Green photochemistry: solarchemical synthesis of 5-amido-1,4-naphthoquinones†

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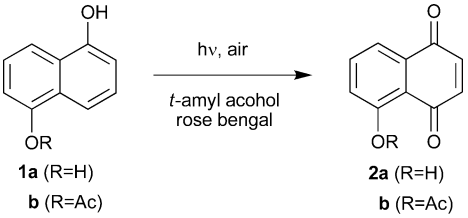
Dye sensitized photooxygenations of 5-amido-1-naphthols were investigated with artificial light and sunlight, and the corresponding 5-amido-1,4-naphthoquinones were isolated in moderate to excellent yields. Under sunny conditions the yields were higher for almost all cases studied. The energy demand of the equipment used was determined, revealing significant energy savings for solar exposures.

Recent concerns regarding global warming and climate change have lead to the establishment of *green chemistry* and its principles in academia and industry.[1] Among the many different *green chemical* approaches, photochemistry can play a central role since light is regarded as a *clean reagent*.[2] So far, however, the high energy demand of most common artificial light-sources has prevented widespread usage of photochemical methods in industry. To overcome this disadvantage, sunlight (direct or concentrated) has recently been applied as sustainable light-source.[3] This concept leads back to the origin of organic photochemistry in the late 19th century.[4] In recent years, we have demonstrated the feasibility of solarchemical syntheses for a number of commodity chemicals.[5] During our ongoing study on photoacylation reactions,[6] we became especially interested in the synthesis of 1,4-naphthoquinones through solar photooxygenations.[7] 1,4-Naphthoquinones are important natural products, serve as valuable building blocks in synthesis and are key-moieties in biologically active compounds.[8] They are most commonly synthesized from the corresponding 1-naphthols by oxidation,[9] but these thermal pathways suffer from severe disadvantages concerning selectivity, sustainability or scale-up.[9a] Dye sensitized photooxygenations represent a useful alternative, and various examples have been reported in the literature.[7,10]

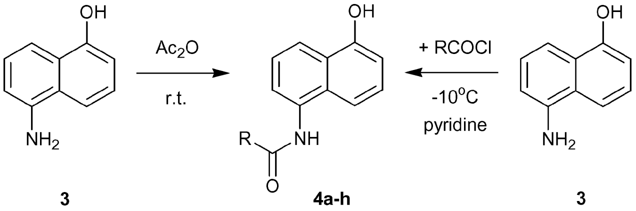
The photooxygenation of 1,5-dihydroxynaphthalene **1** to Juglone (**2**, 5-hydroxy-1,4-naphthoquinone) was selected as a model system to establish the most sustainable reaction conditions (Scheme 1). We were in particular interested in developing an entirely 'green' procedure and, for example, applied the solvent selection criteria developed by Pfizer[11] for the photochemical key-step *and* the subsequent purification.



Scheme 1 Photooxygenation to Juglone **2a** and 5-acetoxy-1,4-naphthoquinone **2b**.

The original irradiation procedures required the usage of the hazardous solvents dichloromethane, acetonitrile or methanol.[10] After extensive optimization we found *tert*-amyl alcohol to be a suitable 'green' substitute instead. Following a standardized procedure, a solution of 1,5-dihydroxynaphthalene **1a** was irradiated in a Schlenk-flask with a 500 W halogen lamp in the presence of rose bengal as a sensitizer while the solution was purged with air. After 2.5 h, Juglone was isolated *via* column chromatography in a yield of 62%. In an attempt to synthesize functionalized derivatives of Juglone, the mono-acetate **1b** was irradiated under the same conditions for 4 to 5.5 h. The outcome of this reaction was somewhat sensitive to workup conditions.‡ When the solvent was evaporated at elevated temperature, Juglone **2a** was isolated in 30% yield as the only product. When the water bath temperature was kept below 40 °C during evaporation, Juglone was only detected in trace amounts by TLC and the 5-acetoxy-1,4-naphthoquinone **2b** was isolated in a yield of 35% instead.

We thus became interested in using 5-amido-1-naphthols as starting materials. Subsequent photooxygenation would yield the corresponding 5-amido-1,4-naphthoquinones, and these compounds are known to show antibiotic properties.[12] The desired starting compounds **4a–h** were readily available through standard acylation from 5-amino-1-naphthol **3** in yields of 15–61% (Scheme 2).[13]



Scheme 2 Synthesis of 5-amido-1-naphthols **4a–h**.

When the amido-derivatives **4a–h** were irradiated for 4 h following the general photooxygenation procedure, the

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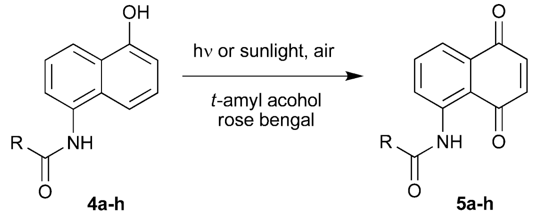
corresponding naphthoquinones **5a–h** were obtained in yields of 12–72% (Scheme 3). When irradiation was extended to 24 h, conversions and consequently yields increased and the desired products were isolated in amounts of 40–96% (Table 1). In July and August 2008, we repeated the photooxygenation reactions under 'outdoor' conditions at Dublin City University (latitude 53°23′ N, 6°15′ W, 50 m above sea level). Solutions of **4a–h** and rose bengal were exposed to direct sunlight for 6 h while the solution was purged with a gentle stream of air. During the course of each illumination the reaction mixture significantly darkened due to the formation of the strongly colored product. All solar experiments went smoothly and gave moderate to excellent yields of **5a–h** without any noticeable side-products or photodecomposition (Table 1). Under sunny or partly sunny conditions, the yields were comparable or higher than those after irradiation with artificial light for 24 h. Even under poor illumination conditions with mainly diffuse radiation the desired products were isolated in moderate to good yields, hence unambiguously proving the feasibility of solar synthesis. Likewise, solar exposure of the diol **1a** under sunny conditions for 4 h furnished Juglone **2a** in 70% yield and excellent quality.



Scheme 3 Photooxygenation of 5-amido-1-naphthols **4a–h**.

In order to compare the energy efficiency of solar exposure *vs.* irradiations with artificial light we measured the energy consumption per hour of operation of all electrical devices applied (Table 2) using a commercially available domestic electricity meter (Nikkai power, N67FU).[14] The 500 W halogen lamp consumed the by far largest amount of electrical power with 0.432 kWh (or 1555.2 kJ). Due to the significant generation of heat by the lamp, the 'indoor' procedure required additional cooling by an electrical fan thus adding 0.018 kW (or 64.8 kJ) for its operation. In contrast, the 'outdoor' procedure solely required the use of an air pump (common for both processes), which consumed just 0.002 kWh (or 7.2 kJ) of energy. Purging additionally avoided the need of a magnetic stirrer. Notably, the mild climate of Dublin (Ireland) in combination with the relatively high boiling point of *tert*-amyl alcohol (102 °C) does not necessarily require the need for cooling water, thus reducing the overall energy demand further.[15] Alternatively, the concept of using natural or artificial water reservoirs as heat sinks has been recently demonstrated by Liu and coworkers.[16] In comparison with the energy demand of a conventional hot plate/magnetic stirrer it is interesting to note that the selected artificial light-source required far more electrical energy per hour of operation.

Conclusions

In conclusion, the photooxygenation of a series of 5-amido-1-naphthols results in the formation of 5-amido-1,4-naphthoquinones in moderate to excellent yields. Solar illuminations under ideal conditions gave significantly higher yields for almost all cases examined. The energy demand of the equipment has been compared for solar exposure *vs.* irradiation for the first time. Significant energy savings could be achieved by completely avoiding artificial light. Hence, this transformation

Table 1 Isolated yields of photooxygenations to **4a–h**

		Artificial light		Sunlight	
5	R	4 h	24 h	6 h	Weather
a	Me	12%	80%	90%	sunny
b	Et	34%	89%	53%	cloudy[a]
c	*cyclo*-Pr	36%	54%	53%	partly sunny
d	*t*-Bu	72%	94%	54%	sunny spells
e	Ph	17%	58%	80%	partly sunny
f	*p*-ClC_6H_4	68%	72%	54%	cloudy[a]
g	*p*-MeC_6H_4	24%	40%	63%	partly sunny
h	*p*-NCC_6H_4	35%	96%	23%	cloudy[a]

[a] Mainly diffuse radiation.

Table 2 Energy consumption of equipment used[a]

	Model	E/kWh	E/kJ
Halogen lamp	IQ group HB-DFL-500, Armley lamp	0.432	1555.2
Air pump	Hagen Elite 800	0.002	7.2
Electric fan	GET, 9″ desk fan, G9DFAN	0.018	64.8
Oil bath (heating to 100 °C)[b]	IKA, yellowline MST basic	0.084	302.4
Oil bath (maintained at 100 °C)[c]	IKA, yellowline MST basic	0.054	194.4

[a] Energy consumption as measured by a Wattmeter for 1 h of operation. [b] Setting to 100 °C on the TC 1 probe (electronic contactthermometer) and 150 °C on the dial; 50 min heat up time, 10 min maintaining the temperature; 14 cm ∅ crystallization dish; 600 ml silicon oil (Fluka). [c] Same settings and conditions as [b].

can be regarded as another example of 'green photochemistry'[17] and a further contribution to Giacomo Ciamician's vision of '*the photochemistry of the future*' (presented at the International Congress of Applied Chemistry in New York in 1912).[18,19]

Experimental

Compound **4a** was synthesized as described by Jindal and co-workers.[13a] All other 5-amido-1-naphthols **4b–h** were prepared following a modified procedure reported by Neidlein and Moller.[13b] **General procedure:** 7.0 g (44 mmol) of 5-amino-1-naphthol **3** were dissolved in 75 ml of pyridine. 60 mmol of the corresponding acid chloride were added dropwise to the solution at −10 °C. After stirring for 3 h, the reaction mixture was poured onto ice-water. The precipitate was filtered off and washed twice with cold water. The crude product was recrystallized from ethanol–water or ethyl acetate–cyclohexane. Exemplary details for **5-pivaloylamino-1-naphthol** (**5d**). Purple solid; m.p.: 258 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 1.31 (s, 9H), 6.86 (dd, ^3J = 6.4, ^4J = 2.4 Hz, 1H), 7.30 (dd, ^3J = 6.4 Hz, 1H), 7.34-7.43 (m, 3H), 8.02 (d, ^3J = 8.0 Hz, 1H), 9.37 (br. s, 1H), 10.17 ppm (br. s, 1H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ = 27.5, 38.9, 108.0, 113.7, 120.2, 124.0, 124.5, 126.3, 125.4, 131.1, 133.8, 153.4, 177.1 ppm; IR (KBr): ν = 3284, 2970, 1655, 1599, 1577, 1493, 1408, 1274, 1209, 1141, 960, 779, 736, 555 cm^{-1}.

General Procedure for photooxygenation

1 mmol of 5-amido-1-naphthol **4** and 50 mg of rose bengal were dissolved in 100 ml of *tert*-amyl alcohol. The clear solution was irradiated (500 W halogen lamp) or exposed to direct sunlight in a Pyrex Schlenk-flask equipped with a cold finger and a reflux condenser for 4, 6 or 24 h at ambient temperature while purging with a gentle stream of air. Evaporated solvent should be refilled whenever necessary. The progress of the reaction was monitored by TLC analysis (SiO$_2$, cyclohexane:ethyl acetate 3:1). The solvent was removed under vacuum, and the residue was purified by column chromatography (SiO$_2$, cyclohexane:ethyl acetate 3:1). Experimental details and results are given in Table 1. Exemplary details for **5-pivaloylamino-1,4-naphthoquinone** (**5d**). Yellow solid; m.p.: 186 °C; ^{1}H NMR (400 MHz, acetone-d$_6$): δ = 1.36 (s, 9H), 7.04 (d, ^2J = 14.4 Hz, 1H), 7.06 (d, ^2J = 14.4 Hz, 1H), 7.78 (dd, ^3J = 7.6, ^4J = 1.2 Hz, 1H), 8.85 (dd, ^3J = 7.6, 8.4 Hz, 1H), 9.14 (dd, ^3J = 8.4, ^4J = 1.2 Hz, 1H), 12.13 ppm (br. s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 27.7, 40.8, 116.4, 121.9, 126.3, 132.3, 135.9, 138.1, 140.1, 141.9, 179.1, 184.7, 189.3 ppm; IR (KBr): ν = 3249, 2965, 1687, 1646, 1604, 1577, 1491, 1408, 1304, 1254, 1152, 1100, 944, 836, 740, 550, 448 cm^{-1}.

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‡ This phenomenon is currently being further investigated. The synthesis of Juglone starting from **1b** has previously been reported.[7b,10g]

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