix[9] and can be easily implemented in the normal chemical laboratory, without the need for expensive or dedicated lithographic facilities. Since packed-solid MRs that use molecular oxygen can be subjected to back pressures, we designed effective female ports for reversible press-fit interconnects and leak-proof operations also in the presence of high pressure drops.

Results and Discussion

Construction of Microreactors

The MRs used in this work have been fabricated through a procedure, introduced by Beers[9] and co-workers, that exploits commercial thiolene optical adhesives. Accordingly, a layer of thiolene, acting as a negative resist, was poured between two glass plates. Upon partial UV light illumination through a mask containing the desired microfluidic network, the adhesive, in the regions not shielded by the mask, undergoes cross-linking and solidifies. Conversely, the fluid, uncured adhesive can be flushed away with ethanol or acetone through proper interconnects, leaving the microfluidic channels behind. We modified Beer's procedure[9] and introduced a new type of interconnects that greatly simplify the coupling of the MR to the external environment (e.g., capillary tubing, sample reservoirs and pumps). Our contribution to the general procedure of polymer MRs fabrication is a versatile press-fit couple composed by a flanged tube (female connector) and another smaller Teflon tube (male connector) with matching inside and outside diameters. Figure 1a shows the flanged tube, integrated in the MR head, and the male connector interconnect. Figure 1b illustrates the mask that has been used for the photo-patterning and a thiolene reactor (Figure 1c) built on glass plates that has been employed for the homogeneous photooxidation of α-terpinene to the corresponding *endo*-peroxide ascaridole. Note the flanged tubes A, B and C that constitute the female ports. Further details on the MR fabrication have been reported in the Supporting Information.

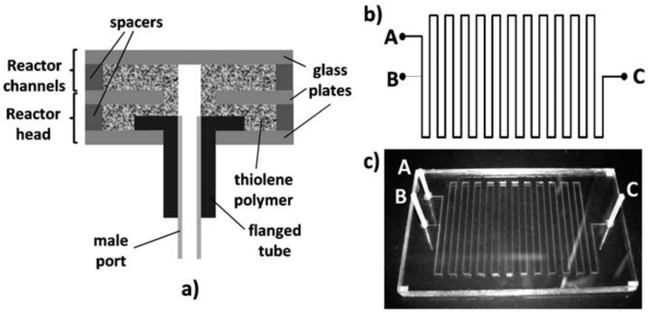

Figure 1. a) Female port design in the MR head that serves as a base for the microchannels network; **b**) mask used for the reactor photo-patterning; c) glass-thiolene reactor with three female ports: substrate inlet (A), oxygen inlet (B), product outlet (C).

The inclusion of a solid-supported [60]fullerene photosensitizer for singlet oxygen generation has been realized in a chamber within the microfluidic network. Figure 2 illustrates a three-chambers (E, H, M) MR with filters (white stripes F1–F3) to confine the photosensitizer (see the Supporting Information for further fabrication details). Inlets A and B are used for reagent and oxygen, respectively. The convergent geometry of the inlets governs the formation of oxygen bubbles within the reagent flow.[5] The serpentine channel (Figure 2, zone C) promotes the oxygenation of the reaction medium. The first chamber (Figure 2, zone E) is directly connected to the oxygenation serpentine whereas the others are not connected for a modular use of the reactor. Therefore, it is possible to employ one, two or three chambers on demand, by series connection with Teflon tubing bridges. In addition, one can collect intermediate samples of the mixture at the outlet of each chamber for reaction monitoring purposes. Each chamber has its own feeding port for an easy photocatalyst loading and replacement. The whole process, from design to working device, can be completed within a few hours.

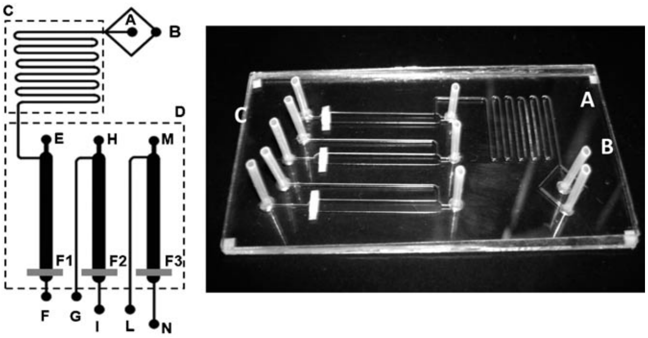

Figure 2. Microfluidic path for the photochemical MR. Oxygen inlet (A), substrate solution inlet (B), oxygenation zone (C), micro-chamber zone (D), photocatalyst feed ports (E, H, M), outlet/connection ports (F, G, I, L, N), paper filter restrains (F1, F2, F3).

Photooxidation of α-Terpinene

The oxidation of α-terpinene to the *endo*-peroxide ascaridole (Figure 3) has been carried out in the presence of [60]fullerene which is a highly stable singlet oxygen photosensitizer with an almost unitary quantum yield over a broad range of wavelengths.[10]

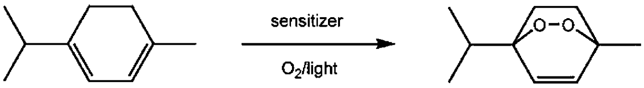

Figure 3. Photooxidation of α-terpinene to ascaridole.

Table 1. Photooxidation of α-terpinene catalyzed by [60]fullerene and Tentagel-supported [60]fullerene (TG-C_{60}).[a]

Entry	Photo catalyst	T [°C]	Substrate flow [mL h^{-1}]	Oxygen flow [mL h^{-1}]	Correlated residence time[f] [sec]	α-Terpinene conversion [%][g]	Ascaridole [%][g]
1	C_{60}	−5[c]	2	5	78	38	30
2	C_{60}	−5	1	3	138	70	40
3	C_{60}	−5	1	2	180	97	51
4	C_{60}	10[d]	1	0.2	138	45	32
5	C_{60}	>50[e]	1	0.7	324	29	25
6	TG-C_{60}[b]	−5	1	2	27	94	52
7	TG-C_{60}	−5	0.5	1	54	97	53
8	TG-C_{60}	−5	0.25	0.5	109	96	53

[a] *Reaction conditions – homogeneous reaction:* a solution containing α-terpinene (195 μL, 1.0 mmol), *n*-tetradecane (130 μL, 0.5 mmol, internal standard for GC analysis) and fullerene (8.8 mg, 0.012 mmol, 1.2% with respect to the substrate) in toluene (10 mL, total volume). *Reaction conditions – heterogeneous reaction:* a solution containing α-terpinene (256 μL, 1.5 mmol), *n*-tetradecane (174 μL, 0.7 mmol, internal standard for GC analysis), and toluene (25 mL, total volume). The reactor contains 14.3 mg of TG-C_{60} corresponding to 0.45 mg of fullerene (0.6 μmol).

[b] Prepared by reacting Tentagel-NH_2 (200 mg, 0.08 mmol amino groups based on a loading of 0.4 mmol of amino groups for gram of dry resin) with [60]fullerene (6.4 mg, 8.8 μmol, 11% of Tentagel-NH_2 loading) in toluene (5 mL).

[c] Ice/sodium chloride mixture.

[d] Water cooling.

[e] Spontaneous temperature due to light source heating without any cooling control.

[f] Calculated total volume of the reactor: 0.152 mL. Correlated residence time (sec) (CRT) = [reactor volume/(oxygen flow + substrate flow] × 3600. For hetereogeneous reactions the "reactor free volume" was evaluated as described in the Experimental Section.

[g] The yields of both residual α-terpinene and ascaridole were determined by GC analysis, using internal standard calibration.

The reaction was first carried out in toluene under oxygen gas/solution two-phases system, and dissolved [60]fullerene, onto the MR reported in Figure 1. Thus, a toluene solution of α-terpinene, [60]fullerene (1.2 mol%) and *n*-tetradecane, as an internal standard for gas-chromatographic quantitation, was introduced through inlet A, whereas pure oxygen was added through inlet B. Owing to the "T" mixer configuration, gas and liquid streams collided head-on generating a gas microbubble train within the microchannel. The chip was layered on an ice/NaCl bath (−5 °C) and irradiated with a 300-W tungsten halogen lamp that was placed 25 cm away from the MR (light intensity = 19000 lux). Ascaridole was collected in brown glass vials and analyzed by GC. The oxidation was also carried out either at 10 °C, by pouring the MR into a water bath, or without any temperature control. In this latter case the lamp heats the MR to about 50 °C. Results are reported in Table 1 (entries 1–5). It is worth noting that the contribution of the gaseous component to the total flow is hard to estimate and that the sum of oxygen and substrate flows does not represent the real residence time of reagents inside the MR. We propose to use the term "correlated residence time" (CRT) as a practical parameter which depends, according to the formula reported in the paper, to the total flow value, calculated as the sum of oxygen and substrate "nominal" flows as set on the syringe pumps, being aware that "nominal" flows are, in turn, proportional to the real ones. CRT (calculated from "nominal" flows rates) is a useful parameter that can be used to optimize product yields, reproduce a set of conditions or highlight a general process trend. However, care must be taken when dealing with solid-supported reagents whose packing characteristics have an important effect on the hydrodynamics of the microreactor and, therefore, on CRT. An increase of the reaction mixture CRT into the MR from 78 (entry 1) to 180 seconds (entry 3), produces an α-terpinene consumption rise from 38% up to 97%. However, the yield of ascaridole (30–51%) is less than the expected, for its known propensity to photochemical degradation.[11] We noted that raising the temperature from −5 °C to 10 °C, while maintaining the same CRT (entries 2 and 4), led to a smaller α-terpinene conversion. This is probably due to a reduced oxygen solubility in toluene as the temperature increases. This was further confirmed by the results of the experiment at T > 50 °C in which an excessive heating gave the lowest substrate conversion observed in our study (25%, entry 5).

Table 1 reports also the heterogeneous photooxidation of α-terpinene that was carried out in the MR illustrated in Figure 2. We used, as solid-supported photosensitizer, Tentagel® resin beads that were functionalized with [60]fullerene. The fullerene-Tentagel® hybrid (TG-C_{60}, Figure 4) was prepared by nucleophilic addition of primary amino groups, that lie at the surface of a commercial amino-Tentagel® resin (TG-NH_2), to [60]fullerene (see the legend of Table 1

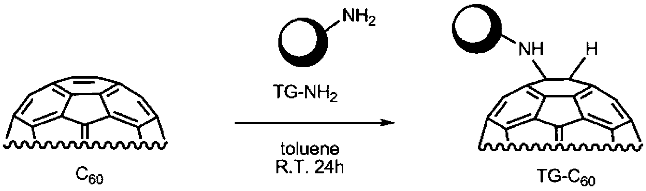

Figure 4. Supporting [60]fullerene on Tentagel® beads.

for details on [60]fullerene loading).[12,13] We note that [60]fullerene polyfunctionalization is very likely to occur as the results of multiple fullerene-amine reactions.

Entries 6–8 in Table 1 show that α-terpinene conversion at −5 °C is almost quantitative (94–97%) in the CRT-range explored. Furthermore, the moderate amount of ascaridole that forms, as a result of some decomposition discussed earlier, is constant (52–53%). The independence of the ascaridole production on CRT in the range 27–109 seconds, suggests a *plateau* condition that prompted us to carry out additional experiments with higher flow rates and, therefore, shorter CRTs. Unfortunately, this led to enhanced back-pressure that made it very difficult to achieve a stable segmented gas-liquid regime for the collection of meaningful data.

Photooxidation of L-Methionine

As a second model reaction, we studied the singlet oxygen photooxidation in water of L-methionine methyl ester to the corresponding sulfoxide with a supported [60]fullerene photosensitizer that was grafted to Tentagel® beads and on SiO_2 particles, commonly used for flash chromatography (Figure 5). We used a functionalized fulleropyrrolidine-SiO_2 hybrid (Si-C_{60}), whose synthesis and characterization were reported earlier,[10c] to overcome the problem of swelling that, for Tentagel® resins, could be an issue in aqueous media.

The oxidation of L-methionine was carried out in D_2O because it turned out very convenient to analyze the thioether to sulfoxide conversion *via* ^{1}H NMR spectroscopy (see Supporting Information). The reaction was first carried out under the irradiation of a 300-W tungsten halogen lamp that was kept 25 cm away from the MR that, in turn, was layered on ice to avoid overheating. Tentagel-based [60]fullerene (TG-C_{60}, entries 1–5 in Table 2) or silica gel-based [60]fullerene (Si-C_{60}, entries 6–8 in Table 2) were used as photosensitizers. Inlets A and B of the MR in Figure 2 were used for methionine solution and oxygen stream, respectively.

A 5×3 array of commercial white LED (Figure 6a) was also employed as an alternative light source to the classical tungsten halogen lamp. LEDs are small in size, cheap and represent a "cold" source of light that can be kept into close contact to the MR at room temperature without any overheating hazard. To this purpose, a polycarbonate case was prepared to contain the MR and the LED array (Figure 6b) that delivered a light intensity equal to 18000 lux.

The photoreaction was monitored by collecting effluent portions that were diluted with D_2O (1:1 v/v) and subjected to ^{1}H NMR analysis to determine the extent of photooxygenation. The results are collected in Table 2.

For TG-C_{60}, under the irradiation of the tungsten lamp, an increase of the CRT from 32 (entry 1) to 102 seconds (entry 5) rises the conversion of methionine from 38 to 85%. The SiO_2-supported fullerene (Si-C_{60}) performs better than TG-C_{60} (entries 5–8) because for a CRT of only 33 seconds a quantitative conversion of methionine was achieved. The oxidation worked nicely also under LED irradiation (entries 9 and 10) since we observed 95% conversion of methionine for a CRT of 42 seconds.

Conclusions

In this paper we have reported the fabrication of a thiolene-based photo-microreactor specifically designed for the inclusion, in the microfluidic network, of a supported photo-catalyst. This MR has been ap-

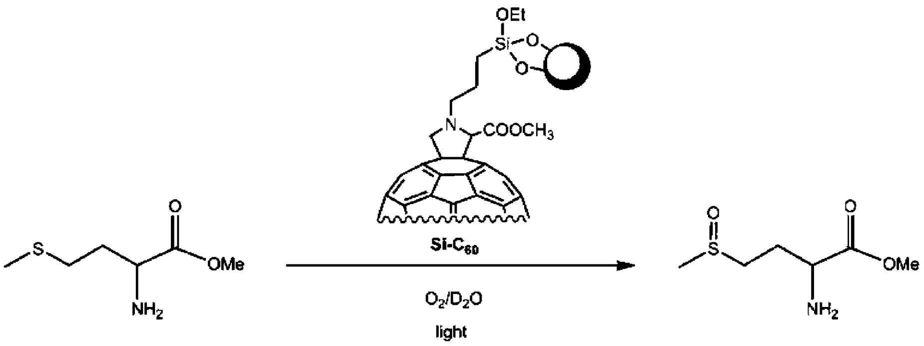

Figure 5. Photooxidation of methionine to methionine sulfoxide.

Table 2. Singlet oxygen photooxidation of methionine methyl ester with Tentagel®- and silica-supported [60]fullerene photosensitizers.[a] < W = 3

Entry	Photo catalyst	*T* [°C]	Substrate flow [mL h^{-1}]	Oxygen flow [mL h^{-1}]	Correlated residence time[f] [sec]	Methionine conversion[g,h] [%]
1	TG-C60[b]	0[d]	1	1.5	32	38
2	TG-C_{60}	0	0.7	1.5	37	40
3	TG-C_{60}	0	0.7	1	48	55
4	TG-C_{60}	0	0.3	0.8	74	59
5	TG-C_{60}	0	0.2	0.6	102	85
6	Si-C_{60}[c]	0	0.7	1.5	21	83
7	Si-C_{60}	0	0.7	2.5	33	100
8	Si-C_{60}	0	0.5	2.0	42	100
9	Si-C_{60}	25[e]	1	2.5	30	89
10	Si-C_{60}	25	0.5	2.0	42	95

[a] *Reaction conditions*: a solution of L-methionine methyl ester hydrochloride (24.1 mg, 0.120 mmol) in D_2O (4 mL) containing also 2 drops of DCl in D_2O is loaded into a gastight Hamilton syringe and delivered to the microreactor at the proper rate.

[b] Prepared by reacting Tentagel-NH_2 (200 mg, 0.08 mmol amino groups based on a loading of 0.4 mmol of amino groups for gram of dry resin) with fullerene (6.4 mg, 8.8 μmol, 11% of Tentagel-NH_2 loading) in toluene (5 mL).

[c] Prepared according to ref.[10c]

[d] The reactor was layered on ice.

[e] Room temperature.

[f] Calculated total volume of the reactor: 0.152 mL. The "reactor free volume" was evaluated as described in the Experimental Section. Correlated residence time (sec) (CRT) = [reactor free volume/(oxygen flow + substrate flow)] × 3600.

[g] Determined by ^{1}H NMR peak integration.

[h] NMR characterization, that has been carried out on reaction mixture aliquots, showed only methionine ester sulfoxide as oxidation product. Therefore, the conversion of methionine ester corresponds numerically to the sulfoxide yield.

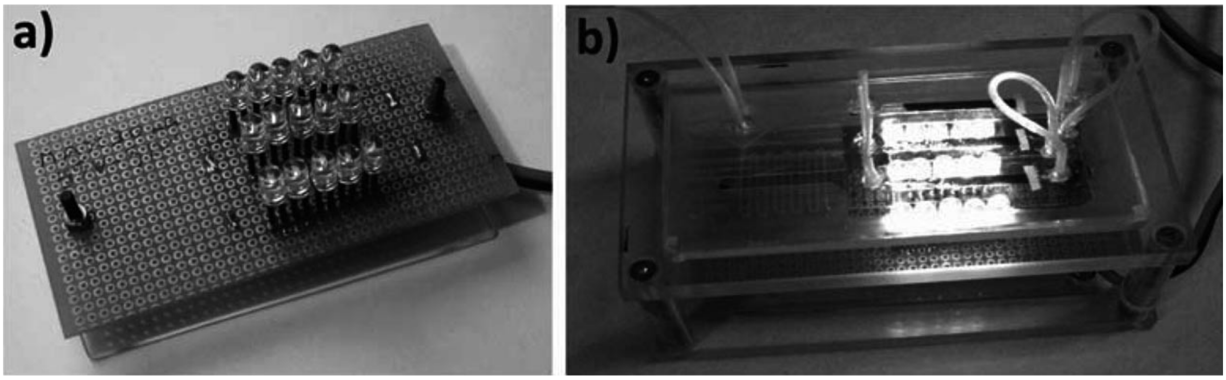

Figure 6. a) LED 5 × 3 array; **b**) MR of Figure 2 with LED source turned on.

plied to the oxidation of α-terpinene to ascaridole and of methionine to methionine sulfoxide with molecular oxygen, using solid-supported [60]fullerene as singlet oxygen sensitizer. Nearly quantitative conversions were achieved for both substrates in about 50 and 40 seconds, respectively, although, in the case of α-terpinene, the moderate yield in ascaridole can be ascribed to its sensitivity to photochemical degradation. The reaction times are considerably shorter when compared to the batch reactor procedure that requires, for the conversion of α-terpinene and methionine ester under comparable reaction conditions, about one hour upon 300-W tungsten halogen lamp illumination. Probably in a microreactor, the narrow channels space favours singlet oxygen diffusion thus determining a faster reaction. Interestingly, the conversion of methionine ester to the corresponding sulfoxide works nicely, in deuterium oxide, under white LED illumination as well. On the other hand, LED irradiation did not produce any ascaridole in toluene. Radiometric characterization gave a light intensity equal to 19000 lux and to 18000 lux for the 300-W tungsten halogen lamp and the LED array, respectively. However, the two sources deliver light in a different spectral range. The LED array emits in the visible, whereas the tungsten halogen lamp has a substantial emission also in the UV region. We believe that the failure of LED with α-terpinene could be ascribed to their limited emission range that probably affects the sensitized production of singlet oxygen, although its lower lifetime in toluene, with respect to D_2O, cannot be ruled out. We are currently purchasing a suitable equipment for an accurate control and metering of light sources to extend this promising photooxidation study also to other functional substrates.

The results reported in this paper were achieved with a simple set-up in which the solid photosensitizer was confined into suitably-designed chambers within the MR that was equipped with original female ports for a quick and easy press-fit connection. The design principles reported in this work should be applicable to the inclusion of other supported molecular structures, such as catalysts, scavengers or bead-based chemosensors, in the microfluidic network. As a final remark, we believe that safety issues should make a microreactor a system to be considered for photochemical oxygenations even if efficiency questions would be in favour of a batch reactor

Experimental Section

Materials and General Methods

Chemical reagents were purchased from Aldrich and used as received. The silica supported, fullerene-based sensitizer was prepared according to a published procedure.[10c] Optical adhesive NOA81 was obtained from Norland Products Inc. A Spectroline SB-100P flood lamp (Spectronics, optimized for 365 nm) was used for pre- and post-curing the optical adhesive. The lamp was housed inside a home-made dark-box that allowed us to place the device 60 and 10 cm away from the lamp during pre-cure (to achieve a degree of beam collimation) and post-cure, respectively. The fluidic path was generated by using a computer drawing package (Canvas ver. 9) and printed out in duplicate on transparency film (KarnaK cod. 2676) using a 1200 dpi laser printer (Epson EPL-6200). The two masks were aligned on top of each other and taped together. Access holes (inlets and outlets) were drilled on glass plates (25×75×1 mm or 50×100×1 mm) using a diamond wheel point (Dremel item n. 7103, bit diameter 2.0 mm, mounted in a variable speed multipro rotary tool fixed to a 220–01 work station drill press). PTFE tubings (OD=1/8 inch, ID=1/16 inch, Supelco, item no. 58699) were flanged with a flanging tool (female ports). PTFE tubing (OD=1/16 inch, ID=1/32 inch, Supelco, item no. 58701) were used for connecting the MR to sample reservoirs and pumps. During the construction of the reactors, in some cases it was necessary to prevent the adhesive to enter into the flanged tubes. In such cases, small pieces of the connection tubes were filled with optical glue, cured beneath the UV lamp, and used as stoppers.

Liquids and gas were delivered to the MR by syringe pumps (KD-Scientific, Mod. KDS200 and KDS100) equipped with 5-mL gas-tight Hamilton syringes. The connection between tubing and syringes was realized with female Luer to female 10–32 adapters in conjunction with 10–32 fingertight fittings for 1/16 inch OD tubing (Upchurch). Proton nuclear magnetic resonance analysis (^{1}H NMR) was carried out on a Bruker AC 250F tuned at 250 MHz. According to the specification sheet available in the internet (www.cnmic.com) for the white LED used (model. ML50W13H-BED) the emission spectrum is in the range 440–630 nm with two broad peaks at 480 and 580 nm. The power supply for the LED-based light source was a HAMEG instrument (model HM7042-S, Elpav Instruments, Padua).

Fabrication of the Reactor Head with Integrated Female Ports

The structure of an integrated female port is depicted schematically in Figure 1a. For its construction, access holes were drilled on two identical glass-slides using the corresponding mask as a reference. One of the two glass-slides was placed in horizontal position and flanged tubes were inserted, flange up, into each of the access holes. Spacers were glued at the corners of the glass plate using a small amount of thiolene resin (UV lamp exposition time of about a minute). Next, the flanged holes were plugged with stoppers and the adhesive was poured over the glass plate. A second glass plate was aligned using the stopper tubes as a guide and carefully layered on the thiolene resin avoiding air bubbles formation. The device was allowed to pre-cure beneath the UV-lamp for two minutes. After removing the stopper tubes with a tweezer, the reactor head was allowed to post cure for 20 min. Finally, the device was thermally cured at 50°C for 12 h to complete the thiolene cross-linking and make the device impervious to organic solvents. The detailed layout of the reactor head construction is reported in the Supporting Information associated to this paper.

Fabrication of the Microstructured Reactor

The head described previously served as the bottom layer for the construction of the photochemical MR. To this purpose, the access holes of the reactor head were plugged with stopper tubes to prevent contamination with the adhesive. Using the mask as a reference, pieces of paper filters (about 2×5×0.3 mm) were placed in the appropriate locations (F1, F2, and F3 in Figure 2) and glued to the glass using small amounts of thiolene adhesive (curing time 1 min). The same kind of paper filter was also used as spacer and glued to the corners of the bottom layer. The adhesive was poured over the glass plate then a second glass plate was carefully layered on the thiolene resin. The mask was placed on the top and the assembly and pre-cured for 45 s beneath the UV lamp at a distance of 60 cm. After removing the stoppers, the channels were emptied by connecting the device to a water aspirator, then extensively washed with methanol alternated to short washings with acetone. The device was dried with a flow of nitrogen. Post curing was carried out by placing the microreactor under the UV lamp for 20 min at a distance of 10 cm from the bulb, followed by thermal curing at 50°C for 12 h to attain mechanical stability and to become impervious to organic solvents. The chambers of the MR, filled with the sensitizer (*vide infra*), were connected in series through small bridges of PTFE tubing. The light source was an array of 15 commercial white LEDs (45 V, 30 mA; Figure 6).

Fullerene Immobilization onto Silica Gel

The procedure for covalently linking [60]fullerene onto silica gel and the characterization of the hybrid singlet oxygen photosensitizer have been reported previously.[10c] The photosensitizer was suspended in toluene and introduced in the MR through the ports (E, H, M in Figure 2). In order to achieve uniform packing of the catalyst, a slight vacuum was applied by a water aspirator at the corresponding outlets. During the experiments, the feeding ports were closed by stoppers. Replacement of the photosensitizer can be achieved by applying a slight vacuum from the feeding port and a concomitant flow of solvent through the outlet port by means of a syringe.

General Procedure for the Evaluation of the "Free Reactor Volume"

An estimation of the "free reactor volume" is needed for the calculation of the CRTs of the reactants inside the MR. To this purpose, an empty reactor was filled with a solution of tetraphenylporphyrin at a known concentration in toluene. The solution was then displaced by using a syringe and collected in a flask and diluted to a known volume with toluene. The absorbance of the solution was measured at the Soret band and from the molecular extinction coefficient it was possible to calculate the total volume of the reactor. Subsequently, the reactor was filled with the resin and the above procedure was repeated to find the total volume of the reactor in the presence of the solid supported photo-catalyst. The subtraction of this value from the previous one allows an estimate of the volume not occupied by the catalyst and the calculation of the CRT according the formula:

CRT (sec) = [Free reactor volume/(Oxygen flow + Substrate flow)] x 3600

Singlet-Oxygen Photooxidation in an MR of α-Terpinene with [60]Fullerene under Homogeneous Conditions

A solution of α-terpinene (195 μL, 1.0 mmol), *n*-tetradecane (130 μL, 0.5 mmol), and pristine [60]fullerene (0.012 mmol) in toluene (10 mL) was passed through the MR reported in Figure 2 for the contact times reported in Table 1 (entries 1–5). The solution that was collected from the MR was diluted 1/10 with toluene and analyzed by GC.

Singlet-Oxygen Photooxidation in an MR of α-Terpinene with [60]Fullerene Supported onto Tentagel® Beads

A solution of α-terpinene (256 μL, 1.5 mmol), *n*-tetradecane (174 μL, 0.7 mmol) in toluene (25 mL) was passed through the MR reported in Figure 2 for the contact times reported in Table 1 (entries 6–8). The MR had the fullerene grafted to Tentagel® (90 mg of a TG-C_{60} resin containing 44 μmol of [60]fullerene for gram of Tentagel®, i.e., 4 μmol of [60]fullerene) which, in turn was placed in the appropriate chambers, as illustrated in Figure 2. The solution collected from the MR was diluted 1/10 with toluene and analyzed by GC.

Singlet-Oxygen Photooxidation of α-Terpinene under Batch-Reactor Conditions

A solution of α-terpinene (195 μL, 1 mmol), *n*-tetradecane (130 μL, 0.5 mmol) and pristine [60]fullerene (0.005 mmol) in toluene (10 mL) were loaded into a glass photochemical reactor, maintained at 20 °C with water cooling, and irradiated with a 300-W tungsten halogen lamp from a distance of 20 cm. During irradiation, oxygen was passed through the reaction mixture *via* a 0.8 mm ID Teflon tube. 100 μL aliquots of the reaction mixture were diluted 1:10 (v/v) with toluene and analyzed by GC-MS to check substrate conversion.

Singlet-Oxygen Photooxidation in an MR of L-Methionine Methyl Ester

A solution of L-methionine methyl ester (24.1 mg, 1.21×10^{-4} mol) in D_2O (4.0 mL) containing two drops of concentrated DCl in D_2O were loaded into a gas-tight Hamilton syringe and delivered to the MR (inlet B, Figure 2) at a rate of 0.5 mL/hour. In the meantime, oxygen was pumped with a gas-tight Hamilton syringe, connected to inlet A at a rate of 2.0 mL/hour. A steady formation of gas bubbles in the aqueous phase was observed (Figure 2, zone C). After this contacting stage, the oxygenated solution with L-methionine methyl ester passed throught the three packed chambers (each of them containing approssimatively 15 mg of [60]fullerene photosensitizer immobilized on silica gel) under the illuminated zone (Figure 2, zone D). The solution at the MR outlet (Figure 2, zone N) was collected, diluted 1:1 (v/v) with D_2O and analyzed by ^1H NMR to determine substrate conversion.

Singlet-Oxygen Photooxidation of Methionine Methyl Ester under Batch-Reactor Conditions

A solution of L-methionine methyl ester (24 mg, 1.2×10^{-4} mol) in D_2O (4 mL) containing two drops of DCl in D_2O and [60]fullerene photosensitizer immobilized on silica silica gel (12.3 mg, 0.87 mg C_{60}, 1.2×10^{-6} mol, 1 mol%) were charged into a glass photochemical reactor, maintained at 20 °C with water cooling, and irradiated with a 300-W tungsten halogen lamp from a distance of 10 cm. During irradiation, oxygen was passed through the reaction mixture via a 0.8 mm ID Teflon tube. 100 μL aliquots of the reaction mixture were diluted 1:5 (v/v) with D_2O (500 μL) and analyzed by ^1H NMR to check substrate conversion.

Supporting Information

Details for the reactor fabrication and ^1H NMR monitoring of methionine oxidation are reported in the Supporting Information.

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