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Large-Scale Photochemical Reactions of Nanocrystalline Suspensions: A Promising Green Chemistry Method

Marcel Veerman, Marino J. E. Resendiz, and Miguel A. Garcia-Garibay*

Department of Chemistry and Biochemistry, University of California,
405 Hilgard Avenue, Los Angeles, California 90095-1569

mgg@chem.ucla.edu

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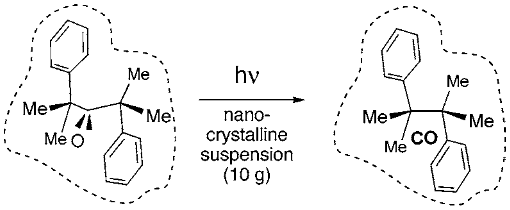
ABSTRACT

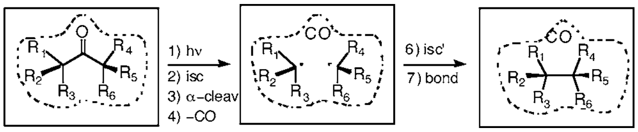


CRYSTAL-TO-CRYSTAL REACTIONS

Photochemical reactions in the solid state can be scaled up from a few milligrams to 10 grams by using colloidal suspensions of a photoactive molecular crystal prepared by the solvent shift method. Pure products are recovered by filtration, and the use of H_2O as a suspension medium makes this method a very attractive one from a green chemistry perspective. Using the photodecarbonylation of dicumyl ketone (DCK) as a test system, we show that reaction efficiencies in colloidal suspensions rival those observed in solution.

The high selectivity and specificity of photochemical reactions in crystals have been known for many years.[1] However, it is only recently that their potential for synthetic transformations has been demonstrated in total synthesis.[2] While there has been some recent progress in the prediction and control of crystallization[3] and solid-state reactivity,[4,5] it is now essential to develop a general method that allows large-scale photochemical reactions to occur in a practical and energetically efficient manner. Having recently identified the photodecarbonylation of crystalline ketones[6] as a promising method for the stereospecific synthesis of quaternary stereogenic centers[7] (Scheme 1) and recognizing its potential in the development of green chemistry strategies,[8,9] we decided to investigate scale-up procedures that may lead to solid-state photochemical reactions in the multigram to

Scheme 1



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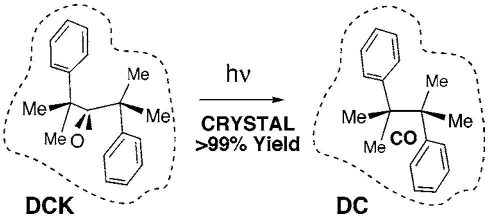
10.1021/ol060978m CCC: $33.50

Scheme 2



kilogram scales. MacGillivray and co-workers have shown the feasibility of such processes.[10]

To investigate these expectations, we selected the readily available dicumyl ketone (**DCK**) as a test system. We have recently shown that irradiation of **DCK** in solution leads to formation of dicumene (**DC**) in 60% yield, isopropylbenzene and α-methylstyrene in ca. 10% yield each, and several other unidentified products (20%). In contrast, finely powdered crystals of **DCK** react in a very clean solid-to-solid reaction to give **DC** as the only product in >99% yield (Scheme 2).[11]

As a starting point, we compared the reaction efficiency of single crystals (ca. 1 × 1 × 2 mm^3) with that of microcrystals grown as a thin film by fast evaporation of diethyl ether over a microscope slide.[12] Both experiments gave **DC** as the only product. However, after 10 h, the single crystals had reacted to only ca. 5% conversion while the smaller crystals had reacted to completion. Large single crystals had turned opaque and tended to splinter, whereas crystals in the film remained birefringent when analyzed under cross polarizers.

To scale up the reaction and promote homogeneous illumination, samples of **DCK** were mechanically ground and suspended in an aqueous solution containing an equivalent mass of sodium dodecyl sulfate (SDS), which was added to reduce surface tension. Microscopic analysis indicated that particle sizes in these experiments were in the range of ca. 15−55 μm. Samples prepared with 40, 80, 120, and 180 mg of **DCK** in 20 mL of water were irradiated with an external light source while being continuously stirred. The extent of reaction was monitored by GC every 2 h and the product recovered by filtration with a cellulose filter (11 μm nominal retention size). As illustrated in Figure 1, the initial kinetics of product formation tended to a zero order law for high particle loadings and are a linear function of irradiation time, as expected for an optically dense medium where photons are the limiting reagent. Notably, the reaction proceeded to >98% conversion within 10−26 h, and the efficiency of product recovery increased with particle loading from 69.9% (at 2 mg/mL) up to 98.1% (at 8 mg/mL) with a relatively constant amount of loss material of ca. 0.25 mg/mL.

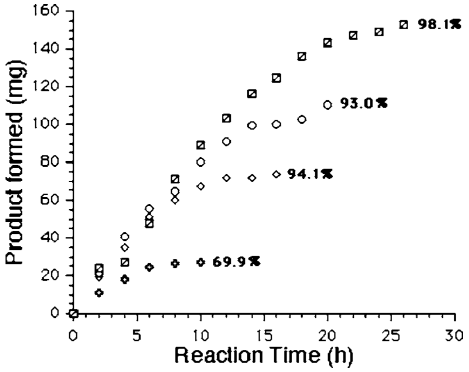


Figure 1. Product formation as a function of irradiation time for microcrystalline samples suspended in 20 mL of H_2O containing SDS. All reactions proceeded to >99% conversion. The percentage product recovery indicated on the right of each trace varied.

Knowing that nanocrystalline suspensions of diolefin monomers are able to retain their single crystalline phase during a photopolymerization reaction,[13] and taking advantage of the reprecipitation method,[14] we were able to increase the scale of the reaction by up to 2 orders of magnitude. Nanocrystalline suspensions were prepared by slowly adding a saturated **DCK** solution in acetone into H_2O with SDS. The method is known to provide stable suspensions with a distribution of particle size from tens of nanometers to microns.[14,15] Suspensions of **DCK** had a milky-white appearance characterized by particle sizes with an average in the 800−1500 nm range, as determined by dynamic light scattering. FT-IR analysis confirmed formation of the same polymorph as that obtained by solvent evaporation.[11] Suspensions prepared in this manner were ideally suited for irradiation with an immersion well (Figure 2a). The progress

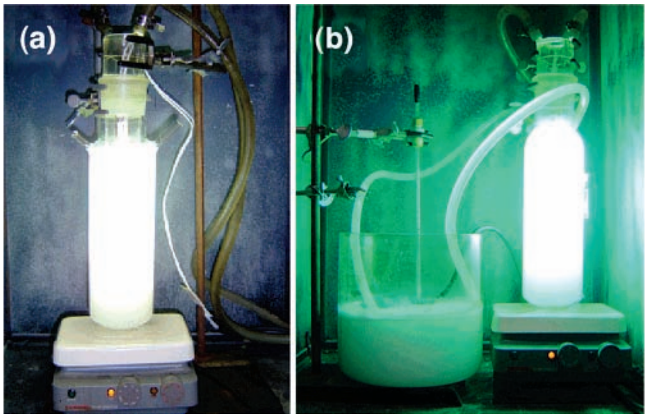


Figure 2. Experimental set up used for the photolysis of 2 and 10 g of **DCK** in H_2O.

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(12) All photochemical experiments were carried using a 400 W medium-pressure Hg-lamp using Pyrex glass as a filter ($\lambda > 290$ nm).

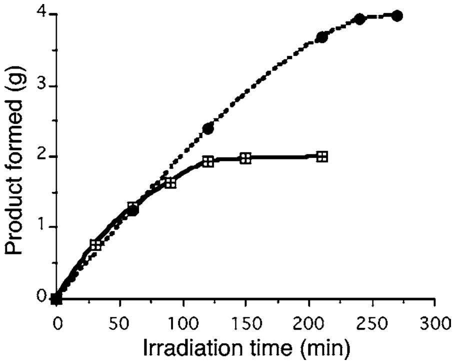

Figure 3. Product formation as a function of irradiation time for samples of 2 and 4 g of **DCK** suspended in 1.0 L of H_2O.

of reactions carried out with suspensions containing 2 and 4 g of **DCK** in a 1 L well revealed a remarkably efficient process with reaction velocities of ca. 1 g/h with the 400 W medium-pressure Hg lamp (Figure 3). Given that suspensions with greater particle loading were not stable, larger reaction scales were explored with a flow reactor consisting of a 5 L vessel and a submersible pump that circulates the suspension through the immersion well. Shown in Figure 2b, a reaction of 10 g of **DCK** in 3.3 L of water (3 g/L) led to 91.2% conversion in 19 h for an apparent rate of ca. 0.5 g/h. Possible reasons for the lower efficiency in the latter experiment may be related to the formation of foam, which ascends to the upper portion of the vessel trapping some of the reactant, and to partial sedimentation of particles during the longer experiment. These problems should be easily solved by using a closed, evacuated system and a suitable stirrer.

The macroscopic homogeneity of the nanocrystalline suspensions and their ability to trap all the absorbable photons emitted by the source suggested an opportunity to determine the absolute quantum yield of the reaction by conventional valerophenone actinometry.[16] We established that the quantum yield of reaction of **DCK** in benzene ($\Phi = 0.41 \pm 0.04$)[17] is only twice as large as that in the solid ($\Phi = 0.20 \pm 0.02$). However, **DC** is the only product formed in crystals. In conclusion, the use of nanocrystalline suspensions is a promising strategy to scale-up photochemical reactions of crystalline solids. Strategies shown here suggest simple ways to scale these reactions to the multi-kilogram scale. We believe that reactions in crystals will provide a practical green chemistry approach for the synthesis of structurally complex, specialty chemicals. This work provides a strong incentive to investigate the formation and control of organic molecular nanocrystals.

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Supporting Information Available: Photochemical procedures and NMR data for **DCK** and **DC**. This material is available free of charge via the Internet at http://pubs.acs.org.

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