Effect of Intramolecular Hydrogen Bonding on Thermolysis of Dioxetane: Unusual Instability of Bicyclic Dioxetanes Bearing a Hydroxynaphthyl Group with Vicinal Substitution Pattern

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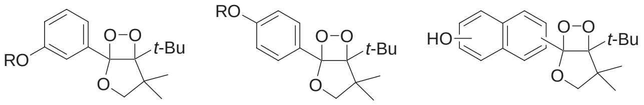
Dioxetanes bearing a 1-hydroxynaphthalen-2-yl group **4(OH)** or 2-hydroxynaphthalen-1-yl group **5(OH)** were found to be significantly unstable thermally in contrast to their methoxynaphthyl-analogs **4(OMe)** and **5(OMe)**. The marked instability of **4(OH)** and **5(OH)** was attributed to the intramolecular hydrogen bonding of a hydroxy group on the naphthalene ring.

Bicyclic dioxetanes bearing a 3-hydroxyphenyl group **1(OH)** or 4-hydroxyphenyl group **2(OH)** are thermally stable like their methoxy-derivatives **1(OMe)** and **2(OMe)**, though they produce by deprotonation unstable dioxetanes bearing an oxidophenyl, which undergo intramolecular charge-transfer-induced chemiluminescence (CTICL).[1–3] Related CTICL-active hydroxynaphthyl-substituted dioxetanes **3** hitherto known are also stable thermally (Figure 1).[4]



1(OH): R = H
1(OMe): R = Me

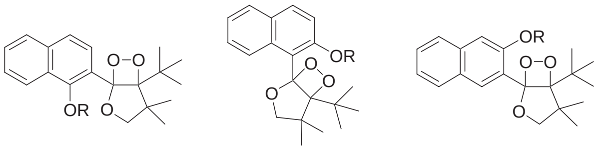
2(OH): R = H
2(OMe): R = Me

3

Figure 1.

In the course of our further investigation of the relationship between the substitution pattern of a hydroxyaryl group and chemiluminescence properties for CTICL of dioxetanes, we attempted to synthesize dioxetanes bearing a 1-hydroxynaphthalen-2-yl group **4(OH)** or 2-hydroxynaphthalen-1-yl group **5(OH)**. Thus, we found that these dioxetanes with a vicinal substitution pattern were very labile thermally beyond our expectation. We report here that unusual thermal instability of dioxetanes bearing a hydroxynaphthyl group is apparently peculiar to those with a vicinal substitution pattern like dioxetanes, **4(OH)** and **5(OH)**, and such phenomenon is attributed to the intramolecular hydrogen bonding of a hydroxy group on the naphthalene ring, based on examination of the thermal stability of their methoxy-analogs **4(OMe)**, **5(OMe)**, and **6(OMe)**, and a hydroxyl-analog **6(OH)** (Figure 2).

Dihydrofuran **7(OH)** bearing a 1-hydroxynaphthalen-2-yl group was irradiated in the presence of tetraphenylporphin (catalytic amount) in toluene-d_8 with Na-lamp under an oxygen atmosphere at −78 °C for 30 min. ^{1}H NMR of the photolysate revealed that dioxetane **4(OH)** was produced exclusively.[5,6] However, dioxetane **4(OH)** was disappointingly unstable thermally even at 25 °C, and 6.5% of **4(OH)** decomposed into keto ester **9(OH)** after 1 h. On the other hand, dioxetane **6(OH)** bearing a naphthalen-2-yl group with a hydroxy at the 3-position but not at the 1-position has been reported to be stable thermally enough to permit handling at room temperature.[4] The significant difference in thermal stability between **4(OH)** and **6(OH)** was thought at first to be attributed to the difference in the oxidation potential between 1-naphthol and 2-naphthol.[2,7,8] Thus, dioxetane **5(OH)** bearing a 2-hydroxynaphthalen-1-yl group was synthesized by the singlet oxygenation of dihydrofuran **8(OH)** similarly to the case of **4(OH)**. Dioxetane **5(OH)** was unstable thermally like **4(OH)**, and 7.3% of dioxetane **5(OH)** decomposed into keto ester **10(OH)** after 1 h at 25 °C (Figure 3). It should be noted here that the ^{1}H NMR spectra (toluene-d_8) of these dioxetanes, **4(OH)** and **5(OH)**, displayed a peak due to a hydroxy proton at δ_H 9.1 and 10.7, respectively.[5] This shows that a hydroxy group would form intramolecular hydrogen bonding with an oxygen of the dihydrofuran ring and/or an oxygen of dioxetane O–O for **4(OH)** and **5(OH)**, since a hydroxy proton not participating in hydrogen bonding displays in general a peak at 4–6 ppm for related hydroxynaphthyldioxetanes.[4] Such intramolecular hydrogen bonding was also observed for dioxetane **6(OH)** (δ_H 7.9), though it was apparently weaker than the cases of **4(OH)** and **5(OH)**.



4(OH) : R = H
4(OMe) : R = Me

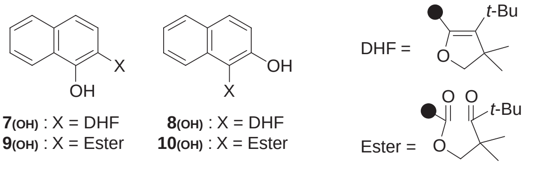
5(OH) : R = H
5(OMe) : R = Me

6(OH) : R = H
6(OMe) : R = Me

Figure 2.

Protection of hydroxy group with methyl for **4(OH)**–**6(OH)** leads to dioxetanes bearing a methoxynaphthyl group, **4(OMe)**–**6(OMe)**, in which no intramolecular hydrogen bonding can be formed. The dioxetanes **4(OMe)**–**6(OMe)**, synthesized from the corresponding dihydrofurans, were quite stable thermally at 25 °C. However, thermal decomposition of these dioxetanes proceeded to give the corresponding keto esters exclusively in *p*-xylene-d_{10} at 120–140 °C. Thus, activation parameters for thermolysis of **4(OMe)**–**6(OMe)** were estimated by Arrhenius plots, the results of which are summarized together with those for dioxetanes **4(OH)**–**6(OH)** in Table 1.

Table 1 reveals that a) methoxynaphthyl-substituted diox-



7(OH) : X = DHF
9(OH) : X = Ester

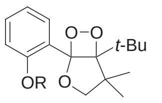
8(OH) : X = DHF
10(OH) : X = Ester

Figure 3.

Table 1. Activation parameters for thermolysis of dioxetanes bearing a hydroxyaryl or methoxyaryl, and chemical shifts of OH proton for dioxetanes bearing a hydroxyaryl

Dioxetane	ΔH /kcal mol^{-1}	$\Delta S^{\ddagger}$ /cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}$ /kcal mol^{-1}	k^{b} /s^{-1}	δ_{H}^{c}
4(OH)	—	—	—	1.8×10^{-5}	9.1
4(OMe)	35.0	9.5	32.2	6.6×10^{-12}	—
5(OH)	—	—	—	2.0×10^{-5}	10.7
5(OMe)	32.1	1.2	31.8	1.2×10^{-11}	—
6(OH)	29.8	1.3	29.5	6.1×10^{-10}	7.9
6(OMe)	33.3	4.1	32.1	7.4×10^{-12}	—
1(OH)	31.5	5.0	30.1	2.2×10^{-10}	3.9
1(OMe)[a]	29.6	−0.1	29.6	4.4×10^{-10}	—
11(OH)	25.2	−9.1	27.9	7.7×10^{-9}	8.1
11(OMe)[a]	28.2	−3.5	31.1	2.5×10^{-11}	—

[a]Ref. 2. [b]Estimated rate constants at 25 °C. [c]In toluene-d_8.



11(OH): R = H
11(OMe): R = Me

Figure 4.

etanes, **4(OMe)** and **5(OMe)**, had marked thermal stability in contrast to hydroxynaphthyl-substituted dioxetanes **4(OH)** and **5(OH)**, and b) only **6(OH)** was stable thermally among three dioxetanes bearing a hydroxynaphthyl group with a vicinal substitution pattern, though it was far less stable than its methoxy-analog **6(OMe)**.

Dioxetane **1(OH)** bearing a 3-hydroxyphenyl group is a typical one in which phenolic hydroxy can not form an intramolecular hydrogen bonding, and has been known to be rather more stable than its methoxy analog **1(OMe)**.[2] On the other hand, dioxetane **11(OH)** bearing a 2-hydroxyphenyl group was capable of forming an intramolecular hydrogen bonding, and was found to be far less stable thermally than its methoxy-analog **11(OMe)** (Table 1). These results suggested strongly that the intramolecular hydrogen bonding acts to destabilize dioxetanes bearing a hydroxyaryl with a vicinal substitution pattern (Figure 4).

The intramolecular hydrogen bonding plays a role not only to fix conformation of the hydroxyaryl ring around the bond joining it to the dioxetane ring but also to make presumably the aromatic ring more negatively charged, thus, more easily oxidized. Therefore, the intramolecular charge-transfer inducing decomposition of dioxetane[8] should occur from the hydroxyaryl to dioxetane far more easily for dioxetanes **4(OH)**–**6(OH)** and **11(OH)** than for the corresponding methoxy-analogs, **4(OMe)**–**6(OMe)** and **11(OMe)**.

Next, we investigated the conformations of dioxetane **4(OH)**–**6(OH)** by the use of NOE technique of ^{1}H NMR. On irradiation of the hydroxy proton at δ_H 7.9, only H_a proton signal increased for dioxetane **6(OH)**. On the other hand, NOE was observed between the hydroxy proton and the *tert*-butyl group but not the H_a nor the H_b proton on the tetrahydrofuran ring for **4(OH)** and **5(OH)**. These results show that a hydroxy group forms hydrogen bonding with an oxygen of the dihydrofuran ring for dioxetane **6(OH)**, while a hydroxy group forms hydrogen bonding with an oxygen of dioxetane O–O for the dioxetanes **4(OH)** and **5(OH)** (Figure 5). Furthermore, when an oxygen of O–O in the dioxetane ring acts as an acceptor of proton for the intramolecular hydrogen bonding for these dioxetanes, the O–O should accept an electron more easily for the intramolecular CT from a hydroxynaphthyl.[9,10] The difference in the proton acceptor, namely, oxygen of the tetrahydrofuran ring or dioxetane O–O, causes most likely the significant difference in thermal stability between **4(OH)**, **5(OH)**, and **6(OH)**, as suggested above.

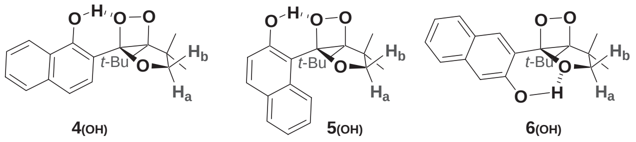


Figure 5.

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References and Notes

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5 ^{1}H NMR (400 MHz, toluene-d_8) for **4(OH)**: δ_H 0.87 (s, 3H), 0.88 (s, 9H), 1.03 (s, 3H), 3.36 (d, $J = 8.5$ Hz, 1H), 4.49 (d, $J = 8.5$ Hz, 1H), 7.19 (d, $J = 8.6$ Hz, 1H), 7.22–7.28 (m, 2H), 7.49 (d with fine coupling, $J = 7.0$ Hz, 1H), 7.71 (broad d, $J = 8.6$ Hz, 1H), 8.54 (d with fine coupling, $J = 7.0$ Hz, 1H), 9.08 (broad s, 1H). ^{1}H NMR (400 MHz, toluene-d_8) for **5(OH)**: δ_H 0.84 (s, 9H), 0.97 (s, 3H), 1.27 (s, 3H), 3.64 (d, $J = 8.8$ Hz, 1H), 4.54 (s, $J = 8.8$ Hz, 1H), 7.08 (d, $J = 9.0$ Hz, 1H), 7.09–7.01 (m, 1H), 7.30 (dd with fine coupling, $J = 8.8$ and 6.8 Hz, 1H), 7.38 (d, $J = 9.0$ Hz, 1H), 7.41 (d, $J = 7.8$ Hz, 1H), 8.51 (d, $J = 8.8$ Hz, 1H), 10.7 (s, 1H).
6 On treatment with tetrabutylammonium fluoride in DMSO, the fresh photolysate gave emission of blue light.
7 It has been reported that a dioxetane bearing an aryl with lower oxidation potential tends to become unstable thermally. For such case, intramolecular charge-transfer-induced decomposition of dioxetane occurs even on simple heating.[2,8]
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9 Catalysts with acidic sites, such as silica gel and alumina, have been reported to accelerate the rate of decomposition of dioxetane.[10]
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