CSIRO PUBLISHING

Aust. J. Chem.
http://dx.doi.org/10.1071/CH15627

Full Paper

Synthesis and Photocleavage of Quinoline Methyl Ethers: A Mild and Efficient Method for the Selective Protection and Deprotection of the Alcohol Functionality*

Anthony A. Provatas,[A,C] *Gary A. Epling,*[B] *and James D. Stuart*[A]

[A]Center for Environmental Sciences and Engineering, University of Connecticut, Building 4 Annex, 3107 Horsebarn Hill Road, Unit 4210 Storrs, CT 06269-4210, USA.
[B]Deceased (9 September 2001). Formerly of University of Connecticut, USA.
[C]Corresponding author. Email: anthony.provatas@uconn.edu

The synthesis and photocleavage of quinolinyl methyl ether-protected alcohols is reported in this study. A variety of quinoline methyl chlorides were synthesized, and protection of the various alcohols was performed via a substitution reaction in the presence of a strong base. Photocleavage of the quinolinyl methyl ether moiety proceeded under visible light with the formation of the charged quinolinyl radical intermediate through a single-electron transfer in the presence of a photosensitizer dye leading to the deprotected alcohol in excellent yields. The utility of triethylamine as a sacrificial reductant and D-sorbitol as a radical scavenger were also investigated in this study.

Manuscript received: 7 October 2015.
Manuscript accepted: 9 December 2015.
Published online: 18 January 2016.

Introduction

A protecting group is often introduced into a molecule during a multi-step synthesis to prevent a particular functional group from reacting in order for a reaction to occur selectively on another site in the molecule.[1] The protecting group is then removed to recover the molecule with the functional group in its unreacted state. It is critical that removal of the protecting group is achieved in high yield with minimal by-product formation. Typical deprotection techniques include chemical,[2–6] electrochemical,[7,8] and photochemical[9,10] processes. Chemical and electrochemical methods often involve significant drawbacks including the usage of reagents such as strong acids. Photochemical methods often proceed slowly and involve side reactions, which can cause reduced yields and impure products. There is precedent for use of the benzyl ether group as a protecting group for alcohols.[11,12] The resulting benzyl ether linkage is highly stable, and as a result, deprotection is difficult and typically facilitated through harsh conditions, including the usage of organometallic compounds, which may affect yield.[13–15] Provatas and Epling demonstrated that under ultraviolet irradiation, a highly light absorbent moiety such as quinoline may be suitable for a protecting group as it produced minimal side photoreaction products and therefore resulted in increased quantum yields and conversion rates of the deprotected alcohol.[16] Quinolinyl methyl protecting groups achieve the dual goal of minimizing side reactions via the presence of a strongly absorbing aryl group, however, proceed rapidly enough that the reaction is viable for synthetic applications. Thus, it is important to investigate the utility of these molecules, such as the quinoline moiety, as an inexpensive and ubiquitous synthetic block. In addition, varying the substituents on the outlying phenyl moiety affects the rate and progression of the reaction, allowing flexibility in synthetic development, due to the strongly absorbing properties of this moiety in the near-ultraviolet region ($\varepsilon = 22400$ at $\lambda_{max} = 347$ nm).[17–19] Various electron-withdrawing and electron-donating groups were used as substituents by Provatas and Epling et al. to examine the effect of substituents on the percentage conversion and yield.[16,18,19]

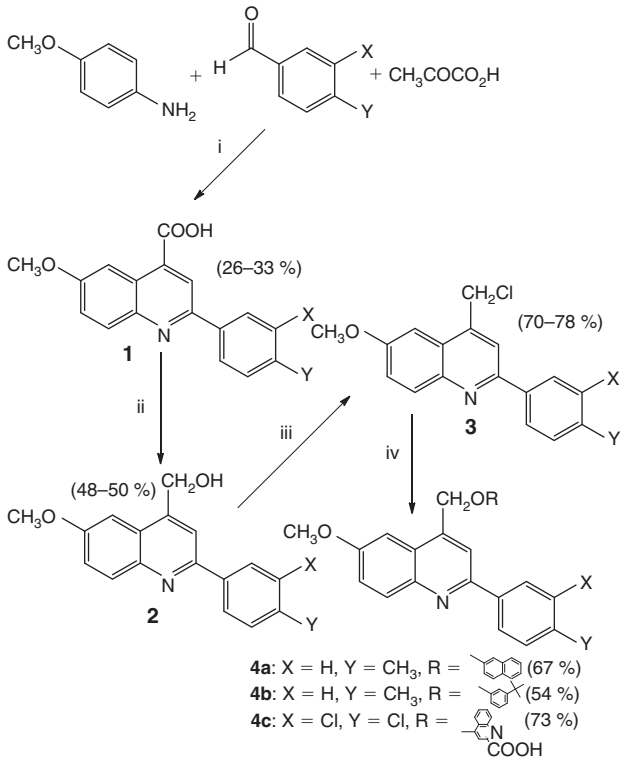
The focal point of this particular study was to investigate the utility of visible light as the energy source underlying the photocleavage process. In a recent publication, an analogous promising approach to this process was presented by Provatas et al. involving the regioselective cleavage of epoxides using visible light and catalytic dyes.[20]

Results and Discussion

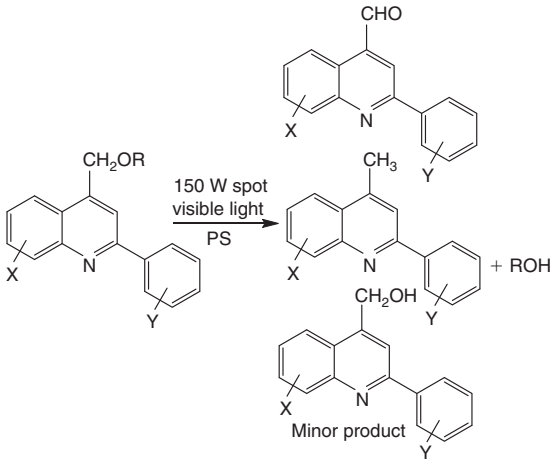
In this study, we demonstrate the effective cleavage of quinolinyl methyl ether-protected alcohols using visible light and a photocatalytic dye (photosensitizer, PS). The radical anion or cation of the quinolinyl methyl ether could be generated through visible light-induced single-electron transfer processes. This radical may lead to the formation of the deprotected alcohol.

The synthesis of the quinoline carboxylic acid used in this experiment was performed by the synthetic route outlined in Scheme 1. The initial step involved Doebner condensation in ethanol, yielding the quinoline carboxylic acid **1**, followed by

*This paper is dedicated to Professor Epling's memory.



Scheme 1. Synthesis of quinoline methyl chloride intermediate product and protection of the candidate alcohol. Reagents and conditions: i, absolute ethanol, reflux, 36 h; ii, $LiAlH_4$, tetrahydrofuran, 20 h; iii, $SOCl_2$, 2 h; iv, ROH, NaOH (or NaH), DMF, 3 h.



Scheme 2. Quinoline products resulting from the photocleavage of the quinolinyl methyl ether.

reduction using lithium aluminium hydride in tetrahydrofuran to yield the quinoline methyl alcohol product **2**. This alcohol was then converted into the quinoline methyl chloride **3** using thionyl chloride. The quinoline methyl chloride in the presence of the candidate alcohol and a strong base via a substitution reaction was converted into the quinolinyl methyl ether-protected alcohol (**4a**–**4c**) in good yields as seen in Scheme 1.

Deprotection of the quinoline methyl ether-protected alcohol was facilitated by a single-electron transfer (SET) process using visible light (150 W spotlight), a variety of photocatalytic dyes and solvent systems, D-sorbitol (0.18 %) as a radical scavenger (observed in unpublished data), and triethylamine as the sacrificial reductant. The products resulting from the photocleavage of the quinolinyl methyl ether are shown in Scheme 2.

A summary of the experiments performed and their results are shown in Table 1.

In Experiment **1** of Table 1, irradiation of substrate **4a** in 90 mL methanol/10 mL distilled water in the presence of methylene green (MG) as the catalytic dye resulted in a 100 % conversion of the substrate and 96 % yield of the deprotected alcohol in 30 min of irradiation time. From Experiments **1**–**3**, it is apparent that increasing the concentration of the photosensitizer dye increased the conversion of the substrate from 30 % to 95 % in 15 min under the same experimental conditions. Similarly, in Experiments **8** and **9** for higher concentration of substrate **4a**, the increase in the concentration of MG increased the substrate conversion from 12 % to 20 % in 5 min of irradiation time.

The presence of triethylamine had an increasing effect on the conversion of the substrate by acting as a proposed sacrificial reductant as shown in Experiments **10**, **11**, and **13**. In Experiment **11**, in the presence of triethylamine, MG, and eosin B (EB), the substrate conversion increased to 33 % when compared with the conversion of 25 % obtained in Experiment **10** in the absence of triethylamine under the same irradiation conditions. Likewise, in Experiment **13** in the presence of MB and triethylamine, the conversion of substrate **4b** was 100 % with a yield of 98 % achieved within 10 min of irradiation time. As a result, it is thought that triethylamine acted as a sacrificial reductant in the photochemical reactions, as evidenced by the increasing effect it had in this particular study on the percentage conversion and yield.[21,22]

In Experiments **4**–**7** and **12**, a methanol/acetic acid solvent system was used, which increased the reaction rate and conversion of the substrate. As reported in Experiment **5**, the substrate conversion was 100 % in 10 min in a solvent system of 95 mL methanol/5 mL acetic acid.

In Experiment **12**, in-house-synthesized dye di-NitroMG was used and increased the conversion of substrate **4a** from 30 % to 40 % when compared with Experiment **6**, wherein MG was used under the same irradiation conditions. Moreover, in Experiment **10**, the addition of EB as a dye in combination with MG increased the conversion of substrate **1** when compared with Experiment **9**, wherein only MG was used under the same experimental conditions.

In Experiment **14**, substrate **4c** was irradiated for 15 min in the presence of MB in a solvent system of acetonitrile/water. A 100 % substrate conversion with a 93 % yield of the corresponding deprotected alcohol was reported.

In Experiments **1**–**12**, D-sorbitol was used as a radical scavenger in order to improve the overall yield. The effect of D-sorbitol has been observed in similar photochemical transformations and data have not been published.

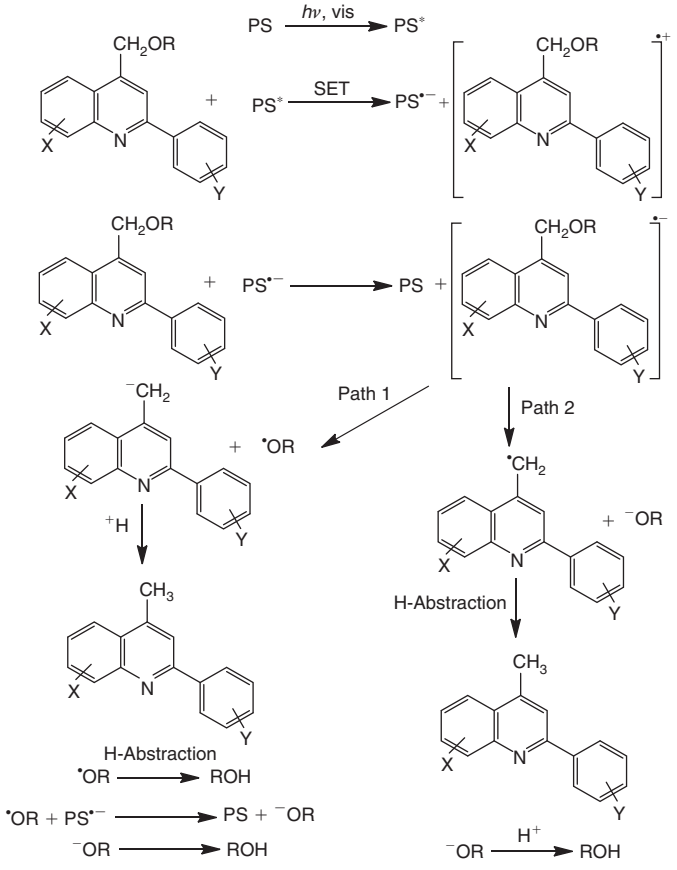
The formation of the deprotected alcohol and quinoline methyl product is rationalized in Scheme 3. Initially, the photosensitizer dye is excited under visible light, followed by the formation of the substrate radical anion. Consequently, the radical anion may be involved in two plausible mechanistic paths. One involved the quinolinyl anion via a H^+ abstraction, and the other involved the quinolinyl radical via a $H^\bullet$ abstraction, with both leading to the deprotected alcohol and the quinolone methyl products.

The formation of the deprotected alcohol and quinoline aldehyde in Scheme 2 can be rationalized by the transformation of the quinoline alcohol (observed as minor product). A plausible mechanism is shown in Scheme 4. The proposed mechanism

Table 1. Experimental results of the photocleavage of quinolinyl methyl ether-protected alcohols in various experimental conditions
MG, methylene green; EB, eosin B; MB, methylene blue; di-NitroMG, dinitro-methylene green; T_{irrad}, irradiation time

Experiment[A]	Substrate	Concentration [mmol]	Dye [mM/mol-%]	Solvent system	T_{irrad} [min]	Conversion [%][B]
1	**4a**	0.049	MG (1.0/67.1)	90 mL methanol/10 mL water	30, 15	100 (96 % yield), 48
2	**4a**	0.049	MG (2.0/80.3)	90 mL methanol/10 mL water	15	95
3	**4a**	0.049	MG (0.5/50.5)	90 mL methanol/10 mL water	15	30
4	**4a**	0.098	MG (2.0/67.1)	99 mL methanol/1 mL acetic acid	10	90
5	**4a**	0.098	MG (2.0/67.1	95 mL methanol/5 mL acetic acid	10	100
6	**4a**	0.196	MG (2.0/50.5)	95 mL methanol/5 mL acetic acid	5	30
7	**4a**	0.196	MG (4.0/67.1)	95 mL methanol/5 mL acetic acid	5	50
8	**4a**	0.196	MG (2.0/50.5)	90 mL methanol/10 mL water	5	12
9	**4a**	0.196	MG (4.0/67.1)	90 mL methanol/10 mL water	5	20
10	**4a**	0.196	MG, EB (4.0/67.1)	90 mL methanol/10 mL water	5	25
11	**4a**	0.196	MG, EB (4.0/67.1)/0.01 M triethylamine	90 mL methanol/10 mL water	5	33
12	**4a**	0.196	di-NitroMG (2.0/50.5)	95 mL methanol/5 mL acetic acid	5	40
13	**4b**	0.049	MB (2.0/80.3)/0.01 M triethylamine	90 mL methanol/10 mL water	10	100 (98 % yield)
14	**4c**	0.040	MB (2.0/83.3)	90 mL acetonitrile/10 mL water	15	100 (93 % yield)

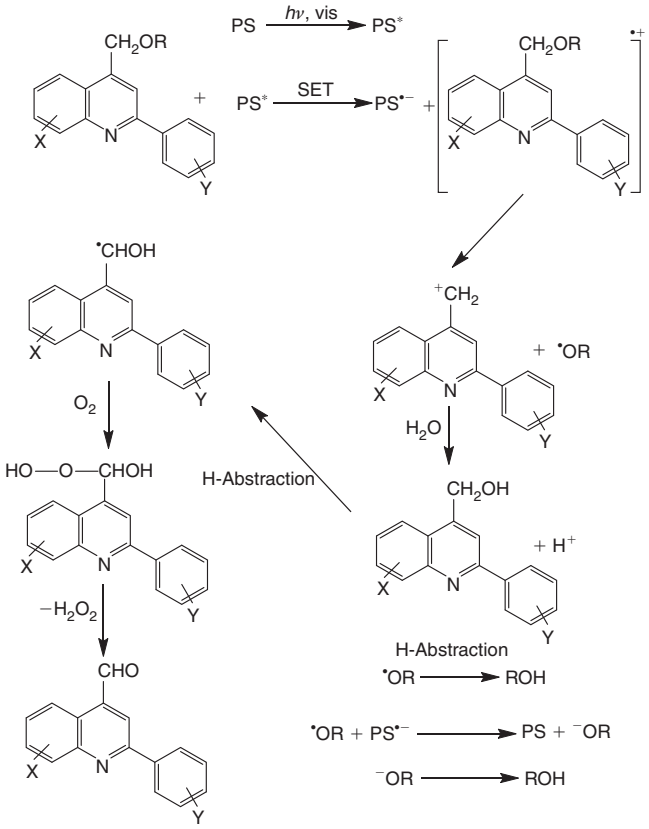
[A]All reactions were carried out in a 100-mL Pyrex round-bottom flask under nitrogen gas. Solutions were purged with nitrogen gas for 5 min before irradiation. D-Sorbitol (0.18 %) was present in Experiments **1**–**12**. Control experiments indicated that in the absence of light and/or catalytic dye, conversion of the substrate was not observed.
[B]Substrate conversion (%) = [(initial moles − moles remaining)/(initial moles)] × 100 %.



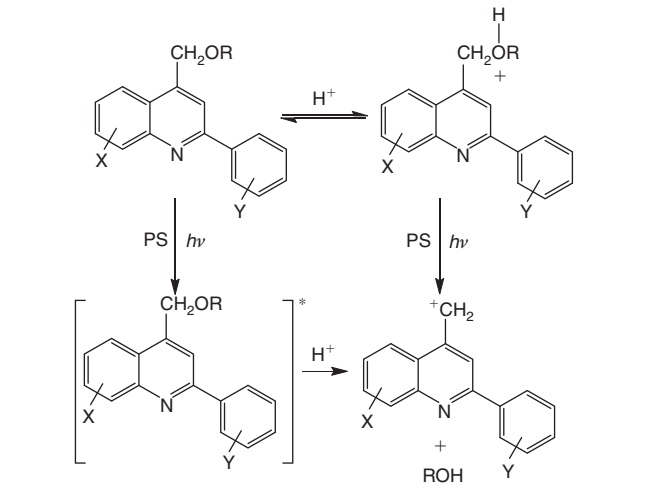
Scheme 3. Proposed mechanism for the formation of the quinoline methyl product and the deprotected alcohol.

involves the initial formation of the quinolinyl radical cation, followed by reaction of the resulting carbocation with water to form the quinoline alcohol and the deprotected alcohol. The quinoline alcohol undergoes an $H^{\bullet}$ abstraction, followed by oxidation and loss of hydrogen peroxide to form the quinoline aldehyde.

Acetic acid (1–5 % v/v) added in the methanol solvent system increased the percentage conversion of the substrate to 100 %



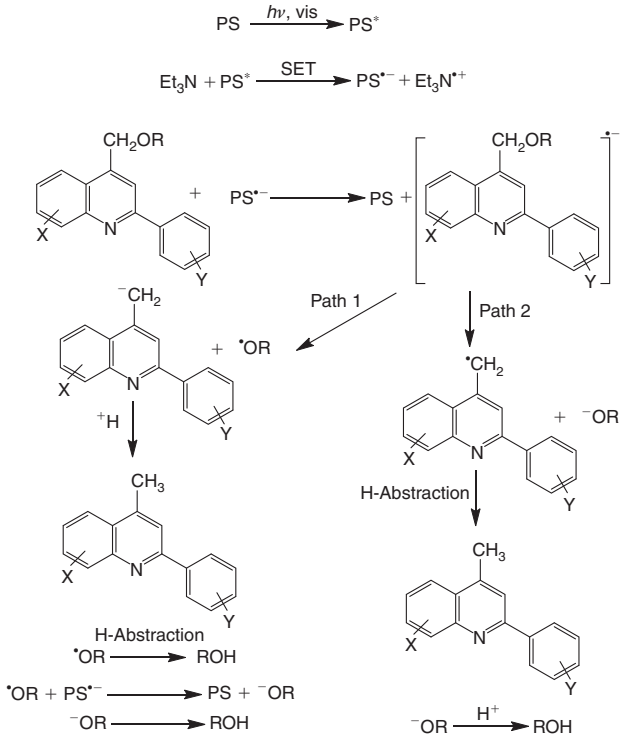
Scheme 4. Proposed mechanism for the formation of the quinoline aldehyde, quinoline alcohol, and the deprotected alcohol.



Scheme 5. Proposed mechanism for acid-induced photolysis.

(Experiment **5**, Table 1). Thus, there was a need to explore dyes that could withstand weak acidic conditions. The dyes used in Experiments **4**–**7** and **12** did not degrade (bleach) and were suitable for use with the addition of acetic acid. In this acid-induced photolysis, protonation of the substrate may occur before or after excitation, leading to the deprotected alcohol and the quinoline product. This is rationalized by the mechanism in Scheme 5.

Triethylamine is hypothesized to act as a sacrificial reductant in the context of this study. The results of the study indicated that the presence of the amine acted to increase the rate and yield of the reaction (Experiment **13**, Table 1). Triethylamine as the reductant promoted the SET process and consequently the formation of the quinolinyl radical anion, finally leading to the deprotected alcohol and the methyl quinoline product. This activity is rationalized by the mechanism in Scheme 6.



Scheme 6. Proposed photolysis mechanism in the presence of triethylamine as a sacrificial reductant.

Conclusion

In summary, the synthesis and photocleavage of quinolinyl methyl ether-protected alcohols under visible light in the presence of a PS dye and D-sorbitol as a radical scavenger provided good quantum yields, enhanced photoreactivity, and increased percentage substrate conversions. It is proposed that the presented photocleavage was initiated through a catalytic dye excitation, followed by a SET propagation. It was observed that this photochemical transformation in the presence of an amine such as triethylamine improved the overall results. Triethylamine is hypothesized to act as a sacrificial reductant in the photocleavage process. Additionally, the presence of acetic acid (1–5 % v/v) increased the percentage conversion of the protected alcohol to the deprotected alcohol, given a PS dye that resisted degradation under such acidic conditions. The utility of various dyes i.e. MG, di-NitroMG, MB, and EB was investigated, and it appeared that MG, MB, and combination of MG and EB are suited for usage in such photochemical applications.

The synthesis and photocleavage of quinolinyl methyl ether-protected alcohols under visible light is a feasible synthetic strategy given the results of this study. This mild and efficient synthetic approach can be an alternative to the existing chemical, electrochemical, and photochemical methods, and may promote further interesting research by other investigators.

Experimental

Materials

Ethyl alcohol was obtained from AAAPER Alcohol and Chemical Co. The solvents used in photolysis were acetonitrile

and methanol. These solvents were all obtained from J.T. Baker and were of photrex grade. No special methods were used to purify the solvents except for tetrahydrofuran and dimethylformamide (DMF) that were purified by fractional distillation. Pyruvic acid (type I-S, free acid) was obtained from Sigma Chemical and vacuum distilled. Formic acid (98–99 %), sodium hydroxide (98.6 %), and anhydrous calcium chloride (4–20 mesh) were purchased from Fisher. Thionyl chloride was purchased from Acros and used with no further purification. Acetic anhydride, acetone, phenol, sodium bicarbonate, anhydrous sodium carbonate (granular), tetrahydrofuran, DMF, chloroform, benzene, diethyl ether, and ethyl acetate were obtained from J.T. Baker. Lithium aluminium hydride (95 %), 3-*tert*-butylphenol (94 %), 2-naphthol, *p*-anisidine (99 %), triethylamine, acetic acid, D-sorbitol (97 %), and 2-carboxyl-4-quinolinol were obtained from Aldrich. Anhydrous sodium acetate (99 %) was obtained from Allied Chemical. The dyes, methylene blue, eosin B, and methylene green, were purchased from Aldrich and were suitable for use directly without further purification. Dinitro-methylene green was made in house.

Each photochemical reaction performed was analyzed by gas chromatography–mass spectrometry (GCMS). The percentage conversion or the percentage yield of the alcohol was calculated based on the integrals and/or weight of the isolated alcohol. For more reliable quantification of the alcohol, the reaction mixture was treated with acetic anhydride and sodium acetate to convert the alcohol into the acetate product. Melting points were recorded on a Thomas-Hoover Mel-Temp apparatus. GCMS was performed using biphenyl as the internal standard. GCMS analysis was done on a Hewlett-Packard 5890A GC/MSD 5970B with a methyl silicone capillary column Hewlett-Packard HP-1 12 m × 0.20 mm of 0.33 μm film thickness, using the Hewlett-Packard ChemStation® software. For sample analysis, two temperature programs were used. In the first program, the temperature was initially maintained at 120°C for 2 min and then raised to 250°C at a rate of 20°C min^{-1}. In the second program, the temperature was initially maintained at 100°C for 2 min and then raised to 270°C at a rate of 20°C min^{-1}.

Flash chromatography was done using a Baker flash chromatography silica gel, with an average particle size of 40 μm. The column used was purchased from Air Glass (part #25, 2.5 cm outer diameter). Thin layer chromatography analysis was done on Merck silica gel 60F254 pre-coated on plastic sheets, with a layer thickness of 0.22 mm. Visualisation was done by using UV light. UV-Visible spectra were recorded on a Hewlett-Packard HP8452A diode array spectrophotometer. All analyses were done using 10-mm path length quartz UV cells.

Proton spectra were recorded on a Bruker AC270 spectrometer and a Bruker DRX400 spectrometer. Chemical shifts were recorded relative to tetramethylsilane as internal standard. The samples were prepared in 10 mm tubes, and the spectra were taken at ambient temperature. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; m, multiplet.

General Procedures

Synthesis of 2-(p-Tolyl)-6-methoxy-4-quinoline Carboxylic Acid (**1a**)

Into a 2-L three-neck round-bottom flask equipped with a stirring bar magnet, a reflux condenser, and a dropping funnel and set above a heating mantle, 148 g (1.23 mol) *p*-tolualdehyde, 151.2 g (1.23 mol) *p*-anisidine, and 624 mL absolute ethanol were introduced. The mixture was stirred and heated gently until *p*-tolualdehyde and *p*-anisidine had dissolved to form a black solution. The mixture was then allowed to reflux for 20 min. In the meantime, a mixture of 85.8 mL (108.2 g, 1.23 mol) pyruvic acid and 250 mL absolute ethanol were prepared and placed in an addition funnel. After the reaction mixture had refluxed for 20 min, the pyruvic acid solution was allowed to drop at a rate of two drops per second into the mixture. Within 45 min, addition of the pyruvic acid solution was complete, and the reaction mixture was allowed to reflux for approximately 3 days. About 94.38 g (26.4 %) of a yellow, powdery compound was collected (suction filtered) and recrystallized from ethanol. This purified quinoline carboxylic acid had a melting point of 243–244°C. δ_H ([D6]DMSO) 13.80 (1H, br), 8.41 (1H, s), 8.14–8.09 (3H, m), 8.02 (1H, d), 7.46–7.43 (1H, d), 7.31–7.29 (2H, d), 3.86 (3H, s), 2.35 (3H, s).

Synthesis of 2-(p-Tolyl)-6-methoxy-4-quinoline Methanol (**2a**)

Into a 1-L three-neck round-bottom flask equipped with a stirring bar magnet and a reflux condenser, 20.0 g (0.07 mol) 2-(*p*-tolyl)-6-methoxy-4-quinoline carboxylic acid (**1a**) and 500 mL dry tetrahydrofuran were introduced. The mixture was stirred until the quinoline carboxylic acid had dissolved to form a yellow solution. Then, 10.0 g (95 %, 0.26 mol) lithium aluminium hydride was added in small portions to the solution. The solution began to reflux. The addition was completed in ~30 min. After the addition process, the reaction was stirred at room temperature for 20 h. Then, 50 mL ethyl acetate was added to the mixture slowly using an addition funnel. After the addition was complete, 10 mL distilled water was added, followed by 10 mL concentrated hydrochloric acid until the pH of the solution was ~3. The solution was stirred for an additional hour. The reaction mixture was suction-filtered and washed with distilled water. The resulting solid was soaked in 150 mL methanol for 2 h. Then, the undissolved solid was filtered, and the methanol filtrate was evaporated using a rotary evaporator. The orange oil that resulted after concentration of the filtrate was solidified after the addition of 80 mL ether and 10 mL ethyl acetate. The yellow solid was collected by suction filtration (4.5 g). The resulting filtrate from the suction filtration of the reaction mixture was extracted twice with 100 mL portions of ethyl acetate. The ethyl acetate extracts were combined and evaporated using a rotary evaporator. The orange–red oil was recrystallized from ether to give 4.7 g solid product. The total pure pale yellow solid was 9.2 g (48 %), mp 145–146°C. δ_H ([D6]DMSO) 8.10 (1H, d), 7.98 (3H, d), 7.28 (4H, m), 5.62 (1H, t), 5.09 (2H, s), 3.93 (3H, s), 2.43 (3H, s). *m*/*z* (electron impact (EI), 70 eV) 279 (1.5×10^5, $[M]^+$), 236 (2.5×10^4), 204 (1.5×10^4), 191 (1.0×10^4), 152 (0.5×10^4), 139 (0.5×10^4), 89 (1.0×10^4), 63 (0.5×10^4).

Synthesis of 2-(p-Tolyl)-6-methoxy-4-quinoline Chloride (**3a**)

Into a 100 mL two-neck round-bottom flask equipped with a magnetic stirrer, an addition funnel, and a reflux condenser with a calcium chloride drying tube, 1.0 g (0.0030 mol) 2-(*p*-tolyl)-6-methoxy-4-quinoline methanol (**2a**) was introduced. Then, 6 mL (9.75 g, 0.082 mol) thionyl chloride was cautiously added. After 2 h, the reaction was quenched by cautious addition of 20 mL formic acid (98–99 %). The mixture was stirred at room temperature for 30 min and after that, 40 mL distilled water was added. A yellow precipitate was formed almost immediately. The reaction mixture was cooled in an ice bath, and this mixture

was suction-filtered and washed with distilled water. The solid collected was recrystallized from methanol to give a pale yellow solid (0.83 g, 78 %), mp 109–110°C. δ_H ($CDCl_3$) 8.16 (1H, d), 8.41 (1H, d), 8.13 (2H, d), 7.99 (1H, s), 7.45–7.25 (4H, m), 5.08 (2H, s), 4.00 (3H, s), 2.44 (3H, s).

*Procedure 4: Synthesis of 2-(*p*-Tolyl)-6-methoxy-4-quinoline 2-Naphthol Ether (**4a**)*

A 100 mL flask was equipped with a magnetic stirring bar. In the flask were added 1.26 g (0.004 mol) 2-(*p*-tolyl)-6-methoxy-4-quinoline chloride (**3a**) and 50 mL dry DMF. The mixture was stirred until the quinoline chloride dissolved completely in DMF (~15 min). Meanwhile, a solution of sodium hydroxide pellets (0.84 g, 0.021 mol) dissolved in a minimum volume of DMF was prepared. Then, 2-naphthol (3.05 g, 0.021 mol) was added to the sodium hydroxide solution. This solution was added slowly with the use of an addition funnel to the quinoline chloride solution. The addition took ~30 min. The reaction mixture was allowed to stir for 3 h. After completion of the reaction, as monitored by thin layer chromatography, 10 mL distilled water and 10 mL concentrated hydrochloric acid were added slowly. A pale yellow precipitation formed. Then, the flask was cooled first to room temperature and then in an ice bath. The solid was collected using suction filtration and washed with distilled water. The solid collected was dissolved in ethyl acetate, and the mixture was extracted from a saturated solution of sodium bicarbonate (or sodium hydroxide) three times. The ethyl acetate layer was evaporated to dryness on a rotary evaporator, and a pale yellow solid was collected (1.085 g, 67 %), mp 122–123°C. δ_H ($CDCl_3$) 8.17 (1H, d), 8.05 (3H, d), 7.85–7.82 (3H, m), 7.45–7.26 (8H, m), 5.65 (2H, s), 3.95 (3H, s), 2.44 (3H, s). *m*/*z* (EI, 70 eV) 405 (5.0×10^4, $[M]^+$), 263 (5.0×10^4), 262 (2.5×10^5), 219 (5.0×10^4), 115 (5.0×10^4), 63 (2.5×10^4).

*Synthesis of 2-(*p*-Tolyl)-6-methoxy-4-quinoline 3-*tert*-Butylphenol Ether (**4b**)*

The procedure for synthesizing compound **4a** was followed using 0.5 g (0.0016 mol) 2-(*p*-tolyl)-6-methoxy-4-quinoline chloride (**3a**), 1.26 g (0.0084 mol) 3-*tert*-butylphenol, and 0.33 g (0.0082 mol) sodium hydroxide were used. Isolation, as performed for **4a**, gave a pale yellow solid (0.35 g, 54 %), mp 117–118°C. δ_H ($CDCl_3$) 8.45 (1H, s), 8.19 (1H, s), 7.64–7.42 (4H, m), 7.41 (1H, s), 6.97–6.66 (5H, m), 5.51 (2H, s), 4.03 (3H, s), 2.41 (3H, s), 1.30 (9H, s). *m*/*z* (EI, 70 eV) 411 (1.0×10^5, $[M]^+$), 341 (0.1×10^5), 262 (5.0×10^5), 219 (1.0×10^5), 102 (0.1×10^5), 91 (0.2×10^5).

*Synthesis of 2-(3,4-Dichlorophenyl)-6-methoxy-4-quinoline Carboxylic Acid (**1c**)*

The procedure for preparing compound **1a** was followed using 150 g (0.857 mol) 3,4-dichlorobenzaldehyde, 105.4 g (0.857 mol) of *p*-anisidine, and 60.7 mL (77.0 g, 0.857 mol) pyruvic acid. Isolation, as performed for **1a**, gave a pale yellow solid (99.3 g, 33 %), mp 267–268°C. δ_H ([D6]DMSO) 14.48–13.94 (1H, br), 8.46 (2H, s), 8.21 (1H, d), 8.09 (2H, d), 7.78 (1H, d), 7.52 (1H, d), 3.92 (3H, s).

*Synthesis of 2-(3,4-Dichlorophenyl)-6-methoxy-4-quinoline Methanol (**2c**)*

The procedure for preparing compound **2a** was followed using 5.0 g (0.0143 mol) 2-(3,4-dichlorophenyl)-6-methoxy-4-quinoline carboxylic acid and 3.0 g (0.079 mol) lithium aluminium hydride. Isolation, as performed for **2a**, gave a pale yellow solid (2.4 g, 50 %), mp 222–224°C. δ_H ([D6]DMSO) 8.42 (1H, s), 8.17–8.00 (3H, m), 7.44 (1H, s), 7.08 (2H, d), 5.72 (1H, t), 5.10 (2H, s), 4.01 (3H, s).

*Synthesis of 2-(3,4-Dichlorophenyl)-6-methoxy-4-quinoline Chloride (**3c**)*

The procedure for preparing compound **3a** was followed using 1.0 g (0.0030 mol) 2-(3,4-dichlorophenyl)-6-methoxy-4-quinoline methanol and 7.0 mL (11.45 g, 0.096 mol) thionyl chloride. Isolation, as performed for **3a**, gave a yellow solid (0.74 g, 70 %), mp 210–212°C. δ_H ([D6]DMSO) 8.46 (1H, s), 8.35–8.21 (3H, m), 7.52 (1H, s), 7.12 (2H, d), 5.37 (2H, s), 4.07 (3H, s).

*Synthesis of 2-(3,4-Dichlorophenyl)-6-methoxy-4-quinoline-2-carboxyl-4-quinolinol Ether (**4c**)*

The procedure for preparing compound **4a** was followed using 0.5 g (0.0014 mol) 2-(3,4-dichlorophenyl)-6-methoxy-4-quinoline chloride, 0.54 g (0.00285 mol) 2-carboxyl-4-quinolinol, and 0.11 g (0.0028 mol) sodium hydroxide. Isolation, as performed for **4a**, gave a yellow solid (0.51 g, 73 %), mp 139–141°C. δ_H ([D6]DMSO) 8.45 (1H, s), 8.29–8.03 (4H, m), 7.96 (1H, s), 7.69 (1H, s), 7.44 (1H, s), 7.12 (2H, d), 6.84 (2H, d), 5.99 (2H, s), 4.06 (3H, s).

General Procedure for Photocleavage of Quinolinyl Methyl Ether-Protected Alcohols under Visible Light

Into a 100 mL round-bottom Pyrex flask, equipped with a stirring bar magnet and a reflux condenser, were added 0.196 mmol quinolinyl methyl ether and $(0.5–4.0) \times 10^{-3}$ M sensitizer dye (methylene green, eosin B, dinitro-methylene green). The reaction mixture was dissolved in a solvent system of choice (90 mL methanol/10 mL distilled water, 99 mL methanol/1 mL acetic acid, 95 mL methanol/5 mL acetic acid). Then, D-sorbitol (0.18 %) was added as a radical scavenger. If pertinent to the trial, 0.01 M triethylamine was then added. The resulting solution was purged with nitrogen gas for 15 min. The solution was irradiated with a 150 W spotlight for 5–30 min. The distance between the centre of the flask and the spotlight was 6 cm. After irradiation was complete, the reaction mixture was diluted in ethyl acetate and washed with a solution of saturated sodium chloride three times. The ethyl acetate layers were combined and evaporated to dryness on a rotary evaporator. Then, GCMS analysis was performed. The percentage conversion of the quinolinyl methyl ether to the alcohol was calculated based on the integrals. The percentage yield of alcohol was determined by the amount of alcohol in the mixture (alcohol fraction obtained by flash chromatography). For more reliable quantification of the alcohol, the reaction mixture was treated with acetic anhydride and sodium acetate to convert the alcohol into the alcohol acetate. GCMS was performed using biphenyl as the internal standard.

Acknowledgements

This project would not have been possible without the invaluable support and guidance of the late Professor Gary Epling. He was a 1967 graduate of the Massachusetts Institute of Technology and received his Ph.D degree from the University of Wisconsin (Zimmerman 1972). His post-doctoral work was conducted at Yale in 1973. He was a professor at Fordham University from 1973 to 1978, when he came to the Chemistry Department at the University of Connecticut and served as the Head. Professor Epling has published over 70 scholarly articles.

References

[1] T. W. Greene, *Organic Synthesis* **1981** (John Wiley and Sons: New York, NY).

[2] L. Jobron, O. Hindsgaul, *J. Am. Chem. Soc.* **1999**, *121*, 5835. doi:10.1021/JA9836085

[3] P. R. Brooks, M. C. Wirtz, M. G. Vetelino, D. M. Rescek, G. F. Woodworth, B. P. Morgan, J. W. Coe, *J. Org. Chem.* **1999**, *64*, 9719. doi:10.1021/JO9910740

[4] C. J. Moody, M. R. Pitts, *Synlett* **1999**, *1999*, 1575. doi:10.1055/S-1999-2904

[5] N. Ikemoto, S. L. Schreiber, *J. Am. Chem. Soc.* **1992**, *114*, 2524. doi:10.1021/JA00033A029

[6] J. P. Kutney, N. Abdurahman, C. Gletsos, P. Le Quesne, E. Piers, I. Vlattas, *J. Am. Chem. Soc.* **1970**, *92*, 1727. doi:10.1021/JA00709A052

[7] V. G. Mairanovsky, *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 281. doi:10.1002/ANIE.197602811

[8] E. A. Mayeda, L. L. Miller, J. F. Wolf, *J. Am. Chem. Soc.* **1972**, *94*, 6812. doi:10.1021/JA00774A039

[9] G. Pandey, A. Krishna, *Synth. Commun.* **1988**, *18*, 2309. doi:10.1080/00397918808082375

[10] R. W. Binkley, D. G. Hehemann, *J. Org. Chem.* **1990**, *55*, 378. doi:10.1021/JO00288A074

[11] K. Yamada, H. Fujita, M. Kunishima, *Org. Lett.* **2012**, *14*, 5026. doi:10.1021/OL302222P

[12] K. W. C. Poon, G. B. Dudley, *J. Org. Chem.* **2006**, *71*, 3923. doi:10.1021/JO0602773

[13] M. Schelhaas, H. Waldmann, *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2056. doi:10.1002/ANIE.199620561

[14] A. Maercker, *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 972. doi:10.1002/ANIE.198709721

[15] A. Fedorov, A. A. Toutov, N. A. Swisher, R. H. Grubbs, *Chem. Sci.* **2013**, *4*, 1640. doi:10.1039/C3SC22256J

[16] G. A. Epling, A. A. Provatas, *Chem. Commun.* **2002**, 1036. doi:10.1039/B201002J

[17] F. R. Stermitz, C. C. Wei, C. M. O'Donnell, *J. Am. Chem. Soc.* **1970**, *92*, 2745. doi:10.1021/JA00712A027

[18] G. A. Epling, K. Y. Lin, A. Kumar, *J. Heterocycl. Chem.* **1988**, *25*, 425. doi:10.1002/JHET.5570250214

[19] G. A. Epling, N. K. Ayengar, E. F. McCarthy, *Tetrahedron Lett.* **1977**, *18*, 517. doi:10.1016/S0040-4039(01)92682-6

[20] A. A. Provatas, G. A. Epling, J. D. Stuart, A. Yeudakimau, *Aust. J. Chem.* **2015**, *68*, 500. doi:10.1071/CH14327

[21] J. M. R. Narayanam, J. R. A. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102. doi:10.1039/B913880N

[22] P. V. Pham, D. A. Nagib, D. W. C. MacMillan, *Angew. Chem., Int. Ed.* **2011**, *50*, 6119. doi:10.1002/ANIE.201101861