SYNTHESIS AND CHEMILUMINESCENCE OF 3-BIPHENYLYL-4,4-DIISOPROPYL-3-METHOXY-1,2-DIOXETANES

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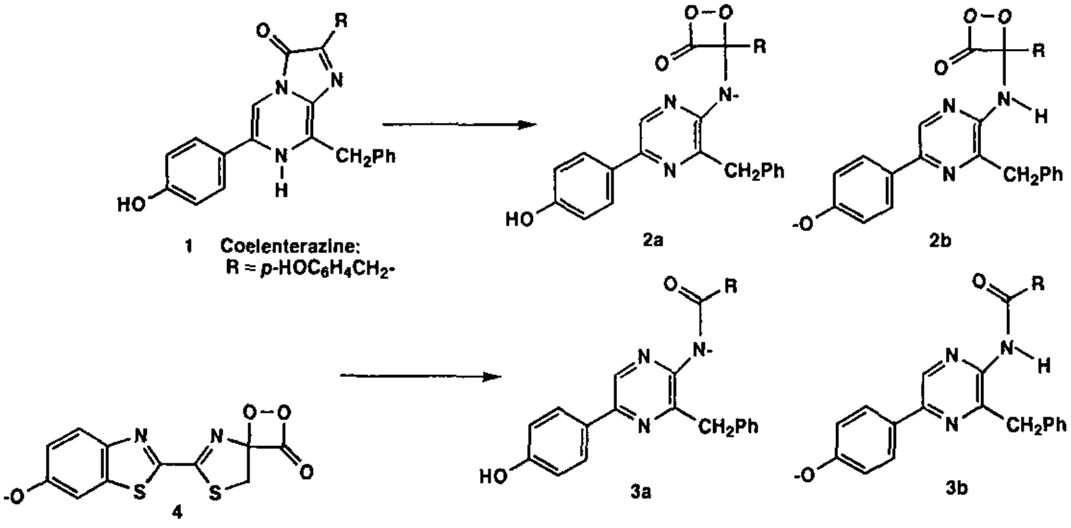
Abstract----- Five 3-biphenylyl-4,4-diisopropyl-3-methoxy-1,2-dioxetanes (**5**) with a *tert*-butyldimethylsiloxy group at the appropriate position on the aromatic ring were synthesized and their fluoride-induced chemiluminescence were examined.

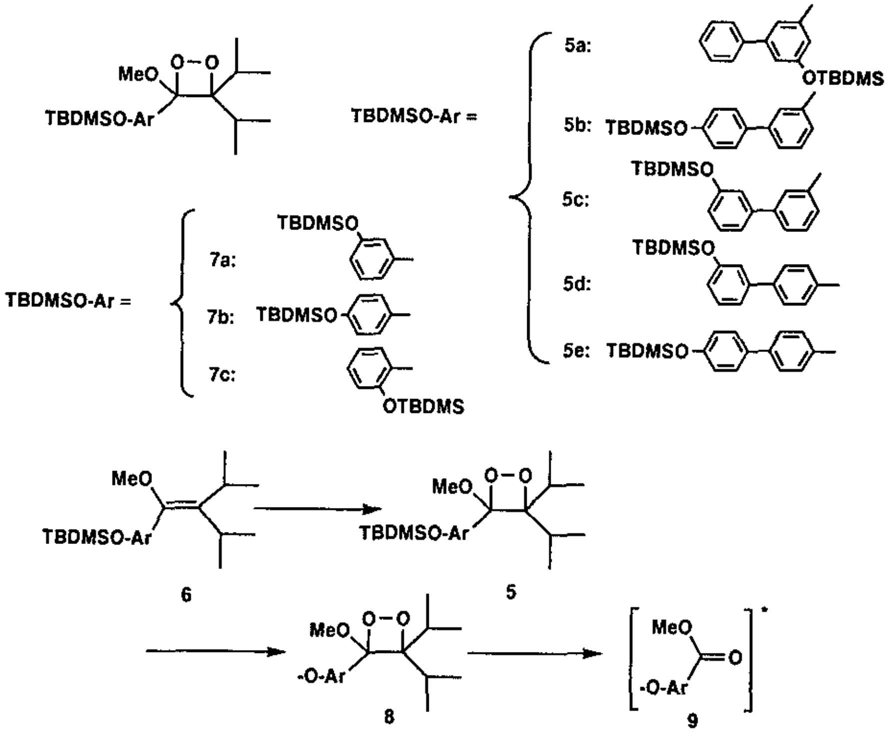
The bioluminescence and the chemiluminescence of coelenterazine and its analogues (**1**) have recently received much attention in connection with the bioluminescence mechanism of the jellyfish, *Aequoria victoria.*[1] Coelenterazines (**1**) are first dioxygenated and emit flash light through intermediary dioxetanones (**2**), which decompose into excited coelenteramides (**3**) and CO$_2$.[2-4] The decomposition of **2** has been suggested to be induced by an intramolecular electron transfer from the anionic biaryl system, 5-(4-hydroxyphenyl)pyrazin-2-amino moiety to a σ^* orbital of O-O in the dioxetanone ring.[3,5,6] It has been reported that the light emitter in the chemiluminescence of **1** is a monoanion (**3a**) of coelenteramide, which likely forms through a nitrogen anion (**2a**) of the dioxetanone.[6,7] Contrary to the chemiluminescence, Hirano has very recently clarified that the light emitter is a monoanion (**3b**), where the formal anionic center is remote from the dioxetanone ring, in the bioluminescence of aequorin, which consists of a complex of apoaequorin (apoprotein), coelenterazine, and dioxygen.[8] It has also been suggested that an intramolecular electron transfer from a phenolic anion of the biaryl-



like conjugate system in an intermediary dioxetanone (**4**) to the peroxidic O-O plays an important role for the firefly luminescence.[5,9] These facts prompted us to synthesize 3,3-diisopropyl-4-methoxy-1,2-dioxetanes (**5**) bearing a biphenylyl with *tert*-butyldimethylsilyloxy (TBDMS-O) group at the appropriate position as a simplified model for coelenterazines and firefly luciferin, and to examine whether the light emission is induced by a phenolic oxide ion on the biphenylyl even if at a distance from the dioxetane ring.

Considering that TBDMS-O should not prevent sterically the overlapping of two aromtaic π-systems in the biphenylyl, we chose five dioxetanes (**5a-e**) to be examined. An enol ether (**6a**) (100 mg, 0.24 mmol) was irradiated together with tetraphenylporphin (5 mg) in CH_2Cl_2 (10 ml) with sodium vapor lamp (940W) under an oxygen atmosphere at -78°C for 2 h. After the irradiation, the reaction mixture was concentrated and chromatographed on silica gel. Elution with hexane-ethyl acetate (20 : 1) gave a dioxetane (**5a**) as a pale yellow viscous oil in 89 % yield. Dioxetanes (**5b-e**) were synthesized similarly by the singlet oxygenation of the corresponding enol ethers (**6b-e**) in 62 - 97 % isolated yields. All the dioxetanes (**5a-e**) were stable enough to handle at room temperature.[10]

A dioxetane (**7a**), which is a mononuclear analogue of **5a**, has recently been reported to emit light with high efficiency ($\lambda_{max} = 463$ nm, $\Phi_{CL} = 0.21$, $t_{1/2} = 6.3$ sec) by treatment with tetrabutylammonium fluoride (TBAF) in DMSO.[11] Before studying on the chemiluminescence of the biphenylyldioxetanes (**5**), we examined the fluoride-induced chemiluminescence of *para*- (**7b**) and *ortho*-isomers (**7c**) of **7a**, which were synthesized by the similar singlet oxygenation of the corresponding enol ethers. The triggering of TBDMS-O was attained by adding a solution of the dioxetane (**7b**) or (**7c**) in DMSO (1.0×10^{-5} mol dm^{-3},1ml) into TBAF solution in DMSO (1.0×10^{-2} mol dm^{-3}, 2ml) under a N_2 atmosphere at 25°C.[12] Both the isomers (**7b**) and (**7c**) emitted spontaneously light, though the efficency (Φ_{CL})[13,14] were far less than the *m*-isomer (**7a**); for **7b**, $\lambda_{max} = 463$



nm, $\Phi_{CL} = 5 \times 10^{-4}$, $t_{1/2} < 1$ sec: for **7c**, $\lambda_{max} = 422$ nm, $\Phi_{CL} = 8 \times 10^{-4}$, $t_{1/2} = 1.5$ sec. The significant difference of Φ_{CL} between *m*-isomer (**7a**) and the other isomers (**7b**) and (**7c**) was in agreement with the suggestion reported.[15]

When the similar fluoride-induced reaction of the dioxetane (**5a**) was made in DMSO, strong light emission occurred with λmax (462 nm) similarly to the case of **7a**, though the efficiency Φ_{CL} (0.08) was somewhat less and the half-life ($t_{1/2} = 10.6$ sec) was a little longer than those for **7a**. The treatment of the dioxetanes (**5b-d**) with TBAF in DMSO caused also the luminescence with $\lambda_{max} = 465$ nm and Φ_{CL} = **5b** :1.0×10^{-4}, **5c** : 1.7×10^{-4}, and **5d** : 1.5×10^{-5}.[16] These results revealed that a phenolic oxide anion at a distance from the dioxetane ring can induce the decomposition of the dioxetanes (**5b-d**) with light. The half-lives ($t_{1/2}$) of the luminescence from **5a-d** were varied by the substitution pattern on the biphenyl; $t_{1/2} = 7.8$ sec for **5b**, 32.0 sec for **5c**, and 12.5 sec for **5d**.

Easiness (rate) of the electron transfer from the phenoxide anion to O-O of the dioxetane ring should be reflected more simply in the half-life of the luminescence than the efficiency Φ_{CL}, which is significantly affected by complex factors such as the energetic relationships between the singlet and triplet excited states of the emitters as well as those of two carbonyl fragments formed by the decomposition of the dioxetane. Thus, the results about the half-lives showed that, after the triggering of TBDMS-O, the *p*- and *o*-phenoxy isomers (**7b**) and (**7c**) cause the electron transfer more easily than the *m*-isomer (**7a**). For the series of the biphenylyldioxetanes (**5a-d**), it was characteristic that the *meta-meta*-substituted (**5c**) possesses the half-life longer significantly than those of the rest isomers (**5a**, **b** and **d**), though it requires further experiments to discuss in detail a relationship between the half-lives and the substitution pattern of the biphenylyl. The difficulty of the electron transfer for the anion of **5c** seemed to be well rationalized as follows; a) the electron transfer to the σ^* orbital of O-O occurs from the position near to the dioxetane ring, that is the aromatic carbon ($C\alpha$) attached to the dioxetane; b) the HOMO of the aromatic π-electron system plays an important role for the electron transfer; and c) in consequence, the larger the HOMO electron density at $C\alpha$ is, the more easily the electron transfer occurs.[18] In accord with the rationalization, the half-life of the chemiluminescence for the *para-para* analogue (**5e**) would be the shortest among those of **5a-e**.[18]

The triggering of the *para-para*-substituted biphenylyldioxetane (**5e**) caused a short duration of luminescence ($t_{1/2} = 2.6$ sec) with $\Phi_{CL} = 3 \times 10^{-5}$ and $\lambda_{max} = 510$ nm. The result disclosed that for **5e**, the electron transfer occurs the most easily among the biphenylyldioxetanes (**5a-e**) and met the expectation described above. The present results also suggested that the electron transfer in the intermediary anion (**8**) formed from **5** might not occur directly through space from the anionic oxygen to the O-O but through the conjugate system of two aromatic rings; if the electron transfer occurs from the anionic oxygen through space, the *para-para* isomer (**5e**), bearing the phenolic oxygen the most remote from the dioxetane, would give the longest duration of the luminescence among **5**.

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16. These chemiluminescences are likely due to the excited ester anions (**8a-d**), since the spectra of the chemiluminescence from **5a-d** were identical to the fluorescence emission spectra of the corresponding spent reaction mixture.
17. Predicted that the aromatic ring plane is in the same conformation in respect to the dioxetane ring for **5a-e**; it has been suggested that the conformation of the aromatic ring plane influences the half-life of the luminescence for **7a** and its analogues.[11] There are possibilities that the HOMO electrons at *o,o'*-positions (neighboring carbons to Cα) act together with the electrons at Cα for the electron transfer.
18. A simple π-MO calculation suggested that the HOMO electron density at Cα is in the order; *para-para* (**5e**) >> *meta-meta* (**5c**).

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