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Synthesis of Thermally Stable 1,2-Dioxetanes Bearing a Phenylethenyl or a Phenylethynyl Moiety and their Base-Induced Decomposition

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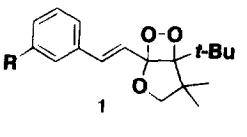
Abstract

Singlet oxygenation of olefins **3** and **6** affords selectively the corresponding 1,2-dioxetanes bearing a phenylethenyl group (**1**) or a phenylethynyl group (**2**), which possess marked thermal stability. Treatment of siloxy-substituted analogs **1b** and **2b** with tetrabutylammonium fluoride in DMSO causes the charge transfer-induced decomposition of the dioxetanes to yield red light.

Keywords: *phenylethenyldioxetane, phenylethynyldioxetane, singlet oxygenation, CIEEL*

High-energy molecules, 1,2-dioxetanes have received considerable attention because of their unique property to decompose thermally to excited carbonyl products, and a wide variety of dioxetanes bearing alkyl and/or aromatic substituents have been synthesized [1,2]. Among them, CIEEL (chemically initiated electron exchange luminescence)-active dioxetanes bearing an aromatic electron donor have been studied extensively from the viewpoints of the design of new efficient chemiluminescent substrates and the mechanistic studies on bioluminescence [3-6]. On the other hand, there have been only several reports on dioxetanes bearing an olefinic moiety, which are in general unstable thermally [7-12] except a rather special tetracyclic dioxetane [13], and little has been known of dioxetanes bearing an acetylenic functionality, though both olefinic and acetylenic π-systems attached to a dioxetane would become also a promising electron donor as well as a fluorophore for CIEEL. These facts prompted us to synthesize thermally stable dioxetanes bearing a phenylethenyl (**1**) or phenylethynyl moiety (**2**) and to examine their base-induced decomposition.



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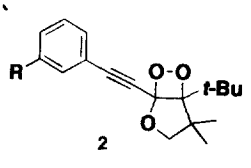

2

a: R = H
b: R = t-BuMe$_2$SiO-

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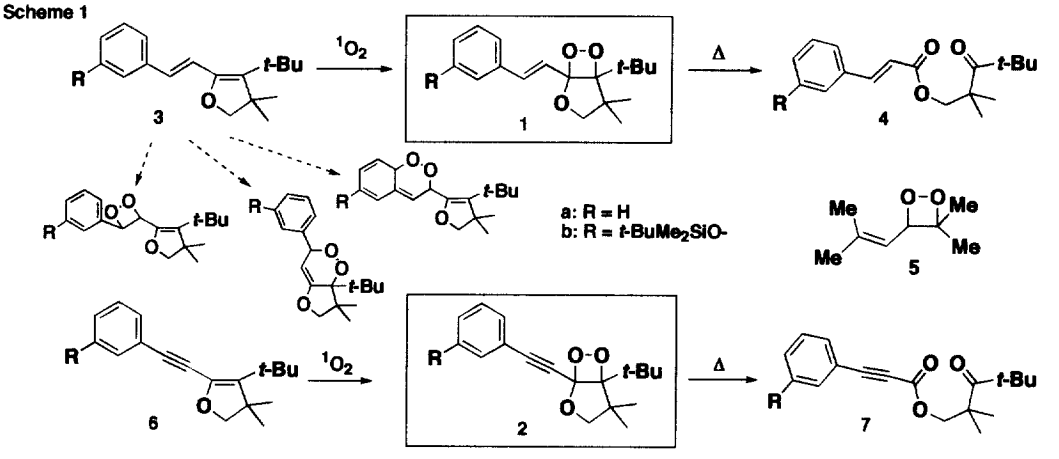
When a solution of a phenylethenyl (styryl)-substituted dihydrofuran **3a** (100 mg)[1] in CH_2Cl_2 (10 mL) was irradiated in the presence of Rose Bengal supported on SiO_2 with a Na-lamp (940 W) under an oxygen atmosphere at -78 °C for 1h, a dioxetane **1a** was produced selectively and was isolated by chromatographic purification (SiO_2 / hexane - AcOEt; 20 : 1) as a pale yellow oil in 76 % yield.[2] It is noteworthy that none of the primary oxygenation products nor the secondary products derived from them other than **1a** was observed, though **3a** is formally capable of undergoing 1,4-addition of singlet oxygen to a conjugated diene system(s) and 1,2-addition to a styryl double bond as illustrated in scheme 1. A dioxetane **1a** decomposed exclusively to a ketoester **4a** by a first-order process in hot toluene. To know its thermal stability, decomposition rates of **1a** were measured in toluene-d_8 at 70 - 100 °C by ^{1}HNMR, and activation parameters for the decomposition were estimated from Arrhenius plots: $\Delta H^{\ddagger}$ = 24.1 kcal mol^{-1}, $\Delta S^{\ddagger}$ = -10.3 cal K^{-1}mol^{-1}, $\Delta G^{\ddagger}$ = 27.2 kcal mol^{-1}, half-life $t_{1/2}$ at 25 °C = 0.85 y in toluene-d_8. This result shows that a dioxetane **1a** is very stable thermally and is in marked contrast to a related olefinic dioxetane **5** ($\Delta H^{\ddagger}$ = 21.6 kcal mol^{-1}, $\Delta S^{\ddagger}$ = -7.6 cal K^{-1}mol^{-1}, $\Delta G^{\ddagger}$ = 23.8 kcal mol^{-1}) [8,10].

Scheme 1



Next, we carried out similar singlet oxygenation of a dihydrofuran **6a** bearing a phenylethynyl moiety. The reaction proceeded smoothly to give a dioxetane **2a** (isolated yield: 80 %),[2] which decomposed also to a keto ester **7a** exclusively, though it was far more stable thermally than a styryl analog **1a** (activation parameters for thermal decomposition of **2a** in toluene-d_8: $\Delta H^{\ddagger}$ = 30.6 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 5.2 cal K^{-1}mol^{-1}, $\Delta G^{\ddagger}$ = 29.0 kcal mol^{-1}, $t_{1/2}$ at 25 °C = 17.4 y). It has been known that an easily oxidized substituent, that has low oxidation potential, on a dioxetane ring tends to decrease the thermal persistency of the

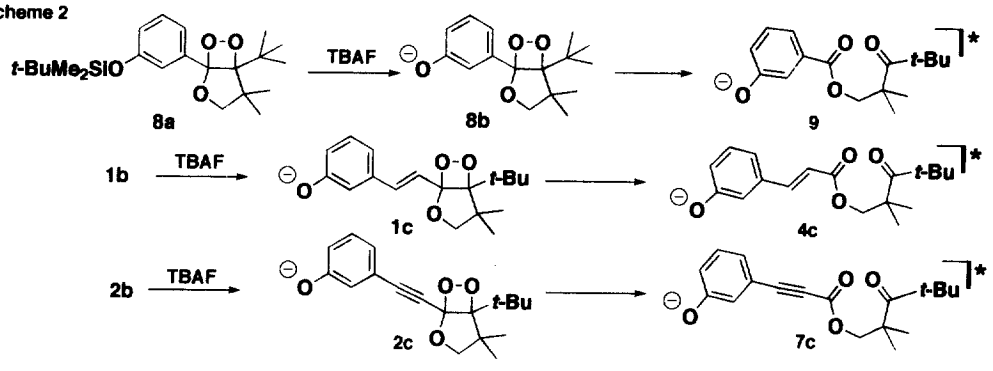
[1] Dihydrofuran **3a** was synthesized from 2,2,4,4-tetramethyl-9-phenyl-6-oxa-8-nonen-3-one by a modification of base-induced cyclization of 2,2,4,4-tetramethyl-7-phenyl-6-oxa-3-heptanone [14]. Dihydrofurans **3b** and **6** were similarly synthesized.

[2] All the dioxetanes synthesized here gave satisfactory spectral data. Selected data for **1a**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.22 (s, 9H), 1.25 (s, 3H), 3.74 (d, J = 8.3 Hz, 1H), 4.54 (d, J = 8.3 Hz, 1H), 6.37 (d, J = 16.1 Hz, 1H), 6.98 (d, J = 16.1 Hz, 1H), 7.28 - 7.38 (m, 3H), 7.42 - 7.46 (m, 2H) ppm. ^{13}CNMR (100 MHz, $CDCl_3$) δ 18.0, 24.8, 27.0, 36.7, 45.7, 80.2, 105.0, 115.3, 123.4, 127.1, 128.8, 135.6, 136.0 ppm. Selected data for **2a**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.28 (s, 3H), 1.39 (s, 9H), 3.79 (d, J = 7.8 Hz, 1H), 4.54 (d, J = 7.8 Hz, 1H), 7.32 - 7.42 (m, 3H), 7.49 - 7.52 (m, 2H) ppm. ^{13}CNMR (100 MHz, $CDCl_3$) δ 17.8, 24.7, 26.4, 29.7, 36.3, 45.6, 81.3, 81.9, 91.7, 105.0, 107.1, 120.9, 128.5, 129.6, 131.8, 132.0 ppm.

dioxetane [15-17], while the steric interaction between *geminal* substituents of a dioxetane (3,3-steric interaction) serves to stabilize the dioxetane ring [18]. Comparing dioxetanes **1a** and **2a** with each other, the oxidation half-wave potential of styrene ($E_{1/2}$ = 1.99 - 2.05 V)[1] as a parent skeleton of a styryl is lower than that of phenylacetylene ($E_{1/2}$ = 2.12 - 2.30 V)[1] as a parent skeleton of a phenylethynyl [19], while the 3,3-steric interaction of a styryl for **1a** should be larger than that of a phenylethynyl group for **2a**.[2] Thus, the difference in thermal stability between **1a** and **2a** is mainly attributed to the difference in the electronic but not in the steric factor(s) of an unsaturated substituent attached to the 1-position of 2,6,7-trioxabicyclo[3.2.0]heptane skeleton.

The fact that singlet oxygenation of **3a** and **6a** affords selectively the corresponding dioxetanes **1a** and **2a**, which possess marked thermal stability, encouraged us to synthesize their CIEEL-active analogs having a *tert*-butyldimethylsiloxy group on a phenyl of the styryl or phenylethynyl moiety. The singlet oxygenation of dihydrofurans **3b** and **6b** was carried out similarly to give dioxetanes **1b** (74 %) and **2b** (90 %), respectively. These dioxetanes were also thermally stable enough to handle at room temperature, though they decomposed quantitatively into the corresponding ketoesters **4b** and **7b** on heating in toluene-d8 (**1b**: $\Delta H^{\ddagger}$ = 26.8 kcal mol^{-1}, $\Delta S^{\ddagger}$ = -2.8 cal K^{-1}mol^{-1}, $\Delta G^{\ddagger}$ = 27.6 kcal mol^{-1}, **2b**: $\Delta H^{\ddagger}$ = 32.7 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 11.1 cal K^{-1}mol^{-1}, $\Delta G^{\ddagger}$ = 29.4 kcal mol^{-1}).

Scheme 2



A dioxetane **8a** bearing a *m*-siloxyphenyl joined directly to the 4-membered ring decomposes through an unstable dioxetane **8b** having a *m*-oxyphenyl anion to give a ketoester **9** with luminescence (blue light, λ_{max} = 467 nm, $t_{1/2}$ = 6.7 s) by removing the silyl group with tetrabutylammonium fluoride (TBAF) in DMSO [21]. When a solution of styryldioxetane **1b** in DMSO (1 x 10^{-4} M, 1 mL) was treated with a solution of TBAF in DMSO (1 x 10^{-1} M, 2 mL) at 25 °C, **1b** decomposed with emission of glow red light (λ_{max} = 644 nm, $t_{1/2}$ = 2,940 s, Φ_{CL} = 2.6 x 10^{-4}). From the spent reaction mixture, an *E*-cinnamate **4c** was obtained with little amount of its *Z*-isomer. The results show that a) even a 2-(3-

1 Solvent system: CH_3CN, Et_4NClO_4, reference electrode: Ag / AgCl, working electrode: Pt [19].

2 A steric interaction between *vicinal* substituents (3,4-steric interaction) of a dioxetane should be related to the stability of a dioxetane to some extent; the phenomenon suggesting such interaction has been observed [20]. The 3,4-steric interaction would be also larger for **1a** than for **2a**.

oxypheny)ethenyl anion acts as an electron donor for the CIEEL-type decomposition of a dioxetane, though the rate is far slower than that of **8a**, and b) the emission of a far longer wavelength-light than for **8a** is exactly attained by expanding the π-conjugate system of a *m*-oxyphenyl anion through a carbon-carbon double bond.

A dioxetane bearing a phenylethynyl group **2b** decomposed to emit weak flash red light (λ_{max} = 630 nm, $t_{1/2}$ = 0.2 s, Φ_{CL} = 3.0 x 10^{-7}), when **2b** was treated similarly with TBAF in DMSO. This result shows that an oxyphenylethynyl anion acts also as an electron donor,[1] though the F^--induced decomposition of **1b** afforded a complex mixture, including an expected ketoester **7c** (23 %)[2] and other products whose structure could not be determined at present.

In conclusion, the present studies show that thermally persistent dioxetanes bearing an olefinic or acetylenic functionality can be realized and both oxyphenylethenyl and oxyphenylethynyl anions act as an electron donor for CT-induced decomposition of dioxetanes to emit red light.

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[1] The rate of intramolecular CT-induced decomposition of a dioxetane has been suggested to be affected by the conformation of an electron donor [20, 22]. Significant difference in chemiluminescent half-life between **1b** and **2b** is likely attributed to the difference in ease of rotation of a styryl or a phenylethynyl as an electron donor to the conformation favorable for the CT; a phenylethynyl would rotate freely for **2b**, while barrier(s) would exist for the rotation of a styryl of **1b**.

[2] Selected data for **7c**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 1.28 (s, 9H), 1.35 (s, 6H), 4.29 (s, 2H), 4.95 (s, 1H), 6.93 (dd, J = 7.8 and 2.0 Hz, 1H), 7.02 (t, J = 2.0 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H) ppm. Selected data for **4c**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 1.28 (s, 9H), 1.34 (s, 6H), 4.29 (s, 2H), 4.82 (s, 1H), 6.35 (d, J = 16.0 Hz, 1H), 6.86 (dd, J = 7.8 and 2.5, 1H), 6.97 (t, J = 2.0 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 7.26 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 16.0 Hz, 1H) ppm.