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SYNTHESIS OF 5-(ADAMANTAN-1-YL)-4,4-DIMETHYL-1-(3-OXYPHENYL)-2,6,7-TRIOXABICYCLO[3.2.0]HEPTANES AND THEIR BASE-INDUCED CHEMILUMINESCENT DECOMPOSITION IN LIQUID/SOLID PHASE

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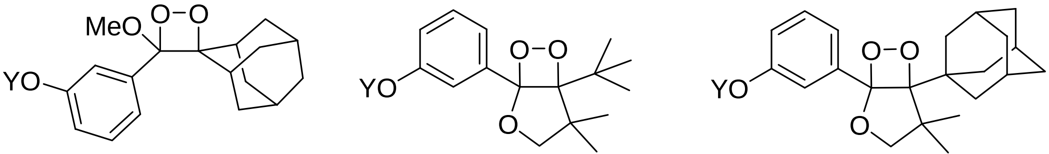
Abstract – Singlet oxygenation of 4-(adamantan-1-yl)-5-(3-hydroxy)phenyl-1,2-dihydrofuran **4a** effectively gave bicyclic dioxetane **3a** as crystals with a high melting point. Dioxetane **3a** decomposed rapidly accompanied by the emission of blue light, when treated with tetrabutylammonium fluoride (TBAF) in DMSO or acetonitrile. The chemiluminescence efficiency for **3a** was as high as those for *tert*-butyl-analog **2**. In addition to chemiluminescent decomposition in a liquid phase, a finely powdered mixture of crystalline **3a** and crystalline dimethylaminopyridine (DMAP) emitted blue light upon heating at 80-110 ºC while maintaining a solid state.

INTRODUCTION

Deprotonation or deprotection of a dioxetane substituted with a phenolic group produces unstable dioxetane bearing an oxidophenyl anion, which decomposes rapidly accompanied by the emission of light by an intramolecular charge-transfer-induced chemiluminescence (CTICL) mechanism.[1-4] For instance, thermally stable dioxetanes, such as 3-oxyphenyl-substituted spiroadamantyldioxetane **1** and 5-*tert*-butyl-4,4-dimethyl-1-(3-oxyphenyl)-2,6,7-trioxabicylo[3.2.0]heptane **2**, have been reported to undergo base-induced decomposition to give a blue light in an aprotic polar solvent (Figure 1).[1,5-8] This phenomenon has received considerable attention in terms of its relation to bioluminescence and its possible application to high-performance biological analysis.[2,3] In the course of our investigation of chemiluminescence from dioxetanes, we attempted, from the perspective of topochemistry, to realize a new type of dioxetane that undergoes CTICL decomposition in a solid phase. We report here that adamantyl-analog **3a** of bicyclic dioxetanes **2** was successfully synthesized as a chemiluminescent substrate with a high melting point, and **3a** underwent fluoride ion-iuduced CTICL decomposition to give light with high efficiency in a liquid phase, and also report a preliminary result that CTICL of **3a** took place even in a solid state, including a crystalline base.



1a: Y = H
1b: Y = *t*-BuMe$_2$Si-
1c: Y = Na$_2$O$_2$(O)P$^-$

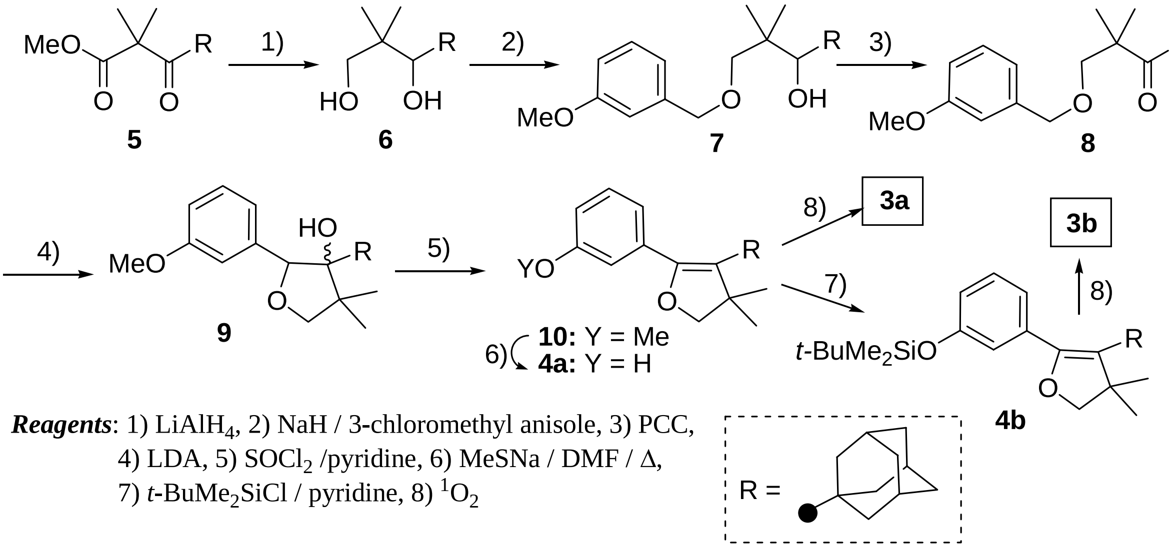
2a: Y = H
2b: Y = *t*-BuMe$_2$Si-
2c: Y = Na$_2$O$_2$(O)P$^-$

3a: Y = H
3b: Y = *t*-BuMe$_2$Si-

Figure 1. Adamantylidenedioxetanes **1** and bicylic dioxetanes bearing a *tert*-butyl group **2** or adamantan-1-yl group **3**.

RESULTS AND DISCUSSION

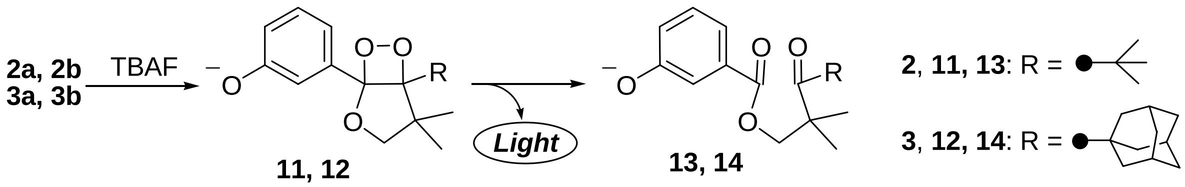
Dioxetanes **3a** and **3b** were effectively synthesized by singlet oxygenation of the corresponding 4-(adamantan-1-yl)-5-(3-oxypheny)-3,3-dimethyl-2,3-dihydrofurans **4a** and **4b**, respectively. Precursor **4a** was synthesized from 1-(adamantan-1-yl)-2,2-dimethylpropan-1,3-diol (**6**) in several steps, as illustrated in Scheme 1. Diol **6** was prepared by LiAlH$_4$-reduction of keto ester **5**, which was easily synthesized by the Claisen condensation of adamantane-1-carboxylic acid chloride with enolate anion of methyl isobutyrate. Williamson reaction of diol **6** with 3-(chloromethyl)anisole gave hydroxy ether **7** in 95 % yield. Oxidation of a hydroxyl group in **7** with PCC (pyridinium chlorochromate) afforded ketone **8** in 97 % yield. LDA (lithium diisopropylamide) mediated the intramolecular cyclization of **8** to give tetrahydrofuran **9**, which was in turn dehydrated with SOCl$_2$ / pyridine to afford dihydrofuran **10** in 93 % yield. The desired precursor **4a** was obtained effectively from **10** by demethylation with MeSNa in hot DMF. Silylation of **4a** with *tert*-butyldimethylsilyl chloride gave dihydrofuran **4b**.



Reagents: 1) LiAlH$_4$, 2) NaH / 3-chloromethyl anisole, 3) PCC, 4) LDA, 5) SOCl$_2$ /pyridine, 6) MeSNa / DMF / Δ, 7) *t*-BuMe$_2$SiCl / pyridine, 8) $^1O_2$

Scheme 1. Synthesis of dioxetanes **3a** and **3b**

Dioxetane **3a** with adamantyl and 3-hydroxyphenyl groups was thus synthesized as a crystalline solid with a high melting point, while its siloxyphenyl-analog **3b** was a viscous oily compound. We first examined their chemiluminescent decomposition in a liquid phase to know whether they could emit light as effectively as the parent dioxetanes **2a**, **2b**. Both the hydroxyphenyl and *tert*-butyldimethylsiloxyphenyl groups are easily deprotonated or desilylated with tetrabutylammonium fluoride (TBAF) to give an oxidophenyl anion in an aprotic solvent such as DMSO or acetonitrile. Thus, dioxetanes **2a** and **2b** undergo chemiluminescent decomposition induced by TBAF through dioxetanes bearing an oxidophenyl anion **11** to give keto ester **13** accompanied by light emission. It has been reported for such TBAF-induced decomposition that the rate follows pseudo-first-order kinetics independent of the TBAF concentration when a large excess of fluoride ion is used.[5] Therefore, we used a large excess of TBAF to simplify the analysis of the decomposition of **3a** and **3b**, which proceeded through intermediary dioxetane **12** to give keto ester **14** in the excited state. When a solution of dioxetane **3a** in DMSO (1.0 x 10^{-5} mol cm^{-3}, 1 mL) was added to a TBAF solution in DMSO (1.0 x 10^{-2} mol cm^{-3}, 2 mL) at 25 °C, **3a** emitted blue light with maximum wavelength λ_{max} = 466 nm, chemiluminescence efficiency Φ^{CTICL} = 0.27, and CTICL rate constant of decomposition k^{CTICL} = 0.10 s^{-1} (half-life, $t_{1/2}$ = 7.0 s) (Scheme 2) (Figure 3, (a)). Siloxyphenyl-analog **3b** showed chemiluminescence with $\lambda_{max}{}^{CTICL}$, Φ^{CTICL}, and k^{CTICL}, which were practically the same as those for **3a**. These results are summarized in Table 1, which shows the chemiluminescence properties of related dioxetanes **2b** and their isopropyl-analog **15** (Figure 2, see also Experimental),[8] which was synthesized similarly to **3a** starting from neopentyl glycol instead of **6** and obtained as an oily compound.



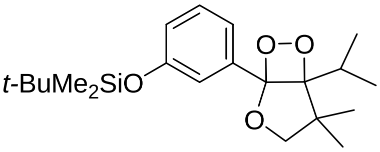
Scheme 2. TBAF-induced chemiluminescent decomposition of **2** and **3.**

Table 1. TBAF-Induced chemiluminescent decomposition of bicyclic dioxetanes.

	DMSO				Acetonitrile			
	$\lambda_{max}{}^{CTICL}$ / nm	Φ^{CTICL}	k^{CTICL} / s^{-1}	$t_{1/2}$ / s	$\lambda_{max}{}^{CTICL}$ / nm	Φ^{CTICL}	k^{CTICL} / s^{-1}	$t_{1/2}$ / s
3a	466	0.27	0.10	7.0	467	0.11	2.9x10^{-2}	23
3b	466	0.26	0.11	6.9	467	0.11	3.6x10^{-2}	19
2b	466	0.27	0.28	4.5	467	0.10	3.6x10^{-2}	19
15	466	0.24	0.29	2.4	467	0.09	5.8x10^{-2}	12

a)All reactions were carried out at 25 ºC. b)Chemiluminescence efficiencies Φ^{CTICL} were estimated based on the value for 3-adamantylidene-4-methoxy-4-(3-*tert*-butyldimethylsiloxy)-phenyl-1,2-dioxetane.[5] c)Although we reported that Φ^{CTICL} for **2b** was 0.20,[8] a revised value is shown here as a result of careful repeated measurements.

Table 1 reveals that a) all cases, i.e., *tert*-butyl- **2b**, adamantyl- **3a**, **3b**, and isopropyl- **15**, gave the same chemiluminescence spectra with λ_{max} at 466 nm, and b) there was practically no difference in chemiluminescence properties between hydroxyphenyl-analog **3a** and siloxyphenyl-analog **3b**, as expected. When we compared **3** with **2** and **15**, the 5-alkyl substituent did not greatly affect the chemiluminescence efficiency Φ^{CTICL}, though isopropyl-analog **15** gave somewhat lower Φ^{CTICL} than *tert*-butyl and adamantyl-analogs **2** and **3**. On the other hand, the rate of decomposition expressed by k^{CTICL} was considerably slower for adamantyl-analogs **3** than for isopropyl-analogs **15**.



15

Figure 2.

Next, the TBAF-induced chemiluminescent decomposition of dioxetanes **3a**, **3b** and **15** was examined in acetonitrile. The results are summarized in Table 1, and revealed that the structural relationship with chemiluminescence properties in acetonitrile resembled the case in DMSO. On the other hand, both Φ^{CTICL} and k^{CTICL} were considerably decreased in acetonitrile compared to those in DMSO, though λ_{max}^{CTICL} was only slightly different between DMSO and acetonitrile (Figure 3, (a, b)).

Adamantyl-substituted dioxetanes **3a** and **3b** were found to emit light as effectively as *tert*-butyl-analog **2** by the action of TBAF in either DMSO or acetonitrile. Next, we sought to determine whether crystalline dioxetane **3a** could emit light while maintaining a solid state. It should be noted here that the expected product, neutral **14**, after thermolysis of **3a** possessed high melting point 129.5−130.0 ºC. However, crystals of **3a** did not give any observable emission of light upon heating, although melted **3a** gave a weak violet light with λ_{max}^{CTICL} = 430 nm at ca 140 °C (Figure 3, (c)). Thus, we examined the decomposition of crystalline **3a** in the presence of a crystalline organic base, even though strong organic bases such as DBU (diazabicycloundecane) and TMG (tetramethylguanidine) induced the decomposition of **1−3** far less effectively than TBAF in DMSO or acetonitrile at room temperature. The crystalline base selected was DMAP (4-dimethylaminopyridine), which melted at 111-114 °C. When a finely powdered mixture of **3a** and DMAP (molar ratio = 1.0 :1.0) was heated at 80-110 °C, it emitted blue light (λ_{max}^{CTICL} = 463 nm) without melt-down (Figure 3, (d)). A cocrystal of **3a** and DMAP (molar ratio = 1.0 :1.0) also gave blue light (λ_{max}^{CTICL} = 465 nm) upon heating at 80-100 °C (Figure 3, (e)). Although these chemiluminescence spectra were somewhat broader than those in TBAF / DMSO or acetonitrile, their λ_{max}^{CTICL} values coincided with those for the solution system. Thus, the major process leading to the emission of light should be through oxido anion **12**. These results may be the first example of the base-induced chemiluminescent decomposition of dioxetane in a crystalline state, though the chemiluminescence

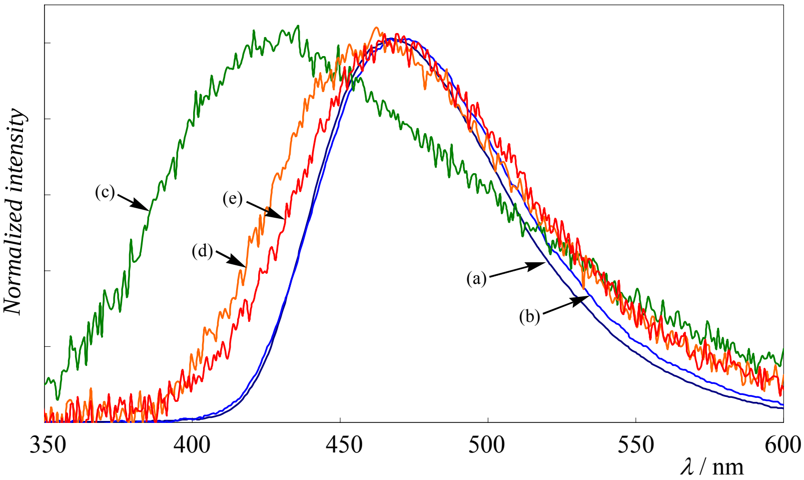


Figure 3. Chemiluminescence spectram of dioxetane **3a**.
(a): TBAF in DMSO solution at 25 °C, (b): TBAF in acetonitrile at 25 °C,
(c): Melted **3a** at 140 °C, (d): Powdered mixture of **3a** and DMAP at 100 °C,
(e): Cocrystal of **3a** and DMAP at 100 °C

efficiencies for these systems could not be estimated at present. It is also intriguing that simple mixing of solid dioxetane **3a** and solid base caused base-induced chemiluminescent decomposition, similar to the case in solution.

CONCLUSION

Bicyclic dioxetanes, 5-(adamantan-1-yl)-4,4-dimethyl-2,6,7-trioxabicylo[3.2.0]heptanes bearing a 3-hydroxyphenyl (**3a**) or 3-*tert*-butyldimethylsiloxyphenyl group (**3b**) at the 1-position were synthesized. Dioxetane **3a** exhibited high melting points, as expected. These dioxetanes underwent TBAF-induced decomposition accompanied by the emission of blue light in DMSO or acetonitrile. Their chemiluminescence efficiencies were as high as those for their *tert*-butyl-analog **2**. In addition to chemiluminescent decomposition in a liquid phase, a finely powdered mixture of crystalline **3a** and crystalline DMAP emitted blue light upon heating at 80−110 ºC without melt-down. Base-induced chemiluminescent decomposition in a crystalline state was also observed for a cocrystal of **3a** and DMAP.

EXPERIMENTAL

Melting points were measured with a Yanako MP-S3 melting point apparatus and were uncorrected. IR spectra were taken on a JASCO FT/IR-300 Fourier transform infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL EX-400 and/or JEOL EPC-500 spectrometers. Mass spectra were obtained by using a JEOL JMS-AX-505H and a JEOL JMS-T-100LC mass spectrometers. Reagents were purchased from Aldrich, Tokyo Chemical Industries, and/or Wako Pure Chemical Industries. Column chromatography was carried out with silica gel, unless otherwise stated.

***Synthesis of 1-(adamantan-1-yl)-2,2-dimethylpropane-1,3-diol* (6).** Butyllithium (1.61 M in hexane, 46.0 mL, 74.1 mmol) was added to a solution of diisopropylamine (12.0 mL, 85.6 mmol) in dry THF (55 mL) at rt under nitrogen atmosphere and stirred for 30 min. To the LDA, solution methyl isobutyrate (7.60 mL, 66.3 mmol) in dry THF (20 mL) was added dropwise over 15 min at –78 °C and stirred for 30 min. To the solution, 1-adamantanecarbonyl chloride (13.0 g, 64.5 mmol) in dry THF (20 mL) was added and stirred for 2 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* to give 17.1 g of crude methyl 3-(adamantan-1-yl)-2,2-dimethyl-3-oxopropionate (**5**) as a pale yellow oil. The crude product **5** was used without further purification for next reaction.

A solution of crude **5** (17.1 g) in dry THF (60 mL) was added to a suspension of $LiAlH_4$ (2.46 g, 64.8 mmol) in dry THF (50 mL) over 30 min under nitrogen atmosphere at 0 °C and stirred at rt for 22 h. To the solution, H_2O was added and stirred for several min. The reaction mixture poured into 3 N aq. HCl and extracted twice with AcOEt. The organic layer was washed with sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a colorless solid. The solid was rinsed with hexane to give 12.3 g of **6** as a colorless solid in 79 % yield. The residue was chromatographed on silica gel with hexane:AcOEt (4:1) to give 1.30g of **6** as a colorless solid in 8 % yield. **6:** colorless needles melted at

134.0-134.5 °C (from AcOEt). ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 1.04 (s, 3H), 1.05 (s, 3H), 1.63-1.83 (m, 12H), 1.95-2.01 (m, 3H), 2.94 (broad s, 1H), 3.07 (s, 1H), 3.40 (d, J = 10.3 Hz, 1H), 3.41 (broad s, 1H), 3.51 (d, J = 10.3 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 21.0, 25.5, 28.6, 37.1, 39.6, 39.7, 40.7, 74.9, 86.0 ppm; IR (KBr): $\tilde{\nu}$ 3370, 2902, 2849, 1043 cm^{-1}; Mass (*m/z*, %): 220 (M$^+$-18, 1), 165 (26), 136 (32), 135 (100); HRMS (ESI): 261.1806, calcd for $C_{15}H_{26}O_2Na$ [M$^+$ + Na] 261.1831.

***Synthesis of 1-(adamantan-1-yl)-3-(3-methoxybenzyl)oxy-2,2-dimethylpropan-1-ol* (7).** 1-(Adamantan-1-yl)-2,2-dimethylpropane-1,3-diol (**6**) (2.50 g, 10.5 mmol) in dry THF (10 mL) was added dropwise over 12 min to a suspension of NaH (60 % in oil, 450 mg, 11.3 mmol) in dry THF (15 mL) at 0 °C under nitrogen atmosphere and stirred for 30 min at rt. A solution of 3-methoxybenzyl chloride (1.5 ml, 10.3 mmol,) in dry DMF (10 mL) was added dropwise over 10 min to the suspension and was stirred for 3 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 with hexane:AcOEt (9:1) to give 3.58 g of **7** as a pale yellow oil in 95 % yield. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 1.04 (s, 3H), 1.10 (s, 3H), 1.63-1.83 (m, 12H), 1.93-1.98 (m, 3H), 3.00 (d, J = 5.6 Hz, 1H), 3.21 (d, J = 5.6 Hz, 1H), 3.23 (d, J = 8.7 Hz, 1H), 3.44 (d, J = 8.7 Hz, 1H), 3.80 (s, 3H), 4.47 (s, 2H), 6.82 (dd, J = 8.2 and 2.5 Hz, 1H), 6.86-6.91 (m, 2H), 7.25 (dd, J = 8.2 and 7.4 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 22.3, 26.1, 28.7, 37.2, 39.6, 39.9, 40.8, 55.1, 73.2, 81.7, 85.1, 112.8, 113.2, 119.7, 129.4, 139.5, 159.7 ppm; IR (liquid film): $\tilde{\nu}$ 3493, 2901, 2849, 1601 cm^{-1}; Mass (*m/z*, %): 358 (M$^+$, 7), 223 (23), 139 (10), 138 (100), 137 (11), 136 (10), 135 (60), 122 (24), 121 (87); HRMS (ESI): 381.2388, calcd for $C_{23}H_{34}O_3Na$ [M$^+$ + Na] 381.2406.

***Synthesis of 1-(adamantan-1-yl)-3-(3-methoxybenzyloxy)-2,2-dimethylpropan-1-one* (8).** A solution of 1-(adamantan-1-yl)-3-(3-methoxybenzyloxy)- 2,2-dimethylpropan-1-ol (**7**) (3.31 g, 9.23 mmol) in CH_2Cl_2 (10 mL) was added to a suspension of PCC (2.5 g, 12 mmol) and Celite (5.0 g) in CH_2Cl_2 (30 mL) at rt and stirred for 16 h. To the reaction mixture 2-propanol (1.4 mL) was added and stirred for 30 min, then Et_2O was added. The reaction mixture was filtered through Celite and concentrated *in vacuo*. The residue was chromatographed on silica gel with Et_2O to give 3.19 g of **8** as a pale yellow oil in 97 % yield. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.27 (s, 6H), 1.64-1.74 (m, 6H), 1.96-2.03 (m, 9H), 3.51 (s, 2H), 3.80 (s, 3H), 4.47 (s, 2H), 6.81 (d with fine coupling, J = 8.3 Hz, 1H), 6.86-6.89 (m, 2H), 7.23 (dd, J = 8.3 and 7.7 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 23.8, 28.3, 36.6, 39.2, 48.8, 50.5, 55.1, 73.0, 77.9, 112.7, 113.1, 119.7, 129.2, 140.1, 159.6, 216.5 ppm; IR (liquid film): $\tilde{\nu}$ 2906, 2851, 1679, 1601 cm^{-1}; Mass (*m/z*, %): 356 (M$^+$, 5), 300 (26), 134 (18), 135 (100), 121 (23); HRMS (ESI): 379.2235, calcd for $C_{23}H_{32}O_3Na$ [M$^+$ + Na] 379.2249.

***Synthesis of 3-(adamantan-1-yl)-3-hydroxy-2-(3-methoxyphenyl)-4,4-dimethyltetrahydrofuran* (9).** Butyllitium (1.61 M in hexane, 10.4 mL, 16.7 mmol) was added to a solution of diisopropylamine (2.60 mL, 18.6 mmol) in dry THF (15 mL) at 0 °C under nitrogen atmosphere and stirred for 30 min. To the LDA solution 1-(adamantan-1-yl)-3-(3-methoxybenzyloxy)-2,2-dimethylpropan-1-one (**8**) (3.00 g, 8.42 mmol) in dry THF (15 mL) was added at –78 °C. The reaction mixture was allowed to warm from –78 °C to rt and stirred for 1 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* to give a colorless solid. The solid was rinsed with hexane to give 2.35 g of 3-(adamantan-1-yl)-3-hydroxy-2-(3-methoxyphenyl)-4,4-dimethyltetrahydrofuran (*trans*-**9**) as a colorless solid in 78 % yield. The residue was chromatographed on silica gel with hexane:AcOEt (9:1) to give 246 mg of *cis*-**9** in 8 % yield as a colorless solid and 320 mg of *trans*-**9** in 11 % yield as a colorless solid.

trans-**9**; colorless plates melted at 127.5-128.5 °C (from CH_2Cl_2-hexane), ^{1}H-NMR (400 MHz, $CDCl_3$):δ_H 1.18 (s, 3H), 1.46 (s, 3H), 1.35-1.93 (m, 15H), 1.99 (s, 1H), 3.65 (d, J = 8.0 Hz 1H), 3.81 (s, 3H), 3.92 (d, J = 8.0 Hz, 1H), 4.96 (s, 1H), 6.80 (d with fine coupling, J = 8.2 Hz, 1H), 7.11-7.16 (m, 2H), 7.21 (dd, J = 8.2 and 7.3 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$):δ_C 22.3, 26.4, 28.5, 36.8, 37.0, 42.2, 47.9, 55.3, 81.5, 88.4, 94.6, 113.1, 114.9, 121.9, 128.5, 143.4, 159.1 ppm; IR (KBr): $\tilde{\nu}$ 3512, 2905, 2847, 1600 cm^{-1}; Mass (m/z, %): 356 (M$^+$, 4), 338 (8), 323 (12), 300 (18), 205 (18), 136 (21), 135 (100); HRMS (ESI): 379.2233, calcd for $C_{23}H_{32}O_3Na$ [M$^+$ + Na] 379.2249.

cis-**9**; colorless needles melted at 85.0-86.0 °C (from CH_2Cl_2-hexane), ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.16 (s, 3H), 1.42 (s, 3H), 1.54-1.78 (m, 12H), 1.87-1.94 (m, 3H), 3.44 (d, J = 7.1 Hz 1H), 3.81 (s, 3H), 4.10 (d, J = 7.1 Hz, 1H), 5.44 (s, 1H), 6.84 (ddd, J = 8.2, 2.6 and 0.9 Hz, 1H), 7.03 (s with fine coupling, 1H), 7.07 (d, J = 7.6 Hz, 1H), 7.26 (dd, J = 8.2 and 7.6 Hz, 1H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 20.3, 26.4, 28.7, 36.9, 37.8, 40.5, 48.3, 55.2, 82.1, 82.8, 84.5, 113.6, 114.4, 121.5, 129.1, 141.9, 159.4 ppm; IR (KBr): $\tilde{\nu}$ 3474, 2905, 2848, 1603 cm^{-1}; Mass (*m/z*, %): 356 (M$^+$, 11), 300 (38), 219 (11), 205 (22), 136 (21), 135 (100); HRMS (ESI): 379.2231, calcd for $C_{23}H_{32}O_3Na$ [M$^+$ + Na] 379.2249.

Synthesis of 4-(adamantan-1-yl)-5-(3-methoxyphenyl)-3,3-dimethyl-2,3-dihydrofuran (**10**). Thionyl chlolide (0.35 mL, 4.80 mmol) was added to a solution of 3-(adamantan-1-yl)-3-hydroxy-2-(3-methoxyphenyl)-4,4-dimethyltetrahydrofuran (*trans*-**9**) (1.32 g, 3.70 mmol) and pyridine (3.0 mL, 37 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C and stirred for 30 min. The reaction mixture was poured into sat. aq. $NaHCO_3$ and then extracted with AcOEt. The organic layer was washed with 2 M HCl and sat. aq. NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on silica gel and eluted with hexane:AcOEt (19:1) to give 1.16 g of **10** as a colorless solid in 93 % yield. **10**: colorless needles melted at 59.0-59.5 °C (from CH_2Cl_2-hexane), ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.35 (s, 6H), 1.52-1.62 (m, 6H), 1.73-1.77 (m, 6H), 1.80-1.87 (m, 3H), 3.81 (s, 3H), 3.83 (s, 2H), 6.82 (s with fine coupling, 1H), 6.85 (dd, J = 8.1 and 2.7 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 7.23 (dd, J = 8.1 and 7.6 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 27.8, 28.7, 35.3, 36.7, 43.1, 47.1, 55.2, 83.1, 113.8, 115.1, 122.4, 126.2, 128.8, 137.7, 150.0, 159.1 ppm; IR (KBr): $\tilde{\nu}$ 2907, 2851, 1651, 1599, 1577 cm^{-1}; Mass (*m/z*, %): 339 (M$^+$+1, 15), 338 (M$^+$, 56), 324 (22), 323 (87), 136 (12), 135 (100); HRMS (ESI): 361.2140, calcd for $C_{23}H_{30}O_2Na$ [M$^+$ + Na] 361.2144.

Synthesis of 4-(adamantan-1-yl)-5-(3-hydroxyphenyl)-3,3-dimethyl-2,3-dihydrofuran (**4a**). Sodium methanethiolate (425 mg, 6.06 mmol) was added to a solution of 4-(adamantan-1-yl)-5-(3-methoxyphenyl)-3,3-dimethyl-2,3-dihydrofuran (**10**) (1.02 g, 3.01 mmol) in dry DMF (10 mL) was added at rt under nitrogen atmosphere and stirred at 140 °C for 2 h. 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 (4:1) to give 901 mg of **4a** as a colorless solid in 92 % yield. **4a**: colorless needles melted at 145.5-147.0 °C (from CH_2Cl_2), ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.34 (s, 6H), 1.52-1.63 (m, 6H), 1.72-1.77 (m, 6H), 1.80-1.87 (m, 3H), 3.82 (s, 2H), 4.68 (s, 1H), 6.75-6.80 (m, 2H), 6.87 (d, J = 7.5 Hz, 1H), 7.19 (dd, J = 7.9 and 7.5 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 27.7, 28.7, 35.3, 36.6, 43.1, 47.0, 82.9, 115.2, 117.0, 122.3, 126.7, 129.0, 137.4, 149.5, 155.1 ppm; IR (KBr): $\tilde{\nu}$ 3366, 2904, 2851, 1651, 1594, 1445 cm^{-1}; Mass (*m/z*, %): 325 (M^++1, 15),324 (M^+, 59), 310 (20), 309 (83), 136 (12), 135 (100), 121 (18), 93 (13); HRMS (ESI): 347.2014, calcd for $C_{22}H_{28}O_2Na$ [M^+ + Na] 347.1987.

***Synthesis of 4-(adamantan-1-yl)-5-[3-(tert-butyldimethylsiloxy)phenyl]-3,3-dimethyl-2,3-dihydrofuran* (4b).** Imidazole (142 mg, 2.09 mmol) and *tert*-butyldimethylsilyl chloride (285 mg, 1.89 mmol) was added to a solution of 4-(adamantan-1-yl)-5-(3-hydroxyphenyl)-3,3-dimethyl-2,3-dihydrofuran (**4a**) (302 mg, 0.931 mmol) in dry DMF (4 mL) under nitrogen atmosphere at rt and stirred for 2 h. 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 (9:1) to give 408 mg of **4b** as a colorless oil in quantative yield. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 0.18 (s, 6H), 0.98 (s, 9H), 1.34 (s, 6H), 1.51-1.62 (m, 6H), 1.71-1.77 (m, 6H), 1.80-1.86 (m, 3H), 3.82 (s, 2H), 6.76 (s with fine coupling, 1H), 6.78 (ddd , J = 8.0, 2.5 and 1.1 Hz, 1H), 6.88 (d with fine coupling, J = 7.6 Hz, 1H), 7.17 (dd , J = 8.0 and 7.6 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 4.4, 18.2, 25.7, 27.8, 28.8, 35.3, 36.7, 43.2, 47.1, 83.1, 119.8, 121.8, 123.1, 126.2, 128.7, 137.8, 150.1, 155.0 ppm; IR (liquid film): $\tilde{\nu}$ 2953, 2925, 2903, 2854, 1593, 1579 cm^{-1}; Mass: *m/z* (%) 439 (M^++1, 34), 438 (M^+, 87), 425 (10), 424 (37), 423 (100), 135 (78); HRMS (ESI): 439.3046, calcd for $C_{28}H_{43}O_2Si$ [M + H^+] 439.3032, 461.2859, calcd for $C_{28}H_{42}O_2SiNa$ [M + Na^+] 461.2852.

Synthesis of 5-(adamantan-1-yl)-1-(3-hydroxyphenyl)-4,4-dimethyl-2,6,7-trioxa-bicyclo[3.2.0]heptane* (3a)**: ***typical procedure. A solution of 5-(3-hydroxyphenyl)-3,3-dimethyl-2,3-dihydrofuran **(4a)** (123 mg, 0.38 mmol) and tetraphenylporphin (TPP) (ca.1 mg) in CH_2Cl_2 (10 mL) was irradiated externally with Na lamp (940 W) under oxygen atmosphere at 0 °C for 1 h. The photolysate was concentrated *in vacuo* and chromatographed on silica gel to give 128 mg of **3a** as a colorless solid in 95 % yield. Similarly to **4a**, dihydrofuran analogs were oxygenated to give the corresponding bicyclic dioxetanes **3b** in 99 % yield. **3a:** colorless needles melted at 123.0-123.5 °C (from CH_2Cl_2-hexane), ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.15 (s, 3H), 1.43 (s, 3H), 1.42-1.60 (m, 6H), 1.75-1.89 (m, 9H), 3.77 (d, J = 8.1 Hz, 1H), 4.55 (d, J = 8.1 Hz, 1H), 4.81 (s, 1H), 6.86 (d with fine coupling, J = 8.1 Hz, 1H), 7.09 (broad s, 1H), 7.20 (broad d, J = 7.8 Hz, 1H), 7.27 (dd, J = 8.1 and 7.8 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 18.6, 25.1, 28.1, 36.3, 36.7, 39.7, 45.7, 80.4, 104.7, 115.2, 116.4, 116.5, 120.7, 129.0, 137.6, 155.1 ppm; IR (KBr): $\tilde{\nu}$ 3428, 2906, 2850, 1595 cm^{-1}; Mass (*m/z*, %): 356 (M^+, 1), 324 (2), 256 (9), 163 (15), 136 (13), 135 (100), 134 (10), 121 (23). HRMS (ESI): 379.1899, calcd for $C_{22}H_{28}O_4Na$ [M^+ + Na] 379.1885.

3b: a pale yellow oil; ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 0.19 (s, 6H), 0.98 (s, 9H), 1.15 (s, 3H), 1.43 (s, 3H), 1.40-1.60 (m, 6H), 1.77-1.88 (m, 9H), 3.76 (d, J = 8.2 Hz, 1H), 4.55 (d, J = 8.2 Hz, 1H), 6.86 (d with fine coupling, J = 8.2 Hz, 1H), 7.09 (broad s, 1H), 7.16-7.28 (m, 2H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C -4.4, 18.2, 18.6, 25.1, 25.7, 28.1, 36.3, 36.6, 39.6, 45.6, 80.3, 104.4, 116.3, 120.1, 121.3, 121.4, 128.8, 137., 155.3 ppm. IR (liquid film): $\tilde{\nu}$ 2949, 2905, 2853, 1602, 1586 cm^{-1}; Mass (*m/z*, %): 470 (M^+, 0.2), 438 (8), 415 (12), 414 (35), 358 (17), 357 (51), 329 (11), 236 (10), 235 (47), 136 (13), 135

(100); HRMS (ESI): 493.2750, calcd for $C_{28}H_{42}O_4SiNa$ [M + Na^+] 493.2750.

***1-(3-Hydroxyphenyl)-5-isopropyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptane*(15):**

Similarly to the case of **3a**, **15** was synthesized from 4-isopropyl-analog of dihydrofuran **4a** as pale yellow oil in 90 % yield. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 0.75 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 1.16 (s, 3H), 1.23 (s with fine coupling, 3H), 2.18-2.29 (m, 1H), 3.87 (d, *J* = 8.3 Hz, 1H), 4.56 (d with fine coupling, *J* = 8.3 Hz, 1H), 5.19 (broad s, 1H), 6.86 (ddd , *J* = 8.1, 2.6 and 1.0 Hz, 1H), 7.05 (dd , *J* = 2.6 and 1.6 Hz, 1H), 7.12 (d with fine coupling, *J* = 7.8 Hz, 1H), 7.28 (dd , *J* = 8.1 and 7.8 Hz, 1H) ppm. ^{13}C-NMR (125 MHz, $CDCl_3$):δ_C 17.1 (CH_3 x 2), 17.5 (CH_3), 22.6 (CH_3), 30.2 (CH), 44.3 (C), 79.7 (CH_2), 103.0 (C), 113.8 (CH), 116.3 (C), 116.6 (CH), 119.0 (CH), 129.7 (CH), 137.0 (C), 155.7 (C) ppm. IR (liquid film): $\tilde{\nu}$3426, 2971, 2895, 1594 cm^{-1}. Mass (EI, m/z, %): 264 (M^+, 1), 232 (2), 209 (11), 208 (28), 138 (11), 122 (10), 121 (100), 93 (11), 71 (23), 70 (21). HRMS (ESI): 287.1274, calcd for $C_{15}H_{20}O_4Na$ [M + Na^+] 287.1259.

Chemiluminescence measurement; general procedure

Chemiluminescence was measured using a Hitachi FP-750 spectrometer and/or a Hamamatsu Photonics PMA-11 multi-channel detector.

Liquid phase: A freshly prepared solution of TBAF (1.0 x 10^{-2} mol/L, 2 mL) in solvent was transferred to a quartz cell (10 x 10 x 45 mm). The quartz cell was placed in the spectrometer, which was thermostated with stirring at 25 °C. A solution of the dioxetane in solvent (1.0 x 10^{-4} mol/L–1.0 x 10^{-6} mol/L 1 mL) was added by a syringe and the 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, which has been reported to have a chemiluminescence efficiency, Φ^{CTICL}, of 0.29 and which was used here as a standard.[5]

Solid phase: Dioxetane **3a** (3.6 mg, 0.01 mmol) and *N,N*-dimethylaminopyridine (DMAP) (1.2 mg, 0.01 mmol) were ground together into fine powder in an agate mortar. The finely powdered mixture was loaded in a glass tube (for measurement of m. p., ϕ = ca 1mm, 2 cm). The tube containing the sample was then placed in a melting point apparatus and heated at 80−110 °C, and light emission was monitored by the spectrometer.

A mixture of dioxetane **3a** (35.6 mg, 0.1 mmol) and DMAP (12.2 mg, 0.1 mmol) was dissolved in CH_2Cl_2 and crystallized at low temperature to give ~~a~~ colorless crystals that melted at 104−108 °C. This cocrystal was similarly heated at 80−100 °C, and light emission was monitored.

***Isolation of 3-(adamantan-1-yl)-2,2-dimethyl-3-oxopropyl 3-hydroxybenzoate (neutral 14) from spent reaction mixture after chemiluminescent decomposition of dioxetane* 3a**. 5-(Adamantan-1-yl)-1-(3-hydroxyphenyl)-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptane (**3a**) (50 mg, 0.14 mmol) in dry DMSO (2 mL) was added to a solution of TBAF (1 M in THF, 0.70 mL, 0.70 mmol) in dry DMSO (1 mL) under N_2 atomosphere at rt and stirred for 15 min. During the reaction, blue light emission was observed. 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 to give 50 mg of neutral **14** as a colorless solid in quantitative yield. Dioxetane **3b** was similarly decomposed to give neutral **14** in quantitative yield.

Neutral **14**: colorless columns melted at 129.5-130.0 °C (from AcOEt-hexane). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 1.37 (s, 6H), 1.66-1.77 (m, 6H), 1.99-2.07 (m, 9H), 4.41 (s, 2H), 5.58 (broad s, 1H), 7.05 (ddd , *J* = 8.2, 2.6 and 0.9 Hz, 1H), 7.30 (dd, *J* = 8.2 and 7.7 Hz, 1H), 7.45 (dd , *J* = 2.6 and 1.5 Hz, 1H), 7.54 (d with fine coupling, *J* = 7.7 Hz, 1H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 23.5, 28.2, 36.5, 39.3, 49.0, 49.7, 71.7, 116.3, 120.5, 121.6, 129.7, 131.1, 156.2, 166.4, 216.1 ppm; IR (KBr): $\tilde{\nu}$ 3437, 2958, 2911, 2883, 2855, 1701, 1676, 1602 cm^{-1}; Mass: *m/z* (%) 356 (M$^+$, 1), 163 (11), 136 (13), 135 (100), 121 (28), 93 (11); HRMS (ESI): 379.1898, calcd for $C_{22}H_{28}O_4Na$ [M + Na$^+$] 379.1885.

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