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In Situ, Simultaneous Irradiation and Monitoring of a Photocatalyzed Organic Oxidation Reaction in a TiO_2-Coated NMR Tube

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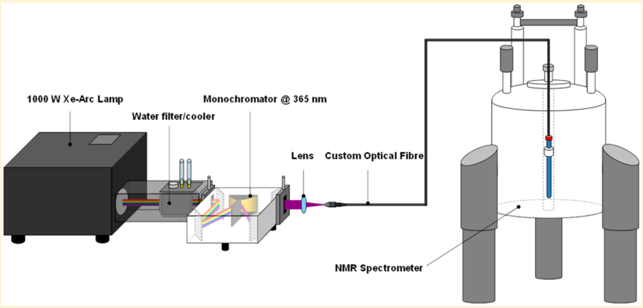
ABSTRACT: The semiconductor photocatalyzed (SPC) oxidation of toluene is performed *inside* an NMR spectrometer and the reaction is monitored simultaneously *in situ*, using a fiber optic probe/diffuser to provide the UV light to activate the titania photocatalyst coating on the inside of the NMR tube. Such a system has great potential for the simple rapid screening of a wide range of SPC mediated organic reactions.



Semiconductor photocatalysis (SPC) in organic synthesis was the subject of significant research in the early 1980s[1] and now appears to be attracting increasing attention as it presents a 'greener' approach to organic synthesis. It also offers a high degree of control (the reaction can be stopped by simply switching off the light); in many cases, selectivity; and the ability to perform redox reactions under ambient conditions of temperature and pressure.[2−4] This photocatalytic approach to organic synthesis has been the subject of recent reviews[4−9] and includes a wide range of organic transformations such as carbon−carbon[10] and carbon−heteroatom[11] coupling, cyclization,[12] reduction,[13] and oxidation.[14] However, most reported photocatalytic organic synthetic processes are not stereo- or region-specific, probably due to the radical nature of the underlying reaction mechanisms.

This group has recently reported the use of sol−gel titania-coated NMR tubes, with *ex situ* irradiation, as a possible fast screening method to assess a range of SPC mediated organic reactions, such as the oxidation of toluene,[15] and the carbon−carbon coupling of phenoxyacetic acid with maleimides,[16] and acrylamide,[17] all of which can be monitored *in situ*. The SPC reactions were performed on a 1 mL scale inside a sealed NMR tube, as opposed to using a more commonly larger scale photoreactor (ca. 75−100 mL), from which samples are removed and prepared for analysis by conventional methods, such as HPLC, GC-MS, FTIR, etc. The advantages of working on this small, 1 mL, scale includes faster reaction times (vide infra) and the ability to use a deuterated solvent (which otherwise would be prohibitive on cost grounds), allowing high resolution ^1H NMR to be employed to monitor the progress of the reactant, intermediates, and product(s) quickly and easily as the photocatalyzed reaction proceeds. The titania-coated NMR tube screening method has been demonstrated to be 10−40 times faster than its more conventional, large scale counterpart, due to the low reaction volume and high surface area of the mesoporous TiO_2 sol−gel film in contact with the reactants in solution.[15,17]

The *in situ* irradiation approach (i) obviates the need to transfer samples to the NMR, (ii) allows time-resolved spectra to be obtained, and (iii) is most useful for observing reactive species that would have otherwise decayed during the transfer process. NMR is preferred as a monitoring tool over the more traditional methods of UV/vis or IR spectroscopies because it gives much greater insight into the structure and bonding in molecules, although the latter techniques can be used to monitor much lower concentrations, i.e. much less than the usual >0.1 mM concentrations required for NMR. It can be argued that the main disadvantage of this method is the requirement of a more complicated, and possibly more expensive, irradiation setup, when compared to performing the same irradiation *ex situ*.

Some of the earliest *in situ* photochemical NMR work was used to observed photochemically induced dynamic polarization (photo-CIDNP) in the late 1960s.[18] The light from high wattage arc lamps was focused on the NMR sample under testing, usually via a purpose made hole in the NMR probe.[18−20] In modern NMR instruments, which utilize superconducting magnets, the sample is much less accessible and such work requires delivery of the light to the sample along the vertical bore of the magnet. Other, nonphoto-CIDNP, photochemical processes have been studied using in situ NMR, including: photochromism,[21] azo-dye transformations,[22] RNA folding,[23] protein refolding,[24] and a photoinduced process involving organometallic compounds.[25] Light sources used for this work are usually arc lamps,[24] lasers,[22] and, more recently, LEDs.[26] The former are relatively inexpensive and provide a broadband output, whereas the lasers are generally more

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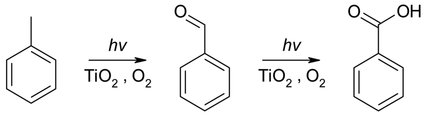
expensive and have more safety issues associated with their operation.

Historically, the most common arrangement for the delivery of the light is through a quartz external light pipe, coming from the bottom of the probe, capped with a mirror, prism etc., so as to deliver the light horizontally to the sample in the NMR probe.[27,28] An attractive alternative is to use a fiber optic to deliver light down the magnet bore, in which the unmodified fiber can be placed above or in solution.[29,30] More recently, Kuprov and Hore have modified a conventional silica fiber so that it has a stepwise tapered tip which allows light to be emitted along its length thereby providing more uniform irradiation along its length.[31]

This note reports on the further and significant development of the rapid screening technique in which a fiber optic diffuser probe is used to deliver UVA light directly inside the sealed TiO_2-coated NMR tube in the NMR spectrometer, thus allowing the reaction solution composition to be monitored simultaneously by NMR as the photocatalytic reaction proceeds. The photocatalytic reaction chosen to demonstrate this method is the SPC oxidation of toluene to benzaldehyde and its subsequent oxidation to benzoic acid (see Scheme 1).[14,15]

Scheme 1. SPC Mediated Oxidation of Toluene to Benzaldehyde, and Then to Benzoic Acid



The majority of commercially available fiber optic diffusers are designed to transmit in the visible and infrared, for applications from pool lighting to photodynamic therapy. Thus, for this work a custom-made, UV diffuser was prepared, in which the end of a 6 m length of fiber optic cable (ThorLabs, Ltd. (BFH37-1500) high OH, 1500 μm core) was stripped of its plastic cladding and the underlying silica core was roughened with careful sanding, using 60-grit sandpaper, to produce the 40 mm long diffuser tip shown in Figure 1a. Its ability to diffuse UVA light is demonstrated in Figure 1b, where the tip was placed in a 10^{-4} M solution of fluorescent brightener 28 to reveal the presence of the emerging UV light, and the other end of the fiber optic cable was coupled to a 1 kW Xe-arc lamp monochromator combination, with the latter set at 365 nm. Figure 1c shows the fiber optic diffuser placed in a sealed NMR tube containing 1 mL of 1 mM toluene in oxygen saturated CD_3CN, and 0.5 μL of 5 M H_2SO_4, with the UV light off and on. Figure 1b illustrates how the light is distributed along the length of the etched fiber core used in this work. In this work, a typical fiber, with its core and cladding stripped off, emitted 90% of the UV light from the tip, whereas, after etching, this figure was reduced to ca. 5%. Clearly, the observed kinetics of photocatalysis will depend upon the amount of UV light emitted from the sides of the fiber optic and so the degree of etching. Whereas we have used sandpaper to perform this task, with reasonable reproducibility (±10%), others have used sand-blasting which has the potential for greater reproducibility.[26]

In a photocatalysed organic synthetic reaction involving O_2, as studied here, it is important that the level of O_2 does not become the limiting reagent, as this would affect the kinetics and possibly the nature and levels of the product(s). Thus, in this work the concentration of O_2 employed (i.e., O_2-saturated = 8.1 mM at 25 °C)[32] far exceeded that of the organic species under testing (1 mM). This potential problem is further mitigated by observation of the following: (i) for most photocatalyzed reactions involving TiO_2, the kinetics are Langmuir−Hinshelwood-like, i.e. saturated type kinetics, and (ii) when using O_2 as a reagent, a saturated rate is usually achieved at an O_2 concentration less than that associated with an air-saturated solution, i.e. 5 times less than that used in this work. For example, in a study of the photocatalysed oxidation of amines to imines in acetonitrile conducted by Zhao et al.,[33] the kinetics were found to be independent of $[O_2]$ at values greater than air-saturated values (1.6 mM). Evidence that O_2 was not a limiting reagent in the nonspun NMR tube in situ work carried out here was provided by the observation that the same intermediates and products were generated, using largely the same system, but with the NMR tube: (i) outside the NMR instrument and (ii) illuminated using a cylindrical photoreactor comprising 12 8-W 365-nm blacklight blue lamps (UV irradiance: 3.5 mW cm^{-2}) and (iii) spun continuously (250 rpm).

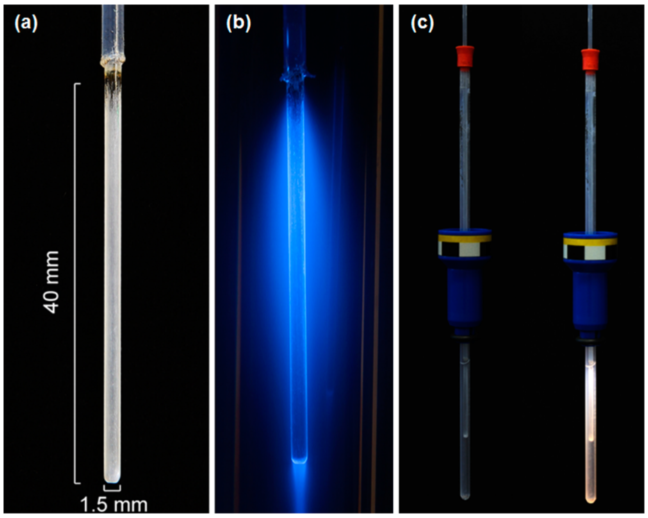


Figure 1. (a) Custom made optical fiber diffuser tip. (b) Irradiation of a 10^{-4} M solution of fluorescent brightener 28, demonstrating the distribution of the diffused 365 nm light from a 1 kW Xe-arc lamp. (c) The optical fiber installed inside a sealed NMR tube, also demonstrating, the UV light off and on, the efficient irradiation of the photocatalyst-coated sides of the NMR tube down the length of the solution.

The sol−gel titania coating inside the NMR tube is typically 1.4 ± 0.2 mg cm^{-2}, and its preparation is described elsewhere.[15] Although there are many reported different methods for the manufacture of TiO_2 sol gel films, of different porosity and phase, the sol gel coating material used here was chosen for its established high activity and reproducibility.[34] Indeed, the same sol−gel is used in the manufacture of dye-sensitized solar cells[35] and available commercially.[36]

In a typical experiment, a 1 mL reaction solution in an NMR tube (i.d. = 0.4 cm) is exposed to ~11 cm^2 of irradiated photocatalyst film. The fiber is held in place using a hollowed out rubber septa cap, shown in Figure 1c.

Figure 2 shows the successful monitoring, by NMR, of the SPC oxidation of toluene via Scheme 1 (with the reaction solution comprising 1 mL of an oxygen saturated CD_3CN solution of 1 mM toluene with 0.5 μL of 5 M H_2SO_4), in an

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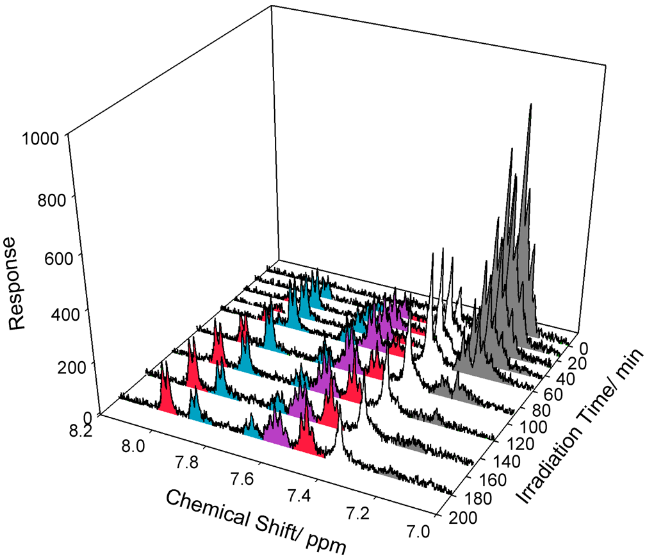

Figure 2. Change in ^{1}H NMR of the SPC oxidation of toluene in a titania coated NMR tube, irradiated *in situ* using a fiber optic probe (λ_{max} = 365 nm, provided by a 1 kW Xe-arc lamp connected to a monochromator). The gray signals correspond to toluene, while the blue and red correspond to benzaldehyde and benzoic acid, respectively. The purple represents the significant area of overlap of triplets from both products.

NMR tube, over a 3 h period sensitized by the TiO_2 coating, when irradiated *in situ* using the fiber optic diffuser, illustrated in Figure 1. Although the products are mainly those outlined in Scheme 1, i.e. benzaldehyde followed by benzoic acid, it is evident from the data in Figure 2 that a small amount of benzene is also produced (with a peak at 7.3 ppm), and this is thought to be via decarboxylation of the radical intermediate in the formation of benzoic acid.

Figure 3 shows more clearly the progress of the SPC oxidation of toluene where the concentration versus irradiation time profiles were generated using the data reported in Figure 2. These results reveal maximum concentrations of benzaldehyde (0.27 mM) and benzoic acid (0.28 mM), after 60 and 150 min, respectively. In this work, there was no evidence of product contamination of the fiber, and so it could be used repeatedly with no loss of efficacy. In the absence of photocatalyst, no photochemical decomposition of the reactant components was observed. In a set of repeated runs, the reproducibility in the measured rates was ca. ±3%.

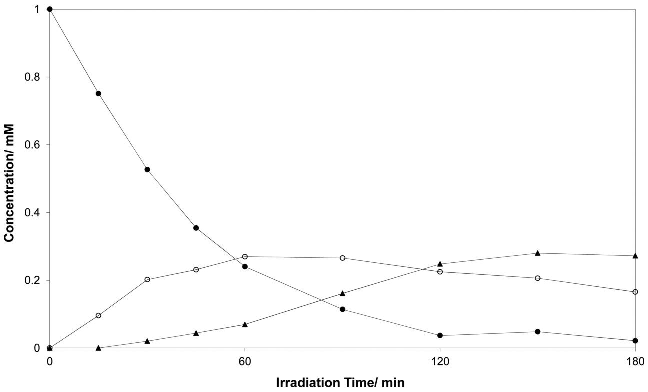

Figure 3. Change in concentration of toluene (●), benzaldehyde (○), and benzoic acid (▲) as a function of irradiation time, determined by NMR analysis, for the optical fiber irradiated sol−gel coated tube.

With all in situ NMR studies, any kinetic analyses must take into consideration how readily the reaction solution is mixed within the NMR sample tube, mainly by convection. Fortunately in our work, with the fiber optic in place, complete mixing of a small (20 μL) plug of test organic injected onto the top of reaction solution in the NMR tube (thermostated at 40 °C as in all this work) took <3 min. Thus, slow photoprocesses, such as the photocatalytic reaction studied here, should not be affected by probe position, as was found to be the case in this work.

Other work showed that, with repeated use of the photocatalyst film, its activity decreases as unidentified organic, UV-absorbing polymeric byproducts accumulated on its surface. However, its activity was readily restored by heating at 450 °C for 30 min.

It has been successfully demonstrated that an optical fiber with a diffuser tip can be used to provide light inside a sol−gel titania-coated NMR tube (held inside an NMR spectrometer) to promote photocatalytic reactions, such as the SPC oxidation of toluene, and allow the simultaneous *in situ* real-time analysis of the photocatalyzed changes in concentration of both the reactants and products. This method allows the rapid screening of an established photocatalyst for mediating a variety of different reactions and the screening of new photocatalysts using established reactions, such as the oxidation of toluene used above.

In addition, as the light is being provided via a monochromator, this system readily lends itself to the acquisition of action spectra data,[37] which are useful when using different or doped semiconductor photocatalyst coatings, so as to help optimize the illumination conditions. Fine control of the wavelength of the incident light is also vital if any of the starting materials or products absorb significantly in the UV region, since careful selection of the wavelength will help minimize/eliminate any possible background (i.e., non-SPC) photochemistry.

This novel approach to monitoring SPC mediated reactions should prove invaluable in screening new photocatalyst material films and a wide range of different organic reactions.

■ EXPERIMENTAL SECTION

Unless otherwise stated, all chemicals used in this work were purchased from Sigma-Aldrich and were used as supplied.

Preparation of TiO_2 Sol−Gel Paste. A paste of titania nanoparticles was prepared using the sol−gel method described by Mills et al.[34] Briefly, the precursor, titanium(IV) isopropoxide (20 mL), was modified by the addition of glacial acetic acid (4.65 g). The modified precursor was then added to a solution of 120 mL of deionized water containing 1.08 g of nitric acid, thus initiating the hydrolysis reaction, which leads to a condensation reaction that produces the hydrous oxide. The colloidal titania particles were then grown via Ostwald ripening using an autoclave set to 220 °C for 12 h. The resulting precipitated particles were dispersed using an ultrasonic probe, and the solution was rotary evaporated until a weight percent of titania of 10−12% was achieved. At this stage 50 wt % of polyethylene glycol was added as a binder to help prevent the formation of cracks in the cast films.

Preparation of TiO_2 Coated NMR Tubes. A few drops of the titania paste were pipetted into a NMR tube and shaken with the cap in place until the paste completely covered the inside of the tube. The cap was then removed, and the NMR tube placed in the chuck of an overhead stirrer turned on its side and rotated horizontal to the floor at 1000 rpm for 5 min to create an even thickness of the paste film on the sides of the NMR tube, before placing it under vacuum using a rotary evaporator to remove all the remaining solvent. The tube was then placed in a furnace and heated to 450 °C for 90 min (ramp rate = 10 °C min^{-1}). The tube was then left overnight to cool slowly inside the furnace to create a final robust, clear coating of anatase titania (ca. 1.4 mg cm^{-2}, thickness ~4 μm) on the inside of an otherwise conventional Pyrex/quartz NMR tube (5 mm o.d., length = 20.3 cm). XRD reveals the annealed TiO_2 film is in its anatase crystal form.[34]

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Notes

The authors declare no competing financial interest.

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