JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

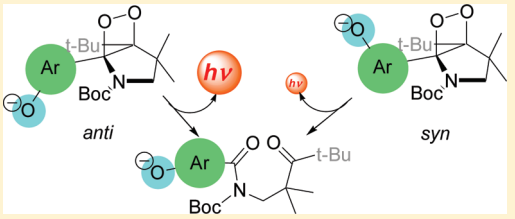
Crucial Dependence of Chemiluminescence Efficiency on the *Syn*/*Anti* Conformation for Intramolecular Charge-Transfer-Induced Decomposition of Bicyclic Dioxetanes Bearing an Oxidoaryl Group

Masakatsu Matsumoto,* Haruna Suzuki, Nobuko Watanabe, Hisako K. Ijuin, Jiro Tanaka, and Chizuko Tanaka

Department of Chemistry, Kanagawa University, Tsuchiya, Hiratsuka, Kanagawa 259-1293, Japan

Supporting Information

ABSTRACT: Thermally stable rotamers of bicyclic dioxetanes bearing 6-hydroxynaphthalen-1-yl (*anti*-**5a** and *syn*-**5a**), 3-hydroxynaphthalen-1-yl (*anti*-**5b** and *syn*-**5b**), and 5-hydroxy-2-methylphenyl groups (*anti*-**5c** and *syn*-**5c**) were synthesized. These dioxetanes underwent TBAF (tetrabutylammonium fluoride)-induced decomposition accompanied by the emission of light in DMSO and in acetonitrile at 25 °C. For all three pairs of rotamers, the chemiluminescence efficiency Φ^{CL} for *anti*-**5** was 8−19 times higher than that for *syn*-**5**, and the rate of CTID (charge-transfer-induced decomposition) for *anti*-**5** was faster than that for *syn*-**5**. The chemiluminescence spectra of the rotamers for **5a** and **5c**, respectively, were different. This discrepancy in the chemiluminescence spectra between rotamers can presumably be attributed to the difference in the structures of *de novo* keto imide *anti*-**14** and *syn*-**14** in an excited state, which inherit the structures of the corresponding intermediary anionic dioxetanes *anti*-**13** and *syn*-**13**. The important difference in chemiluminescence efficiency between *anti*-**5** and *syn*-**5** is discussed from the viewpoint of a chemiexcitation mechanism for CTID of oxidophenyl-substituted dioxetane.



INTRODUCTION

Intramolecular charge-transfer-induced decomposition (CTID) of a 1,2-dioxetane bearing an aromatic electron donor has promising potential that could lead to highly efficient chemiluminescence[1−5] and is now believed to play a key role in the bioluminescence of various organisms.[6] Thus, extensive research has been conducted to elucidate the chemiexcitation process in chemiluminescence and bioluminescence. CTID has furthermore stimulated the development of high-performance dioxetane-based chemiluminescence systems that may be useful for modern biological and clinical analysis.[7−9] However, it is still unclear how chemiluminescence is related to the structure and stereochemistry of dioxetanes. For instance, it is unclear how the conformation of an aryl group affects the chemiluminescence efficiency for CTID-active dioxetane **1** bearing an oxidophenyl group (Scheme 1). In addition, there have been few studies or discussions of the efficiency of bioluminescence in the firefly from the viewpoint of the stereochemistry of intermediary dioxetanone **2** and/or excited oxyluciferin **3** (Scheme 1).[10−13] Against this background, we found an unprecedented phenomenon that sheds light on the relationship between the stereochemistry of aryl-substituted dioxetanes and their chemiluminescence efficiency.

Dioxetanes **4** bearing a 3-hydroxyphenyl group have very recently been found to show, at room temperature, *syn*/*anti* rotational isomerism of an aromatic ring caused by steric hindrance from adjacent *N*-acyl and *tert*-butyl groups (Scheme 2).[14,15] This finding suggested that the introduction of a substituent at the 2- or 6-position of a phenyl group in dioxetane such as **4** would make rotation of the aromatic ring more difficult, so that the *syn*/*anti* rotamers could become individually isolable. This idea was realized in the form of three pairs of *syn*/*anti* rotamers of 2-Boc-5-*tert*-butyl-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane bearing a 6-hydroxynaphthalen-1-yl **5a**, 3-hydroxynaphthalen-1-yl **5b**, or 5-hydroxy-2-methylphenyl group **5c** (Chart 1).[16,17] We report here that the chemiluminescence of these dioxetanes in CTID changed with the stereochemistry of the rotamers, and the efficiencies of chemiluminescence were decisively different between the rotamers.

RESULTS AND DISCUSSION

1. Synthesis of Thermally Stable *Syn*/*Anti* Rotamers of *N*-(Boc)amino-Substituted Bicyclic Dioxetanes. First, we synthesized dioxetane **5a** to examine whether or not *syn*/*anti* rotamers of aryl-substituted dioxetane could be isolated individually in a stable form. The key precursor **6a** was synthesized as follows (Scheme 3). The first step of the synthetic sequence was *N*-substitution of 1-(*N*-Boc)amino-2,2,4,4-tetramethylpentan-3-one[14] **7** with 1-chloromethyl-6-methoxynaphthalene **8a** to give 1-[*N*-Boc-*N*-(6-methoxynaphthalen-1-yl)methylamino]-2,2,4,4-tetramethylpentan-3-one **9a**, which was in turn subjected to

Received: April 2, 2011
Published: May 16, 2011

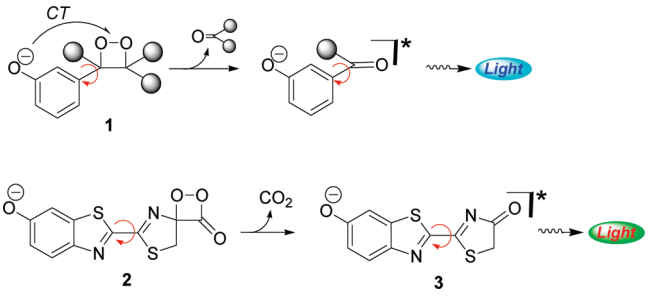
LDA-mediated cyclization to give a stereoisomeric mixture of hydroxypyrrolidine **10a**. Dehydration of **10a** gave dihydropyrrole **11a**, the methoxynaphthyl group of which was finally demethylated with MeSNa in hot DMF to give **6a**. When **6a** was irradiated in the presence of a catalytic amount of Rose Bengal in ethyl acetate with a Na lamp under an oxygen atmosphere at 0 °C, singlet oxygenation smoothly took place to exclusively give dioxetane *anti*-**5a** (Scheme 4). This result shows that singlet oxygen selectively attacked the less-crowded π-face of **6a**. The structure of *anti*-**5a** was determined by ^{1}H NMR, ^{13}C NMR, IR, Mass, HRMass spectral data and elemental analysis. The stereochemistry of *anti*-**5a** was finally determined by X-ray single crystallographic analysis,[17] and the ORTEP view is shown in Figure 1.

When *anti*-**5a** was heated in toluene at 110 °C for 15 min, isomerization occurred to give a mixture of *anti*-**5a** and *syn*-**5a** rotamers (70:30) along with a small amount of a decomposition product, i.e., keto imide **12a** (Scheme 4). Prolonged heating of *anti*-**5a** did not change the *syn*/*anti* ratio and only resulted in increased **12a**. Fortunately, rotamer *syn*-**5a** could be isolated in pure form by column chromatography (SiO_2) and gave satisfactory analytical data similar to the case of *anti*-**5a**. The stereochemistry of *syn*-**5a** was determined by X-ray single crystallographic analysis (Figure 1). The isomerization of *syn*-**5a** similarly occurred to give a 70:30 mixture of *anti*-**5a** and *syn*-**5a** together with a small amount of **12a**, when heated in refluxing toluene for 15 min. Such isomerization between *anti*-**5a** and *syn*-**5a** was practically not observed at room temperature.

The results described above encouraged us to synthesize other pairs of rotamers, *anti*-**5b**/*syn*-**5b** and *anti*-**5c**/*syn*-**5c**. Precursors **6b** and **6c** were similarly prepared as in the case of **6a**, starting from 1-chloromethyl-3-methoxynaphthalene **8b** or 5-methoxy-2-methylbenzyl chloride **8c** in the place of **8a** (Scheme 3). Singlet oxygenation of **6b** and **6c** was carried out to exclusively give the *syn*-form of the dioxetanes, *syn*-**5b** and *syn*-**5c**, respectively. This result shows that $^1O_2$ attacked with high π-face selectivity for **6b** and **6c** as well as for **6a** (Scheme 4). Thermal isomerization of these dioxetanes was carried out as in the case of *anti*-**5a** to give a mixture of *syn*/*anti* rotamers: *anti*/*syn* = 20:80 for **5b** and 50:50 for **5c**. Thus, we isolated *anti*-**5b** and *anti*-**5c** by column chromatography. Dioxetanes *anti*-**5b**, *syn*-**5b**, *anti*-**5c**, and *syn*-**5c** gave satisfactory analytical data, and their stereochemistries were determined by X-ray single crystallographic analysis (Figure S1 in the Supporting Information).

2. Base-Induced Chemiluminescent Decomposition of *Syn*/*Anti* Rotamers of Hydroxyaryl-Substituted Bicyclic Dioxetanes. When a solution of *anti*-**5a** in DMSO was added to a solution containing a large excess of tetrabutylammonium fluoride (TBAF) in DMSO at 25 °C, CTID of *anti*-**5a** took place according to pseudo-first-order kinetics to give an orange light (Figure 2) with maximum wavelength λ_{max}^{CL} = 678 nm, chemiluminescence efficiency $\Phi^{CL} = 2.8 \times 10^{-4}$,[18,19] and rate of CTID $k^{CTID} = 3.2 \times 10^{-2}$ s^{-1}. These chemiluminescence properties are summarized in Table 1. TBAF-induced chemiluminescent decomposition of *syn*-**5a** also took place under the same conditions. However, it showed unexpectedly weak chemiluminescence, the Φ^{CL} of which was only 1/19 of that for *anti*-**5a**, and both λ_{max}^{CL} and k^{CTID} were different from those for *anti*-**5a**, as shown in Table 1 and Figure 2. *Syn*/*anti* isomerization did not occur during TBAF-induced CTID: when the chemiluminescent

Scheme 1. Chemiluminescence of Oxidophenyl-Substituted Dioxetane and Bioluminescence of the Firefly



Scheme 2. Rotamers of Dioxetane 4

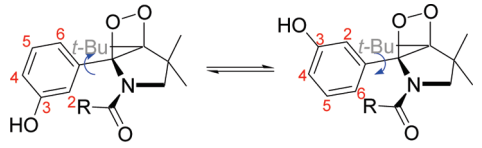
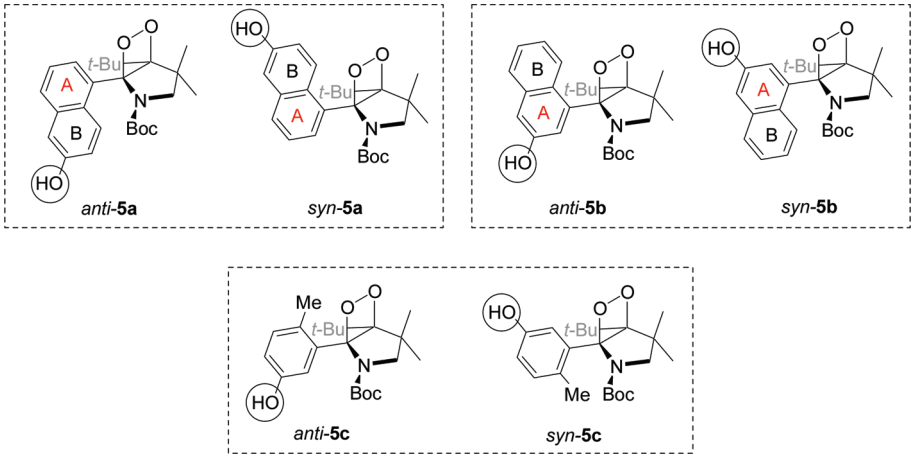
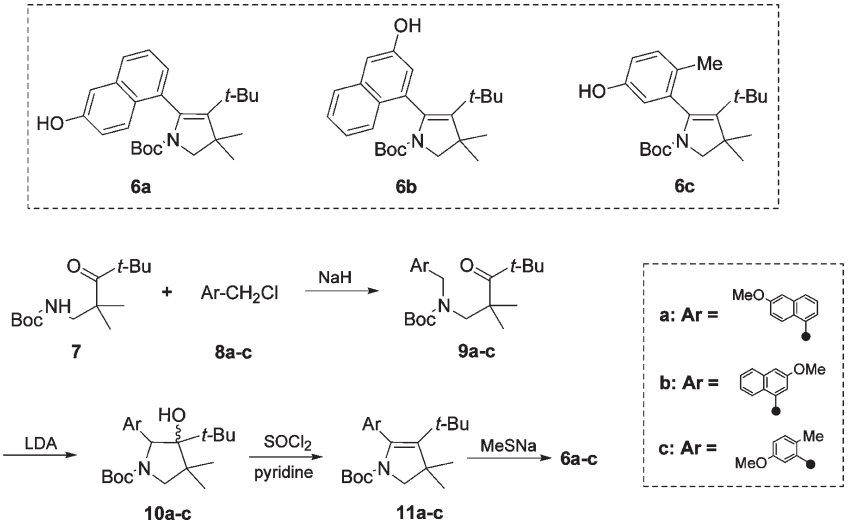


Chart 1. Rotamers of Dioxetanes 5a−c

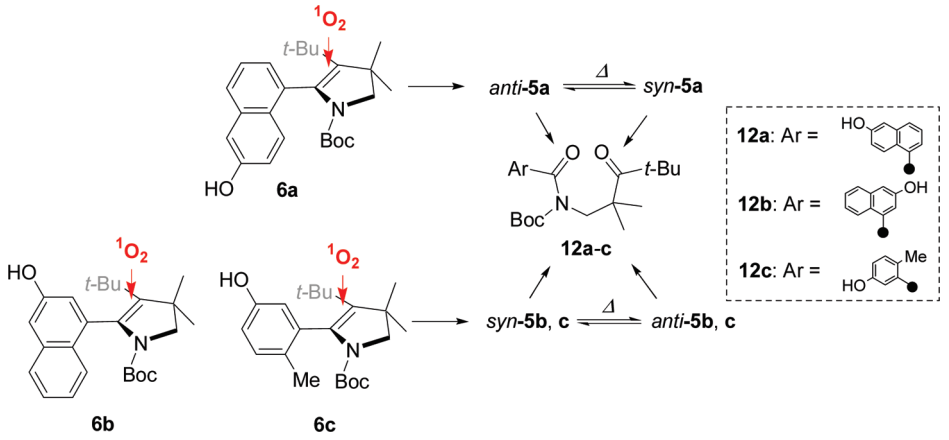


dx.doi.org/10.1021/jo2006945 |J. Org. Chem. 2011, 76, 5006–5017

Scheme 3. Synthetic Pathway of Precursors 6a−c for the Synthesis of Dioxetanes 5a−c



Scheme 4. Singlet Oxygenation of Dihydropyrroles 6a−c, Isomerization of Dioxetanes 5a−c, and Their Thermal Decomposition to Keto Imides 12a−c



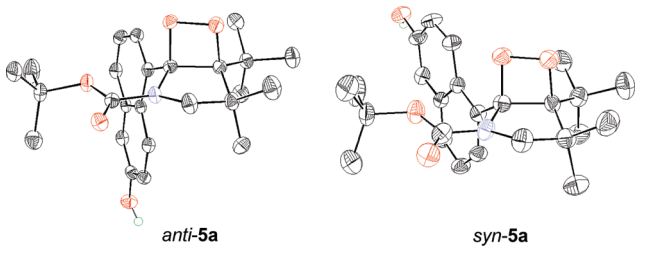


Figure 1. ORTEP views of dioxetane *anti*-**5a** and *syn*-**5a**.

reactions of *anti*-**5a** and *syn*-**5a** were individually quenched midway, intact *anti*-**5a** and *syn*-**5a** were both confirmed to have retained their stereochemistry.

The above results posed two questions. The first was whether this phenomenon was due to the difference in the conformation of the naphthalene ring itself[20] or to a difference in the conformation of the entire hydroxynaphthalene ring. The second was whether this result was specific for naphthyl-substituted dioxetane **5a** or could similarly be observed for a rather simple phenolic dioxetane. Thus, TBAF-induced decomposition was examined for a pair of isomers, i.e. *anti*-**5b** and *syn*-**5b**, in DMSO. The results summarized in Table 1 show that Φ^{CL} for *anti*-**5b** was 8 times higher than that for *syn*-**5b**, and k^{CTID} for *anti*-**5b** was considerably faster than that for *syn*-**5b**, while both λ_{max}^{CL}'s were observed at 594 nm. These results showed that the marked *syn*/*anti* difference in chemiluminescence properties could be attributed to the difference in the conformation of the entire hydroxynaphthalene ring.

Next, we examined the TBAF-induced decomposition of **5c**, which bore a 3-hydroxyphenyl group substituted with a 6-methyl group to prevent rotation of the aromatic ring. The results summarized in Table 1 show that Φ^{CL} for *anti*-**5c** was 10 times higher than that for *syn*-**5c**, k^{CTID} for the *anti*-rotamer was slightly faster than that for the *syn*-rotamer, and λ_{max}^{CL} for the *syn*-rotamer was longer than that for the *anti*-rotamer. Thus, the rotamer-dependence of chemiluminescence properties was also seen for a phenolic dioxetane.

As described above, by comparing the chemiluminescence properties between *anti*- and *syn*-rotamers of **5a−c**, we can see

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

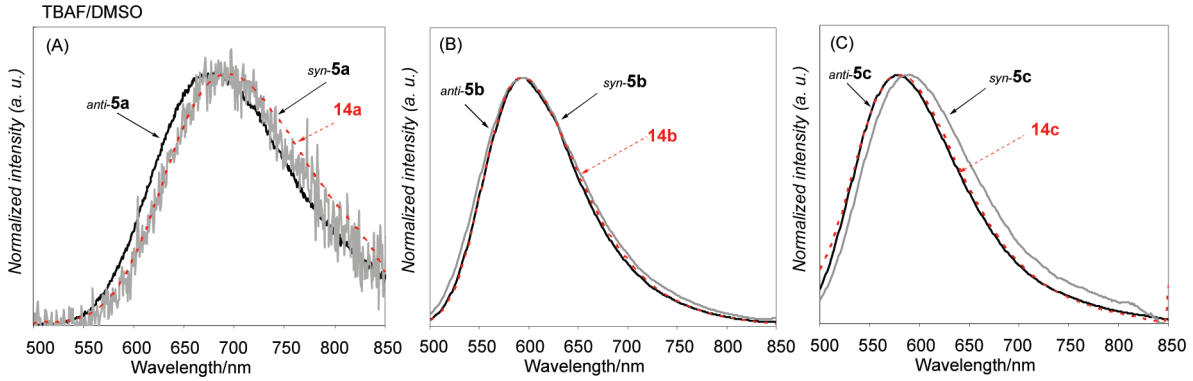


Figure 2. Chemiluminescence (CL) spectra of rotamers of dioxetanes **5a**−**c** and fluorescence (FL) spectra of oxido anions **14a**−**c** in DMSO: (A) CL of *anti*-**5a** and *syn*-**5a** and FL of **14a**; (B) CL of *anti*-**5b** and *syn*-**5b**, and FL of **14b**; (C) CL of *anti*-**5c** and *syn*-**5c**, and FL of **14c**.

Table 1. TBAF-Induced Chemiluminescent Decomposition of Rotamers of Dioxetanes 5a−c in DMSO[a]

	λ_{max}^{CL}/ nm	Φ^{CL} [b]	Φ^{fl}	Φ_S	k^{CTID}/ s^{-1}	relative Φ^{CL} *anti*/*syn*
anti-**5a**	678	2.8×10^{-4}	1.2×10^{-3}	2.3×10^{-1}	3.2×10^{-2}	19
syn-**5a**	688	1.5×10^{-5}		1.3×10^{-2}	5.7×10^{-3}	
anti-**5b**	594	1.2×10^{-2}	3.6×10^{-1}	3.3×10^{-2}	2.7×10^{-2}	8
syn-**5b**	594	1.5×10^{-3}		4.2×10^{-3}	1.4×10^{-3}	
anti-**5c**	578	2.0×10^{-3}	1.0×10^{-2}	2.0×10^{-1}	2.8×10^{-2}	10
syn-**5c**	584	2.1×10^{-4}		2.1×10^{-2}	1.7×10^{-2}	

[a] All reactions were carried out at 25 °C. [b] Based on a value reported for the chemiluminescent decomposition of 3-adamantylidene-4-(3-*tert*-butyldimethylsiloxy-phenyl)-4-methoxy-1,2-dioxetane in TBAF/DMSO.[18,19]

Table 2. TBAF-Induced Chemiluminescent Decomposition of Rotamers of Dioxetanes 5a−c in Acetonitrile[a]

	λ_{max}^{CL}/ nm	Φ^{CL} [b]	Φ^{fl}	Φ_S	k^{CTID}/ s^{-1}	relative Φ^{CL} *anti*/*syn*
anti-**5a**	690	1.0×10^{-4}	5.8×10^{-4}	1.7×10^{-1}	6.5×10^{-3}	12
syn-**5a**	701	8.3×10^{-6}		1.4×10^{-2}	6.5×10^{-4}	
anti-**5b**	598	4.6×10^{-3}	1.5×10^{-1}	3.1×10^{-2}	2.8×10^{-3}	18
syn-**5b**	598	2.5×10^{-4}		1.6×10^{-3}	3.4×10^{-4}	
anti-**5c**	582	7.7×10^{-4}	5.1×10^{-3}	1.5×10^{-1}	9.4×10^{-4}	10
syn-**5c**	594	7.9×10^{-5}		1.5×10^{-2}	5.7×10^{-4}	

[a] All reactions were carried out at 25 °C. [b] Based on a value reported for the chemiluminescent decomposition of 3-adamantylidene-4-(3-*tert*-butyldimethyl-siloxyphenyl)-4-methoxy-1,2-dioxetane in TBAF/DMSO.[18,19]

that (a) Φ^{CL} values for *anti*-rotamers were an order of magnitude, or more, greater than those for the corresponding *syn*-rotamers, and (b) *anti*-rotamers tended to decompose more rapidly to give chemiluminescence with a shorter wavelength compared to *syn*-rotamers.

TBAF-induced decomposition was carried out in acetonitrile for these three pairs of stereoisomeric dioxetanes **5a**−**c**, as in DMSO. As summarized in Table 2, the results show that there was a marked difference in Φ^{CL} between *anti*- and *syn*-isomers, though the Φ^{CL} values in acetonitrile tended to be somewhat smaller than those in DMSO. All of the chemiluminescence spectra for **5a**−**c** were observed in the region a little longer than in DMSO, as shown in Figure 3. Rates of CTID in acetonitrile were somewhat slower than those in DMSO.

The results described above raise important questions related to the singlet-chemiexcitation mechanism for the CTID of dioxetanes. It is not surprising that k^{CTID} changed depending on the conformation of the aromatic ring, since the structure of dioxetanes has often been reported to affect k^{CTID}.[7] However, before the present findings, we hardly expected the marked difference in chemiluminescence efficiency between the *anti*-**5a**−**c** and *syn*-**5a**−**c** rotamers. The difference in the chemiluminescence spectra between *anti*- and *syn*-rotamers observed for **5a** and **5c** was also rather unusual, since both rotamers, as expected, gave the same decomposition product in CTID.

Thus, we attempted to investigate the fluorescence of emitters produced from stereoisomeric **5a**−**c** to understand chemiexcitation for the present CTID. Freshly spent reaction mixtures from *anti*-**5a**

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

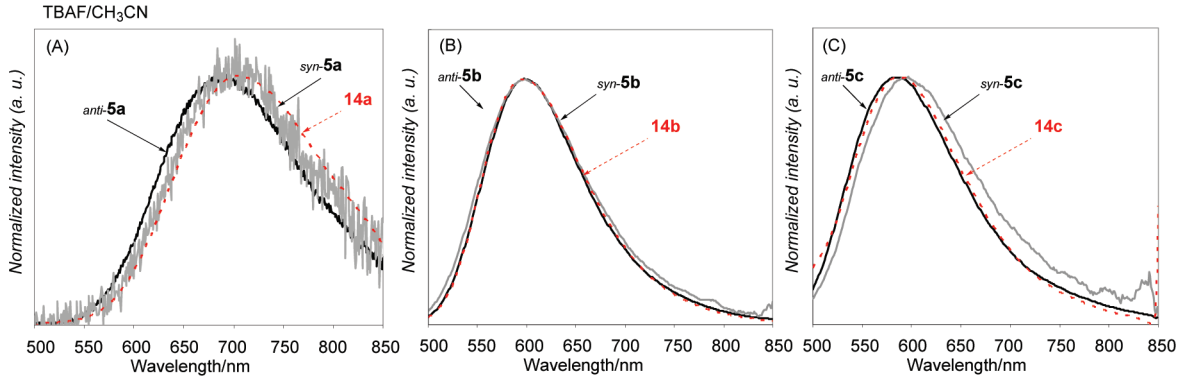


Figure 3. Chemiluminescence (CL) spectra of rotamers of dioxetanes **5a**−**c** and fluorescence (FL) spectra of oxido anions **14a**−**c** in acetonitrile: (A) CL of *anti*-**5a** and *syn*-**5a** and FL of **14a**; (B) CL of *anti*-**5b** and *syn*-**5b**, and FL of **14b**; (C) CL of *anti*-**5c** and *syn*-**5c**, and FL of **14c**.

Scheme 5. Light Emission from *de novo* Keto Imide 14 for the Decomposition of Dioxetane 5 and Light Emission from Authentic Keto Imide 14

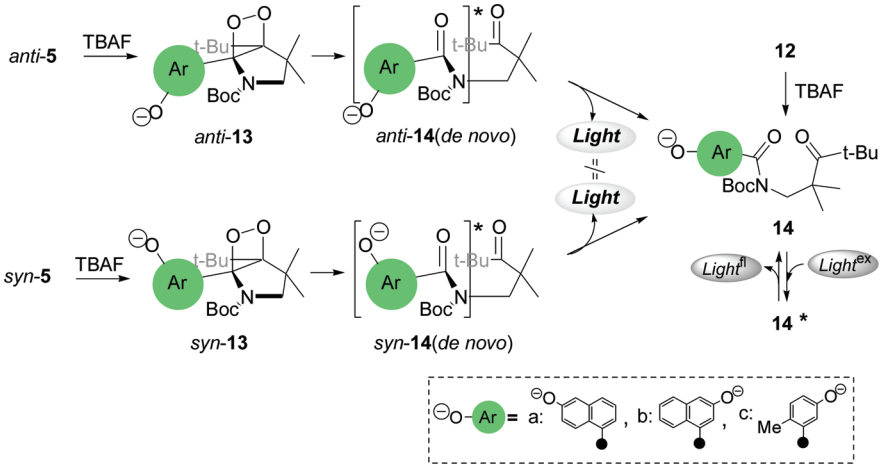
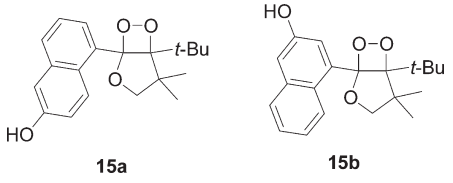


Chart 2. Dioxetanes 15a and 15b Fused with a Tetrahydrofuran Ring



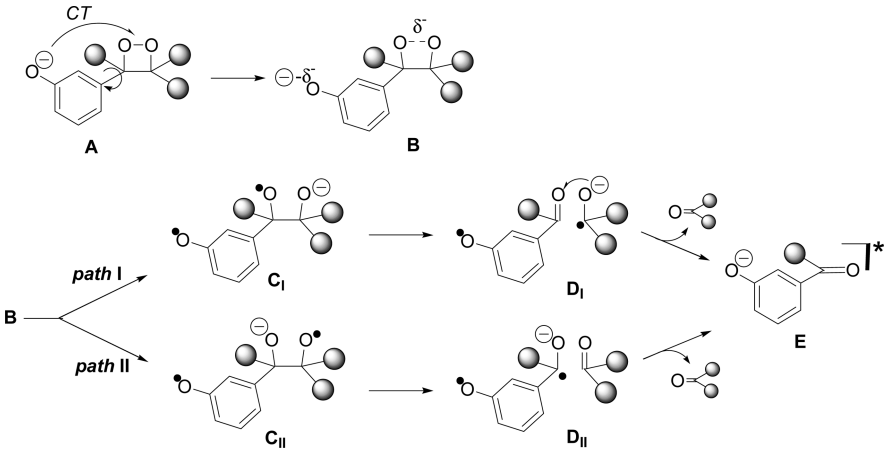
and *syn*-**5a** gave the same keto imide **12a** in high yields after careful neutralization. Similarly, **5b** and **5c** gave **12b** and **12c** in high yields. These results strongly suggest that CTIDs of both *anti*-**5** and *syn*-**5** produced oxido anion **14** of keto imide **12** accompanied by the emission of light through intermediary oxidoaryl-substituted dioxetane *anti*-**13** and *syn*-**13**, respectively (Scheme 5). Oxido anions **14a**−**c** generated *in situ* from the corresponding authentic **12a**−**c** gave fluorescence in TBAF/DMSO, as shown in Figure 2. The fluorescence spectrum of **14b** practically coincided with the chemiluminescence spectra of both *anti*- and *syn*-**5b**, while those of **14a** and **14c** coincided only with the chemiluminescence spectra of *syn*-**5a** and *anti*-**5c**, respectively. A similar tendency in the relationship between chemiluminescence spectra of **5** and the corresponding fluorescence spectra of **14** was observed in acetonitrile (Figure 3). Fluorescence efficiencies (Φ^{fl}'s) for **14a**−**c** in DMSO and in acetonitrile are shown in Tables 1 and 2. Based on these values, singlet chemiexcitation efficiency, $\Phi_S = \Phi^{CL}/\Phi^{fl}$, values were estimated for *syn*-**5a**, *anti*- and *syn*-**5b**, and *anti*-**5c**. The results are summarized in Tables 1 and 2.

On the other hand, Φ_S's for *anti*-**5a** and *syn*-**5c** could not be reliably estimated since the fluorescence spectra of authentic **14a** and **14c** deviated to some extent from the corresponding chemiluminescence spectra. Thus, we formally estimated Φ_S's for *anti*-**5a** and *syn*-**5c** as shown in Tables 1 and 2, by using the Φ^{fl}'s of authentic **14a** and **14c**. The formal Φ_S's for *anti*-**5a** and *anti*-**5b** in DMSO were close to the values of Φ_S reported for the corresponding tetrahydrofuran analogs **15a** and **15b**: $\Phi_S = 0.22$ and 0.09 for **15a** and **15b** respectively (Chart 2).[21] These estimations suggest that the marked difference in Φ^{CL} between *anti*-**5** and *syn*-**5** can be attributed to a difference in singlet-chemiexcitation efficiency (*vide infra*).

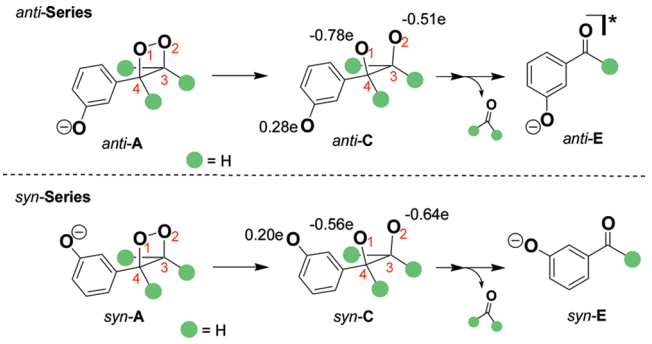
As noted above, the chemiluminescence spectra of *anti*-**5a** and *syn*-**5a** did not coincide with each other, though both isomers of **5a** exclusively produced the same keto ester **12a**. This discrepancy is likely due to the difference in stereochemistry between the two *de novo* keto imides in an excited state; i.e. *anti*-**14a**(*de novo*) formed from *anti*-**5a** and *syn*-**14a**(*de novo*) from *syn*-**5a**. Thus,

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

Scheme 6. Plausible Mechanism for the Intramolecular CT-Induced Decomposition of Oxidophenyl-Substituted Dioxetane



Scheme 7. Charge Distribution on Biradical Anion *anti*-C and *syn*-C for the Intramolecular CT-Induced Decomposition of Oxidophenyl-Substituted Dioxetane



anti-**14a**(*de novo*) and *syn*-**14a**(*de novo*) may more or less inherit the corresponding conformations from intermediary dioxetanes *anti*-**13a** and *syn*-**13a**, as illustrated in Scheme 5. If we consider that the fluorescence spectra of authentic **14a** coincided with the chemiluminescence spectra of *syn*-**5a** in both solvent systems (DMSO and acetonitrile), *syn*-**14a**(*de novo*) had a structure similar to that of authentic **14a**. This was also the case for **5c**.

These results suggest that the features of chemiexcitation for *anti*-**5** should not be the same as those for *syn*-**5**. Thus, we finally attempted to elucidate how the chemiexcitation process was affected by the *syn*/*anti* conformational isomerism of a dioxetane bearing an oxidoaryl group. A plausible mechanism of chemiexcitation proposed for the CTID of oxidophenyl-substituted dioxetane **A** is illustrated in Scheme 6, where the reaction proceeds as follows:[7]

(i) Intramolecular CT takes place from an oxidoaryl anion to O−O for dioxetane **A** to form **B** in the transition state.

(ii) The O−O bond of **B** cleaves to give two types of biradical anion, $\mathbf{C_I}$ and/or $\mathbf{C_{II}}$, as a canonical structure.

(iii) Cleavage of the C−C bond in biradical anion $\mathbf{C_I}$ gives a radical ion pair $\mathbf{D_I}$, which is annihilated by intermolecular backward electron transfer (BET) to form excited oxidophenyl carbonyl **E** (*path* **I**). On the other hand, cleavage of biradical anion $\mathbf{C_{II}}$ gives excited oxidophenyl carbonyl **E** directly or through intramolecular BET of $\mathbf{D_{II}}$ (*path* **II**).

Baader and his co-workers have very recently suggested that *path* **II**, rather than *path* **I**, effectively leads to chemiexcitation.[22] According to this mechanism, we attempted to explain the *syn*/*anti* difference in chemiluminescence efficiency for the CTID of oxidophenyl-substituted dioxetane **A** as a simple model. We performed time-dependent DFT (TDDFT) calculations at the B3LYP/6-31G+(d) level individually for the *anti*- and *syn*-forms of 3-oxidophenyl-substituted dioxetane **A** and calculated the charge distribution in **C** for each *anti*- and *syn*-series. The results in Scheme 7 show that a negative charge is distributed more on O_1-C_4 (−0.78e) than on O_2-C_3 (−0.51e) for species *anti*-**C** before C−C bond cleavage into *anti*-**E**, whereas a negative charge is distributed more on O_2-C_3 (−0.64e) than on O_1-C_4 (−0.56e) for *syn*-**C**. We can see from Scheme 7 that *anti*-**C** favors *path* **II** more than *syn*-**C**. Therefore, chemiexcitation presumably occurs more effectively for the *anti*-isomer of **A** than for its *syn*-isomer. However, we cannot at present explain what causes the difference in the distribution of the negative charge between *anti*-**C** and *syn*-**C**, although an MO calculation suggested that they had different dipole moments.

CONCLUSION

We successfully synthesized three pairs of thermally stable isomeric bicyclic dioxetanes bearing 6-hydroxynaphthalen-1-yl (*anti*-**5a** and *syn*-**5a**), 3-hydroxynaphthalen-1-yl (*anti*-**5b** and *syn*-**5b**), and 5-hydroxy-2-methylphenyl groups (*anti*-**5c** and *syn*-**5c**). TBAF-induced decomposition of these dioxetanes showed chemiluminescence, the properties of which were different between *anti*-**5** and *syn*-**5**. Among these differences, the most prominent was a marked discrepancy in chemiluminescence efficiency between the rotamers: *anti*-**5a**−**c** emitted 8−19 times more light than the corresponding *syn*-**5a**−**c**. Thus, if such a phenomenon occurs in general for a nonisolable *syn*/*anti* mixture of oxidoaryl-substituted dioxetanes, chemiluminescence would appear to practically arise only from the *anti*-rotamer. The chemiluminescence spectra of the *anti*- and *syn*-rotamers of **5a** and **5c** were also different to some extent. This phenomenon can presumably be attributed to the difference in structure between *de novo* keto imide *anti*-**14** and *syn*-**14** in an excited state, which inherit the structures of the corresponding intermediary anionic dioxetanes *anti*-**13** and *syn*-**13**.

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

The present findings should stimulate further studies of the mechanism of the singlet-chemiexcitation process for dioxetane-based chemiluminescence as well as bioluminescence and should provide new insight into the design of high-performance chemiluminescent compounds.

EXPERIMENTAL SECTION

General. Melting points were uncorrected. IR spectra were taken on an FT/IR infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a 400 and 500 MHz spectrometers. Mass spectra were obtained by using double-focusing mass spectrometers and an ESI-TOF mass spectrometer. Column chromatography was carried out using silica gel or NH-silica gel.

Synthesis of 1-[*N*-Boc-*N*-(6-methoxynaphthalen-1-yl)methyl]-amino-2,2,4,4-tetramethylpentan-3-one (9a). Typical Procedure. A solution of 1-(*N*-Boc)amino-2,2,4,4-tetramethylpentan-3-one (7) (10.3 g, 40.0 mmol) in dry DMF (25 mL) was added dropwise over 5 min to a suspension of sodium hydride (60% in oil, 1.71 g, 42.8 mmol) in dry DMF (80 mL) under a nitrogen atmosphere at 0 °C and stirred at room temperature for 1 h. To the solution, 1-chloromethyl-6-methoxynaphthalene (**8a**) (8.88 g, 43.0 mmol) was added at 0 °C and stirred at room temperature for 16 h. The reaction mixture was poured into sat. aq. NH_4Cl and then extracted with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on silica gel and eluted with hexane−AcOEt (9:1) to give 1-[*N*-Boc-*N*-(6-methoxynaphthalen-1-yl)methyl]amino-2,2,4,4-tetramethylpentan-3-one (**9a**) as a colorless solid (14.6 g, 86% yield). According to the procedure described above, 1-[*N*-Boc-*N*-(3-methoxynaphthalen-1-yl)methyl]amino-2,2,4,4-tetramethylpentan-3-one (**9b**) and 1-[*N*-Boc-*N*-(5-methoxy-2-methylbenzyl)]amino-2,2,4,4-tetramethylpentan-3-one (**9c**) were synthesized by using 1-chloromethyl-3-methoxynaphtalene (**8b**) and 5-methoxy-2-methylbenzyl chloride (**8c**) instead of **8a** in 84% and 90% yield, respectively. **9a**−**9c** were observed as a mixture of stereoisomers by ^{1}H and ^{13}C NMR.

9a: Coloress granules, mp 79.0−80.0 °C (from AcOEt−hexane) (mixture of stereoisomers). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.15−1.60 (m, 24H), 3.34−3.63 (m, 2H), 3.92 (s, 3H), 4.85 (broad s, 2H), 7.00−7.20 (m, 3H), 7.39 (dd, J = 8.1 and 7.3 Hz, 1H), 7.65 (d, J = 8.1 Hz), 7.73−7.97 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 25.2 (CH_3 × 2), 28.0 (CH_3 × 3), 28.2 (CH_3 × 3), 46.1 (C), 49.0 and 49.8 (broad CH_2), 51.4 (C), 53.8 and 55.6 (broad CH_2), 55.2 (CH_3), 79.8 (broad C), 106.7 (CH), 118.5 (CH), 120.8 and 122.7 (broad CH), 124.1 and 124.9 (broad CH), 125.9 (CH), 126.3 (broad C), 126.2 and 126.6 (broad CH), 133.2 and 133.7 (broad C), 135.1 (C), 156.7 (C), 157.3 (C), 217.7 (C) ppm. IR (KBr): ν 2978, 2965, 2934, 1699, 1675, 1626 cm^{-1}. Mass (m/z, %): 427 (M^+, 4), 200 (26), 172 (17), 171 (100), 128 (10), 57 (11). HRMS (ESI): 450.2607, calcd for $C_{26}H_{37}NO_4Na$ [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$: C, 73.03; H, 8.72; N, 3.28; Found: C, 72.98; H, 9.05; N, 3.29.

9b: Colorless plates, mp 91.0−91.5 °C (from AcOEt−hexane) (mixture of stereoisomers). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.20−1.60 (m, 24H), 3.47−3.61 (m, 2H), 3.91 (s, 3H), 4.84 (broad s, 2H), 6.87 (d, J = 2.2 Hz, 1H), 7.03 (d, J = 2.2 Hz, 1H), 7.35 (dd, J = 8.1 and 6.8 Hz, 1H), 7.44 (dd, J = 8.1 and 6.8 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.69−7.89 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 25.2 (CH_3 × 2), 28.0 (CH_3 × 3), 28.2 (CH_3 × 3), 46.0 (C), 48.7 and 49.6 (broad CH_2), 51.3 (C), 54.5 and 55.7 (broad CH_2), 55.1 (CH_3), 79.8 and 80.2 (broad C), 104.7 and 105.0 (broad CH), 115.9 and 116.9 (broad CH), 122.4 and 122.9 (broad CH), 123.6 (CH), 126.1 (CH), 126.6 and 126.9 (broad C), 127.5 (CH), 134.8 and 135.6 (broad C), 135.2 (C), 156.5 (C), 157.2 (C), 217.5 (C) ppm. IR (KBr): ν 3006, 2979, 2965, 2938, 1703, 1670, 1631, 1605 cm^{-1}. Mass (m/z, %): 427 (M^+, 6), 200 (15), 199 (13), 172 (15), 171 (100), 149 (14), 141 (11), 128 (16), 69 (17), 57 (69), 56 (19), 55 (20). HRMS (ESI):450.2638, calcd for $C_{26}H_{37}NO_4Na$ [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$: C, 73.03; H, 8.72; N, 3.28. Found: C, 72.94; H, 8.97; N, 3.24.

9c: Colorless oil (mixture of stereoisomers). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.20−1.58 (m, 24H), 2.15 (s, 3H), 3.43−3.58 (m, 2H), 3.76 (s, 3H), 4.25−4.40 (m, 2H), 6.56 (broad s, 1H), 6.68 (dd, J = 8.2 and 2.8 Hz, 1H), 7.03 (d, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 17.9 (CH_3), 25.1 (CH_3 × 2), 27.9 (CH_3 × 3), 28.1 (broad CH_3 × 3), 46.0 (C), 49.0 and 50.0 (broad CH_2), 51.1 (C), 54.8 and 55.7 (broad CH_2), 55.0 (CH_3), 79.5 and 80.0 (broad C), 111.3 and 111.6 (CH), 111.4 (CH), 126.8 and 127.3 (C), 130.9 (CH), 136.6 and 137.7 (C), 156.5 (C), 158.0 (C), 217.5 (C) ppm. IR (liquid film): ν 2974, 2935, 1697, 1682, 1612, 1581 cm^{-1}. Mass (m/z, %): 391 (M^+, 1), 208 (13), 164 (42), 136 (11), 135 (100), 134 (28), 57 (57). HRMS (ESI): 414.2645, calcd for $C_{23}H_{37}NO_4Na$ [M + Na^+] 414.2620.

Synthesis of 1-Boc-3-*tert*-butyl-3-hydroxy-2-(6-methoxy-naphthalen-1-yl)-4,4-dimethyl-pyrrolidine (*cis*-10a and *trans*-10a). Typical Procedure. BuLi (1.65 M in hexane, 12.0 mL, 19.8 mmol) was added to a solution of diisopropylamine (3.0 mL, 21 mmol) in dry THF (35 mL) under a nitrogen atmosphere at 0 °C and was stirred at room temperature for 30 min. To the solution, 1-[*N*-Boc-*N*-(6-methoxynaphthalen-1-yl)methylamino]-2,2,4,4-tetramethylpentan-3-one (**9a**) (4.27 g, 10.0 mmol) in dry THF (15 mL) was added dropwise over 3 min at 40 °C and stirred for 15 min. The reaction mixture was quenched with H_2O, poured into sat. aq. NH_4Cl, and then extracted with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel and eluted with hexane−AcOEt (5:1) to give 1-Boc-3-*tert*-butyl-*c*-3-hydroxy-*r*-2-(6-methoxynaphthalen-1-yl)-4,4-dimethylpyrrolidine (*cis*-**10a**) as a pale yellow solid (2.30 g, 54% yield) and 1-Boc-3-*tert*-butyl-*t*-3-hydroxy-*r*-2-(6-methoxynaphthalen-1-yl)-4,4-dimethylpyrrolidine (*trans*-**10a**) as a pale yellow solid (1.73 g, 41% yield).

According to the procedure described above, 1-Boc-3-*tert*-butyl-3-hydroxy-2-(3-methoxynaphthalen-1-yl)-4,4-dimethylpyrrolidine, *cis*-**10b** and *trans*-**10b**, were synthesized from **9b** in 54% and 40% yield, respectively. 1-Boc-3-*tert*-butyl-3-hydroxy-2-(5-methoxy-2-methylphenyl)-4,4-dimethylpyrrolidine, *cis*-**10c** and *trans*-**10c**, were also synthesized from **9c** in 79% and 16% yield, respectively. *cis*-**10a**−*cis*-**10c** were observed by ^{1}H and ^{13}C NMR as a mixture of rotamers, and only the main isomers were assigned by ^{1}H and ^{13}C NMR.

cis-**10a**: Colorless plates, mp 178.5−179.0 °C (from CH_2Cl_2−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.72 (s, 9H), 0.90 (broad s, 9H), 1.27 (s, 3H), 1.39 (s, 3H), 1.86 (s, 1H), 3.37 (d, J = 10.3 Hz, 1H), 3.75 (d, J = 10.3 Hz, 1H), 3.94 (s, 3H), 5.96 (s, 1H), 7.15 (d, J = 2.7 Hz, 1H), 7.20 (dd, J = 9.3 and 2.7 Hz, 1H), 7.38−7.45 (m, 2H), 7.67 (d with fine coupling, J = 6.8 Hz, 1H), 8.20 (d, J = 9.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 21.4 (CH_3), 26.3 (CH_3), 27.8 (CH_3 × 3), 28.1 (CH_3 × 3), 39.3 (C), 46.5 (C), 55.2 (CH_3), 59.4 (CH), 61.1 (CH_2), 79.1 (C), 85.8 (C), 106.6, (CH), 118.5 (CH), 124.1 (CH), 125.8 (CH), 125.8 (CH), 126.9 (CH), 128.1 (C), 135.0 (C), 138.5 (C), 154.3 (C), 157.0 (C) ppm. IR (KBr): ν 3581, 3446, 2977, 2884, 1685, 1626, 1601 cm^{-1}. Mass (m/z, %): 427 (M^+, 17), 371 (29), 327 (29), 326 (100), 314 (21), 244 (11), 213 (20), 200 (20), 199 (32), 198 (55), 186 (20), 171 (57), 57 (39). HRMS (ESI): 450.2612, calcd for $C_{26}H_{37}NO_4$-Na [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$: C, 73.03; H, 8.72; N, 3.28. Found: C, 73.04; H, 9.05; N, 3.25.

trans-**10a**: Colorless granules, mp 182.5−183.0 °C (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 076 (broad s, 9H), 0.79 (broad s, 9H), 1.34 (s, 3H), 1.58 (s, 3H), 2.14 (broad s, 1H), 3.69 (s, 2H), 3.93 (s, 3H), 5.67 (broad, 1H), 7.13 (d, J = 2.7 Hz, 1H), 7.16 (dd, J = 9.3 and 2.7 Hz, 1H), 7.36 (dd, J = 8.1 and 7.1 Hz, 1H), 7.60 (d, J = 7.1 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 8.20−8.30 (m, 1H) ppm.

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

^{13}C NMR (125 MHz, $CDCl_3$): δ_C 26.7 (CH_3), 27.8 (CH_3), 27.8 (CH_3 × 3), 28.3 (broad CH_3 × 3), 39.3 (C), 46.6 (broad C), 55.1 (CH_3), 61.9 (CH_2), 70.0 (CH), 79.2 (C), 90.5 (broad C), 106.3 (CH), 118.0 (CH), 123.9 (CH), 125.5 (CH), 126.3 (CH), 126.6 (CH), 127.7 (C), 135.1 (C), 139.7 (C), 154.6 (C), 156.8 (C) ppm. IR (KBr): ν 3389, 2978, 2959, 2933, 1669, 1627, 1603 cm^{-1}; Mass (m/z, %): 427 (M^+, 12), 371 (30), 327 (31), 326 (100), 314 (21), 244 (13), 243 (13), 240 (13), 213 (23), 200 (26), 199 (51), 198 (93), 186 (30), 183 (10), 172 (12), 171 (72), 57 (43). HRMS (ESI): 450.2610, calcd for $C_{26}H_{37}NO_4$Na [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$ + 1/10hexane: C, 73.24; H, 8.87; N, 3.21. Found: C, 73.00; H, 9.15; N, 3.30.

cis-**10b**: Colorless granules, mp 138.5−139.0 °C (from CH_2Cl_2−hexane). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.72 (s, 9H), 0.91 (broad s, 9H), 1.27 (s, 3H), 1.38 (s, 3H), 1.88 (s, 1H), 3.38 (d, J = 10.5 Hz, 1H), 3.74 (d, J = 10.5 Hz, 1H), 3.88 (s, 3H), 5.97 (s, 1H), 7.08 (broad s, 1H), 7.30 (d, J = 2.8 Hz, 1H), 7.37 (dd, J = 8.2 and 6.9 Hz, 1H), 7.42 (dd, J = 8.2 and 6.9 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 8.20 (d, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 21.4 (CH_3), 26.3 (CH_3), 27.8 (CH_3 × 3), 28.0 (CH_3 × 3), 39.2 (C), 46.5 (C), 55.1 (CH_3), 59.0 (CH), 61.0 (CH_2), 79.1 (C), 85.9 (C), 105.9 (CH), 119.2 (CH), 123.4 (CH), 124.1 (CH), 125.9 (CH), 127.8 (CH), 128.2 (C), 135.0 (C), 140.4 (C), 154.2 (C), 156.8 (C) ppm. IR (KBr): ν 3500, 2977, 2964, 2928, 2889, 1689, 1664, 1626, 1604 cm^{-1}. Mass (m/z, %): 427 (M^+, 14), 371 (25), 327 (26), 326 (100), 314 (13), 213 (15), 200 (13), 199 (22), 198 (55), 186 (13), 184 (10), 171 (46), 58 (12), 57 (65), 56 (25), 55 (19). HRMS (ESI): 450.2642, calcd for $C_{26}H_{37}NO_4$Na [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$: C, 73.03; H, 8.72; N, 3.28. Found: C, 73.02; H, 8.97; N, 3.29.

trans-**10b**: Colorless granules, mp 187.0−188.0 °C (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.80 (broad s, 18H), 1.34 (s, 3H), 1.61 (s, 3H), 2.15 (s, 1H), 3.68 (s, 2H), 3.90 (s, 3H), 5.67 (s, 1H), 7.06 (s with fine coupling, 1H), 7.33−7.48 (m, 3H), 7.73 (d, J = 7.8 Hz, 1H), 8.25 (broad d, J = 7.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 26.6 (CH_3), 27.8 (CH_3 × 4), 28.4 (broad CH_3 × 3), 39.3 (C), 46.7 (C), 55.2 (CH_3), 61.7 (CH_2), 69.6 (C), 79.3 (C), 90.5 (C), 105.7 (CH), 118.9 (CH), 123.1 (CH), 124.6 (CH), 125.8 (CH), 127.6 (CH), 127.9 (C), 135.1 (C), 141.7 (C), 154.5 (C), 156.7 (C) ppm. IR (KBr): ν 3443, 3006, 2978, 2932, 2881, 1683, 1627, 1606 cm^{-1}. Mass (m/z, %): 427 (M^+, 2), 326 (29), 252 (11), 240 (30), 213 (10), 200 (12), 199 (34), 198 (100), 197 (17), 186 (18), 185 (11), 184 (21), 183 (16), 171 (49), 154 (18), 141 (11), 128 (16), 127 (15), 115 (12), 57 (93), 56 (15), 55 (18). HRMS (ESI): 450.2632, calcd for $C_{26}H_{37}NO_4$Na [M + Na^+] 450.2620. Anal. Calcd for $C_{26}H_{37}NO_4$: C, 73.03; H, 8.72; N, 3.28. Found: C, 73.06; H, 9.03; N, 3.27.

cis-**10c**: Colorless granules, mp 100.5−101.0 °C (from hexane−AcOEt). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.98 (broad s, 9H), 1.08 (s, 9H), 1.23 (s, 3H), 1.29 (s, 3H), 1.72 (s, 1H), 2.42 (s, 3H), 3.30 (d, J = 10.1 Hz, 1H), 3.65 (d, J = 10.1 Hz, 1H), 3.75 (s, 3H), 5.26 (s, 1H), 6.74 (dd, J = 8.3 and 2.7 Hz, 1H), 6.88 (d, J = 2.7 Hz, 1H), 7.02 (d, J = 8.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (CH_3), 21.2 (CH_3), 26.2 (CH_3), 27.9 (CH_3 × 3), 28.0 (CH_3 × 3), 39.2 (C), 46.1 (C), 55.2 (CH_3), 60.6 (CH), 61.1 (CH_2), 79.3 (C), 86.0 (C), 113.0 (CH), 113.6 (CH), 129.1 (C), 131.5 (CH), 141.6 (C), 154.1 (C), 157.8 (C) ppm. IR (KBr): ν 3585, 3435, 2976, 2954, 2871, 1687, 1606 cm^{-1}. Mass (m/z, %): 391 (M^+, 5), 291 (21), 290 (100), 278 (14), 204 (11), 177 (11), 164 (17), 163 (22), 162 (25), 150 (15), 148 (13), 135 (33), 134 (15), 57 (59). HRMS (ESI): 414.2639, calcd for $C_{23}H_{37}NO_4$Na [M + Na^+] 414.2620. Anal. Calcd for $C_{23}H_{37}NO_4$: C, 70.55; H, 9.52; N, 3.58. Found: C, 70.49; H, 9.91; N, 3.57.

trans-**10c**: Coloress granules, mp 134.5−135.5 °C (from hexane−AcOEt). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.90 (s, 9H), 1.08 (broad s, 9H), 1.29 (s, 3H), 1.54 (s, 3H), 2.09 (broad s, 1H), 2.42 (broad s, 3H), 3.59 (broad s, 2H), 3.74 (s, 3H), 4.97 (broad s, 1H), 6.70 (dd, J = 8.3 and 2.8 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 7.06 (d, J = 2.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.1 (CH_3), 26.5 (CH_3), 27.5 (CH_3), 28.0 (broad CH_3 × 3), 28.4 (broad CH_3 × 3), 39.3 (C), 46.2 (broad C), 55.3 (CH_3), 61.8 (broad CH_2), 71.2 (CH), 79.3 (C), 90.6 (broad C), 112.6 (CH), 114.0 (CH), 128.9 (C), 131.5 (CH), 142.4 (broad C), 154.6 (C), 157.4 (C) ppm. IR (KBr): ν 3477, 2974, 2931, 2881, 1691, 1608 cm^{-1}. Mass (m/z, %): 391 (M^+, 3), 291 (21), 290 (100), 278 (13), 204 (25), 164 (14), 163 (19), 162 (29), 150 (12), 148 (13), 135 (30), 134 (13), 57 (57), 56 (12), 55 (11). HRMS (ESI): 414.2628, calcd for $C_{23}H_{37}NO_4$Na [M + Na^+] 414.2620. Anal. Calcd for $C_{23}H_{37}NO_4$: C, 70.55; H, 9.52; N, 3.58. Found: C, 70.52; H, 9.89; N, 3.56.

Synthesis of 1-Boc-4-*tert*-butyl-5-(6-methoxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (11a). Typical Procedure. Thionyl chloride (1.38 mL, 18.9 mmol) was added to a solution of 1-Boc-3-*tert*-butyl-*t*-3-hydroxy-*r*-2-(6-methoxynaphthalen-1-yl)-4,4-dimethylpyrrolidine (*trans*-**10a**) (6.24 g, 14.6 mmol) and pyridine (12 mL, 150 mmol) in dry THF (60 mL) under a nitrogen atmosphere at 0 °C and was stirred at room temperature for 1 h. The reaction mixture was poured into sat. aq. $NaHCO_3$ and extracted with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel and eluted with hexane−AcOEt (4:1) to give 1-Boc-4-*tert*-butyl-5-(6-methoxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**11a**) as a colorless solid (5.58 g, 94% yield).

Dehydration of *trans*-**10b** and *trans*-**10c** were similarly carried out to give 1-Boc-4-*tert*-butyl-5-(3-methoxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**11b**) and 1-Boc-4-*tert*-butyl-5-(5-methoxy-2-methylphenyl)-3,3-dimethyl-2,3-dihydropyrrole (**11c**) in 98% and 95% yield, respectively.

11a: Colorless granules, mp 100.0−101.5 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.67 (s, 9H), 0.87 (s, 9H), 1.41 (s, 3H), 1.45 (s, 3H), 3.60 (q_{AB}, J = 10.7 Hz, 2H), 3.92 (s, 3H), 7.08 (d, J = 2.4 Hz, 1H), 7.11 (dd, J = 9.0 and 2.4 Hz, 1H), 7.17 (dd, J = 7.1 and 1.2 Hz, 1H), 7.35 (dd, J = 8.3 and 7.1 Hz, 1H), 7.64−7.70 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 27.4 (CH_3 × 3), 28.1 (CH_3), 28.7 (CH_3), 32.0 (CH_3 × 3), 34.4 (C), 43.8 (C), 55.2 (CH_3), 63.6 (CH_2), 79.0 (C), 105.6 (CH), 118.4 (CH), 125.3 (CH), 126.1 (CH), 126.6 (CH), 127.8 (CH), 129.5 (C), 133.6 (C), 134.3 (C), 134.9 (C), 136.5 (C), 152.4 (C), 157.2(C) ppm. IR (KBr): ν 2976, 2958, 1678, 1626 cm^{-1}. Mass (m/z, %): 409 (M^+, 29), 354 (15), 353 (55), 339 (19), 338 (74), 309 (32), 308 (11), 296 (18), 295 (25), 294 (100), 282 (14), 253 (10), 252 (45), 238 (46), 197 (19), 183 (19). HRMS (ESI): 432.2504, calcd for $C_{26}H_{35}NO_3$Na [M + Na^+] 432.2515. Anal. Calcd for $C_{26}H_{35}NO_3$: C, 76.25; H, 8.61; N, 3.42. Found: C, 76.20; H, 8.88; N, 3.43.

11b: Colorless columns, mp 148.0−148.5 °C (from AcOEt). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.67 (s, 9H), 0.90 (s, 9H), 1.41 (s, 3H), 1.45 (s, 3H), 3.61 (q_{AB}, J = 10.7 Hz, 2H), 3.92 (s, 3H), 7.01 (d, J = 2.6 Hz, 1H), 7.08 (d, J = 2.6 Hz, 1H), 7.29 (ddd, J = 8.5, 6.8, and 1.2 Hz, 1H), 7.38 (ddd, J = 8.3, 6.8, and 1.2 Hz, 1H), 7.68 (d with fine coupling, J = 8.3 Hz, 1H), 7.69 (d with fine coupling, J = 8.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 27.4 (CH_3 × 3), 28.1 (CH_3), 28.6 (CH_3), 32.0 (CH_3 × 3), 34.4 (C), 43.8 (C), 55.3 (CH_3), 63.6 (CH_2), 79.0 (C), 105.7 (CH), 120.9 (CH), 123.5 (CH), 126.0 (CH), 126.0 (CH), 126.7 (CH), 129.7 (C), 132.9 (C), 134.2 (C), 136.5 (C), 136.7 (C), 152.3 (C), 156.6 (C) ppm. IR (KBr): ν 2958, 2929, 2870, 1680, 1628, 1597 cm^{-1}. Mass (m/z, %): 409 (M^+, 18), 353 (31), 339 (11), 338 (46), 309 (25), 307 (17), 295 (23), 294 (100), 292 (26), 277 (10), 262 (13), 252 (34), 239 (10), 238 (58), 236 (11), 197 (15), 183 (17), 69 (20), 57 (48), 56 (20), 55 (24). HRMS (ESI): 432.2526, calcd for $C_{26}H_{35}NO_3$Na [M + Na^+] 432.2515. Anal. Calcd for $C_{26}H_{35}NO_3$: C, 76.25; H, 8.61; N, 3.42. Found: C, 76.14; H, 8.83; N, 3.41.

11c: Coloress needles mp 83.5−84.5 °C (from hexane). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.96 (s, 9H), 1.06 (s, 9H), 1.33 (s, 3H), 1.35 (s, 3H), 2.14 (s, 3H), 3.48 (q_{AB}, J = 10.7 Hz, 2H), 3.77 (s, 2H), 6.68 (d,

J = 2.7 Hz, 1H), 6.74 (dd, J = 8.2 and 2.7 Hz, 1H), 6.98 (d, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.7 (CH_3), 27.8 (CH_3), 27.9 ($CH_3 \times 3$), 28.4 (CH_3), 31.9 ($CH_3 \times 3$), 34.2 (C), 43.5 (C), 55.3 (CH_3), 63.4 (CH_2), 79.2 (C), 113.2 (CH), 116.6 (CH), 129.7 (CH), 129.9 (C), 134.3 (C), 134.5 (C), 137.5 (C), 152.3 (C), 156.8 (C) ppm. IR (KBr): ν 2976, 2958, 2927, 2870, 1672, 1618, 1601, 1576 cm^{-1}. Mass (m/z, %): 373 (M^+, 12), 317 (25), 302 (44), 259 (17), 258 (100), 202 (44), 57 (36), 55 (10). HRMS (ESI): 396.2519, calcd for $C_{23}H_{35}NO_3$Na [M + Na$^+$] 396.2515. Anal. Calcd for $C_{23}H_{35}NO_3$: C, 73.96; H, 9.44; N, 3.75. Found: C, 73.78; H, 9.82; N, 3.72.

Synthesis of 1-Boc-4-*tert*-butyl-5-(6-hydroxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (6a). Typical Procedure. A solution of 1-Boc-4-*tert*-butyl-5-(6-methoxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**11a**) (2.37 g, 5.79 mmol) and sodium thiomethoxide (5.12 g, 69.5 mmo) in dry DMF (80 mL) was stirred under a nitrogen atmosphere at 150 °C for 40 min. The reaction mixture was poured into sat. aq. NH_4Cl and extracted with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel and eluted with hexane−AcOEt (3:1 to 2:1) to give of 1-Boc-4-*tert*-butyl-5-(6-hydroxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**6a**) as a colorless solid (2.05 g, 90% yield).

Demethylation of **11b** and **11c** were similarly carried out to give 1-Boc-4-*tert*-butyl-5-(3-hydroxynaphthaeln-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**6b**) and 1-Boc-4-*tert*-butyl-5-(5-hydroxy-2-methylphenyl)-3,3-dimethyl-2,3-dihydropyrrole (**6c**) in 81% and 69% yield, respectively.

6a: Colorless granules mp, 200.0−200.5 °C (from 1,2-dichloroethane−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.69 (s, 9H), 0.88 (s, 9H) 1.41 (s, 3H), 1.45 (s, 3H), 3.62 (q_{AB}, J = 10.5 Hz, 2H), 5.32 (broad s, 1H), 7.04 (dd, J = 9.0 and 2.4 Hz, 1H), 7.07 (d, J = 2.4 Hz, 1H), 7.17 (dd, J = 7.1 and 1.2 Hz, 1H), 7.34 (dd, J = 8.1 and 7.1 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 9.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, acetone-d_6): δ_C 28.1 ($CH_3 \times 3$), 28.7 (CH_3), 29.2 (CH_3), 32.8 ($CH_3 \times 3$), 35.3 (C), 44.8 (C), 64.9 (CH_2), 79.3 (C), 110.2 (CH), 119.4 (CH), 126.3 (CH), 126.8 (CH), 127.4 (CH), 129.1 (CH), 130.2 (C), 135.5 (C), 136.1 (C), 136.1 (C), 136.8 (C), 153.0 (C), 156.2 (C) ppm. IR (KBr): ν 3278, 2971, 1682, 1633, 1577 cm^{-1}. Mass (m/z, %): 395 (M^+, 17), 339 (33), 325 (12), 324 (48), 296 (12), 295 (47), 281 (24), 280 (100), 238 (27), 224 (52), 183 (25), 169 (23), 57 (13). HRMS (ESI): 418.2348, calcd for $C_{25}H_{33}NO_3$Na [M + Na$^+$] 418.2358. Anal. Calcd for $C_{25}H_{33}NO_3$ + 1/15CH_2ClCH_2Cl: C, 75.07; H, 8.34; N, 3.48. Found: C, 75.26; H, 8.54; N, 3.51.

6b: Colorless needles mp 204.0−206.0 °C (from 1,2-dichloroethane−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.71 (s, 9H), 0.89 (s, 9H) 1.40 (s, 3H), 1.46 (s, 3H), 3.62 (q_{AB}, J = 10.5 Hz, 2H), 5.71−5.77 (m, 1H), 6.97 (d, J = 2.4 Hz, 1H), 7.08 (d, J = 2.4 Hz, 1H), 7.28 (ddd, J = 8.3, 6.8, and 1.3 Hz, 1H), 7.37 (ddd, J = 8.1, 6.8, and 1.3 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 27.6 ($CH_3 \times 3$), 27.9 (CH_3), 28.6 (CH_3), 31.9 ($CH_3 \times 3$), 34.5 (C), 44.0 (C), 63.7 (CH_2), 79.7 (C), 109.5 (CH), 120.1 (CH), 123.3 (CH), 126.0 (CH), 126.1 (CH), 126.5 (CH), 129.5 (C), 132.7 (C), 134.5 (C), 136.5 (C), 137.4 (C), 152.7 (C), 153.1 (C) ppm. IR (KBr): ν 3234, 2989, 2966, 2927, 2862, 1649, 1618, 1595 cm^{-1}. Mass (m/z, %): 395 (M^+, 18), 339 (35), 325 (13), 324 (63), 295 (11), 281 (22), 280 (100), 278 (21), 238 (13), 224 (51), 222 (19), 69 (11), 57 (88), 55 (14). HRMS (ESI): 418.2377 calcd for $C_{25}H_{33}NO_3$Na [M + Na$^+$] 418.2358. Anal. Calcd for $C_{25}H_{33}NO_3$: C, 75.91; H, 8.41; N, 3.54. Found: C, 75.95; H, 8.81; N, 3.54.

6c: Coloress granules mp 176.5−177.5 °C (from AcOEt). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.96 (s, 9H), 1.09 (s, 9H), 1.32 (s, 3H), 1.33 (s, 3H), 2.13 (s, 3H), 3.47 (s, 2H), 4.88 (s, 1H), 6.62 (d, J = 2.8 Hz, 1H), 6.67 (dd, J = 8.1 and 2.8 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.8 (CH_3), 27.7 (CH_3), 28.0 ($CH_3 \times 3$), 28.4 (CH_3), 31.9 ($CH_3 \times 3$), 34.3 (C), 43.6 (C), 63.5 (CH_2), 79.7 (C), 114.5 (CH), 117.8 (CH), 129.6 (C), 129.9 (CH), 134.2 (C), 134.8 (C), 137.4 (C), 152.6 (C), 153.2 (C) ppm. IR (KBr): ν 3288, 2989, 2970, 2927,2871, 1645, 1601 cm^{-1}. Mass (m/z, %): 359 (M^+, 10), 303 (25), 289 (11), 288 (54), 245 (17), 244 (100), 228 (11), 188 (48), 186 (11), 57 (69), 56 (11), 55 (13). HRMS (ESI): 382.2361, calcd for $C_{22}H_{33}NO_3$Na [M + Na$^+$] 382.2358. Anal. Calcd for $C_{22}H_{33}NO_3$: C, 73.50; H, 9.25; N, 3.90. Found: C, 73.28; H, 9.59; N, 3.87.

Singlet Oxygenation of 1-Boc-4-*tert*-butyl-5-(6-hydroxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (6a): Typical Procedure. A solution of 1-Boc-4-*tert*-butyl-5-(6-hydroxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydropyrrole (**6a**) (150 mg, 0.379 mmol) and Rose Bengal (1.8 mg) in AcOEt (25 mL) was irradiated externally with a 940 W Na lamp under an oxygen atmosphere at 0 °C for 3 h. After the photolysate was concentrated *in vacuo*, the residue was chromatographed on silica gel and eluted with hexane−AcOEt (2:1) at low temperature to give 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo-[3.2.0]heptane (*anti*-**5a**) as a colorless solid (155 mg, 96% yield).

According to the procedure described above, dihydropyrroles **6b** and **6c** were transformed to the corresponding dioxetanes 2-Boc-5-*tert*-butyl-1-(3-hydroxy-naphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*syn*-**5b**) and 2-Boc-5-*tert*-butyl-1-(5-hydroxy-2-methylphenyl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*syn*-**5c**) in respective yields of 92% and 88%.

anti-**5a**: Pale yellow granules, mp 181.5−184.0 °C (dec.) (from AcOEt). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.69 (s, 9H), 0.88 (s, 9H), 1.26 (s, 3H), 1.60 (s, 3H), 3.95 (d, J = 10.5 Hz, 1H), 4.20 (d, J = 10.5 Hz, 1H), 5.27 (s, 1H), 7.07 (dd, J = 9.3 and 2.7 Hz, 1H), 7.19 (d, J = 2.7, 1H), 7.45 (dd, J = 8.3 and 7.6 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.97 (dd, J = 7.6 and 1.2 Hz, 1H), 8.42 (d, J = 9.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 22.0, 26.8, 26.9, 27.2, 37.9, 43.1, 63.1, 81.3, 104.3, 107.5, 111.1, 117.5, 125.3, 126.0, 126.3, 127.5, 128.5, 132.7, 135.5, 153.3, 154.3 ppm. IR (KBr): ν 3321, 3006, 2979, 2930, 2891, 1703, 1664, 1637, 1604 cm^{-1}. Mass (m/z, %): 427 (M^+, 10), 395 (M^+-O_2, 4), 327 (21), 271 (32), 270 (94), 243 (11), 242 (19), 214 (10), 213 (16), 187 (20), 172 (14), 171 (100). HRMS (ESI): 450.2258, calcd for $C_{25}H_{33}NO_5$Na [M + Na$^+$] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$ + 1/5AcOEt: C, 69.61; H, 7.83; N, 3.15. Found: C, 69.61; H, 7.74; N, 3.22.

syn-**5b**: Colorless needles, mp 170.0−171.5 °C (dec.) (from AcOEt−CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.74 (s, 9H), 0.91 (s, 9H), 1.27 (s, 3H), 1.63 (s, 3H), 3.96 (d, J = 10.5 Hz, 1H), 4.21 (d, J = 10.5 Hz, 1H), 5.46 (broad s, 1H), 7.17 (d, J = 2.6 Hz, 1H), 7.30 (ddd, J = 8.5, 7.0, and 1.3 Hz, 1H), 7.39 (ddd, J = 8.1, 7.0, and 1.0 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.80 (d, J = 2.6 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 22.2, 26.9, 27.0, 27.3, 38.0, 43.2, 63.1, 80.9, 103.9, 107.8, 111.2, 122.1, 123.6, 124.4, 125.9, 126.8, 127.7, 135.0, 135.2, 152.6, 153.7 ppm. IR (KBr): ν 3383, 2979,1671, 1635 cm^{-1}. Mass (m/z, %): 427 (M^+, 6), 271 (13), 270 (37), 242 (12), 213 (13), 187 (10), 172 (12), 171 (100), 115 (33), 57 (45), 56 (30), 55 (14). HRMS (ESI): 450.2266, calcd for $C_{25}H_{33}NO_5$Na [M + Na$^+$] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$: C, 70.23; H, 7.78; N, 3.28. Found: C, 70.06; H, 7.91; N, 3.33.

syn-**5c**: Coloress needles, mp 177.0−178.0 °C (dec.) (from hexane−CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.02 (s, 9H), 1.07 (s, 9H), 1.19 (s, 3H), 1.49 (s, 3H), 2.34 (s, 3H), 3.71 (d, J = 10.3 Hz, 1H), 4.05 (d, J = 10.3 Hz, 1H), 5.08 (s, 1H), 6.74 (dd, J = 8.1 and 2.9 Hz, 1H), 6.97 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 2.9 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.9, 22.2, 26.4, 26.5, 27.6, 38.0, 43.0, 63.1, 80.7, 103.9, 107.3, 115.3, 117.9, 127.7, 132.6, 136.8, 153.5, 153.9 ppm. IR (KBr): ν 3408, 2979, 2933, 1676, 1612 cm^{-1}. Mass (m/z, %): 391 (M^+, 2), 359 (M^+-O_2,14), 334 (14), 303 (27), 288 (18), 278 (15), 244 (15), 234 (46), 149 (11), 135 (100), 134 (18), 107 (18), 57 (87), 56 (26), 55 (17). HRMS (ESI): 414.2270, calcd for $C_{22}H_{33}NO_5$Na [M + Na$^+$] 414.2256. Anal. Calcd for $C_{22}H_{33}NO_5$: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.48; H, 8.75; N, 3.52.

Thermal Isomerization of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*anti*-5a) to *syn*-5a Isomer. Typical Procedure. A solution of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*anti*-**5a**) (92.5 mg, 0.216 mmol) in toluene (5 mL) was stirred at 110 °C for 15 min. The reaction mixture was concentrated *in vacuo*, and the residue was chromatographed on silica gel and eluted with benzene−AcOEt (10:1) to give *syn*-**5a** as a colorless solid (18.9 mg, 20% yield).

Similarly, dioxetanes *syn*-**5b** and *syn*-**5c** were individually isomerized thermally to the corresponding dioxetanes *anti*-**5b** and *anti*-**5c** in respective isolated yields of 13% and 48%.

syn-**5a**: Pale yellow plates, mp 148.0−148.5 °C (from benzene−CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.81 (broad s, 9H), 0.92 (s, 9H), 1.15 (s, 3H), 1.53 (s, 3H), 3.77 (d, J = 10.0 Hz, 1H), 4.18 (d, J = 10.0 Hz, 1H), 6.35−6.60 (m, 1H), 6.85−7.20 (m, 2H), 7.27−7.37 (m, 2H), 7.62 (d, J = 7.8 Hz, 1H), 8.79 (d, J = 9.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 21.3, 26.4, 27.4, 27.6, 38.0, 43.5, 63.1, 81.3, 108.0, 108.9, 109.9, 118.4, 124.1, 124.4, 127.8, 128.2, 129.5, 134.6, 135.8, 153.3, 154.7 ppm. IR (KBr): ν 3369, 2979, 2930, 1703, 1667, 1626, 1602 cm^{-1}. Mass (m/z, %): 427 (M^+, 2), 395 (M^+-O_2, 1), 327 (11), 271 (15), 270 (45), 242 (11), 187 (17), 172 (13), 171 (100), 143 (21), 57 (19). HRMS (ESI): 450.2257, calcd for $C_{25}H_{33}NO_5Na$ [M + Na^+] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$ + 2/3benzene: C, 72.62; H, 7.78; N, 2.92. Found: C, 72.86; H, 7.86; N, 2.81.

anti-**5b**: Pale yellow granules, mp 154.5−155.5 °C (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.76 (broad s, 9H), 0.96 (s, 9H), 1.16 (s, 3H), 1.55 (s, 3H), 3.74 (d, J = 10.0 Hz, 1H), 4.16 (d, J = 10.0 Hz, 1H), 5.13 (s, 1H), 7.14 (d, J = 2.6 Hz, 1H), 7.17 (d, J = 2.6 Hz, 1H), 7.32 (ddd, J = 8.6, 6.8, and 1.7 Hz, 1H), 7.38 (dd with fine coupling, J = 8.0 and 6.8 Hz, 1H), 7.64 (d with fine coupling, J = 8.0 Hz, 1H), 8.81 (d, J = 8.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 21.3, 26.5, 27.5, 38.0, 43.4, 63.1, 81.7, 108.1, 108.5, 111.3, 118.9, 123.8, 126.0, 127.1, 127.5, 128.0, 135.5, 136.5, 152.0, 154.8 ppm. IR (KBr): ν 3340, 2979, 2933, 2888, 1696, 1671, 1633, 1623, 1604, 1578 cm^{-1}. Mass (m/z, %): 427 (M^+, 0.8), 395 (M^+-O_2, 0.3), 270 (19), 187 (17), 172 (13), 171 (100), 115 (44), 57 (36), 56 (20), 55 (11). HRMS (ESI): 450.2266, calcd for $C_{25}H_{33}NO_5Na$ [M + Na^+] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$: C, 70.23; H, 7.78; N, 3.28. Found: C, 70.30; H, 8.09; N, 3.27.

anti-**5c**: Coloress granules, mp 156.0−157.0 °C (from hexane−CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.03 (s, 9H), 1.10 (s, 3H), 1.12 (s, 9H), 1.46 (s, 3H), 2.42 (s, 3H), 3.64 (d, J = 10.1 Hz, 1H), 4.04 (d, J = 10.1 Hz, 1H), 5.60 (broad s, 1H), 6.68 (dd, J = 8.2 and 2.7 Hz, 1H), 6.73 (d, J = 2.7 Hz, 1H), 6.91 (d, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 21.1, 22.2, 26.5, 27.1, 27.8, 37.8, 43.1, 63.0, 81.3, 107.2, 107.8, 115.2, 115.2, 129.9, 133.4, 137.5, 152.7, 154.4 ppm. IR (KBr): ν 3396, 2976, 2933, 1674, 1612 cm^{-1}. Mass (m/z, %): 391 (M^+, 1), 359 (M^+-O_2,10), 334 (11), 303 (20), 288 (15), 278 (12), 244 (12), 234 (43), 135 (100), 134 (16), 107 (18), 57 (69), 56 (18), 55 (11). HRMS (ESI): 414.2266, calcd for $C_{22}H_{33}NO_5Na$ [M + Na^+] 414.2256. Anal. Calcd for $C_{22}H_{33}NO_5$: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.23; H, 8.79; N, 3.53.

Thermal Decomposition of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo-[3.2.0]heptane (*anti*-5a) to *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-6-hydroxynaphthalene-1-carboxamide (12a). Typical Procedure. A solution of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*anti*-**5a**) (32.7 mg, 0.0765 mmol) in *p*-xylene (1 mL) was refluxed under a nitrogen atmosphere for 1 h. After being allowed to cool, the reaction mixture was concentrated *in vacuo*. The residue was chromatographed on silica gel and eluted with hexane−AcOEt (3:1) to give *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-6-hydroxynaphthalene-1-carboxamide (**12a**) as a colorless solid (27.3 mg, 83% yield).

Dioxetanes *syn*-**5a**, *anti*- and *syn*-**5b**, and *anti*- and *syn*-**5c** were similarly decomposed thermally to give the corresponding keto imides *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-6-hydroxynaphthalene-1-carboxamide (**12a**) (89% yield), *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-3-hydroxynaphthalene-1-carboxamide (**12b**) (87% yield from *anti*-**5b**, 99% yield from *syn*-**5b**) and *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-5-hydroxy-2-methylbenzamide (**12c**) (92% yield from *anti*-**5c**, 87% yield from *syn*-**5c**).

12a: Colorless granules, mp 104.0−105.0 °C (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.75 (s, 9H), 1.35 (s, 9H), 1.42 (s, 6H), 4.19 (broad s, 2H), 5.29 (broad s, 1H), 7.12 (dd, J = 9.0 and 2.4 Hz, 1H), 7.15 (d, J = 2.4 Hz), 7.32 (dd, J = 7.1 and 1.0 Hz, 1H), 7.38 (dd, J = 8.3 and 7.1 Hz, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 25.1, 26.8, 28.3, 46.3, 50.7, 52.1, 83.4, 109.9, 119.1, 120.9, 125.1, 125.2, 126.9, 128.2, 134.9, 136.4, 153.7, 154.1, 172.8, 217.1 ppm. IR (KBr): ν 3460, 2984, 2934, 1738, 1716, 1677, 1669, 1626 cm^{-1}. Mass (m/z, %): 427 (M^+, 6), 327 (10), 271 (15), 270 (46), 242 (12), 213 (14), 187 (13), 172 (15), 171 (100), 143 (20), 57 (19). HRMS (ESI): 450.2246, calcd for $C_{25}H_{33}NO_5Na$ [M + Na^+] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$: C, 70.23; H, 7.78; N, 3.28. Found: C, 70.28; H, 7.99; N, 3.33.

12b: Colorless needles, mp 151.5−152.0 °C (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.75 (s, 9H), 1.36 (s, 9H), 1.43 (s, 6H), 4.20 (broad s, 2H), 5.77−5.87 (m, 1H), 7.18 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 2.6 Hz, 1H), 7.35 (ddd, J = 8.3, 7.0, and 1.3 Hz), 7.41 (ddd, J = 8.1, 7.0, and 1.1 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 25.0, 26.7, 28.2, 46.3, 50.7, 52.0, 83.7, 111.3, 115.8, 124.3, 124.6, 125.1, 126.6, 126.7, 134.9, 137.6, 152.9, 153.4, 172.2, 217.8 ppm. IR (KBr): ν 3328, 2994, 2982, 2971, 1736, 1672, 1642, 1627, 1606, 1578 cm^{-1}. Mass (m/z, %): 427 (M^+, 5), 271 (13), 270 (35), 242 (11), 213 (15), 172 (13), 171 (100), 115 (40), 57 (57), 56 (21), 55 (15). HRMS (ESI): 450.2265, calcd for $C_{25}H_{33}NO_5Na$ [M + Na^+] 450.2256. Anal. Calcd for $C_{25}H_{33}NO_5$: C, 70.23; H, 7.78; N, 3.28. Found: C, 70.08; H, 8.10; N, 3.26.

12c: Coloress granules, mp 135.5−136.0 °C (from hexane). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.08 (s, 9H), 1.33 (s, 9H), 1.35 (s, 6H), 2.24 (s, 3H), 4.07 (broad s, 2H), 6.18 (s, 1H), 6.75−6.88 (m, 2H), 7.02 (d, J = 7.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.2, 25.0, 27.1, 28.2, 46.3, 50.7, 51.8, 83.5, 112.8, 116.4, 126.6, 131.7, 139.0, 153.6, 153.7, 172.7, 217.5 ppm. IR (KBr): ν 3275, 2974, 2933, 1734, 1678, 1645, 1618, 1581 cm^{-1}. Mass (m/z, %): 391 (M^+, 1), 234 (37), 149 (17), 135 (100), 134 (14), 107 (16), 57 (66), 56 (34), 55 (20). HRMS (ESI): 414.2278, calcd for $C_{22}H_{33}NO_5Na$ [M + Na^+] 414.2256. Anal. Calcd for $C_{22}H_{33}NO_5$: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.11; H, 8.89; N, 3.54.

Base-Induced Decomposition of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo-[3.2.0]heptane (*anti*-5a) to *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-6-hydroxynaphthalene-1-carboxamide (12a). Typical Procedure. TBAF (1 M in THF, 0.50 mL, 0.50 mmol, 5.0 equiv) in DMSO (1.5 mL) was added dropwise over 50 s to a solution of 2-Boc-5-*tert*-butyl-1-(6-hydroxynaphthalen-1-yl)-4,4-dimethyl-2-aza-6,7-dioxabicyclo[3.2.0]heptane (*anti*-**5a**) (10.0 mg, 0.0234 mmol) in DMSO (1.0 mL) and stirred for 4 min. The reaction mixture was poured into sat. aq. NH_4Cl and extracted with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on silica gel and eluted with benzene−AcOEt (4:1) to give 10.0 mg of *N*-Boc-*N*-(2,2,4,4-tetramethyl-3-oxopentyl)-6-hydroxynaphthalene-1-carboxamide (**12a**) as a pale yellow solid in a quantitative yield.

Dioxetanes *syn*-**5a**, *anti*- and *syn*-**5b**, and *anti*- and *syn*-**5c** were similarly decomposed to give the corresponding keto imides **12a** (48% yield, conversion yield 97%), **12b** (94% yield from *anti*-**5b**; 48%

dx.doi.org/10.1021/jo2006945 |*J. Org. Chem.* 2011, 76, 5006–5017

yield, conversion yield 97%, from *syn*-**5b**), and **12c** (86% yield from *anti*-**5c**, 89% yield from *syn*-**5c**).

Chemiluminescence Measurement and Time Course for the Charge-Transfer-Induced Decomposition of Dioxetanes. General Procedure. Chemiluminescence was measured using a spectrophotometer and/or a multichannel detector.

A freshly prepared solution (2.0 mL) of TBAF (1.0×10^{-1} or 1.0×10^{-2} mol/L) in DMSO or acetonitrile was transferred to a quartz cell ($10 \times 10 \times 50$ mm), and the latter was placed in the spectrometer, which was thermostatted with stirring at 25 °C. After ca. 1 min, a solution of the dioxetane *anti*-**5a**−**c** or *syn*-**5a**−**c** in DMSO or acetonitrile (1.0×10^{-3} or 1.0×10^{-5} mol/L, 1.0 mL) was added by a syringe, and measurement was started immediately. The time course of the intensity of light emission was recorded and processed according to first-order kinetics. The total light emission was estimated by comparing it to that of an adamantylidene-dioxetane, the chemiluminescence efficiency Φ^{CL} of which has been reported to be 0.29 and which was used here as a standard.[18,19]

Fluorescence Measurement of Authentic Emitters 13a−d. A freshly prepared solution of 2.0×10^{-5}−3.0×10^{-4} mol dm^{-3} of **12a**−**d** and 1.0×10^{-3} mol dm^{-3} of TBAF in DMSO or acetonitrile was transferred to a quartz cell ($10 \times 10 \times 50$ mm^3), and the latter was placed in the spectrometer, which was thermostatted with stirring at 25 °C. Thus, the fluorescence spectra of **13a**−**d** were measured, and their fluorescence efficiencies (Φ^{fl}'s) were estimated using fluorescein as a standard.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H/^{13}C NMR spectra of **5a**−**c**, **6a**−**c**, **9a**−**c**, **10a**−**c**, **11a**−**c**, **12a**−**c**, and ORTEP views and crystallographic information files for *anti*-**5b**−**c** and *syn*-**5b**−**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: matsumo-chem@kanagawa-u.ac.jp.

■ ACKNOWLEDGMENT

We gratefully acknowledge financial assistance provided by Grants-in-aid (Nos. 22550046 and 21550052) for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

■ REFERENCES

(1) For reviews of 1,2-dioxetane, see: (a) Bartlett, P. D.; Landis, M. E. In *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979; pp 243−286. (b) Adam, W. In *The Chemistry of Peroxide*; Patai, S., Ed.; Wiley: New York, 1983; pp 829−920. (c) Adam, W. In *Small Ring Heterocycles*; Hassner, A., Ed.; Wiley: New York, 1986; pp 351−429. (d) Adam, W.; Heil, M.; Mosandl, T.; Saha-Möller, C. R. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1992; pp 221−254. (e) Saha-Möller, C. R.; Adam, W. In *Comprehensive Heterocyclic Chemistry II A Review of the Literature 1982−1995*; Padwa, A., Ed.; Pergamon: New York, 1996; pp 1041−1082. (f) Adam, W.; Trofimov, A. V. In *The Chemistry of Peroxides*; Rappoport, Z., Ed.; Wiley: New York, 2006; Vol. 2, pp 1171−1209.

(2) Schaap, A. P.; Gagnon, S. D. *J. Am. Chem. Soc.* **1982**, *104*, 3504–3506.

(3) (a) Schaap, A. P.; Handley, R. S.; Giri, B. P. *Tetrahedron Lett.* **1987**, *28*, 935–938. (b) Schaap, A. P.; Chen, T. S.; Handley, R. S.; DeSilva, R.; Giri, B. P. *Tetrahedron Lett.* **1987**, *28*, 1155–1158.

(4) The chemiluminescent (CL) decomposition of hydroxyphenyl-substituted dioxetanes has been proposed to proceed by the CIEEL[5] (chemically initiated electron exchange luminescence) mechanism, where an initially formed radical ion pair is annihilated by back electron transfer (BET) to give an excited aromatic carbonyl compound. However, the question of whether such a CL reaction includes BET as a fundamental process is still being argued. Therefore, we have recently been using the term CTID, which includes CIEEL and other CT-induced mechanisms.

(5) (a) Koo, J.-Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1977**, *99*, 6107–6109. (b) Koo, J.-Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1978**, *100*, 4496–4503. (c) Zaklika, K. A.; Kissel, T.; Thayer, A. L.; Burns, P. A.; Schaap, A. P. *Photochem. Photobiol.* **1979**, *30*, 35–44. (d) Catalani, L. H.; Wilson, T. *J. Am. Chem. Soc.* **1989**, *111*, 2633–2639. (e) McCapra, F. J. *Photochem. Photobiol. A: Chem.* **1990**, *51*, 21–28. (f) Adam, W.; Bronstein, I.; Trofimov, T.; Vasil'ev, R. F. *J. Am. Chem. Soc.* **1999**, *121*, 958–961. (g) Adam, W.; Matsumoto, M.; Trofimov, T. *J. Am. Chem. Soc.* **2000**, *122*, 8631–8634. (h) Nery, A. L. P.; Weiss, D.; Catalani, L. H.; Baader, W. J. *Tetrahedron* **2000**, *56*, 5317–5327.

(6) (a) White, E. H.; Steinmetz, M. G.; Miano, J. D.; Wildes, P. D.; Morland, R. *J. Am. Chem. Soc.* **1980**, *102*, 3199–3208. (b) Orlova, G.; Goddard, J. D.; Brovko, L. Y. *J. Am. Chem. Soc.* **2003**, *125*, 6962–6971. (c) McCapra, F. *Acc. Chem. Res.* **1976**, *9*, 201–208. (d) Wilson, T. *Photochem. Photobiol.* **1995**, *62*, 601–606. (e) Mager, H. I. X.; Tu, S.-C. *Photochem. Photobiol.* **1995**, *62*, 607–614. (f) Isobe, H.; Takano, Y.; Okumura, M.; Kuramitsu, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2005**, *127*, 8667–8679. (g) Chung, L. W.; Hayashi, S.; Lundberg, M.; Nakatsu, T.; Kato, H.; Morokuma, K. *J. Am. Chem. Soc.* **2008**, *130*, 12880–12881. (h) Liu, F.; Liu, Y.; Vico, L.; Lindh, R. *Chem. Phys. Lett.* **2009**, *484*, 69–75. (i) Liu, F.; Liu, Y.; Vico, L.; Lindh, R. *J. Am. Chem. Soc.* **2009**, *131*, 6181–6188.

(7) (a) Beck, S.; Köster, H. *Anal. Chem.* **1990**, *62*, 2258–2270. (b) Adam, W.; Reihardt, D.; Saha-Möller, C. R. *Analyst* **1996**, *121*, 1527–1531. (c) Matsumoto, M. *J. Photochem. Photobiol. C: Photochem. Rev.* **2004**, *5*, 27–53. (d) Matsumoto, M.; Watanabe, N. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1899–1920. (e) Baader, W. J.; Stevani, C. V.; Bastos, E. L. In *The Chemistry of Peroxides*; Rappoport, Z., Ed.; Wiley: New York, 2006; Vol. 2, p 1211.

(8) (a) Bronstein, I.; Edwards, B.; Voyta, J. C. *J. Biolumin. Chemilumin.* **1989**, *4*, 99–111. (b) Schaap, A. P.; Akhavan-Tafti, H.; Romano, L. J. *Clin. Chem.* **1989**, *35*, 1863–1864. (c) Edwards, B.; Sparks, A.; Voyta, J. C.; Bronstein, I. *J. Biolumin. Chemilumin.* **1990**, *5*, 1–4. (d) Martin, C.; Bresnick, L.; Juo, R. R.; Voyta, J. C.; Bronstein, I. *BioTechniques* **1991**, *11*, 110–113. (e) Mariscal, A.; Garcia, A.; Carnero, M.; Gomez, M.; Fernandez-Crehuet, J. *BioTechniques* **1994**, *16*, 888–893. (f) Trofimov, A. V.; Vasil'ev, R. F.; Mielke, K.; Adam, W. *Photochem. Photobiol.* **1995**, *62*, 35–43. (g) Adam, W.; Bronstein, I.; Edwards, B.; Engel, T.; Reinhardt, D.; Schneider, F. W.; Trofimov, A. V.; Vasil'ev, R. F. *J. Am. Chem. Soc.* **1996**, *118*, 10400–10407. (h) Buxton, R. C.; Edwards, B.; Juo, R. R.; Voyta, J. C.; Bethell, R. *Anal. Biochem.* **2000**, *280*, 291–300. (i) Sabelle, S.; Renard, P.-Y.; Pecorella, K.; de Suzzoni-Dèzard, S.; Crèminon, C.; Grassi, J.; Mioskowski, C. *J. Am. Chem. Soc.* **2002**, *124*, 4874–4880.

(9) Edwards, B.; Sparks, A.; Voyta, J. C.; Bronstein, I. In *Bioluminescence and Chemiluminescence, Fundamentals and Applied Aspects*; Campbell, A. K., Kricka, L. J., Stanley, P. E., Eds.; Wiley: Chichester, 1994; pp 56−59.

(10) It has been suggested that color tuning is related to a change in the stereochemistry of **3**, which may be caused by a change in the microenvironment; i.e., the pocket of luciferase has been suggested to play a role in the color tuning of bioluminescence in the firefly.[11,12] However, recent reports have suggested that the color tuning is caused by the polarity of the luciferase pocket or protonation of anionic oxyluciferin in the excited state rather than the change of stereochemistry of oxyluciferin.[13]

(11) McCapra, F. In *Chemiluminescence and Bioluminescence*; Hastings, J. W., Kricka, L. J., Stanley, P. E., Eds.; Wiley: New York, 1996; pp 7−15.
(12) Branchini, B. R.; Murtiashaw, M. H.; Magyer, R. A.; Portier, N. C.; Ruggiero, M. C.; Stroh, J. G. *J. Am. Chem. Soc.* **2002**, *124*, 2112–2113.
(13) (a) Cai, D; Marques, M. A. L; Nogueria, F. *J. Phys. Chem. B* **2011**, *115*, 329–332. (b) Milane, B. F.; Marques, M. A. L.; Nogueria, F. *Phys. Chem. Chem. Phys.* **2010**, *12*, 14285–14293. (c) Naumov, P.; Kochunnoonny, M. *J. Am. Chem. Soc.* **2010**, *132*, 11566–11579. (d) Navizet, I.; Liu, Y.-J.; Ferre, N.; Xiao, H.-Y.; Fang, W.-H.; Lindh, R. *J. Am. Chem. Soc.* **2010**, *132*, 706–712. (e) Hirano, T.; Hasumi, Y; Ohtsuka, K.; Maki, S.; Niwa, H.; Yamaji, M.; Hashizume, D. *J. Am. Chem. Soc.* **2009**, *131*, 2385–2396. (f) Nakatani, N.; Hasegawa, J.; Nakatsuji, H. *Chem. Phys. Lett.* **2009**, *469*, 191–194. (g) Naumov, P.; Ozawa, Y.; Ohkubo, K.; Fukuzumi, S. *J. Am. Chem. Soc.* **2009**, *131*, 11590–11605.
(14) (a) Matsumoto, M.; Sano, M.; Watanabe, N.; Ijuin, H. K. *Chem. Lett.* **2006**, *35*, 852–853. (b) Watanabe, N.; Sano, Y.; Suzuki, H.; Tanimura, M.; Ijuin, H. K.; Matsumoto, M. *J. Org. Chem.* **2010**, *75*, 5920–5926.
(15) For convenience sake, we call a rotamer an *anti*-form when the dioxetane O−O and a hydroxyl group on an aromatic ring are on opposite sides of the pyrrolidine ring, while in the *syn*-form the dioxetane O−O and a hydroxyl group on an aromatic ring are on the same side of the pyrrolidine ring.
(16) Part of this work has been reported as a preliminary communication.[17]
(17) Matsumoto, M.; Suzuki, H.; Sano, Y.; Watanabe, N.; Ijuin, H. K. *Tetrahedron Lett.* **2008**, *49*, 5372–5375.
(18) Φ^{CL} was estimated based on the value 0.29 for the chemiluminescent decomposition of 3-adamantylidene-4-methoxy-4-(3-siloxyphenyl)-1,2-dioxetane in a TBAF/DMSO system.[19]
(19) Trofimov, A. V.; Mielke, K.; Vasil'ev, R. F.; Adam, W. *Photochem. Photobiol.* **1996**, *63*, 463–467.
(20) The B-ring of a naphthalene-1-yl group and dioxetane O−O are on opposite sides of the pyrrolidine ring for *anti*-**5a**, and the B-ring and dioxetane O−O are on the same side of the pyrrolidine ring for *syn*-**5a**.
(21) Hoshiya, N.; Fukuda, N.; Watanabe, N.; Matsumoto, M. *Tetrahedron* **2006**, *62*, 5808–5820.
(22) Francisco, L.; Ciscato, M. L.; Bartoloni, F. H.; Weiss, D.; Beckert, R.; Baader, W. J. *J. Org. Chem.* **2010**, *75*, 6574–6580.