Performances of Homogeneous and Heterogenized Methylene Blue on Silica under Red Light in Batch and Continuous Flow Photochemical Reactors

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Supporting information

1. General information

Reagents and solvents were used as received, without further purification, unless otherwise noted. Oxygen (>99.5%) was obtained from Air Liquide and used as received. β-citronellol, 1,3-dimethoxybenzene, methylene blue, triphenylphosphine, phenyl acetate and tetraethoxyorthosilane (TEOS) were purchased from TCI Chemicals. NH_4OH (28-30 %) was purchased from Merck. Silica (60M, 0.04-0.063 mm for column chromatography) was purchased from Macherey-Nagel. Acetonitrile (CH_3CN) ACS reagent grade, ethyl acetate and absolute ethanol were purchased from Carlo Erba.

Reactions were monitored by GC-MS analysis on a Shimadzu GC-2010 Plus equipped with aRxi®-1 ms column capillary (12 m x 0.2 mm, 0.33 μm df) linked to a quadripole mass spectrometer QP2010 SE (start at 50 °C, ramp to 280 °C at 20 °C/min). Aliquots were taken from the reaction medium and diluted with ethyl acetate before analysis. ^{1}H NMR spectra were recorded on a 400 MHz Bruker Advance Spectrometer in $CDCl_3$ (7.26 ppm). ^{1}H NMR analysis was used to confirm GC-MS conversion results and calculate reaction yield. UV–Visible spectra were obtained with a Shimadzu UV-2600. Dynamic Light Scattering (DLS) measurements were performed on Malvern ZetaSizer ZEN3600 instrument equipped with a 633 nm laser (scattering angle 175°) at 25°C on SiO_2 nanoparticles solution (1 mM) diluted in water (RI 1.33, viscosity 0.8872). Three replicate measurements were performed by analysis in a cuvette ZEN0118 (200 μl). An instrumental algorithm was used to supply the hydrodynamic diameters as number distributions (silica RI 1.4701, absorption 2.988). Fluorescence images were taken with Observer AXIO A1 from Zeiss. Scanning Electron Microscopy (SEM) images were taken with a FEI Magellan400 at 5-10 KV to visualize the shape and the size of the synthesized nanoparticles.

2. Reactors description

Batch photoreactor description

A jacketed reactor of 200 mL was used for batch experiments (Figure S1). In the outer jacket, a temperature regulated mixture of water/ethylene glycol (80/20) was circulated to control the reaction temperature. A condenser was used to limit vaporization of solvents and oxygen was supplied to the reaction mixture by a balloon. Red LED strip was purchased from Dichroled. 304 LEDs (120 LED/ m, 12 W/ m), which corresponds to a 30 W power, were attached to an aluminium tube.

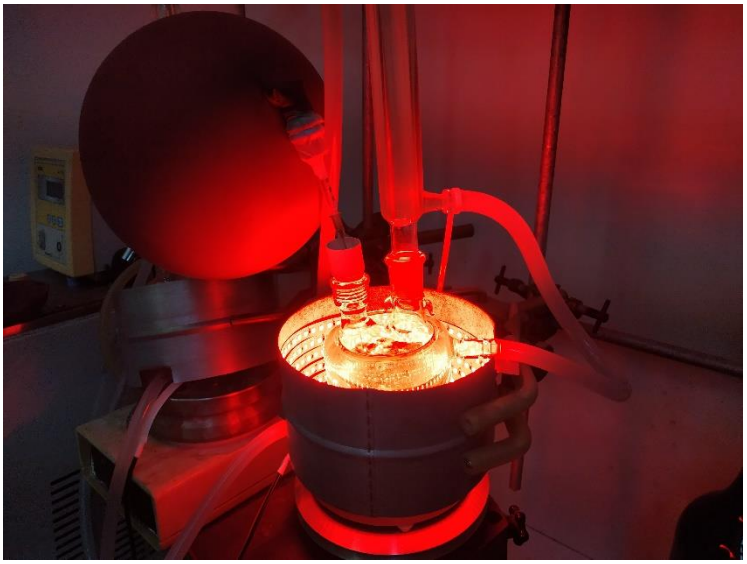


Figure S1. Picture of one of the two thermoregulated batch reactors used this study

Continuous flow photoreactor description (Corning®)

Continuous flow reactions were monitored using a Corning advanced-flow lab reactor system (Figure S2a). The organic solution containing the substrate in CH_3CN was pumped by an HPLC pump in a 1/8'' PFA tube. Oxygen was dosed and injected into the system via a gas mass/flow controller. The solution and O_2 were mixed in the fluidic photoreactor (Figure S2). The fluidic module is a 2,7 mL transparent plate with narrow channels and a heart-shaped static mixer (Figure S2b). It contains three layers: 1 layer dedicated to the reactant and 2 external layers dedicated to thermal fluid circulation in order to regulate the reactor temperature. The plate is irradiated with interchangeable tuneable LEDs with modulable intensity but in this study we focused on the use of 620 nm LEDs (40 LEDs, Radiant power received by the fluidic module: 75,42 mW/cm^2). The pressure on the reactor was controlled using a Zaiput back pressure regulator.

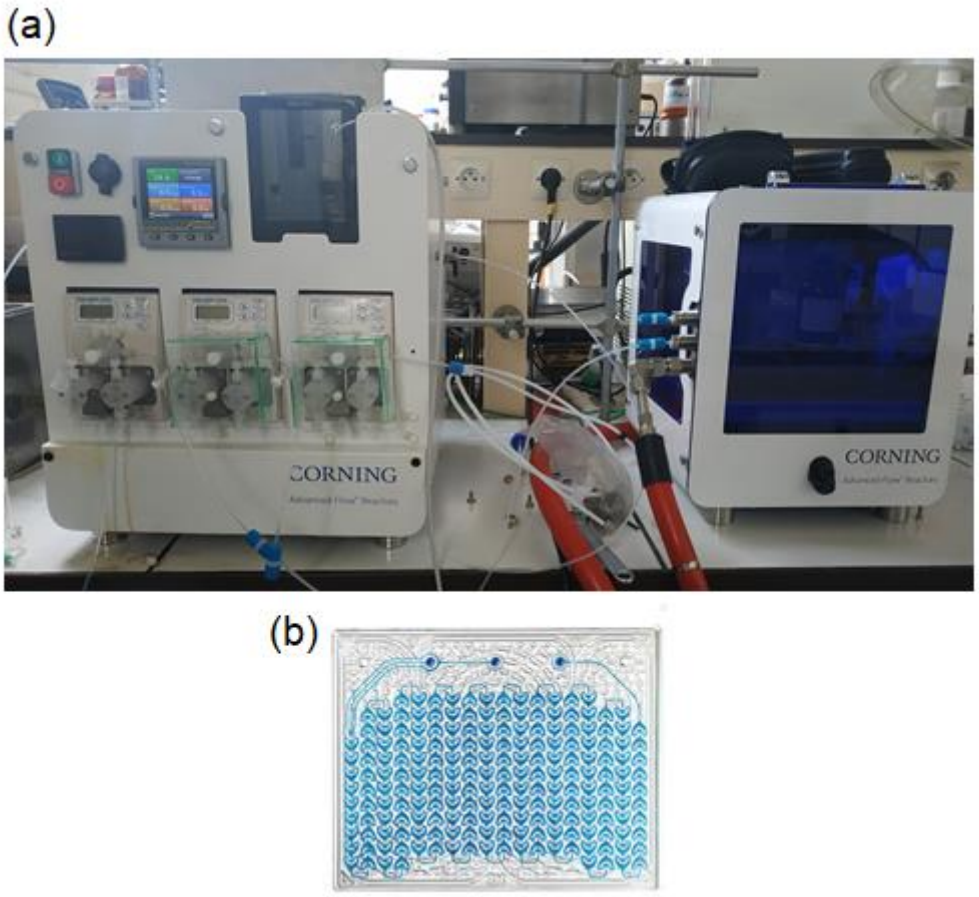


Figure S2. (a) Picture of Corning advanced-flow reactor lab reactor system (b) Picture of the fluidic module

3. TON and STY calculations:

Table S1. TON and STY equations for batch and flow reactions

	TON	STY (g. h^{-1}. L^{-1})
Batch reaction	$\frac{n(citronellol) * \eta}{n(catalyst)}$	$\frac{[citronellol] * \eta * M(product)}{\Delta t * 100}$
Flow reaction	$\frac{n(citronellol) * \eta(third\ cycle)}{n(catalyst)}$	$\frac{D * 60 * [citronellol] * M(Product) * \eta}{V(reactor) * 100}$

n(citronellol): number of moles of citronellol introduced at t_0; η = conversion of photooxidation (%) ; n(PC) = number of moles of PC introduced ; [citronellol] = Molar concentration of β-citronellol at t0 (mol/L) ; M(product) : Molar mass of products 2 and 3 of the photooxidation (M = 172,26 g/mol), Δt = time of reaction; η(third cycle) : conversion of the photooxidation after the third cycle ; D = flow ($mL \cdot min^{-1}$); V(reactor) = Volume of the fluidic module (2,7 mL)

4. Preparation and characterization of MB@SiO_2 on micro- and nanoparticles

Preparation of SiO_2 nanoparticles:

SiO_2 nanoparticles were prepared using the Stöber method presented by Thomassen et al. 200 mL of ethanol, 6 mL of distillated water and 10 mL of NH_4OH (28-30 %) were added in a 500 mL three-neck round bottom flask under stirring (700 rpm). Tetraethoxyorthosilane (8 mL) was added dropwise to the solution. The solution was left under stirring (700 rpm) for 48 hours at room temperature. Then, SiO_2 nanoparticles were removed by centrifugation (3 times, 6500 rpm, 45 minutes), redispersed in distillated water and lyophilized. Finally, around 1 g of SiO_2 nanoparticles were obtained with an average hydrodynamic size of 150 ± 45 nm to 190 ± 50 nm in number.

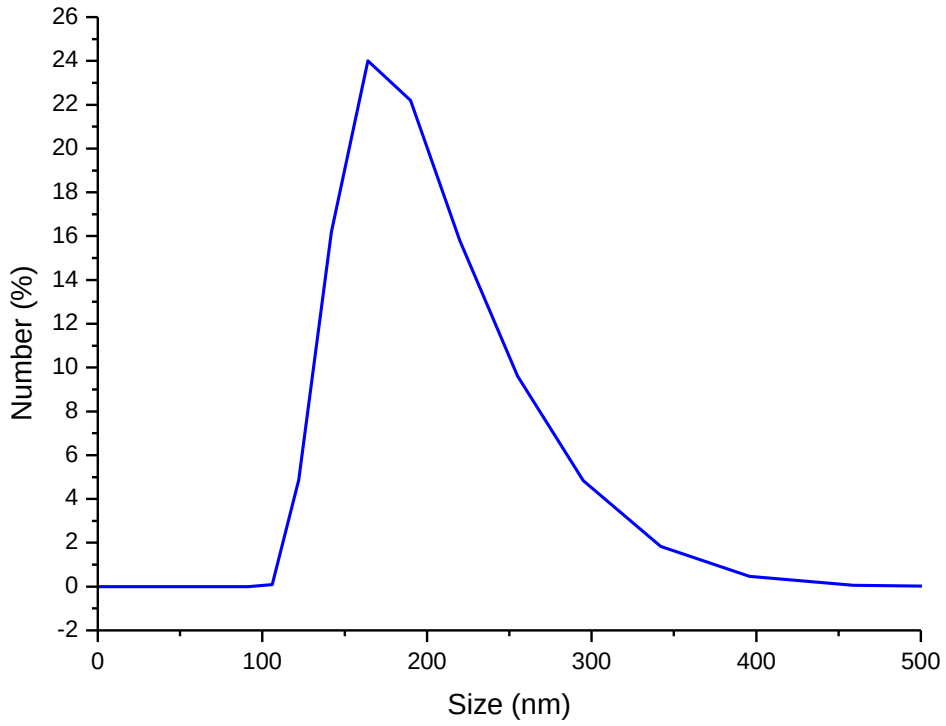


Figure S3. DLS analysis of SiO_2 nanoparticles (in number); Size = 192 ± 50 nm

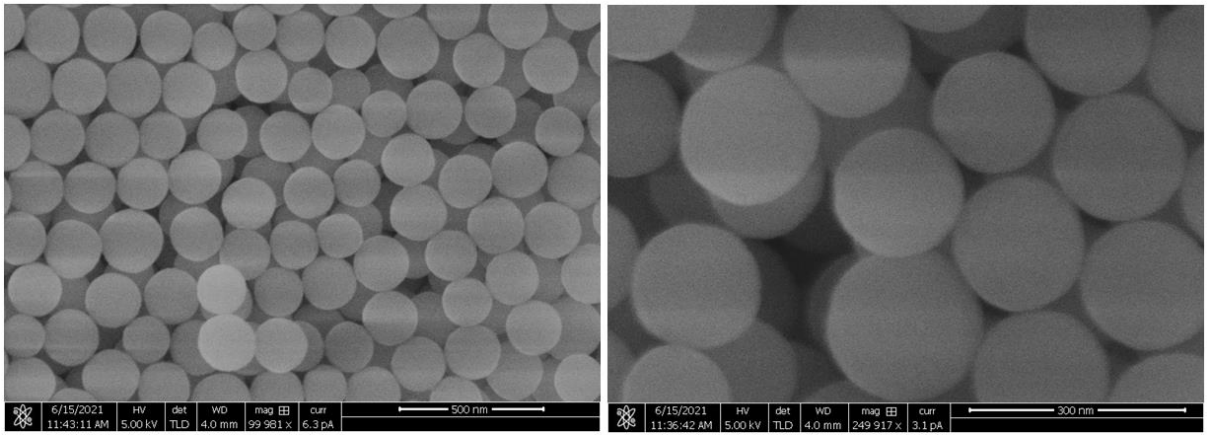


Figure S4. SEM Images of SiO_2 nanoparticles; Size ≈ 187,2 nm

Immobilization of MB on micro and nanoparticles:

1,25 mL of MB (1 g/L aqueous solution) was added to 200 mL of distillated water. 1.0 g of micro- or nano-silica was added to this solution. The mixture was left under stirring for 2 hours at room temperature and filtered. MB@SiO_2 was finally dried in an oven at 80°C overnight.

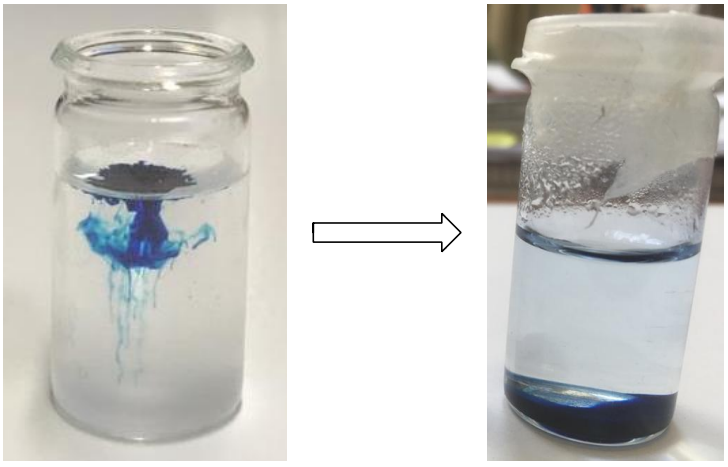


Figure S5. Photographs of the MB dye when freshly added to water and after addition of micro-SiO_2

Fluorescence microscopy experiments:

300 mg of MB@SiO_2 was added in a 100 mL erlenmeyer filled with 100 mL of distillated water. 152 mg of SiO_2 was added to this solution and the heterogeneous mixture was left under stirring for 2 hours. The solid was filtered, dried and analyzed by fluorescence microscopy. The adsorption of MB on all

SiO_2 particles (Figure S6d) was observed as compared to the reference (Figure S6c), which consists of a mixture of MB@SiO_2 and pure SiO_2 added in the same quantity but without solvent. This experiment demonstrates the non-covalent nature of the link between MB and SiO_2.

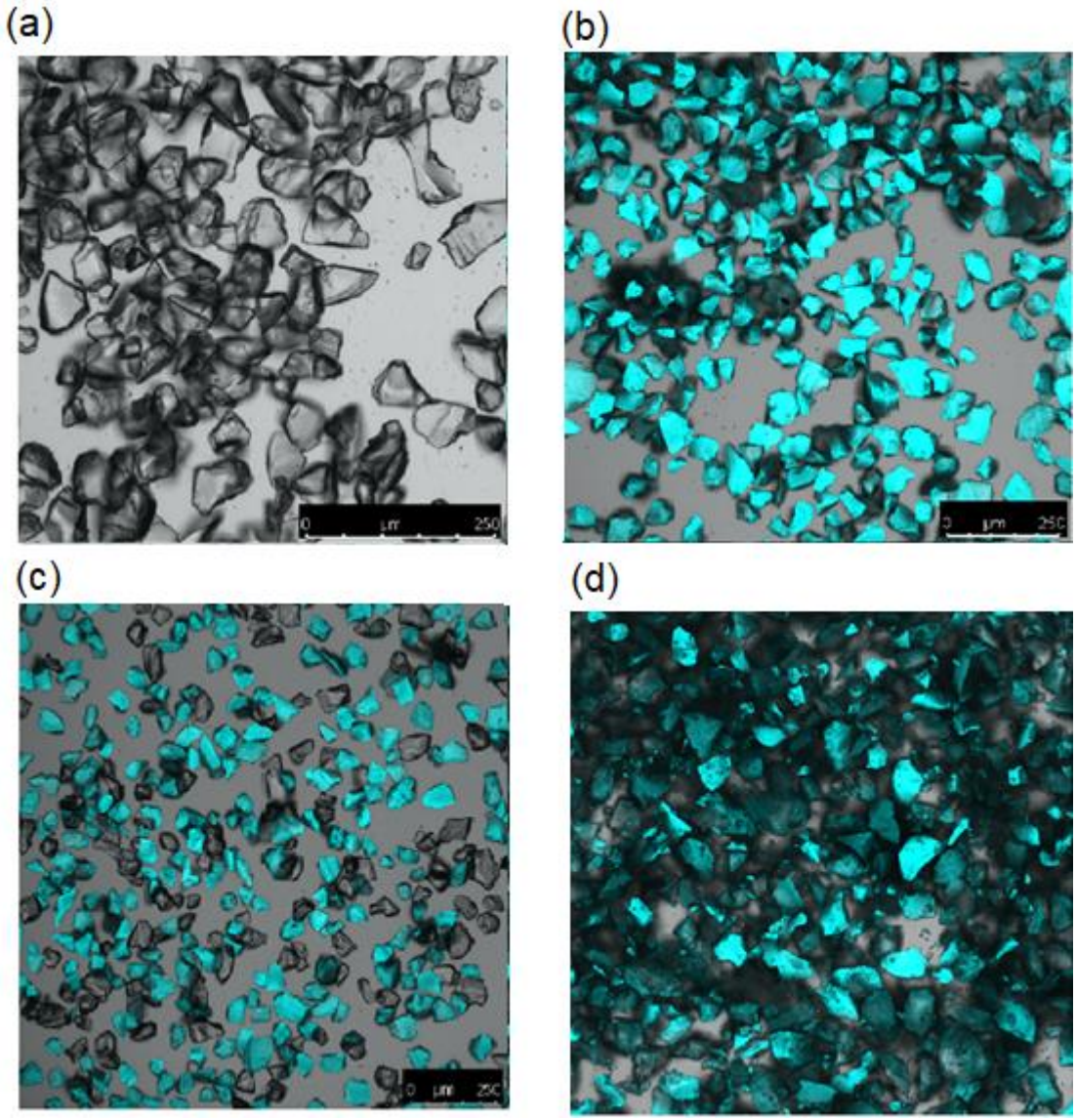
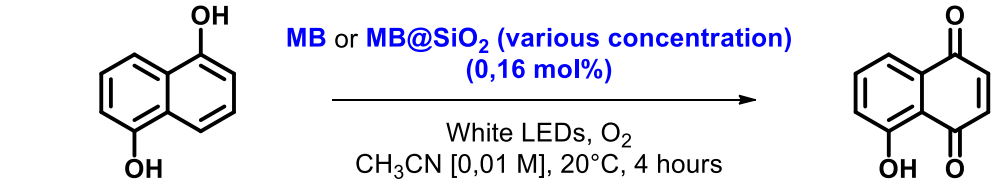


Figure S6. Fluorescence microscopy experiment to prove the non-covalent link between MB and SiO_2 (a) pure SiO_2; (b) MB@SiO_2 MPs; (c) MB@SiO_2 MPs + SiO_2 without solvent; (d) MB@SiO_2 MPs + SiO_2 mixed in H_2O

5. Screening of optimal concentration

We initially performed control experiments on the conversion of 1,5-dihydroxynaphthalene to produce juglone. In these experiments the performance of various MB/SiO_2 density were assessed and we found that 1,25 mg/g of MB/SiO_2 was the optimal concentration.



1,5-dihydroxynaphthalene

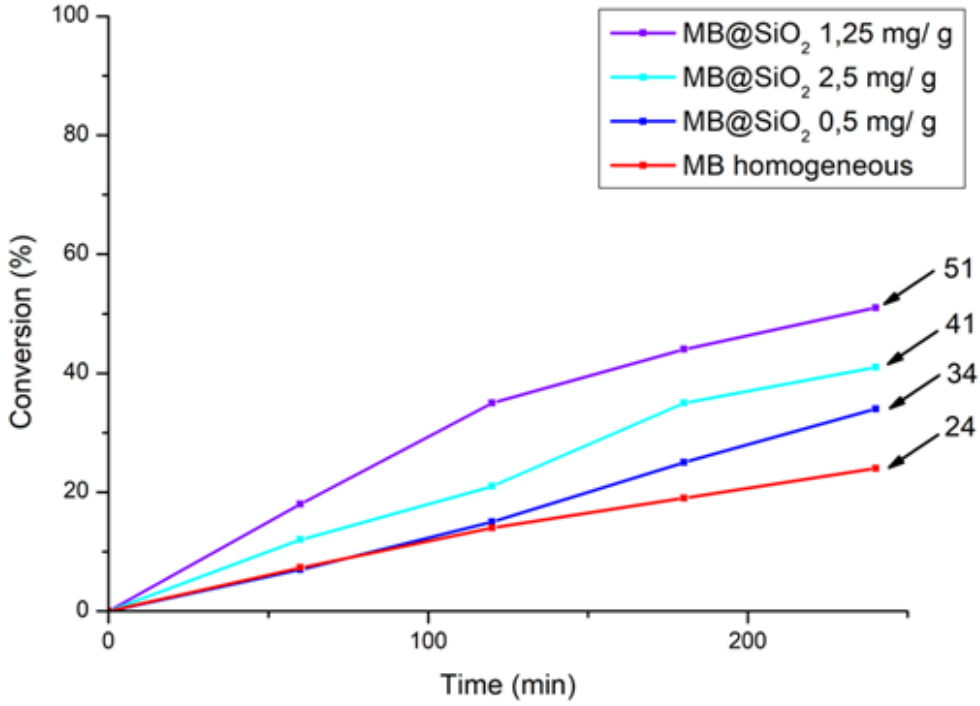


Figure S7. Screening of optimal concentration of MB/SiO_2 on the photo-oxidation of 1,5-dihydroxynaphthalene

6. Influence of the temperature on the conversion of β-citronellol

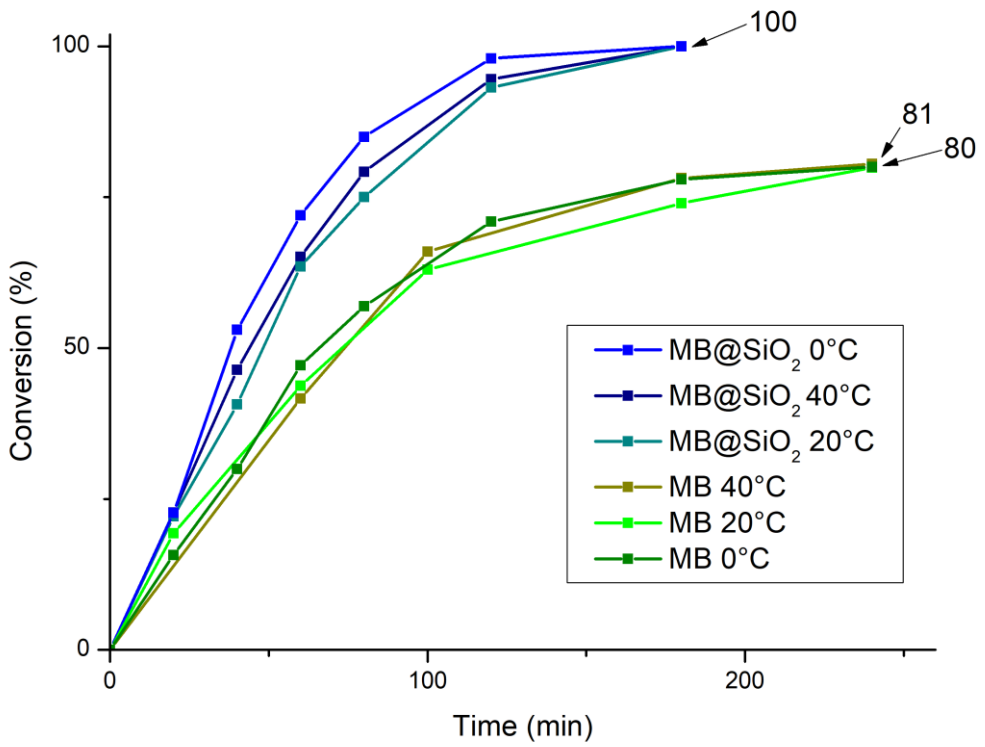


Figure S8. Study of the effect of the temperature on the β-citronellol photo-oxidation

7. Control experiments

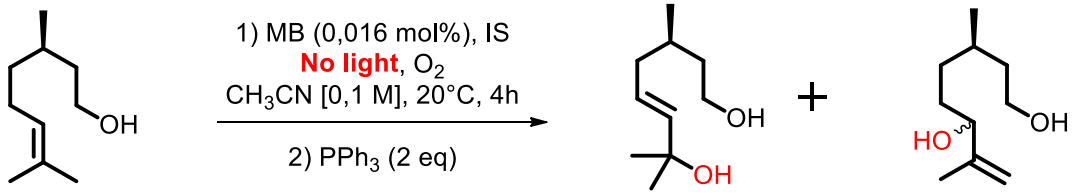
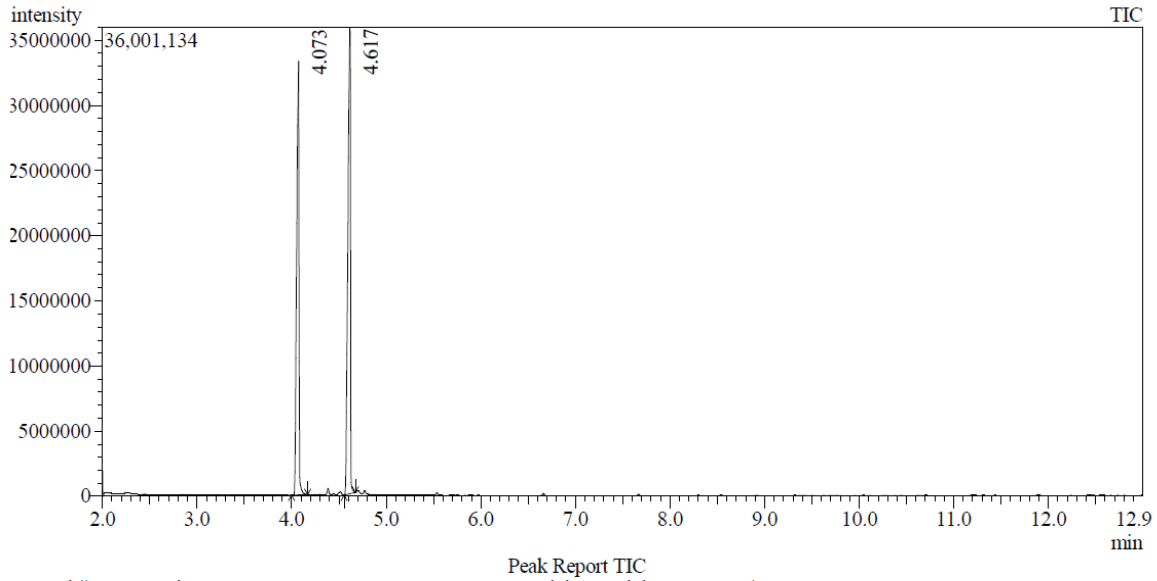


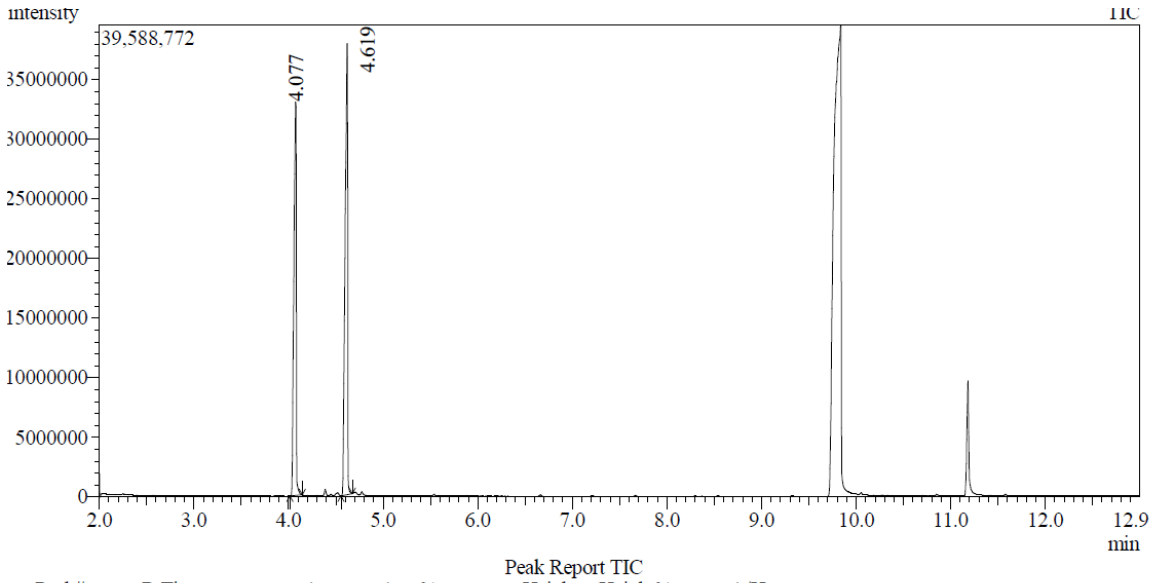
Figure S9. Control experiment without light



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	A/H
1	4.073	56699777	45.70	33281555	48.18	1.70
2	4.617	67371638	54.30	35795959	51.82	1.88
		124071415	100.00	69077514	100.00	

Figure S10. Control experiment without light at t_0



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	A/H
1	4.077	58531351	45.37	32983741	46.58	1.77
2	4.619	70465689	54.63	37830445	53.42	1.86
		128997040	100.00	70814186	100.00	

Figure S11. Control experiment without light after 4 hours of reaction

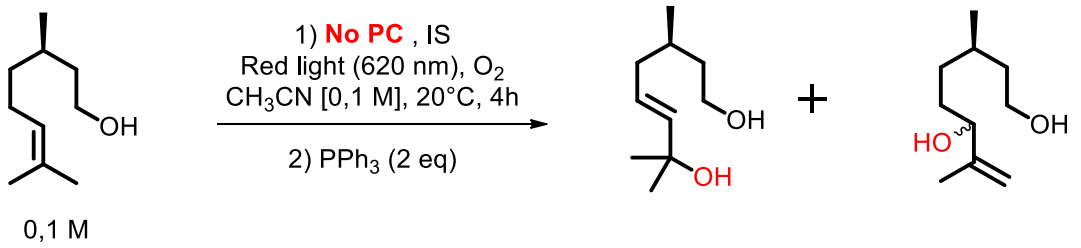
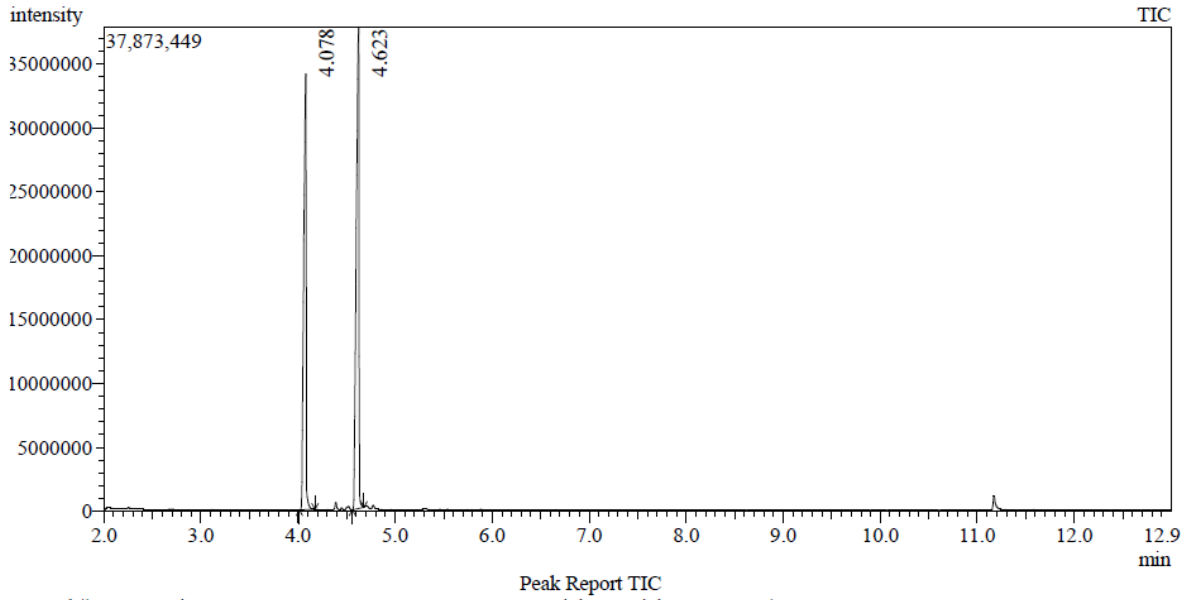


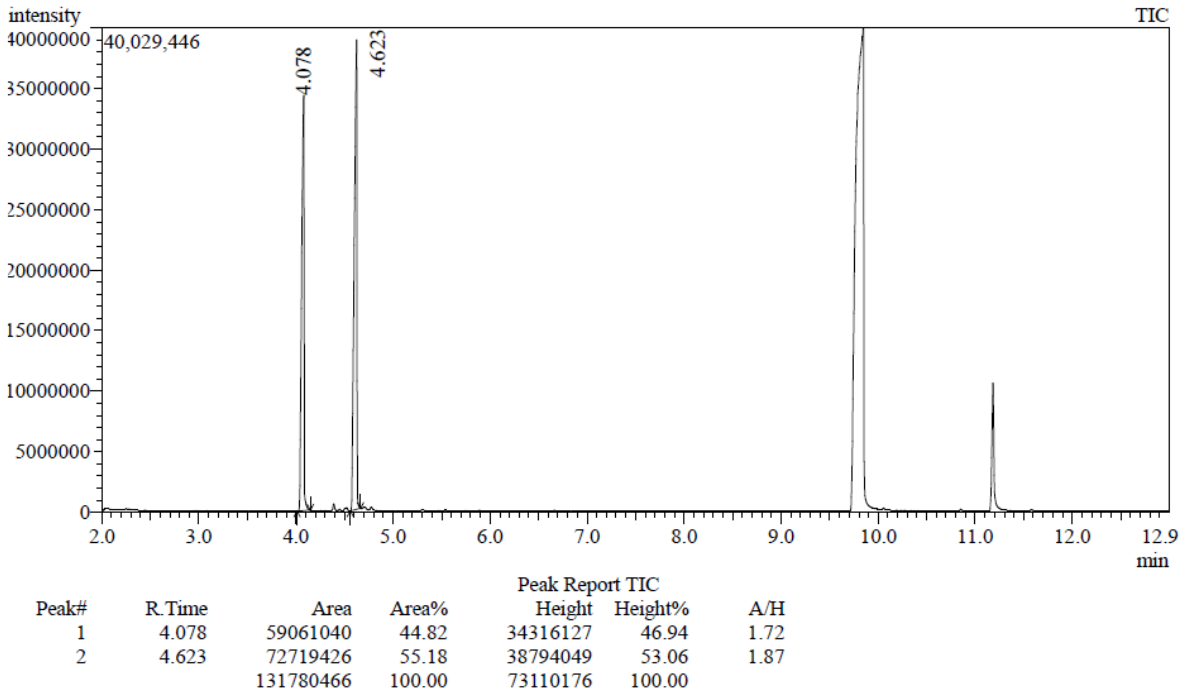
Figure S12. Control experiment without PC



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	A/H
1	4.078	59730083	45.20	34107918	47.53	1.75
2	4.623	72413705	54.80	37659874	52.47	1.92
		132143788	100.00	71767792	100.00	

Figure S13. Control experiment without PC at t_0



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	A/H
1	4.078	59061040	44.82	34316127	46.94	1.72
2	4.623	72719426	55.18	38794049	53.06	1.87
		131780466	100.00	73110176	100.00	

Figure S14. Control experiment without PC after 4 hours of reaction

8. β-citronellol photooxidation in batch and flow photoreactors

Batch reactions

Homogeneous Conditions: A 100 mL mixture of β-citronellol (10 mmol, 1,82 mL) and 1,3-dimethoxybenzene (10 mmol, 1,3 mL) was prepared in CH_3CN and sonicated for 5 minutes. This solution was analyzed by GC-MS in order to calculate the response factor. Then, 0,51 mL of MB solution (1 g/L solution in CH_3CN) was added to the solution. An oxygen balloon with a needle bubbling in the liquid was used to continuously oxygenate the solution. The solution was irradiated under red light (620 nm) and stirred for 4 hours. Aliquots were taken and quenched with 2 equivalents of PPh_3 before GC-MS analysis.

Heterogeneous Conditions: A 100 mL mixture of β-citronellol (1 eq, 1,82 mL) and 1,3-dimethoxybenzene (1 eq, 1,3 mL) was prepared in CH_3CN. This solution was analyzed by GC-MS in order to calculate the response factor. Then, 409 mg of MB@SiO_2 (MPS or NPs) (1,25 mg/g) was added to the solution. An oxygen balloon with a needle bubbling in the liquid was used to continuously oxygenate the solution. The solution was irradiated under red light (620 nm) and stirred for 4 hours.

Aliquots were taken and quenched with 2 equivalents of PPh_3 and filtered on celite before GC-MS analysis.

Flow reactions:

Homogeneous Conditions: A 100 mL mixture of β-citronellol (1 eq, 1,82 mL) and 1,3-dimethoxybenzene (1 eq, 1,3 mL) was prepared in CH_3CN. This solution was analyzed by GC-MS in order to calculate the response factor. Then, 0,51 mL of MB solution (1 g/L solution in CH_3CN) was added to the solution. A pressure of 6 bars was fixed in the system and the desired flowrate was fixed to reach the appropriate residence time. The reaction temperature was regulated at 20°C and the fluidic photo-reactor was irradiated at 610 nm with 100 % intensity. Aliquots were taken and quenched with 2 equivalents of PPh_3 before GC-MS analysis.

Heterogeneous Conditions: A 100 mL mixture of β-citronellol (1 eq, 1,82 mL) and 1,3-dimethoxybenzene (1 eq, 1,3 mL) was prepared in CH_3CN. This solution was analyzed by GC-MS in order to calculate the response factor. Then, 409 mg of MB@SiO_2 NPs (1,25 mg/g) was added in solution. A pressure of 6 bars was fixed in the system and a correct flow to reach an appropriate residence time. The system was thermoregulated at 20°C and fluidic photo-reactor was irradiated at 610 nm with 100 % intensity. Aliquots were taken and quenched with 2 equivalents of PPh_3 and filtered on celite before GC-MS analysis.

Experiments for tTON calculation in the continuous flow reactor:

Homogeneous Conditions: A 70 mL mixture of β-citronellol (1 eq, 1,28 mL) and phenyl acetate (internal standard, 1 eq, 0,8 mL) was prepared in CH_3CN. This solution was analyzed by GC-MS in order to calculate the response factor. Then, 35 µL of a 1g/ L MB solution was added in this solution. A pressure of 6 bars, a 0.25 $mL \cdot min^{-1}$ flow and a 1 $mL \cdot min^{-1}$ O_2 flow were fixed. The system was thermostated at 20°C and fluidic module was irradiated at 610 nm with 100 % intensity. Aliquots were taken and quenched with 2 equivalents of PPh_3 before GC-MS analysis. The same procedure was repeated during three cycles by recirculating the crude solution mixture. The cumulated conversion was calculated after each cycle.

Heterogeneous conditions: A 70 mL mixture of β-citronellol (1 eq, 1,28 mL) and phenyl acetate (1 eq, 0,89 mL) was prepared in CH_3CN. 28 mg of MB@SiO_2 NPs was added to this solution. A pressure of 6 bars, a 0.25 mL/ min flow and a 1 mL/ min O_2 flow were fixed. The system was thermostated at 20°C and fluidic module was irradiated at 610 nm with 100 % intensity. Aliquots were quenched with 2 equivalents of PPh_3 and filtered on celite before GC-MS analysis. The same procedure was used during three cycles by recirculating the crude solution mixture. The cumulated conversion was calculated after each cycle.

9. Reaction analysis

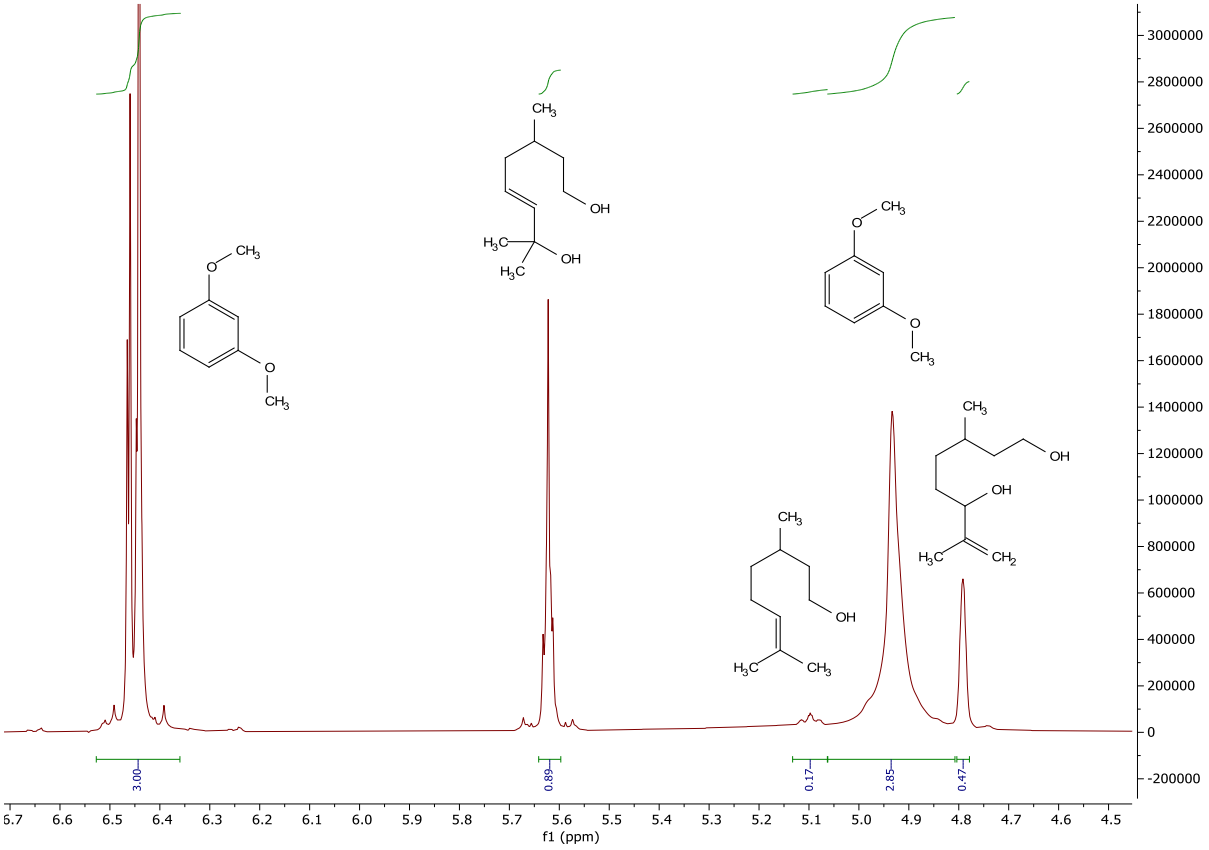


Figure S15. Example of NMR spectra for crude product with a conversion of 83 % and a 49:51 selectivity

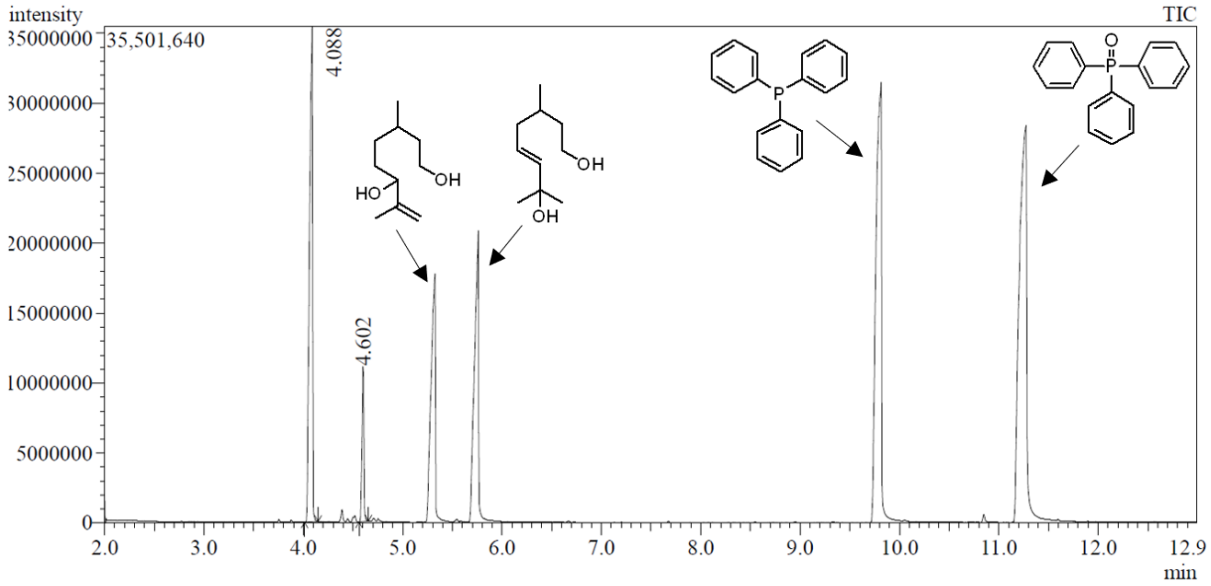


Figure S16. GC-MS spectrum of β-citronellol photooxidation. β-citronellol tr = 4,602 min; 1,3-dimethoxybenzene tr = 4,088 min

Thomassen, L. C. J., Aerts, A., Rabolli, V., Lison, D., Gonzalez, L., Kirsch-Volders, M., et al. (2010). Synthesis and Characterization of Stable Monodisperse Silica Nanoparticle Sols for *in Vitro* Cytotoxicity Testing. *Langmuir* 26, 328–335. doi:10.1021/la902050k.