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Synthesis and photochemistry of two quinoline analogs of the perimidinespirohexadienone family of photochromes

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ABSTRACT

We report the detailed synthesis and photochemistry of two analogs (specifically 3,5-di-*tert*-butyl-7′-methyl- and 3,5-di-*tert*-butyl-7′,9′-dimethyl-1′,3′-dihydrospirocyclohexa[2,5]diene-1,2′-pyrido[4,3,2-de]quinazolin-4-one) of the perimidinespirohexadienone (3,5-di-*tert*-butyl-1′,3′-dihydrospirocyclohexa[2,5]diene-1,2′-perimidin-4-one) family of photochromes in which the naphthalene moiety of the parent is replaced by a quinoline, and compare them to the parent compound. Molar absorptivities of both the short wavelength spirocyclic isomer (SW) and long wavelength quinonimine isomer (LW) of each were determined by a combination of proton NMR and UV–vis spectroscopy in solvents of varying polarity. Quantum yield measurements for photoisomerization of SW to LW are reported in those same solvents, with qualitative extrapolation to additional solvents. The position and rate of the thermal equilibrium reverting LW to SW is estimated for these compounds. The 9′-methyl in SW (6-methyl in LW) is found to be essential for complete reversion of LW to SW in the dark. Finally one-dimensional NOE NMR spectroscopy was used to conclusively determine the structure of LW for the quinoline analogs as the 4-(5-aminoquinolin-4-ylimino)-2,6-di-*tert*-butylcyclohexa-2,5-dienone resulting from opening toward the quinoline nitrogen, rather than the 4-(4-aminoquinolin-5-ylimino) structure that would result from spirocyclic ring opening away from the quinoline nitrogen which had been initially proposed by Minkin et al. for very similar compounds [V.I. Minkin, V.N. Komissarov, V.A. Kharlanov, Perimidinespirocyclohexadienones, in: J.C. Crano, R.J. Guglielmetti (Eds.), Organic Photochromic and Thermochromic Compounds, vol. 1, Plenum Press, New York, 1999, pp. 315–340, and references therein].

1. Introduction

We have recently been investigating analogs of the perimidinespirohexadienone photochrome family studied almost exclusively over the past 20 years by Minkin and co-workers (Scheme 1) [1–5]. We are ultimately interested in designing a new class of "gateable" intermolecular photooxidants based on photochromic rearrangement of a non-photooxidizing short wavelength isomer (SW, a "pro-photooxidant") to a potentially photooxidizing long wavelength isomer (LW). The perimidinespirohexadienones are promising in this regard, as they meet several necessary criteria: photochromic coloration of SW to LW with UV or short wavelength visible light; purely thermal reversion of LW to SW (leaving LW's photochemical "channel" available for intermolecular photoinduced charge transfer); distinct and non-interfering absorbance bands in SW and LW; sufficiently slow thermal fade (LW → SW) to make use of an appreciable concentration of LW; and a large difference in ground state reduction potential (E^0_{red}) between LW and SW (with LW more reducible). With respect to this last point, the electrochemical data available for **1b**/**2b** already indicate that the difference in E^0_{red} between LW and SW is similar to or slightly greater than the difference in excitation energy between SW and LW. The flexibility to modify the naphthalene moiety of **1** without substantially impacting the photochromic rearrangement nor the reduction potential of **1** (assuming the dienone moiety is the likely electrophore in **1**, as surmised by Minkin and co-workers) has led us to investigate more electron deficient replacements for the naphthalene moiety.

Minkin and co-workers have reported some investigations of the corresponding analogs where a quinoline replaces the naphthalene in the parent system (compounds **3c**–**e**), dubbing these analogs of the perimidinespirohexadienones to be quinazolinespirohexadienones (Scheme 2) [2,5]. However, unable to devise a suitable synthesis to the necessary aminochloroquinoline precursor with the same substitution pattern, we opted to forego the 5′-methyl at R^3 and devised our own synthesis to prepare compounds **3a**,**b** (analogous to Minkin's **3c**,**d**) from 2-methyl- and 2,4-dimethylaniline, respectively, based in large part on the work

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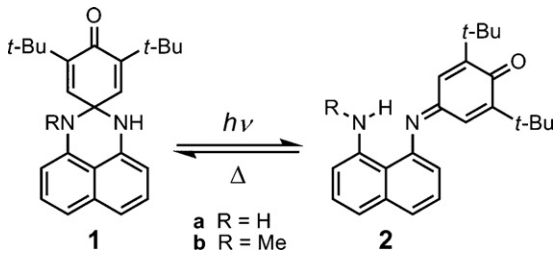
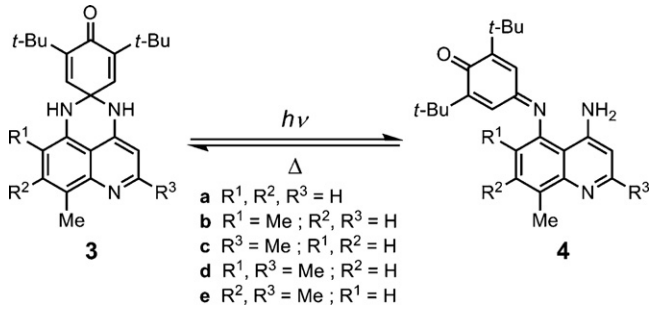


Scheme 1. Perimidinespirohexadienone photochromes.



Scheme 2. Quinoline analogs – quinazolinespirohexadienones.

of Siim et al. [6]. In this work, we report the synthesis and detailed study of the photochromic rearrangement of **3a**,**b**, including a conclusive study of the structure of the photochemically generated LW of these compounds. A separate report on the experimentally determined reduction potentials (in comparison to those predicted computationally based on our recently published methods [7]) and on the nature of the electrogenerated LW isomer will be forthcoming.

2. Materials and methods

2.1. Instrumentation

UV–vis spectroscopy was performed on argon-purged 3 mL or 4 mL solutions in standard 1 cm quartz cuvettes using an Agilent 8453 diode-array spectrophotometer.

Photochemical irradiations were performed on argon-purged 3 mL or 4 mL solutions in standard 1 cm quartz cuvettes (NSG) held in a Newport Oriel 13950 cuvette holder, approximately 30 cm from the source. The source used was a 350 W Newport 6286 mercury arc lamp in a Newport 66942 research arc lamp housing powered by a Newport 69910 power supply. The output of this lamp was partially diffused using the integral collimator, passed through a Newport 6117 water filter, and shuttered with a Newport Oriel 71445 electronic shutter controlled by a Newport 68945 digital exposure controller. The output was ultimately filtered through either a Newport 59470 GG-385 long pass filter (for broad band irradiations above 385 nm), or this long pass filter and a Newport 56541 404.7 nm mercury line interference filter (for the monochromatic irradiations necessary for quantum yields). Control experiments to test for wavelength dependence were performed using alternative filter sets (Newport 59814 BG-3 "355 nm" Band Pass Filter and either a Newport 56531 365.0 nm or Newport 56521 334.1 nm mercury line interference filter) on this apparatus.

NMR spectroscopy was performed on samples in clear quartz or amber borosilicate glass 5 mm NMR tubes (Wilmad), in the deuterated solvents (Cambridge Isotope Labs) indicated, on a Varian Mercury 400 MHz NMR.

One-dimensional NOE experiments on the LW isomer were performed using a 3.5 mL, argon-purged, *ca.* 4 mM acetone–d_6 solution. The solution was irradiated with a mercury arc lamp passed through a Newport 59470 GG-385 long pass filter sufficiently to achieve a substantial % LW (*ca.* 50–60%). The solution was argon-purged and concentrated to *ca.* 0.7 mL using dry argon gas; the concentrated solution was transferred to an NMR tube. A 1D NOE experiment was run collecting 256 manually interleaved scans with a 2 s delay, targeting a single peak per experiment. Successive peaks were targeted on freshly prepared or re-photolyzed solutions in individual NMR experiments lasting under 30 min.

Melting points were determined on a Thomas Hoover 6406-K capillary melting point apparatus and are uncorrected.

GC/MS characterization was performed on an Agilent HP 6890 Series Gas Chromatograph with an Agilent HP 5973 Mass Selective Detector. A 30 m × 0.25 mm × 0.25 μm Agilent HP-5 ms or equivalent capillary column was used. One of two GC methods were used with injector temperature = 250 °C, flow rate = 1.2 mL/min, detector temperature = 280 °C and electron impact ionization at 70 eV. Method A: initial temperature = 50 °C, initial time = 4 min, ramp = +10 °C/min, final temperature = 300 °C, final time = 5 min; Method B: initial temperature = 100 °C, initial time = 0 min, ramp = +20 °C/min, final temperature = 320 °C, final time = 10 min.

2.2. Materials

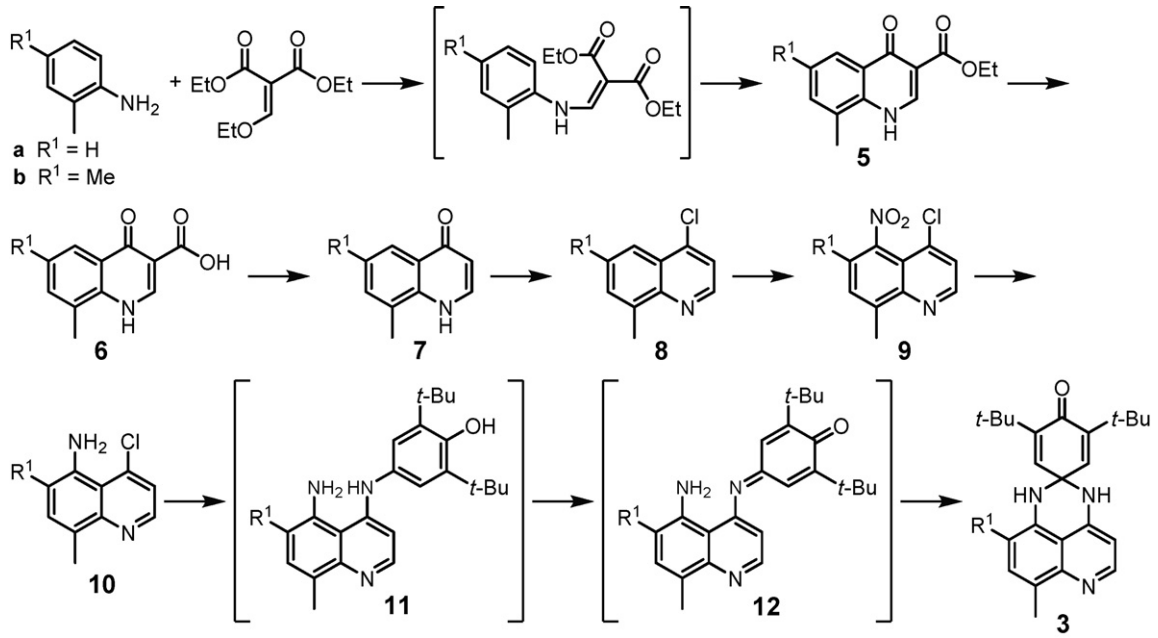
All solvents were the highest purity spectrophotometric or HPLC grade available, and used as received, except for toluene, dichloromethane, acetonitrile, and dimethyl sulfoxide which were dispensed through a nitrogen-purged MBraun MB-SPS 07-299 solvent purification system.

Photochromes **1a**,**b** were prepared by the literature methods [2], with yields similar to those reported though in our hands longer reaction times were required. We investigated the effect of removing water from the refluxing condensation reaction of diaminonaphthalene with di-*tert*-butylbenzoquinone in 1-propanol using either 3A or 4A molecular sieves (freshly activated by oven-drying at least overnight at 350 °C, then briefly flame drying under vacuum and back-filling with dry argon), either directly in the reaction or contained in a Soxhlet extractor. However we found that none of these four combinations of sieve porosity and placement substantially increased either the rate or the yield of this reaction over the method reported in the literature.

Photochromes **3a**,**b** were prepared in *ca.* 30% overall yield from 2-methyl and 2,4-dimethylaniline, respectively, in nine steps as shown in Scheme 3. Square brackets indicate a compound not routinely isolated or characterized in the synthesis.

Ethyl 6,8-*dimethyl*-4-*oxo*-1,4-*dihydroquinoline*-3-*carboxylate* (**5b**). In an adaptation of a literature method [6], 2,4-dimethylaniline (5.844 g, 48.2 mmol) and 10.57 g (48.9 mmol) of diethyl(ethoxymethylene)malonate were combined neat and stirred at 120 °C for 1 h. To this dark-red mixture was added 95 mL (599 mmol) of diphenyl ether. The solution was refluxed for 24 h. Approximately 1/3 to 1/2 of the diphenyl ether was then distilled from the orange-red solution. On cooling to room temperature, a tan solid precipitated. This precipitate was isolated by vacuum filtration, washed with hexane to remove excess diphenyl ether, and vacuum dried to yield 9.765 g (39.7 mmol, 83%) of a pale tan solid. mp 263–265 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 11.58 (broad s, 1H), 8.35 (s, 1H), 7.81 (s, 1H), 7.39 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H), 2.46 (s, 3H), 2.37 (s, 3H), 1.27 (t, J = 7.2, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 173.50, 164.81, 144.06, 135.54, 134.59, 133.74, 127.47, 126.85, 122.93, 109.40, 59.57, 20.72, 16.88, 14.34; GC/MS (Method A): rt 22.153 min (*m*/*z* 245, 199, 143, 115).

Ethyl 8-*methyl*-4-*oxo*-1,4-*dihydroquinoline*-3-*carboxylate* (**5a**) was prepared from 2-methylaniline in a manner analogous to **5b**, in 92% yield. mp 282–284 °C; ^{1}H NMR (DMSO–d_6): δ 11.63 (s, 1H)



Scheme 3. Synthesis of quinazolinespirohexadienones **3a**,**b**.

8.40 (s, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.56 (d, J = 6.7 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.51 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 173.61, 164.78, 144.54, 137.51, 133.25, 127.46, 126.99, 124.37, 123.57, 109.71, 59.65, 16.98, 14.33; GC/MS (Method A): rt 21.256 min (m/z 231, 185, 129, 102, 77).

6,8-*Dimethyl*-4-*oxo*-1,4-*dihydroquinoline*-3-*carboxylic acid* (**6b**). In an adaptation of a literature method [8], potassium hydroxide pellets (34.35 g, 0.61 mol) were dissolved in a mixture of water (28 mL) and methanol (122 mL). To this solution, 19.09 g (78 mmol) of **5b** was added and the reaction heated to 80 °C for 45 min. After cooling to room temperature, the amber solution was washed with 150 mL of diethyl ether. The aqueous layer was acidified with 6 M hydrochloric acid (100 mL) at 0 °C, precipitating a white-yellow solid. This solid was isolated by vacuum filtration, washed with water, and vacuum dried to yield 16.00 g (783.7 mmol, 95%) of a white solid. mp 294–298 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 12.89 (broad s, 1H), 8.62 (d, J = 7.1 Hz, 1H),[1] 7.60 (s, 1H), 7.95 (s, 1H), 2.58 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 178.35, 166.50, 143.86, 136.30, 135.71, 128.15, 124.62, 122.07, 111.85, 107.29, 20.77, 17.21. A GC/MS method sufficient to keep the acid from decarboxylating (either in the injection port or on the column) has not been found.

8-*Methyl*-4-*oxo*-1,4-*dihydroquinoline*-3-*carboxylic acid* (**6a**) was prepared from **5a** in a manner analogous to **6b**, in 89% yield. mp 283–284 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 12.66 (s, 1H), 8.61 (s, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 7.0 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 2.58 (s, 3H), acid H not observed; ^{13}C NMR (DMSO–d_6): δ (ppm) 178.87, 166.84, 144.75, 138.27, 135.12, 128.51, 126.30, 124.76, 123.15, 107.64, 17.42.

6,8-*Dimethylquinoline*-4(1*H*)-*one* (**7b**). In an adaptation of a literature method [6], a neat powder of **6b** (8.692 g, 40.0 mmol) was first carefully purged under nitrogen or argon with stirring, then slowly heated past its melting point to 320 °C under inert atmosphere with continued stirring. The reaction was cooled to room temperature 5 min after the evident evolution of carbon dioxide ceased. The resulting pale, brown solid was dissolved in a 1:9 MeOH/$CHCl_3$ solution. This solution was filtered to remove any insoluble material, then the solvent was removed by rotary evaporation. Upon vacuum drying, 6.795 g (39.3 mmol, 98%) of a tan solid was obtained. mp 222–225 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 11.08 (broad s, 1H), 7.79 (d, J = 7.4 Hz, 1H), 7.75 (s, 1H), 7.33 (s, 1H), 6.04 (d, J = 7.4 Hz, 1H), 2.44 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 176.62, 139.22, 136.81, 133.88, 132.01, 126.40, 125.63, 122.02, 108.27, 20.69, 17.26; GC/MS (Method B): rt 8.211 min (m/z 173, 158, 144, 130, 115).

8-*Methylquinoline*-4(1*H*)-*one* (**7a**) was prepared from **6a** in a manner analogous to **7b**, in 98% yield. mp 214–217 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 11.09 (s, 1H), 7.95 (d, 8.2 Hz, 1H), 7.82 (d, J = 7.1 Hz, 1H), 7.49 (d, J = 7.1 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 6.06 (d, J = 7.1 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 177.23, 139.36, 138.67, 132.32, 126.31, 125.91, 122.91, 122.70, 108.80, 17.24; GC/MS (Method B): rt 7.786 min (m/z 159, 130, 103, 77).

4-*Chloro*-6,8-*dimethylquinoline* (**8b**). In adaptation of literature methods [9,10], phosphorous oxychloride (54 mL, 590 mmol) was added drop-wise to 10.75 g (62.5 mmol) of solid **7b**. The reaction was purged with nitrogen or argon then refluxed under inert atmosphere for 30 min. Approximately 2/3 of the $POCl_3$ was then distilled off. Toluene (50 mL) was added and distilled to azeotropically remove remaining $POCl_3$. The addition and azeotropic distillation of toluene was repeated. After cooling to room temperature, 10% aqueous ammonium hydroxide was added until the solution was basic. The product was extracted using 100 mL of chloroform. The organic layer was dried over anhydrous sodium sulfate. Removal of the solvent by rotary evaporation and vacuum drying yielded 11.13 g of gray-brown solid (58.3 mmol, 93%). mp 89–90 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 8.80 (d, J = 4.7 Hz, 1H), 7.84 (s, 1H), 7.76 (d, J = 4.7 Hz, 1H), 7.61 (s, 1H), 2.71 (s, 3H), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$): δ (ppm) 147.59, 146.93, 141.97, 137.31, 137.24, 132.90, 126.48, 121.04, 120.90, 21.83, 18.32; GC/MS (Method A): rt 17.222 min (m/z 191/193, 176/178, 156, 128, 77).

4-*Chloro*-8-*methylquinoline* (**8a**) was prepared from **7a** in a manner analogous to **8b**, in 93% yield. mp 94–96 °C; ^{1}H NMR (DMSO–d_6): δ (ppm) 8.86 (d, J = 4.7 Hz, 1H), 8.06 (d, J = 8.6 Hz, 1H), 7.78 (d, J = 4.7 Hz, 1H), 7.75 (d, J = 7.0 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR (DMSO–d_6): δ (ppm) 149.35, 147.53, 141.37, 137.30, 130.70, 127.80, 125.52, 121.55, 121.47, 17.98; GC/MS (Method B): rt 4.974 min (m/z 177/179, 142, 115, 89, 63).

[1] Splitting of the vinylic proton is observed sporadically; a singlet at 8.62 ppm has also been observed for the same sample.

4-*Chloro*-6,8-*dimethyl*-5-*nitroquinoline* (**9b**). In an adaptation of a literature method [6], 9.80 g (48.2 mmol) of **8b** was slowly added to 40 mL concentrated sulfuric acid at 0 °C. A mixture of fuming nitric acid (5 mL, 53.1 mmol) and 6 mL of concentrated sulfuric acid was added drop-wise. The reaction mixture was stirred at 0 °C for 20 min and then divided into four flasks, each containing 50 g of ice for workup. The solutions were neutralized slowly with saturated aqueous sodium carbonate (200 mL). The product was extracted from each flask using dichloromethane (100 mL). The organic layers were combined, rinsed with water, and dried over anhydrous sodium sulfate. Removal of the solvent by rotary evaporation followed by vacuum drying yielded 10.70 g (45 mmol, 88%) of a tan solid. mp 110–112 °C; ^{1}H NMR ($CDCl_3$): δ (ppm) 8.80 (d, J = 4.7 Hz, 1H), 7.58 (d, J = 4.7 Hz, 1H), 7.53 (s, 1H), 2.81 (s, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$): δ (ppm) 148.74, 146.91, 143.60, 140.85, 138.19, 132.32, 129.95, 124.62, 117.78, 18.87, 17.76; GC/MS (Method B): rt 7.357 min (*m*/*z* 236/238, 201, 190, 171, 154, 143, 127).

4-*Chloro*-8-*methyl*-5-*nitroquinoline* (**9a**) was prepared from **8a** in a manner analogous to **9b**, in 85% yield. mp 139–140 °C; ^{1}H NMR ($CDCl_3$): δ (ppm) 8.89 (d, J = 4.7 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 4.7 Hz, 1H), 2.87 (s, 3H); ^{13}C NMR ($CDCl_3$): δ (ppm) 149.60, 148.15, 145.04, 143.08, 139.07, 128.38, 124.65, 123.04, 117.94, 19.05; GC/MS (Method B): rt 7.186 min (*m*/*z* 222/224, 187, 157, 149, 141, 114).

5-*Amino*-4-*chloro*-6,8-*dimethylquinoline* (**10b**). As in the literature method [11], a solution of five drops glacial acetic acid in 20 mL of water was prepared, and 11.5 mL of this solution was added to 7.986 g (17.9 mmol) of iron filings. A solution of 2.9102 g of **9b** (12.3 mmol) in 50 mL of *o*-xylene was added to the iron/acetic acid mixture and then refluxed for 16.5 h. Sodium hydroxide (2 M, 4.5 mL) was added, and the mixture refluxed an additional 15 min. The iron was removed by vacuum filtration through diatomaceous earth and washed with chloroform (20 mL). The organic and aqueous layers were separated, and the organic layer was dried over sodium sulfate. Solvents were removed by rotary evaporation and the resulting solid was purified by column chromatography through 230–400 mesh silica gel eluted with a solution of 0.05% triethyl amine, 0.45% methanol, and 99.5% chloroform. Removal of the eluent by rotary evaporation and vacuum drying yielded 1.6198 g (7.8 mmol, 64%) of a pale yellow solid. mp 122–123; ^{1}H NMR ($CDCl_3$): δ 8.62 (d, J = 4.3 Hz, 1H), 7.37 (s, 1H), 7.31 (d, J = 4.7 Hz, 1H), 5.04 (broad s, 2H), 2.65 (s, 3H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$): δ (ppm) 148.75, 147.04, 139.85, 138.69, 134.07, 125.82, 121.73, 118.08, 115.53, 18.38, 18.27; GC/MS (Method A): rt 20.881 min (*m*/*z* 206/208, 191/193, 169, 155, 103).

5-*Amino*-4-*chloro*-8-*methylquinoline* (**10a**) was prepared from **6a** in a manner analogous to **10b**, in 64% yield. mp 128–131 °C; ^{1}H NMR ($CDCl_3$): δ (ppm) 8.67 (d, J = 4.7 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 4.7 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 5.00 (broad s, 2H), 2.65 (s, 3H); ^{13}C NMR ($CDCl_3$): δ (ppm) 149.87, 147.91, 141.91, 140.57, 130.87, 126.84, 121.60, 116.11, 112.05, 18.54; GC/MS (Method B): rt 6.943 min (*m*/*z* 192/194, 155, 128).

3,5-*Di*-*tert*-*butyl*-7′,9′-*dimethyl*-1′,3′-*dihydrospiro*[*cyclohexa*[2,5]*diene*-1,2′-*pyrido*[4,3,2-*de*]*quinazolin*]-4-*one* (**3b**). As in the literature method [2], a solution of 1.133 g of 4-amino-2,6-di-*tert*-butylphenol (5.13 mmol, prepared according to the literature method from 2,6-di-*tert*-butylphenol via 2,6-di-*tert*-butyl-4-nitrosophenol [12]) and 0.622 g (3.02 mmol) of **10b** in 15 mL of *o*-xylene were refluxed for 3 h under argon. After cooling to room temperature, 8 mL of a 1:7 saturated aqueous ammonium hydroxide/chloroform solution was added. The reaction mixture was stirred open to the atmosphere for 18 h. The resulting dark red solution was dried over anhydrous sodium sulfate. Volatiles were removed by rotary evaporation and the resulting dark red solid vacuum dried. The product was purified by column chromatography through 230–400 mesh silica gel eluted with 1.5:8.5:90 triethylamine/methanol/dichloromethane. The eluent was removed by rotary evaporation and the resulting residue was vacuum dried to yield 0.851 g (2.19 mmol, 72.5%) of reddish-brown solid. mp 204–206 °C; ^{1}H NMR ($CDCl_3$): δ (ppm) 8.56 (d, J = 5.1 Hz, 1H), 7.28 (s, 1H), 6.67 (s, 2H), 6.46 (d, J = 5.1 Hz, 1H), 4.74 (broad s, 1H) 4.07 (broad s, 1H), 2.66 (s, 3H), 2.25 (s, 3H), 1.21 (s, 18H); ^{13}C NMR ($CDCl_3$): δ (ppm) 185.37, 149.26, 149.24, 147.66, 145.26, 137.837, 133.75, 132.40, 125.78, 114.09, 107.04, 101.35, 62.55, 34.89, 29.43, 17.548, 16.297; GC/MS (Method A): rt 29.628 min (*m*/*z* 389, 374, 332, 318, 305).

3,5-*Di*-*tert*-*butyl*-7′-*methyl*-1′,3′-*dihydrospiro*[*cyclohexa*[2,5]*diene*-1,2′-*pyrido*[4,3,2-*de*]*quinazolin*]-4-*one* (**3a**) was prepared from **10a** in a manner analogous to **3b**, in 74% yield. mp 160–162 °C; ^{1}H NMR ($CDCl_3$): δ (ppm) 8.60 (d, J = 5.1 Hz, 1H), 7.34 (d, J = 7.4 Hz, 1H), 6.67 (s, 2H), 6.52 (d, J = 7.4 Hz, 1H), 6.48 (d, J = 5.1 Hz, 1H), 4.90 (broad s, 1H), 4.34 (broad s, 1H), 2.67 (s, 3H), 1.20 (s, 18H); ^{13}C NMR (DMSO–d_6): δ (ppm) 185.70, 149.61, 146.58, 146.39, 144.97, 139.08, 137.37, 130.51, 123.02, 106.13, 104.94, 100.53, 61.38, 34.28, 29.20, 17.27; GC/MS (Method A): rt 30.268 min (*m*/*z* 375, 360, 318, 304, 291).

2.3. Extinction coefficients

Molar extinction coefficients of the short wavelength isomers of the photochromes were readily determined using Beer's law from the OD at λ_{max}(SW) measured on freshly prepared solutions of known concentration of **1a**, **3a**, or **3b** in each solvent studied.

Long wavelength molar extinction coefficients had to be determined using NMR and UV–vis spectroscopies in tandem, and are therefore technically the extinction coefficients in the deuterated solvents, and are only reported for solvents which are affordably available in perdeuterated form. Individual vials were charged with a known amount of **1a** (0.2010 mg), **3a** (0.2526 mg), or **3b** (0.3066 mg) by a procedure of serial dilution and evaporation/vacuum drying from acetonitrile solutions. To a given vial was added 1 mL deuterated solvent (benzene–d_6, toluene–d_8, acetone–d_6, acetonitrile–d_3, or isopropyl alcohol–d_8) and the resulting solution was charged into a 1 cm quartz cuvette containing a micro-stirbar. The cuvette was elevated so the solution was held in the beam path of the optical bench. The solution was irradiated using the mercury arc lamp filtered with a 385 nm long pass filter to an OD at λ_{max}(LW) of *ca.* 1.0 as indicated by UV–vis spectroscopy, with magnetic stirring. This solution was then transferred to an NMR tube and a ^{1}H NMR spectrum was acquired (256 scans, 2 s delay, *ca.* 17 min experiment). The solution was transferred back to the quartz cuvette and a second UV–vis spectrum was taken, with no more than a 25% decrease in OD at λ_{max}(LW). The average absorbance before and after NMR was used, along with the concentration of LW as determined by NMR spectroscopy, to determine the molar extinction coefficient of the LW isomer according to Beer's Law.

2.4. Quantum yields

Photochromic solutions (0.5–0.8 mM, 3 mL) in hexane, benzene, toluene, acetone, acetonitrile, and isopropyl alcohol were irradiated with the mercury arc lamp filtered with both the 385 nm long pass and 404.7 nm interference filters, with magnetic stirring (with the stirbar kept below the beam path). UV–vis spectra were taken periodically to determine the extent of conversion.

Photon flux (in photons per second through the sample holder) was determined in duplicate, before and after each set of quantum yield experiments without altering the apparatus, by chemical actinometry. A benzene solution of *ca.* 0.8 M phenanthrenequinone and 0.10 M trans-stilbene was used, according to literature protocol (monitoring disappearance of phenanthrenequinone by UV–vis

Table 1
Photochemical data for PSHD **1a**/**2a** and QSHDs **3a**/**12a**, **3b**/**12b**.

Compound	Solvent	SW λ_{max} (nm)	ε_{SW} (M^{-1} cm^{-1})	LW λ_{max} (nm)	ε_{LW} [a] (M^{-1} cm^{-1})	Dark %LW[b] (equilib.)	Max %LW[b] after $h\nu$	$\phi_{SW\rightarrow LW}$ [b] (mol/Einstein)
1a/**1b**	n-C_6H_{14}	406	1807	584		11	59	0.33 ± 0.01
1a/**1b**	C_6H_6	413	2044	588	3840 ± 714	6	94	0.140 ± 0.006
1a/**1b**	Toluene	414	1667	590	4380 ± 100	7	23	0.151 ± 0.001
1a/**1b**	TBME	420	1944	593		1	37	
1a/**1b**	EtOAc	410	1917	590		1	93	
1a/**1b**	THF	418	1699	599		<1	91	
1a/**1b**	CH_2Cl_2	398	2170	571		8	17	
1a/**1b**	Acetone	408	2249	589	3390 ± 110	<1	98	0.0085 ± 0.0006
1a/**1b**	CH_3CN	396	2271	564	3570 ± 200	6	15	0.0069 ± 0.0003
1a/**1b**	DMSO	420	2315	607		~0	67	
1a/**1b**	*i*-BuOH	407	1595	576		2	100	
1a/**1b**	*i*-PrOH	410	1723	580	3172 ± 260	<1	100	0.0229 ± 0.0001
1a/**1b**	EtOH	408	1830	576		1	3	
3b/**12b**	n-C_6H_{14}	396	1916	594		16	100	0.28 ± 0.03
3b/**12b**	C_6H_6	403	2333	592	1812 ± 54	16	95	0.131 ± 0.005
3b/**12b**	Toluene	399	2106	598	1844 ± 28	10	80	0.140 ± 0.005
3b/**12b**	TBME	406	2097	596		3	99	
3b/**12b**	EtOAc	400	2093	589		1	77	
3b/**12b**	THF	405	1991	600		<1	85	
3b/**12b**	CH_2Cl_2	389	2524	566		10	64	
3b/**12b**	Acetone	403	2592	587	1540 ± 140	2	88	0.0162 ± 0.0008
3b/**12b**	CH_3CN	390	2630	558	1619 ± 31	3	77	0.0102 ± 0.0005
3b/**12b**	DMSO	409	2445	601		<1	61	
3b/**12b**	*i*-BuOH	405	2242	567		3	68	
3b/**12b**	*i*-PrOH	407	2514	571	1647 ± 17	2	86	0.0184 ± 0.0001
3b/**12b**	EtOH	406	2759	556		3	38	
3a/**12a**	n-C_6H_{14}	390	1760	565		45	78	0.29 ± 0.02
3a/**12a**	C_6H_6	393	1656	555	1649 ± 16	33	80	0.146 ± 0.009
3a/**12a**	Toluene	388	1770	559	1827 ± 22	29	76	0.144 ± 0.001
3a/**12a**	TBME	399	1517	564		16	58	
3a/**12a**	EtOAc	387	1750	556		12	43	
3a/**12a**	THF	394	2126	565		13	53	
3a/**12a**	CH_2Cl_2	383	1949	541		32	47	
3a/**12a**	Acetone	396	1978	553	1790 ± 145	20	61	0.0085 ± 0.0002
3a/**12a**	CH_3CN	385	1879	541	1660 ± 280	15	45	0.0087 ± 0.0002
3a/**12a**	DMSO	405	1842	566		17	47	
3a/**12a**	*i*-BuOH	403	2440	527		10	29	
3a/**12a**	*i*-PrOH	406	2635	529	1571 ± 33	9	50	0.01010 ± 0.00001
3a/**12a**	EtOH	405	2896	527		9	26	

[a] As determined in the corresponding deuterated solvent.

[b] For solvents with an experimentally determined ε_{LW}, this value was used in determining %LW and ϕ_{isom}. For solvents where ε_{LW} has not been determined, it was approximated as follows: ε_{LW} of hexane approximated as the average ε_{LW} of benzene and toluene, ε_{LW} of DMSO approximated as the average ε_{LW} of acetone and acetonitrile, ε_{LW} of isobutyryl and isopropyl alcohols approximated as the ε_{LW} of ethyl alcohol, all other undetermined ε_{LW} approximated as the average ε_{LW} of benzene, toluene, acetone, and acetonitrile.

at 412 nm). Photon flux was calculated according to Eq. (1), as the quantum yield for this photochemical bleaching reaction is known (ϕ_{act} = 0.067), as is the molar absorptivity of phenanthrenequinone at 412 nm (ε_{PQ} = 1800 M^{-1} cm^{-1}) [13–15].

$$I = \frac{|dOD/dt| \cdot V \cdot N_A}{\phi_{act} \cdot \varepsilon_{PQ}} \quad (1)$$

A fit of the linear portion of a plot of the increase in OD at λ_{max}(LW) vs. time of irradiation of the photochromic solution, along with the known volume of the solution, the necessary extinction coefficients, and the photon flux determined by actinometry enabled the calculation of initial quantum yields for the isomerization of SW to LW (ϕ_{isom}) according to equation (2).

$$\phi_{isom} = \frac{|dOD/dt| \cdot V \cdot N_A}{I \cdot \varepsilon_{LW}} \quad (2)$$

3. Results and discussion

The syntheses reported above for **3a**,**b** were effective, ultimately yielding gram quantities of these compounds for structural and photochemical study, in an overall yield of about 30% over nine chemical steps.

First we studied the photochromic rearrangement in several solvents of varying polarity to obtain the longest wavelength λ_{max} of each compound in its SW and LW isomer. As Minkin and co-workers have noted for similar compounds, solutions of **3a** contain a substantial amount of the LW isomer which slightly increases to an equilibrium value on prolonged standing in the dark in all solvents save the alcohols. (In alcoholic solvents, the equilibrium amount of LW isomer on prolonged standing was notably less than when first prepared.) For **3b** (like **1a**,**b**) the amount of LW is negligible upon initial dissolution but increases on prolonged standing in the dark to a value that is minimal but non-zero in most solvents. The position of the equilibria in each case was reproducible in a given solvent, and also corresponded to the position reached after irradiation of SW → LW followed by thermal fade of LW → SW. This effect of R^1 has been documented by Minkin and co-workers as well. Interestingly, we found that it was impossible to obtain a solid sample of the LW compound of either **3a** or **3b** (as well as **1a**,**b**) from an irradiated solution – upon even the fastest rotary evaporation of solvent, the photochrome reverted to its SW isomer upon solidifying.

While we did not conduct a careful study of the thermal reversion reaction, we note that thermal reversion of LW → SW in all cases was "complete" in that it reached the same equilibrium value (Table 1) as unirradiated solutions kept in the dark. There was no

irreversibility to the photocoloration reaction if irradiations were performed under reasonably anaerobic conditions. The rate of the thermal fade was dependent on both substrate and solvent, but to a lesser extent than Minkin and co-workers have reported [2,5]: in all cases thermal reversion to the equilibrium state was reached within 12–36 h.

For both **3a** and **3b**, proton NMR indicated (to the limits of detection, ca. 2–5%) that a single LW isomer was produced upon

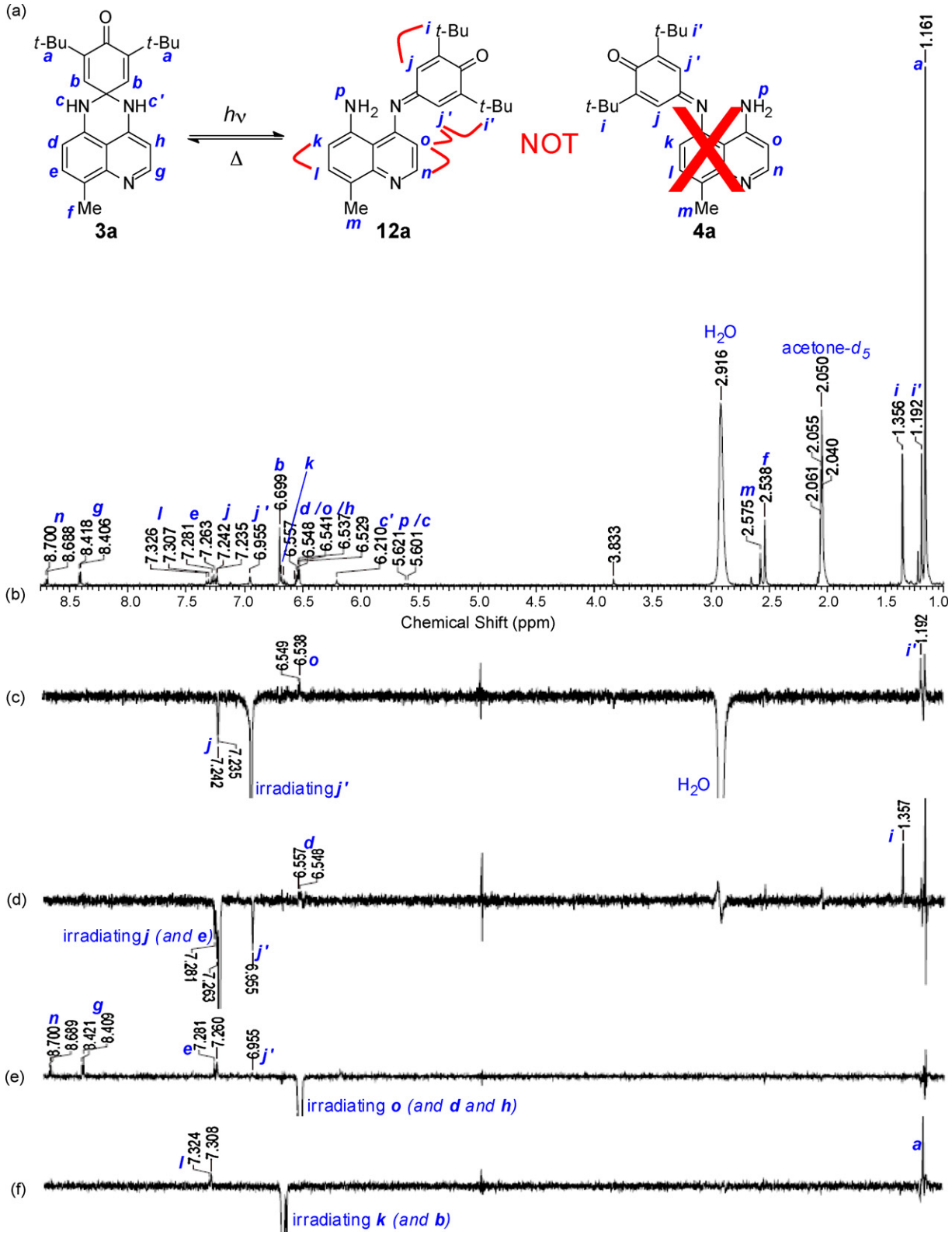


Fig. 1. NOE results for LW of **3a**, indicating structure **12a** rather than **4a**: (a) relevant structures and proton-labeling scheme for NOE experiments; (b) routine 1D proton NMR on a photochemically irradiated solution of **3a** in acetone–d_6; (c) saturating proton *j'* shows positive NOE to protons *o* and *i'*; (d) saturating proton *j* (and *e*) shows positive NOE to proton *i* (and *d*); (e) saturating proton *o* (and *d* and *h*) shows positive NOE to protons *j'* and *n* (and *e* and *g*); (f) saturating proton *k* (and *b*) shows positive NOE to proton *l* (and *a*).

photolysis of **3**. The same LW isomer is produced regardless of irradiation using a mercury arc lamp filtered with solely a 385 nm long pass filter, or monochromatically using either the 404.7 or the 365.0 nm lines. Irradiation with the 334.1 nm line led to minimal conversion in reasonable times. Broad band irradiation (over ca. 280–380 nm) with a UVP Model UVM-57 "302 nm" Mid-Range UV handheld lamp led almost exclusively to the same isomer, with trace amounts of either another LW isomer or a secondary photoproduct.

Interested in the observed difference in dark equilibration/thermal reversion of **3a** vs. **3b**, which are apparently dependent

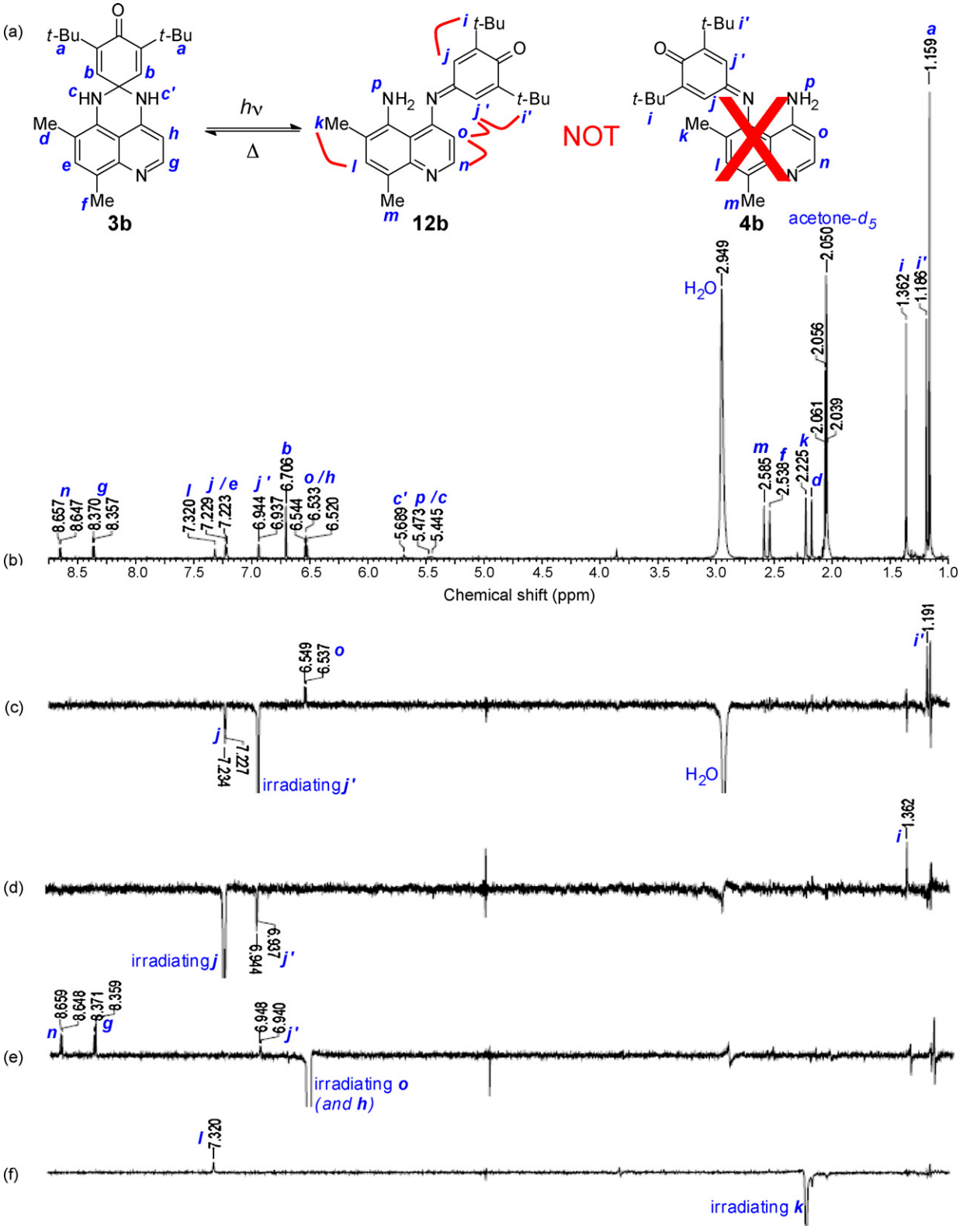


Fig. 2. NOE results for LW of **3b**, indicating structure **12b** rather than **4b**; (a) relevant structures and proton-labeling scheme for NOE experiments; (b) routine 1D proton NMR on a photochemically irradiated solution of **3a** in acetone–d_6; (c) saturating proton *j'* shows positive NOE to protons *o* and *i'*; (d) saturating proton *j* shows positive NOE to proton *i*; (e) saturating proton *o* (and *h*) shows positive NOE to protons *j'* and *n* (and *g*); (f) saturating proton *k* shows positive NOE to proton *l*.

solely on substitution at R^1, and aware that a simple proton NMR was insufficient to distinguish compounds **12** from compounds **4** (but that NMR indicated one or the other, not both), we embarked on a challenging set of NOE experiments to determine the structure. We had two possible hypotheses: either (1) both **3a** and **3b** opened to **4a**,**b**, and the difference in thermal reversion was the added steric driving force for reversion given by the methyl at R^1 in **4b** or (2) that **3b** opened to **12b**, not **4b**, due to steric hindrance in the latter compound, while **3a** did indeed open to **4a**, and that the difference in reversion was due to some inherent difference between structures **12** and **4**. The NOE data, however, fail to support either hypothesis. The experiment is non-trivial due to the need to rapidly obtain NMR spectra on a sample sufficiently dilute for photolytic conversion from SW → LW before significant thermal reversion can occur. Thus individual one-dimensional NOE experiments were conducted, irradiating each relevant proton (labeled *j*, *j*′, *k*, and *o* on the corresponding structures) in the LW isomer of **3a** and **3b** (compounds **12a**/**4a** and **12b**/**4b**, respectively) and observing the positive NOE enhancements at those protons close in space to the irradiated proton. As indicated in Figs. 1 and 2, the data clearly show that the correct structure of the LW isomer is **12** in both cases – *j*′ has an NOE contact with *o* and vice versa, while neither *j* nor *j*′ have an NOE contact with *k* (which in turn only has an NOE contact with *l*). All relevant contacts were reciprocally reproduced by irradiating either of the interacting protons.

Based on this conclusive structure determination of the LW isomers of **3a**,**b** as **12a**,**b**, the effect of R^1 becomes all the more surprising and remains unexplained. Ring opening is not differential based on R^1, but is away from R^1 in all cases. Therefore differences in steric effects on ring closing of **12a** vs. **12b** are likely negligible. One potential remaining explanation yet to be explored is that the slight additional effect of a weak electron donating group at R^1 might make the NH_2 in **12b** just slightly more nucleophilic than in **12a**, thus slightly increasing the preference for ring closure in **12b** over **12a**. This explanation remains to be explored experimentally and computationally.

We next determined the extinction coefficients (molar absorptivities, ε) of each of these compounds (**3a**,**b** and **12a**,**b**, as well as **1a** and **2a** for comparison) at the indicated longest wavelength λ_{max} for each compound in selected solvents. For the SW isomers (**3a**,**b** as well as **1a**), this is a trivial experiment as long as the solutions are very freshly prepared, such that essentially no LW isomer is present. We are therefore able to report ε_{SW} values for each compound in all solvents studied. However to quantify the amount of LW isomers (**12a**,**b** as well as **2a**) in solution, either on standing or after irradiation, proton NMR had to be used. Thus we are only able to determine extinction coefficients of LW isomers of our compounds in solvents which we could affordably obtain in perdeuterated form. Knowing the total concentration of the two isomers ([**3**] + [**12**]) in the solution as prepared from dissolving **3**, and the ratio of the concentrations by NMR, it was possible to determine the absolute concentration of each isomer, and therefore the extinction coefficients by Beer's Law.

For those solvents in which we had LW extinction coefficient data, we could (assuming ε_{LW} in deuterated and non-deuterated solvents were essentially the same, as is likely the case, particularly in the four aprotic solvents studied) determine accurate equilibria positions for the dark isomerization/thermal fade reaction, as well as maximal extent of conversion to LW we were able to achieve photochemically. For solvents where we did not have ε_{LW} we could estimate the amount of LW by using the average ε_{LW} in all solvents for which we had data, or the ε_{LW} in the most similar solvent. Specifically, hexane was approximated using the average value of benzene and toluene, DMSO was approximated using the average value of acetone and acetonitrile, all alcohols studied were approximated using the ε_{LW} determined in isopropyl alcohol, and all other solvents were approximated using the average ε_{LW} of all four aprotic solvents. Extinction coefficients of the individual LW isomers were found to be within 20% of each other regardless of solvent, and the absorptivity of the LW isomers of the quinoline analogs **12** was roughly half that of the parent compound **2**. The extinction coefficients of the individual SW isomers showed somewhat greater variability, exhibiting a roughly 1.5-fold increase in absorptivity from least polar to most polar solvents, but were more similar between the parent compound **1** and the quinoline analogs **3**.

We were able to use chemical actinometry and known ε_{LW} to allow us to determine initial quantum yields (ϕ_{isom}) for the photochemical isomerization of SW to LW in solvents where we had ε_{LW}. Our results for **1a** → **2a** (and **3a**,**b** → **12a**,**b**) in hexane are similar to Minkin's results in octane for **1b** → **2b** [2]. The quantum yields of the quinazolinespirohexadienones **3a**,**b** are qualitatively and quantitatively quite similar to those of the parent perimidinespirohexadienone **1a**. Notably non-polar solvents give appreciably higher quantum yields than either dipolar aprotic or protic solvents (as Minkin and co-workers had already noted for acetonitrile [2]). To confirm that this was not an artifact of solely using aromatic solvents as our non-polar solvents, a quantum yield was determined in hexane, approximating ε_{LW} for this solvent (not affordably available in perdeutero form) by the average ε_{LW} of benzene and toluene. Of the polar solvents, it appears that the quantum yields are just slightly higher in protic solvents. Interestingly, **3b** shows a slightly higher quantum yield in polar solvents than either **1a** or **3a**, though it is still much less than that of any of the compounds studied in non-polar solvents.

All the accumulated photochemical data on **3a**/**12a** and **3b**/**12b**, along with **1a**/**2a** for comparison, that are discussed above are summarized in Table 1.

4. Conclusions and future work

While we have unfortunately not found a suitable explanation for the differences in thermal reversion of **12a** → **3a** vs. **12b** → **3b**, we have conclusively determined the structure of the photolytically generated LW isomers of **3a**,**b** as **12a**,**b** (rather than **4a**,**b**), respectively, by the observed NOE enhancements. We note that this implies, but does not conclusively demonstrate, analogous structures **12c**–**e** as the likely LW isomers generated by photolysis of **3c**–**e**. (As far as we are aware, Minkin and co-workers have not conclusively demonstrated the structure of the long wavelength isomers of their quinazolinespirohexadienones **3c**–**e**, and have at times drawn both **4c**–**e** and **12c**–**e**, but have generally seemed to favor structure **4** [2,5].)

Moreover, the work reported herein gives us an important understanding of structure necessary for analyzing the electrochemical results we have obtained to date for **3a**,**b** and **12a**,**b**. We have preliminary evidence that indicates that electrolysis of **3a**,**b** does not yield **12a**,**b**, but instead another compound that behaves similarly, likely **4a**,**b**. This work will be described in detail in a forthcoming manuscript.

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