Photochemistry of A1E, a Retinoid with a Conjugated Pyridinium Moiety: Competition between Pericyclic Photooxygenation and Pericyclization

Steffen Jockusch, Rex X. Ren,[†] Young Pyo Jang, Yasuhiro Itagaki,
Heidi R. Vollmer-Snarr,[‡] Janet R. Sparrow,[§] Koji Nakanishi,* and Nicholas J. Turro*

*Contribution from the Department of Chemistry, Columbia University, 3000 Broadway,
New York, New York 10027*

Received October 14, 2003; E-mail: kn5@columbia.edu; njt3@columbia.edu

Abstract: The photochemistry of the retinoid analogue A1E shows an oxygen and solvent dependence. Irradiation of A1E with visible light ($\lambda_{irr} = 425$ nm) in methanol solutions resulted in pericyclization to form pyridinium terpenoids. Although the quantum yield for this cyclization is low ($\sim 10^{-4}$), nevertheless the photochemical transformation occurs with quantitative chemical yield with remarkable chemoselectivity and diastereoselectivity. Conversely, irradiation of A1E under the same irradiation conditions in air-saturated carbon tetrachloride or deuterated chloroform produced a cyclic 5,8-peroxide as the major product. Deuterium solvent effects, experiments utilizing endoperoxide, phosphorescence, and chemiluminescence quenching studies strongly support the involvement of singlet oxygen in the endoperoxide formation. It is proposed that, upon irradiation, in the presence of oxygen, A1E acts as a sensitizer for generation of singlet oxygen from triplet oxygen present in the solution; the singlet oxygen produced reacts with A1E to produce cyclic peroxide. Thus, the photochemistry of A1E is characterized by two competing reactions, cyclization and peroxide formation. The dominant reaction is determined by the concentration of oxygen, the concentration of A1E, and the lifetime of singlet oxygen in the solvent employed. If the lifetime of singlet oxygen in a given solvent is long enough, then oxidation (peroxide formation) is the major reaction. If the singlet oxygen produced is quenched by the protonated solvent molecules faster than singlet oxygen reacts with A1E, then cyclization dominates.

Introduction

The chromophore A2E, **1** (Chart 1), a pyridinium bisretinoid,[1,2] accumulates with age in retinal pigment epithelial cells of the eye[3–5] and in patients with a juvenile form of macular degradation (Stargardt's disease).[6] Many studies suggest that A2E contributes to age-related macular degeneration,[7–9] which is the leading cause of blindness among the elderly in the developed world. In a previous study we showed that A2E undergoes photooxidation during irradiation with blue light (430 nm), producing epoxide rings initially at positions 7, 8 and 7′, 8′ (**2**) under involvement of singlet oxygen.[10] It was proposed that, upon irradiation, A2E acts as a sensitizer for generation of singlet oxygen from triplet oxygen, and that subsequently the singlet oxygen reacts with A2E to produce epoxides. The extent of epoxidation (number of epoxide rings per A2E molecule) is dependent on the intensity and duration of irradiation with blue light.[8] MS analysis showed that epoxidation proceeds to give the nonaoxirane **3**.[10] In a study in which A2E epoxides were loaded into RPE cells, we found that the A2E epoxides induce cell damage directly, independent of damage by singlet oxygen.[11]

To elucidate the mechanism of photooxygenation of the bisretinoid A2E, the nonphysiological monoretinoid A1E (**4**) was synthesized. A1E possesses a structure identical to A2E except that it has a single side arm, whereas A2E has two (Chart 1). The photophysics and photochemistry of A1E were studied using a multitechnique approach, including steady-state and time-resolved optical absorption and luminescence spectroscopy

† Current address: Department of Chemistry, Wesleyan University, Middletown, CT 06459.

‡ Current address: Department of Chemistry & Biochemistry, Brigham Young University, Provo, UT 84602.

§ Department of Ophthalmology, Columbia University, New York, NY 10028.

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Chart 1. Structures of A2E, A1E, and Their Photoproducts
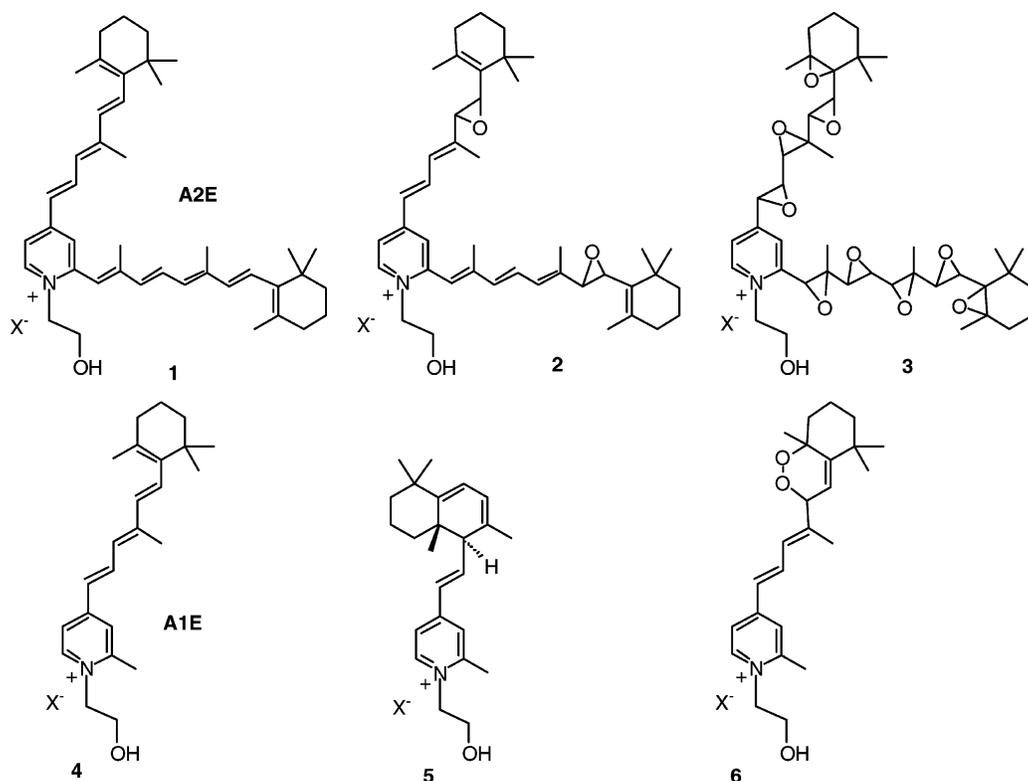
Scheme 1. Synthesis of A1E
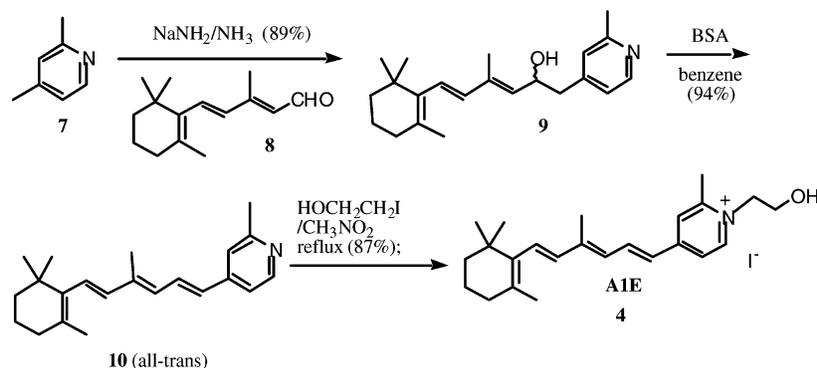
and product studies after irradiation at various conditions using MS and NMR techniques.

Results and Discussion

A1E was synthesized as shown in Scheme 1. Site-specific deprotonation[12,13] of 2,4-dimethylpyridine (**7**) with NaNH$_2$ in liquid ammonia, followed by addition of retinoidyl aldehyde **8**, led to alcohol **9**, which was subjected to acid-catalyzed elimination to give all-trans pyridyl retinoid **10**. Alkylation of **10** with 2-iodoethanol in nitromethane under reflux afforded the pyridinium substrate A1E (**4**).

A1E exhibits an intense optical absorption in methanol solution centered at 417 nm ($\epsilon = 28950$ M^{-1} cm^{-1}). At room temperature A1E shows only a weak fluorescence ($\lambda_{max} = 560$ nm; ethanol solution) with a low fluorescence quantum yield

($\Phi_f^{23\,°C} = 0.002 \pm 0.001$). In agreement with the low fluorescence quantum yield, a short fluorescence lifetime was observed ($\tau_f^{23\,°C} < 0.15$ ns) which is shorter than the time resolution of our instrumental setup. In a frozen ethanol matrix at 77 K the fluorescence quantum yield and lifetime increase strongly ($\Phi_f^{77\,K} > 0.6$; $\tau_f^{77\,K} = 1.7 \pm 0.1$ ns). The low fluorescence quantum yield and lifetime at room temperature are consistent with efficient trans–cis isomerization of the double bonds from the singlet excited state of A1E, which was also observed for other retinoids.[14–16] In a matrix at 77 K the trans–cis isomerization is suppressed, and therefore, a strong fluorescence was observed in ethanol glass.

To investigate the photochemistry, methanol solutions of A1E were irradiated at 425 nm and the reaction was monitored via

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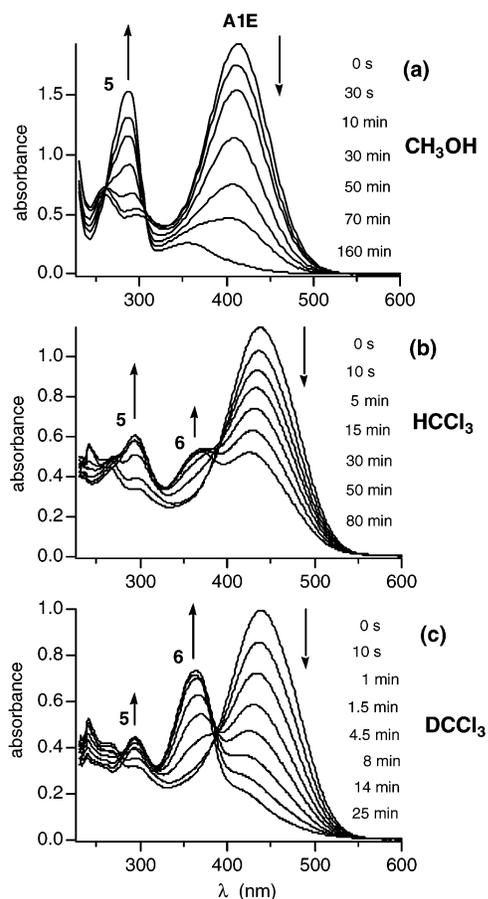
Figure 1. Optical absorption spectra recorded after irradiation of A1E in air-saturated solutions of methanol (6.7×10^{-5} M) (a), chloroform (3.9×10^{-5} M) (b), and deuterated chloroform (3.4×10^{-5} M) (c) at $\lambda_{ex} = 425$ nm.

Figure 2. Optical absorption spectra recorded after different times of dark reaction of A1E in the presence of the endoperoxide of 1,4-diphenylnaph-thalene (17 mM) in solutions of methanol (a) and deuterated methanol (b) at 25 °C.

UV−vis absorption spectroscopy. Figure 1a shows the absorbance after different irradiation times. With continuing irradiation, the band at 417 nm decreases and two new hypsochromically shifted maxima appear (λ_{max} at 288 nm and λ_{max} at 356 nm). In addition, two isosbestic points at 308 and 260 nm were observed. To investigate the structure of the photoproduct, preparative irradiations were performed employing a 1000 W Xe lamp in conjunction with an aqueous filter solution (1 M NaNO₂; $\lambda_{irr} > 400$ nm).[17] NMR analysis showed that irradiation in methanol yields a single diastereomeric bicyclic pyridinium drimadiene (racemic) (**5**) with an almost quantitative yield. The structure of **5** was confirmed on the basis of NOE studies (for details see the Supporting Information).

The quantum yield for this photoreaction in methanol solution was estimated ($\Phi \sim 10^{-4}$) on the basis of the disappearance of **4** by employing Aberchrome 540 as actionmeter.[18] No change in quantum yield of the photoproduct was observed, whether the methanol solution was deoxygenated by argon bubbling or saturated with oxygen. Furthermore, irradiation of A1E in solvents such as acetonitrile and water gave the same photoproduct.

In contrast, irradiation of A1E in air-saturated deuterated chloroform (CDCl₃) at 425 nm produced a completely different
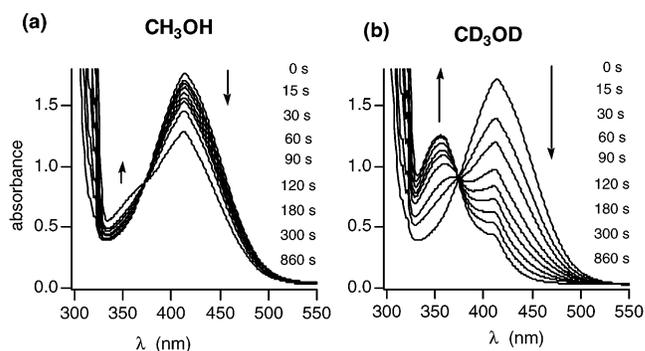
type of photoproduct. Figure 1c shows the absorbance after different irradiation times. With continuing irradiation, A1E bleaches and a new hypsochromically shifted absorption appears ($\lambda_{max} = 363$ nm) (**6**). In addition to the major peak at 363 nm, a weak peak at 294 nm appeared. Because this absorption ($\lambda_{max} = 294$ nm) was also observed during photolysis in a methanol solution (Figure 1a), we assign the peak at 294 nm to the cycloreaction product **5**. Irradiation of A1E in CHCl₃ at 425 nm yielded a similar absorption spectrum with maxima at 294 nm (major peak) and 363 nm (minor peak) (Figure 1b), but the peak intensities are reversed. In addition, the rate of disappearance of the absorption of A1E is 13-fold slower in CHCl₃ compared to the rate in CDCl₃. This strong deuterium effect is a signature of the involvement of singlet oxygen, whose lifetime possesses an extraordinary dependence on the occurrence of CH versus CD bonds in the solvent.[19−21] Due to the longer lifetime of singlet oxygen in CDCl₃ (7 ms)[22] compared to CHCl₃ (0.23 ms),[22] reactions involving singlet oxygen are expected to proceed faster in deuterated solvents. A detailed structural analysis of the reaction product **6** associated with the absorption at 363 nm will be given below. In photolysis experiments of A1E in deoxygenated CDCl₃ solutions (deoxygenation by five freeze−pump−thaw cycles) the cyclization product **5** was observed almost exclusively, showing that molecular oxygen is necessary to generate **6**.

As a direct test of the involvement of singlet oxygen in the formation of **6**, singlet oxygen was generated from the decomposition of the aromatic endoperoxide **11**.[23] The latter was selected because of its convenient half-life (approximately 5 h at 25 °C), and the fact that it decomposes nearly exclusively into 1,4-dimethylnaphthalene (**12**) and singlet oxygen (eq 1).[24]
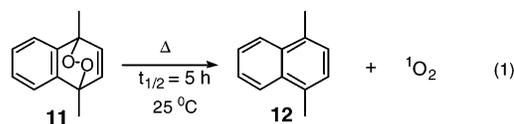
Solutions of A1E and endoperoxide in CH₃OH and CD₃OD were stored in the dark for 12 h at room temperature. Figure 2

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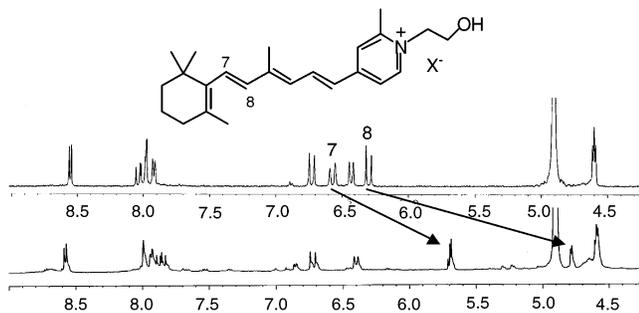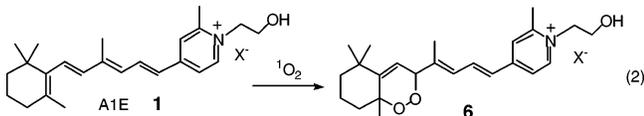(24) Adam, W.; Prein, M. *Acc. Chem. Res.* **1996**, *29*, 275−283.

Figure 3. ¹H NMR spectra of A1E (top) and **6** (bottom) (400 MHz, CD₃-OD). The upfield-shifted protons of the 7 and 8 positions correlated with 115.6 and 82.6 ppm of the ¹³C NMR resonance in the HSQC study, respectively.

Figure 4. Right: phosphorescence spectrum of singlet oxygen generated by sensitization with A1E (λ_{ex} = 425 nm) in CCl₄ at 25 °C. Left: excitation spectrum for the singlet oxygen phosphorescence (λ_{em} = 1270 nm), which resembles the A1E absorption spectrum.

Figure 5. Transient optical absorption spectra of A1E recorded 0.6, 1.3, 2.2, and 4.3 μs following laser excitation (400 nm, ca. 7 mJ/pulse) of argon-saturated benzene solutions at 23 °C.

shows optical absorption spectra after different reaction times. In CD₃OD (Figure 2b) the reaction proceeds approximately 8-fold faster than in CH₃OH (Figure 2a), as is expected due to the longer lifetime of singlet oxygen in CD₃OD (270 μs)[25] compared to CH₃OH (9.5 μs).[22] In both solvents, CH₃OH and CD₃OD, the same reaction product (**6**) was formed as shown by mass spectrometry.

To investigate the structure of the product **6**, the reaction of A1E with singlet oxygen (generated from endoperoxide) (eq 2) was performed on a preparative scale (A1E, 46 mg;

endoperoxide, 200 mg; CH₃OH, 2 mL; 25 °C). The high endoperoxide concentration compared to that of the experiment described in Figure 2a was chosen to increase the conversion of A1E in CH₃OH solutions. After 20 h, approximately 80% of A1E was converted into products (determined by UV–vis spectroscopy). The oxygenation product **6** was isolated by preparative HPLC. FAB-MS studies showed that two oxygen atoms were incorporated into A1E by oxidation (see the Supporting Information). NMR studies of **6** including ¹H and ¹³C NMR, magnitude COSY, and HSQC revealed the structure of **6** as a cyclic 5,8-peroxide (Figure 3).

The large deuterium isotope effect in the photooxidation and thermal oxidation utilizing endoperoxide demands the involvement of singlet oxygen in both instances. Thus, we conclude that irradiation of A1E in the presence of oxygen must lead to the production of singlet oxygen through the quenching of an excited state of A1E. To demonstrate that singlet oxygen can be generated by electronically excited states (S₁ or T₁) of A1E, the phosphorescence of singlet oxygen centered at 1270 nm was used as a spectroscopic probe.[26] Air-saturated solutions of A1E in CCl₄ were irradiated at 425 nm, and the photoluminescence spectra were recorded from 1100 to 1400 nm. The resulting spectrum shown in Figure 4 (right) is consistent with that reported for singlet oxygen phosphorescence.[26] To determine the species responsible for producing the phosphorescence, luminescence excitation spectra were recorded. The excitation
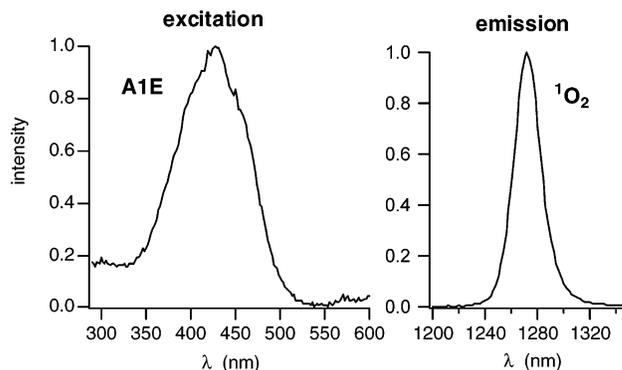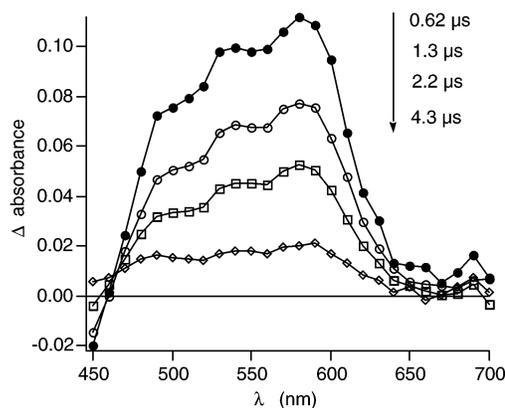
spectrum (Figure 4, left) is very similar to the optical absorption spectrum of A1E. Therefore, we conclude that A1E is the active species whose absorption results in an excited state that generates singlet oxygen. Given the very short fluorescence lifetime (S₁ state) of A1E (see above), we conclude that the triplet state (T₁) is probably the excited state of A1E that produces singlet oxygen.
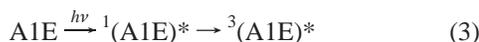
Laser flash photolysis experiments were performed to determine if triplet states of A1E are involved in the singlet oxygen sensitization. Irradiation of argon-saturated benzene solutions of A1E with laser pulses (400 nm) afforded readily detectable transient absorption spectra with a broad absorption from 480 to 620 nm (Figure 5), which decayed by pseudo-first-order kinetics (τ = 1 μs). This transient was assigned to the triplet state of A1E (eq 3), because the transient was efficiently quenched by the triplet quencher canthaxanithin, a carotin (E^T = 88–105 kJ/mol),[27] with a diffusion-controlled rate constant ($k_q \approx 1 \times 10^{10}$ M⁻¹ s⁻¹). In addition, the transient was also quenched by molecular oxygen ($k_{O_2} \approx 1 \times 10^{10}$ M⁻¹ s⁻¹) probably with simultaneous formation of singlet oxygen (eq 4). Subsequently, the generated singlet oxygen could react with A1E (eq 5).

The rate constant for quenching of singlet oxygen by A1E (eq 5) was determined by luminescence quenching experiments.

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$$A1E \xrightarrow{h\nu} {}^1(A1E)^* \rightarrow {}^3(A1E)^* \tag{3}$$

$${}^3(A1E)^* + {}^3O_2 \xrightarrow{k_{O_2}} A1E + {}^1O_2 \tag{4}$$

$$A1E + {}^1O_2 \xrightarrow{k_{A1E}} 6 \tag{5}$$

CCl$_4$ solutions of the endoperoxide of 1,4-dimethylnaphthalene show a strong chemiluminescence of singlet oxygen centered at 1270 nm (Figure 6, left). In the presence of A1E the luminescence intensity was gradually reduced with increasing A1E concentration, suggesting an efficient quenching (Figure 6, left). The rate constant of the singlet oxygen quenching (eq 5) was determined by a Stern–Volmer treatment of the luminescence intensities.[28] The lifetime of singlet oxygen in CCl$_4$ under our experimental conditions (high concentrations of the endoperoxide) is expected to be significantly shorter than in pure CCl$_4$ (59 ms; sensitization with 5,10,15,20-tetraphenylporphine).[22] Therefore, the singlet oxygen lifetime ($\tau = 3.4$ ms) was determined by luminescence quenching with 1-methyl-1-cyclohexane using its known quenching rate constant (3.6 × 10^5 M^{-1} s^{-1}).[29] This lifetime led to an estimation of the rate constant for the quenching of singlet oxygen by A1E of $k_{A1E} \approx 4 \times 10^7$ M^{-1} s^{-1}.

Discussion

The photochemistry of A1E, a retinoid, was investigated in different solvents. Two major reaction products were observed: the cyclization product pyridinium terpenoid **5** and the cyclic 5,8-peroxide **6**. Deuterium solvent effects (Figure 1b,c), experiments utilizing an endoperoxide (Figure 2), phosphorescence (Figure 4), and chemiluminescence quenching experiments (Figure 6) show that singlet oxygen reacts with A1E to form the peroxide **6**. The formation of similar cyclic peroxides was also observed for other retinoids.[30] The singlet oxygen was generated by quenching photoexcited states of A1E, which was demonstrated by the observation of the singlet oxygen phosphorescence after photoexcitation of A1E (Figure 4). Theoretically, singlet oxygen can be generated from both electronic excited states, S$_1$ and T$_1$. Laser flash photolysis experiments showed the formation of triplet excited states of A1E (Figure 5), which were quenched by molecular oxygen with a diffusion-controlled rate constant, and probably resulted in the formation of singlet oxygen. Singlet excited states are also known to be quenched by oxygen under formation of singlet oxygen.[31] Nevertheless, because of the short singlet lifetime of A1E ($\tau_f^{23\,°C} < 0.15$ ns), oxygen quenching of the S$_1$ state is the unlikely source of singlet oxygen. Therefore, we propose that the singlet oxygen is generated from quenching of triplet excited states of A1E (which are generated after photoexcitation and intersystem crossing), by molecular oxygen. Afterward, the singlet oxygen reacts with A1E to form the cyclic 5,8-peroxide **6**, or the singlet oxygen is deactivated (e.g., by solvent molecules) to ground-state triplet oxygen. As expected, the highest yields of **6** were observed in solvents with long singlet oxygen lifetime, such as
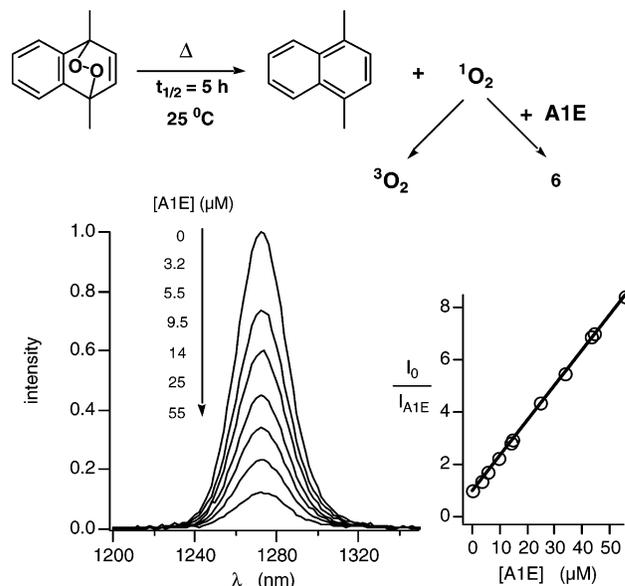

Figure 6. Left: chemiluminescence spectra of singlet oxygen generated from the endoperoxide of 1,4-diphenylnaphthalene (2.0 mM) in the presence of A1E at different concentrations (0–55 μM) in CCl$_4$ at 25 °C. Right: the corresponding Stern–Volmer plot to determine the quenching rate constant, where I_0 is the intensity of the chemiluminescence at 1270 nm in the absence of A1E and I_{A1E} is the intensity in the presence of A1E.

Scheme 2. Photocyclization of A1E
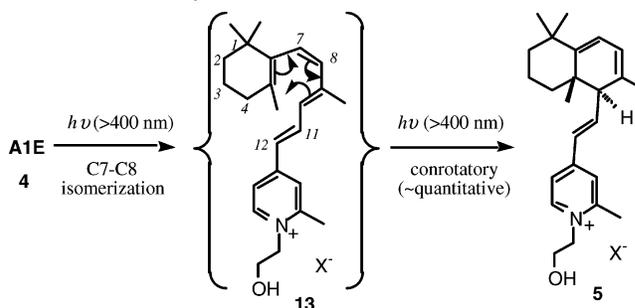
CCl$_4$ and CDCl$_3$. In addition, an increase in concentration of A1E also increases the yield of **6** (see the Supporting Information).

If the singlet oxygen is quenched by the solvent faster than it can react with A1E, pericyclization (Scheme 2) dominates. Because no change in the quantum yield of the formation of the photoproduct **5** was observed in the presence or absence of oxygen, we propose that the pericyclization occurs from the singlet excited state. The singlet excited state is too short lived ($\tau_f^{23\,°C} < 0.15$ ns) to be quenched by oxygen, whereas the triplet state lives long enough for efficient oxygen quenching ($\tau_T^{23\,°C} = 1$ μs; laser flash photolysis). Mechanistically, the pericyclization should most likely involve the initial photoisomerization of the C7–C8 double bond, leading to intermediate **13**, followed by ring closure (to produce **5**) in a separate photochemical step (Scheme 2). Similar cyclization reactions were reported for vitamin A derivatives.[32] It is known that photochemical cyclizations in the vitamin A series are limited to the 6π-electron reaction of the C5–C6, C7–C8, and C9–C10 double bonds regardless of the length of the polyene chains.[32] The quantum yield for the cyclization reaction is very low ($\Phi \approx 10^{-4}$), probably because of efficient photoisomerization of

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the 7-cis isomer **13** back to the all-trans isomer of A1E, which competes with the cyclization reaction. For all the photoreactions carried out on A1E, the UV−vis spectra corresponding to the all-trans pyridinium retinoid starting material (Figure 1, first spectrum in a series) do not pass the isosbestic points. This should indicate a very rapid photoisomerization of the C7−C8 double bond with much higher quantum efficiencies to the photostationary state, which is a mixture of the all-trans isomer of A1E and the cis isomer **13** (Figure 1, second spectrum in a series). The isosbestic points observed in the experiments (Figure 1a) indicate that the 6π-electropericyclic reaction is indeed a unimolecular process[33] with respect to the initial C7−C8 double bond isomerization. The diastereospecificity originating from the conrotatory mode can be accounted for by the Woodward− Hoffmann rule[34] regarding pericyclic reactions of the conjugated triene moiety under photochemical conditions.

Summary and Conclusions

The photochemistry of the retinoid analogue A1E was investigated in different solvents. Irradiation of A1E with visible light ($\lambda_{irr} = 425$ nm) in methanol solutions resulted in pericyclization to form pyridinium terpenoids **5**. Although the quantum yield for this cyclization is low ($\sim 10^{-4}$), the photochemical transformation occurs with quantitative chemical yield and with remarkable chemioselectivity and diastereoselectivity. Conversely, irradiation of A1E under the same irradiation conditions in air-saturated carbon tetrachloride or deuterated chloroform produced a cyclic 5,8-peroxide (**6**) as the major product. Deuterium solvent effects, experiments utilizing endoperoxide, phosphorescence, and chemiluminescence quenching studies strongly support the involvement of singlet oxygen in the endoperoxide formation. We propose that, upon irradiation, in the presence of oxygen, A1E acts as a sensitizer for generation of singlet oxygen from triplet oxygen present in the solution; the singlet oxygen produced reacts with A1E to produce the cyclic peroxide. Thus, the photochemistry of A1E is characterized by two competing reactions, cyclization and peroxide formation. Which reaction dominates depends on the concentrations of oxygen and A1E and the lifetime of singlet oxygen in the solvent employed. If the concentrations of oxygen and A1E are high enough and the lifetime of singlet oxygen in the solvent is long enough, then the peroxide is the major reaction product. Even if the oxygen concentration is high enough to quench the excited states of A1E to produce singlet oxygen, if the singlet oxygen produced is quenched by the protonated solvent molecules faster than singlet oxygen reacts with A1E, then cyclization dominates.

Previously, we found that the bisretinoid A2E (**1**) forms epoxides (**2, 3**) upon reaction with singlet oxygen.[10] In this study we showed that the monoretinoid A1E forms a cyclic 5,8-peroxide (**6**) in the reaction with singlet oxygen. The cause of the entirely different reaction products of A2E and A1E with singlet oxygen is currently under investigation and the subject of an upcoming paper.

Experimental Section

Synthesis of A1E. The requisite precursor was synthesized as shown in Scheme 1. Site-specific deprotonation[12,13] of 2,4-dimethylpyridine

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(**7**) with NaNH$_2$ in liquid ammonia followed by addition of retinoidyl aldehyde **8** led to alcohol **9**, which was subjected to acid-catalyzed elimination to give all-trans pyridyl retinoid **10**. Alkylation with 2-iodoethanol, or methyl iodide in nitromethane under reflux, or treatment with methyl triflate in diethyl ether at room temperature, afforded pyridinium substrate A1E (**4**).

The oxidation product of A1E (**6**) was isolated and purified by HPLC (HP 1100 series with DAD detector) equipped with a reversed-phased preparative column (Vydac, C18, 10 μm, 22 × 250 mm) and using a gradient solvent system mode (water/methanol with 0.1% TFA, 25:75 to 5:95).

^{1}H NMR spectra were recorded using a Varian VXR 400 spectrometer at 400 MHz. ^{13}C NMR spectra were recorded using a Varian Gemini 300 MHz spectrometer at 75 MHz in CDCl$_3$. NOE difference spectra were performed on a 500 MHz Bruker NMR spectrometer. Chemical shifts are given in δ (ppm) using the solvent as the internal reference, and the coupling constants (*J*) are in hertz (Hz). Low-resolution and high-resolution FAB mass spectra were measured on a JEOL JMS-HX110/110A tandem mass spectrometer (Tokyo, Japan) using an *N*-nitrobenzyl alcohol (NBA) matrix and Xe gas (6 kV). ESI mass spectra were obtained on a Q-TOF (Micromass, Manchester, U.K.). UV−vis spectra were recorded on an Agilent 8453 or 8452A spectrometer. Luminescence spectra were recorded on a Fluorolog-2 spectrometer (SPEX) in conjunction with an EO-817L Ge-diode detector (North Coast Scientific Corp.) The laser flash photolysis experiments were performed by Elizabeth Gaillard at Northern Illinois University, DeKalb. The setup employed the pulses from a Continuum Powerlite 9010 injection-seeded Nd:YAG-pumped Sunlite optical paramagnetic oscillator (400 nm; $\sim$7 mJ/pulse) and a computer-controlled system described elsewhere.[35]

The quantum yields were obtained by continuous irradiation of a 3 mL solution in a 1 × 1 cm quartz cell at 417 nm (15 nm bandwidth, 30 mW/cm^2) employing a Xe lamp (LX300 UV) in conjunction with a monochromator (Kratos, Schoeffel Instruments). The changes in optical absorption were measured on an Agilent 8452A spectrophotometer. The absorbed dose was determined by actinometry using Aberchrome 540 (Aberchromics Ltd., U.K.).[18] The preparative irradiations were performed with visible light using a Xe lamp (XBO 1000, Hanovia) and a filter 1 M NaNO$_2$(aq) solution to block the UV light, giving cutoff at about 400 nm.[17]

NMR of 10. ^{1}H NMR (CDCl$_3$, ppm) δ 8.33 (d, 1H, *J* = 5.1 Hz), 7.28 (dd, 1H, *J* = 15.5, 11.4 Hz), 7.06 (s, 1H), 7.02 (d, 1H, *J* = 5.1 Hz), 6.36 (d, 1H, *J* = 15.4 Hz), 6.22 (d, 1H, *J* = 16 Hz), 6.15 (d, 1H, *J* = 11.4 Hz), 6.10 (d, 1H, *J* = 16 Hz), 2.48 (s, 3H), 1.95 (m, 5H), 1.61 (m, 5H), 1.41 (m, 2H), 0.97 (s, 6H); ^{13}C NMR (CDCl$_3$, ppm) δ 158.5, 149.2, 145.2, 139.1, 137.6, 137.1, 129.8, 129.3, 129.1, 128.9, 128.5, 119.9, 117.6, 39.5, 34.2, 33.0, 29.0, 24.3, 21.7, 19.1, 12.8.

NMR of A1E (4). ^{1}H NMR (CDCl$_3$, ppm) δ 9.0 (d, 1H, *J* = 6.7 Hz), 7.72 (m, 2H), 7.58 (s, 1H), 6.52 (m, 2H), 6.3 (m, 2H), 4.8 (t, 2H, *J* = 4.6 Hz), 4.2 (t, 2H, *J* = 4.6 Hz), 2.9 (s, 3H), 2.2 (s, 3H), 2.1 (m, 2H), 1.76 (s, 3H), 1.62 (m, 2H), 1.52 (m, 2H), 1.1 (s, 6H); ^{13}C NMR (CDCl$_3$, ppm) δ 153.7, 153.3, 146.3, 145.3, 138.3, 137.5, 136.5, 132.3, 131.7, 128.7, 125.1, 124.8, 121.1, 59.8, 58.7, 39.6, 34.2, 33.2, 28.9, 21.7, 21.5, 19.0, 13.7.

NMR of 5. ^{1}H NMR (CDCl$_3$, ppm) δ 9.15 (d, 1H, *J* = 6.7 Hz), 7.75 (d, 1H, *J* = 6.7 Hz), 7.65 (s, 1H), 7.05 (dd, 1H, *J* = 15.5, 11 Hz), 6.6 (d, 1H, *J* = 15.5 Hz), 5.9 (d, 1H, 5.7 Hz), 5.84 (m, 1H), 4.9 (t, 2H, *J* = 4.6 Hz), 4.2 (m, 2H), 3.0 (m, 4H), 1.72 (s, 3H), 1.7−1.2 (m, 6H), 1.17 (s, 3H), 1.15 (s, 3H), 1.1 (s, 3H); ^{13}C NMR (CDCl$_3$, ppm) δ 154.5, 152.9, 151.8, 146.5, 146.3, 132.3, 128.4, 125.8, 121.2, 117.8, 59.7, 59.1, 58.3, 41.0, 39.9, 38.9, 35.4, 31.9, 31.8, 21.9, 21.5, 18.4, 17.8.

Supporting Information Available: Synthetic protocols, mass spectrometry of **6**, and A1E concentration dependence of photooxygenation (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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