

pH sensitive photophysical and photochemical properties of a pentaazadentate porphyrin-like gadolinium (III) complex

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1. ABSTRACT

The electronic absorption spectra, photobleaching property, emission, and triplet excited state characteristics of a pentaazadentate porphyrin-like gadolinium(III) complex have been investigated at acidic and basic conditions. The electronic absorption spectrum of this complex exhibits a Soret band at ca. 449 nm and a Q-like band at ca. 880 nm when the pH value of the solution is lower than 6.6. At basic conditions, the Q-like band blue shifts to ca. 624 nm, while the Soret band only shows an approximate 20 nm hypsochromic shift. The acidic solution is relatively stable upon exposure to ambient light, but the basic solution photobleached to colorless in approximately 3 hours. Irradiation of the Soret band of basic solutions at 420 nm causes faster photobleaching than irradiation of the Q-like band (624 nm). The emission of this complex at pH = 6.5 appears at ca. 915 nm (max.) and 1016 nm, which is a mirror image of the Q-like band, indicating the nature of the emitting state being the lowest singlet excited state. At pH = 9.0, the emission band shifts to ca. 585 nm (max.) and 630 nm (shoulder). The triplet transient difference absorption spectrum of the solution at pH = 6.5 exhibits a bleaching band at ca. 460 nm, a narrow positive band at ca. 450 nm, and a broad, moderately intense absorption band from 480 nm extending to the near-IR region (700 nm). The triplet excited state lifetime deduced from the decay of the transient absorption is approximately 81 ns.

2. INTRODUCTION

Texaphyrins (1-3) and their analog pentaazadentate porphyrin-like metal complexes (4-6) are a promising class of expanded porphyrins. They can form planar, aromatic complexes with metal cations, exhibit selective biolocalization, and possess energy transfer capabilities. The larger core size of the pentaazadentate ligands creates a stable coordination environment for large cations such as lanthanum(III) to form a coplanar configuration, resulting in extensively delocalized conjugated pi-electron systems. This unique structural feature causes substantial red-shift of the lowest energy Q-like band to 700 - 900 nm, and gives rise to strong third-order nonlinearities (7-10). In addition, the structures of the complexes can be readily modified by alternation of functional groups on the periphery of the pentaazadentate ring and by insertion of different metal ions in order to change chemical, optical, and biological properties. To date, the photophysical properties, photodynamic therapeutic effects, and third-order nonlinear optical responses of a series of Texaphyrins and pentaazadentate porphyrin-like metal complexes have been systematically investigated (1-15). They have been proven to be promising second-generation photosensitizers and optical limiting materials. However, the lutetium(III) texaphyrin that has been demonstrated to be feasible for treatment of

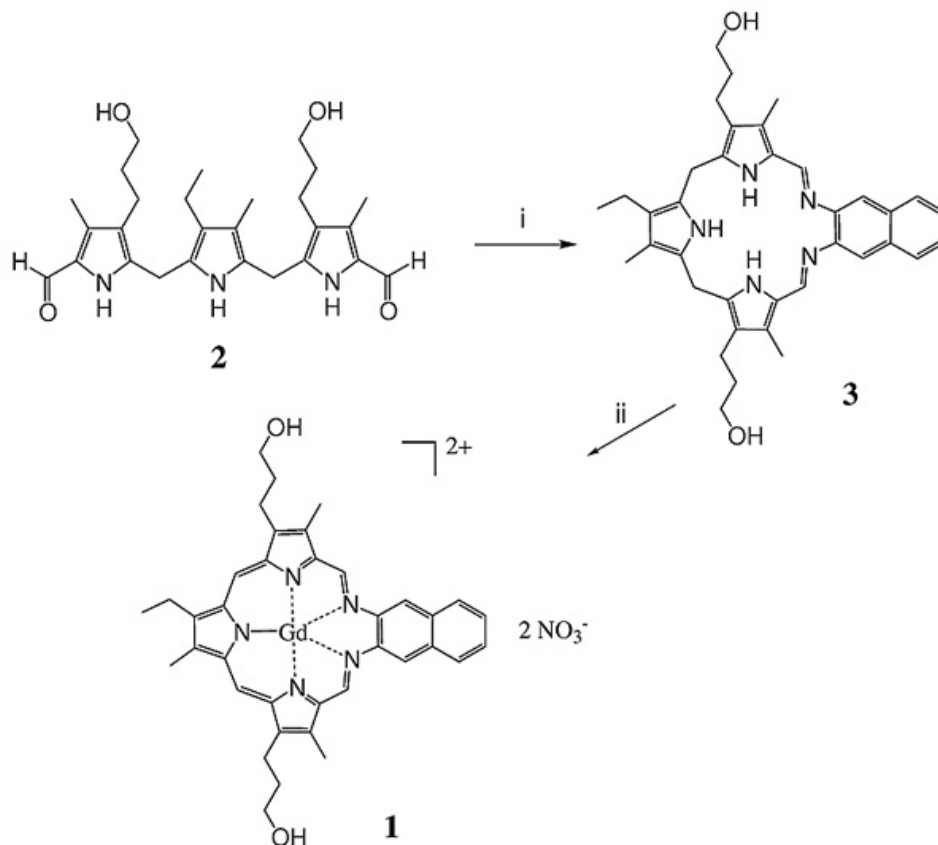


Figure 1. Reagents and conditions: (i) 2,3-Diaminonaphthalene, cat. HCl, toluene/MeOH (3.5:1), reflux; (ii) $\text{Gd}(\text{NO}_3)_3 \cdot \text{H}_2\text{O}$, Et_3N , MeOH, air, reflux.

locally recurrent breast cancer (11-14) exhibits a relatively low efficiency to generate singlet oxygen ($\Phi_{\Delta} = 0.11$), while a gadolinium(III) pentaazadentate porphyrin-like complex that shows dramatic photosensitizing damage to the murine ascitic hepatoma (AH) cell *in vitro* and AH solid tumors *in vivo* (15) has limited water solubility. In addition, the potential application of these complexes in sensing has not been explored yet.

To remedy these deficiencies, a partially water-soluble pentaazadentate porphyrin-like gadolinium complex **1** (Figure 1) has been synthesized and characterized in our group. A naphthyl ring is used to replace the phenyl ring in order to further shift the Q-like band to the near-IR region. The hydroxypropyl groups are introduced to increase the water solubility. Because the photodynamic therapeutic effects and nonlinear optical effects are closely related to the excited state characteristics of the complex, such as the energy levels and the lifetimes of the triplet excited state, it is essential for us to understand the photophysics of the complex first. Therefore, a detailed spectroscopic study, including the electronic absorption and emission spectra, triplet excited state characteristics, and the photobleaching properties of **1** at both acidic and basic conditions, has been carried out. As shown in the following sections, the pH sensitive electronic absorption and emission properties suggest that this complex could possibly be a colorimetric

and luminescent pH sensor in addition to its potential applications in photodynamic therapy and optical limiting.

3. MATERIALS AND METHODS

3.1. Materials

All solvents were reagent grade and were purchased from VWR International or Aldrich. Acetone was purified through refluxing with KMnO_4 , distilled, and then dried over anhydrous K_2CO_3 . Absolute methanol and ethanol were obtained through refluxing with Mg/I_2 . Tetrahydrofuran was dried over Na/benzophenone. Toluene was distilled before use. EM Science 60 (230-400 mesh) silica gel and Aldrich Brockmann I activated neutral alumina (150 mesh) were used for column chromatography.

3.2. Synthetic procedures

The tripyrrane dialdehyde precursor **2**, the pentaazadentate ligand **3**, and the gadolinium complex **1** were synthesized according to procedures reported by Sessler and co-workers for lanthanide(III) Texaphyrins (1). As shown in Figure 1, **3** was prepared by Schiff-base condensation reaction of the tripyrrane dialdehyde (**2**) with 2,3-diaminonaphthalene in degassed dried toluene/absolute methanol (3.5:1) in the presence of 0.25 mL hydrochloric acid catalyst. The reaction mixture was heated to reflux for ~ 7 h. After cooling down, Na_2CO_3 was added to

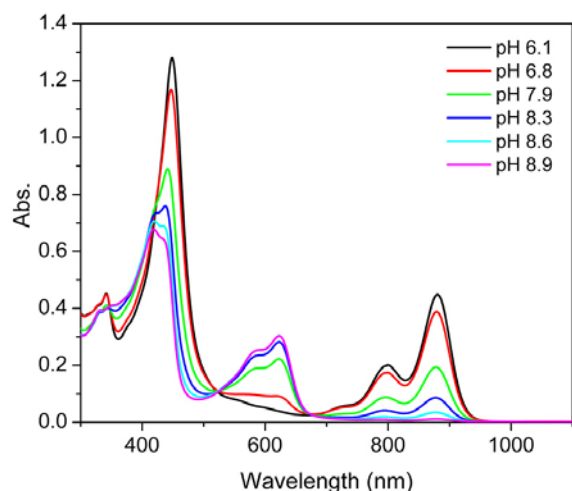


Figure 2. Electronic absorption spectra of complex **1** in methanol solutions at different pH values.

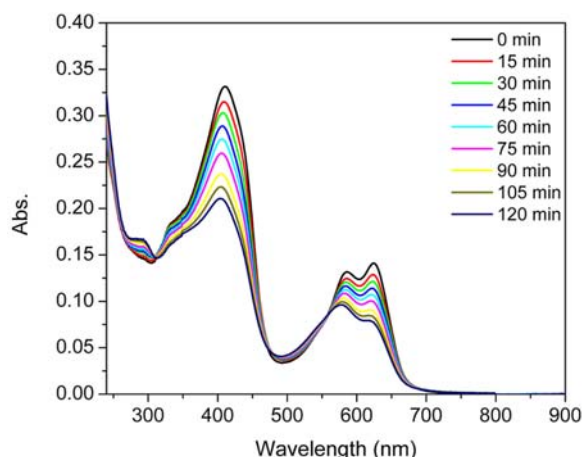


Figure 3. Time-dependent electronic absorption spectra of a basic methanol solution of complex **1** exposed to ambient light.

neutralize the solution. The undissolved Na_2CO_3 was filtered, and the solvent in the filtration was removed under reduced pressure. The crude product was recrystallized in $\text{CHCl}_3/\text{hexane}$.

1 was synthesized by reaction of one equivalent of **3** with 3 equiv. of gadolinium(III) nitrate and ca. 1 mL triethylamine in air-saturated methanol under refluxing. During the reaction, the metal insertion and ligand oxidation occurred simultaneously. The completion of the reaction was monitored by UV/vis spectroscopy. After removal of the solvent under reduced pressure, the crude product was separated using column chromatography through silica gel using CHCl_3 containing increasing amounts of methanol (0–20%) as the eluent. The product was washed out when the percentage of methanol in the eluent was increased to 20%. The product was further purified through recrystallization in $\text{CH}_3\text{OH}/\text{CHCl}_3/\text{diethyl ether}$ to afford dark-green powders. UV-vis (CH_3OH): 342 nm (2.00×10^4), 449 nm (6.25×10^4), 799 nm (1.03×10^4), 880 nm (2.33×10^4); HRMS calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{154+}$:

800.2113, found: 800.2434 (10%); calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{155+}$: 801.2132, found: 801.2289 (47%); calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{156+}$: 802.2127, found: 802.2224 (69%); calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{157+}$: 803.2245, found: 803.2172 (76%); calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{158+}$: 804.2205, found: 804.2111 (100%); calcd for $[\text{C}_{37}\text{H}_{38}\text{N}_6\text{O}_5\text{Gd}]^{160+}$: 806.2177, found: 806.2251 (70%); elemental analysis calcd. for $\text{C}_{37}\text{H}_{38}\text{N}_5\text{O}_2\text{Gd} \cdot 2\text{NO}_3 \cdot 0.5\text{SiO}_2 \cdot 6\text{H}_2\text{O}$: C: 44.22%; H: 4.99%; N: 9.77%; found: C: 43.64%; H: 5.28%; N: 10.57%.

3.3 Structural characterization and spectroscopic studies

Electrospray ionization (ESI) high-resolution mass spectrometry analyses were conducted on a 3-Tesla Finnigan FTMS-2000 Fourier Transform mass spectrometer. Elemental analyses were performed by Midwest Microlab, LLC. UV-vis absorption spectra were obtained using a CARY 500 Dual Beam Scanning UV-vis-NIR spectrophotometer. The complex was dissolved in methanol. The emission spectrum at pH = 9.0 was measured in a methanol solution on a SPEX Fluorolog-3 fluorimeter/phosphorimeter, and the emission spectrum at pH = 6.5 was obtained using a Jobin Yvon Triax 550 Imaging Spectrograph equipped with an ISA Spectrumone CCD detector and a germanium NIR detector. The triplet transient difference absorption spectra were measured on an Edinburgh LP920 laser flash photolysis spectrometer. The sample was excited by the third harmonic output (355 nm) of a Quantel Brilliant Nd:YAG laser; the laser pulsewidth (FWHM) was 4.1 ns and the repetition rate used was 1 Hz. The photobleaching studies were performed at 420 nm and 880 nm for acidic solutions and 420 nm and 624 nm for basic solutions. The light source was provided by an EKSPLA PG 401 optical parametric generator (OPG) pumped by the third harmonic frequency (355 nm) of an EKSPLA PL2143A Nd:YAG laser (The pulsewidth was 21 ps and the repetition rate was 10 Hz). The power of the OPG at selected wavelengths was adjusted to the same level of ~3.2 mW and the spectra were monitored every 15 minutes for 2 hours. The room was kept dark except for the laser irradiation to reduce the interference by the ambient light. The sample solution was stirred by a magnetic stirrer during irradiation to keep uniformity of the solution.

4. RESULTS AND DISCUSSION

4.1. UV-vis absorption spectra and photobleaching studies

Figure 2 presents the electronic absorption spectra of complex **1** in methanol at different pH values. When pH < 6.6, the spectrum possesses a Soret-band at ca. 440 nm and a Q(0,0) band at ca. 880 nm. In comparison with the corresponding Texaphyrin cadmium complex (**16**), the Q-like band of the gadolinium complex exhibits a red-shift of 20 nm. When pH > 6.6, a broad band appears at ca. 624 nm. With increased basicity of the solution, the intensity of this band increases, while the absorptivities of the initial Soret and Q-like bands decrease. When the pH value is increased to 8.8, the original Q-like band completely disappears; instead, the band at ca. 624 nm reaches the maximum. In

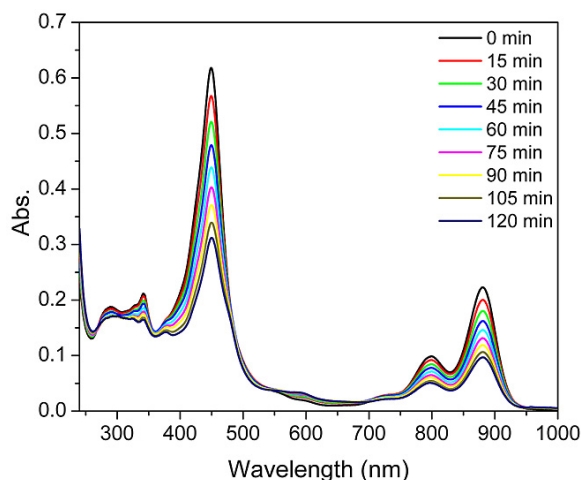


Figure 4. Time-dependent electronic absorption spectra of an acidic methanol solution of complex **1** exposed to 420 nm laser light.

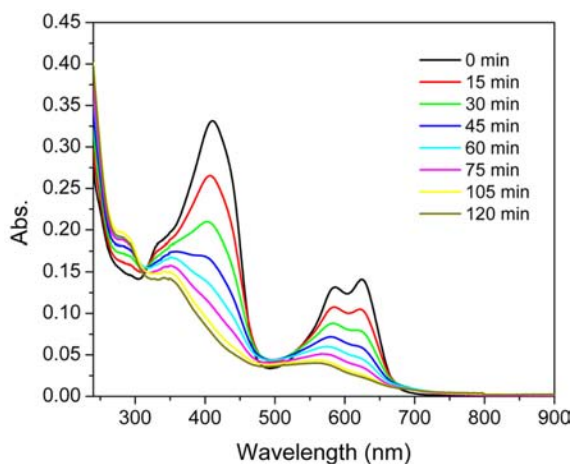


Figure 5. Time-dependent electronic absorption spectra of a basic methanol solution of complex **1** exposed to 420 nm laser light.

contrast to the Q-like band, the position of the Soret band only blue-shifts ~ 20 nm with a decreased absorptivity and broadening of the band. Most importantly, the spectrum can be converted back to its original form when the pH is adjusted to lower than 6.6. Such a convertibility and the appearance of three isosbestic points suggest that there are two interconvertible forms for complex **1** in methanol solution that are pH dependent; and the overall process is reversible. The basic form is presumably attributed to H-aggregates that cause the dramatic hypsochromic shift of the Q-like band. Alternatively, similar to the Texaphyrin ion(II) complex that forms sandwich-type μ -oxo dimers at basic conditions (3), complex **1** could possibly form oxygen bridged dimers, which distorts the planarity of the complex and results in a dramatic blue shift of the Q-like band.

To elucidate the structure of complex **1** at basic condition, high resolution mass spectrometry analysis of the

solids obtained from the basic solution by evaporation of the solvent was conducted. An identical molecular ion peak was observed for the solid obtained from the basic solution and the solid obtained from the acidic solution. This result seems to support the premise of H-aggregation at a basic solution. However, the possibility of formation of μ -oxo dimers still can not be ruled out. To completely determine the structure of complex **1** at basic conditions, X-ray crystallography needs to be carried out. Unfortunately, single crystals were unable to be obtained because of the instability of basic solutions. As will be discussed in the following paragraphs, photobleaching occurs rapidly when the solution is exposed to light. The green color of the solution completely bleaches in approximately 3 hours under ambient light. Even though the solution is kept in the dark, decomposition is still detectable from the UV-vis spectroscopy after 2 hours (shown in Figure 6).

Figure 3 displays the changes of the electronic absorption spectrum for a basic solution of complex **1** over a 120-min. period upon exposure to ambient light. The absorbances of both Soret band and Q-like band decrease. In addition, both bands exhibit a slight blue shift (~ 6 -8 nm). In contrast, the absorbance in the UV region increases, and a new band at ca. 300 nm appears. The appearance of this new band, along with three isosbestic points, suggests that during the photobleaching process, new species that absorb in the UV region are generated. Although the structure of these photobleaching products is not clear, it is probably small in size considering their absorption in the UV region. The photobleaching shows a linear profile up to 120 min., with a rate constant of $5.2 \times 10^{-4} / \text{min}$ for the Q(0,0) band at ca. 624 nm. In contrast to the basic solution of complex **1**, the acidic solution exhibits excellent photostability. No change is observed in the electronic absorption spectrum after exposure to ambient light for several weeks.

To further investigate the photostability of complex **1**, the electronic absorption spectra of complex **1** at acidic and basic solutions were monitored at different irradiation conditions. For acidic solutions, 420 nm and 880 nm laser lights were employed, which correspond to the maximum positions of the Soret and Q-like bands, respectively. For basic solutions, photolysis was conducted using 420 nm and 624 nm laser lights. It is found that the short visible light (420 nm) causes stronger and faster photobleaching than that of the near-IR lights. For acidic solutions, the spectrum remains the same after 2 h. exposure to the 880 nm light. In contrast, upon exposure to 420 nm light, the absorptivities of the Soret and Q-like bands decrease, but all of the bands remain at the same position as those of the initial solution (Figure 4). In addition, two new bands in the region of 550-680 nm and below 260 nm are formed during the photobleaching process. The varied photobleaching characteristic under different irradiation wavelengths probably can be attributed to the molar extinction coefficient difference of complex **1** at different wavelengths. For basic solutions, a similar trend is observed. Laser lights induce faster photobleaching than that of the ambient light, and the photobleaching caused by 420 nm light (Figure 5) is faster than that induced by 624 nm light (Figure 6). It is noted

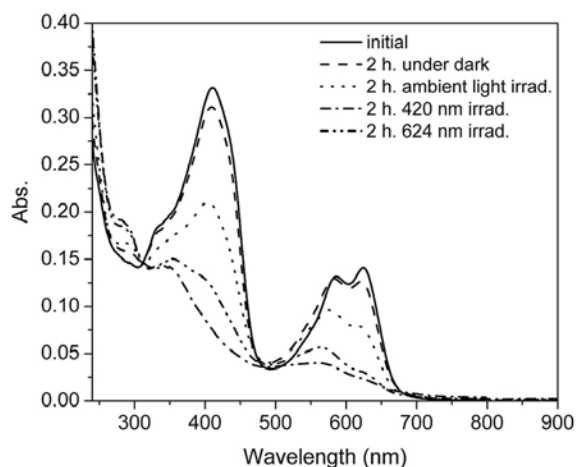


Figure 6. Photobleaching of basic solutions of complex **1** at different irradiation conditions.

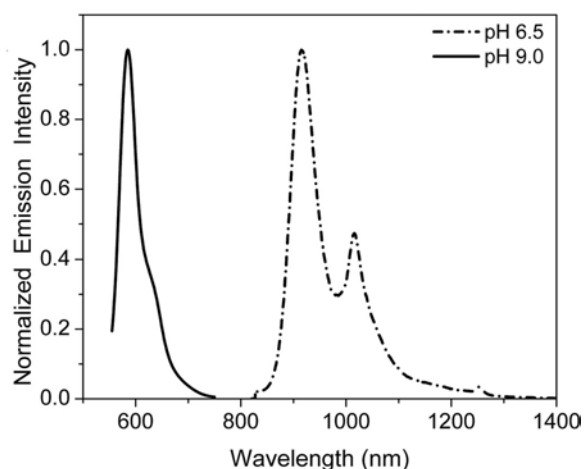


Figure 7. Emission spectra of complex **1** in methanol solutions at different pH values. The excitation wavelength for acidic solution is 774 nm; for basic solution is 567 nm.

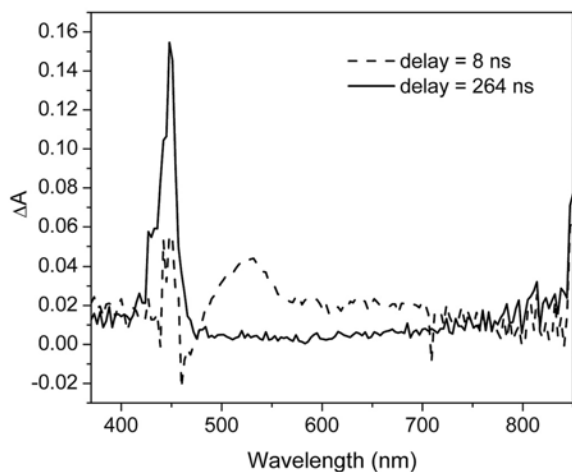


Figure 8. Triplet transient difference absorption spectra of complex **1** in a degassed methanol solution at pH=6.5. The concentration of the solution is 6.0×10^{-4} mol/L. The excitation wavelength is 355 nm.

that, for both acidic and basic solutions, the time course of photobleaching induced by laser lights does not show linear profile anymore. With prolonged irradiation, the photobleaching rate decreases. However, the photobleaching of the acidic solution appears to be much slower than that of the basic solution when both of them are irradiated with the 420 nm light at the same power. Upon exposure to 420 nm laser light, the absorbance of the Q(0,0) band at 880 nm for acidic solution decreases to 43% of that of the initial solution, while the band at ca. 624 nm for basic solution drops to 16% of the initial absorbance after two-hour irradiation. This further demonstrates that acidic solutions are much more stable than those of the basic solutions.

4.2 Emission and transient difference absorption spectra

In line with the electronic absorption spectra, the emission spectra of complex **1** also appear to be pH sensitive. As shown in Figure 7, at pH = 6.5, the emission shows two distinct bands at ca. 915 nm and 1016 nm. The spacing between these two bands is approximately 1086 cm^{-1} , corresponding to the spacing ($\sim 1152 \text{ cm}^{-1}$) between the Q(0,0) band and the Q(0,1) band in the electronic absorption spectrum. This suggests that the spacing between the vibrational states in the singlet excited state resembles that of the ground state. Thus, the emitting state can be assigned as the lowest singlet excited state. At pH = 9.0, the emission band appears at ca. 585 nm, with a shoulder at ca. 630 nm. This is also reminiscent of the Q-like band of the electronic absorption spectrum at basic condition. However, a broad band rather than two distinct bands is observed for basic solution, indicating that the separation of the vibrational levels of the lowest singlet excited state becomes smaller at basic condition.

For photosensitizers that will be applied to photodynamic therapy, the efficiency to generate reactive oxygen species, such as singlet oxygen and superoxide anion, is determined by the energy level and lifetime of the triplet excited state. Therefore, the triplet excited state characteristics of complex **1** need to be evaluated. A kinetic transient difference absorption measurement was conducted for an acidic solution to measure the triplet excited state lifetime. As shown in Figure 8, the transient difference absorption spectrum, recorded 8 ns after the 355 nm laser excitation, exhibits a bleaching band at ca. 460 nm, a narrow positive band at ca. 450 nm, and a broad, moderately intense absorption band from 480 nm extending to the near-IR region (700 nm). The triplet excited state lifetime deduced from the decay of the transient absorption is approximately 81 ns. A reliable transient difference absorption spectrum could not be obtained for the basic solution due to its instability. In comparison with the much longer triplet excited state lifetimes (tens of μs) of diamagnetic transition-metal Texaphyrin complexes (17), the extremely short lifetime for complex **1** is likely attributed to the much lower energy level of the excited states due to the extensive conjugation, which facilitates the nonradiative decay from the excited state to the ground state. In addition, as a general rule, the paramagnetic gadolinium ion also gives rise to a

much shorter excited state lifetime, as reported for a series of paramagnetic lanthanide(III) Texaphyrin complexes (2).

5. SUMMARY

The extensively conjugated pentaazadentate gadolinium(III) complex **1** exhibits pH sensitive electronic absorption and emission spectra, as well as photobleaching properties. The acidic solutions are more stable than those of the basic solutions. The acidic solution shows a moderately intense, broad triplet transient absorption band from 480 nm to 700 nm. The strong electronic absorption band in the near-IR region suggests that this complex could be a potential candidate for photodynamic therapy application, and the pH sensitive electronic absorption and emission property make it a possible colorimetric and luminescence pH sensor. Moreover, the extensive π -conjugation and the broad triplet excited state absorption at acidic condition suggest that this complex could be useful for broadband optical limiting application, which is currently under investigation.

6. ACKNOWLEDGMENT

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