# Thermal decomposition of 1-(aminophenyl)-5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptanes: unusual O–O bond cleavage competing with normal fragmentation of 1,2-dioxetanes

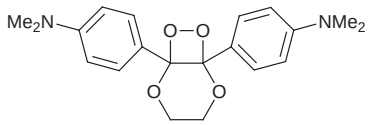
**Masakatsu Matsumoto,* Hiroyuki Murakami and Nobuko Watanabe**

*Department of Materials Science, Kanagawa University, Tsuchiya, Hiratsuka, Kanagawa 259-12, Japan.*
*E-mail: matsumo@info.kanagawa-u.ac.jp*

***Received (in Cambridge, UK) 2nd September 1998, Accepted 21st September 1998***

**A dioxetane (*ortho*-3a) decomposes thermally to give the normal carbonyl product while dioxetanes (*ortho*-3b–c) decompose at low temperature to afford heterocycles 6 and 7 in high yields.**

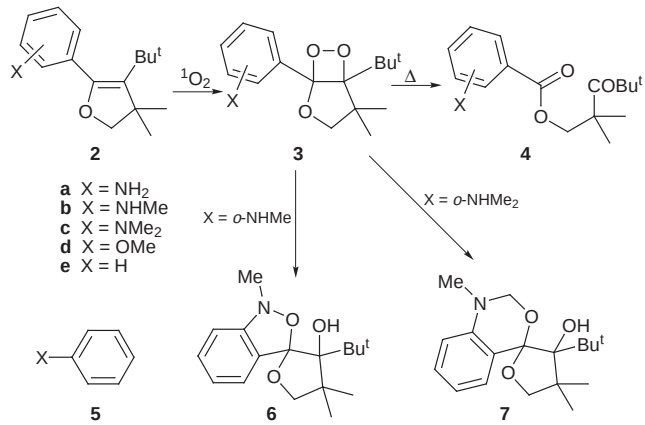
Thermal decomposition of rather simple 1,2-dioxetanes gives in general two carbonyl products.[1] Charge transfer (CT)-induced decomposition of dioxetanes bearing an electron donor also affords two carbonyl fragments, although its mechanistic aspects and accompanying luminescence should be differentiated from those of simple thermolysis.[2–4] A dioxetane



**1**

bearing *p*-(*N*,*N*-dimethylamino)phenyl groups (**1**) is a typical example of species that undergo CT-induced decomposition.[5] In the course of our investigations on highly efficient chemiluminescent substrates, we found that dioxetanes (*ortho*-**3b–c**) bearing a phenyl substituted with an *N*-methylamino or *N*,*N*-dimethylamino group at the *ortho* position suffer unusual decomposition competing with normal fragmentation, although their unsubstituted *o*-amino (*ortho*-**3a**), *p*-amino (*para*-**3**), and *m*-amino analogues (*meta*-**3**) undergo thermal decomposition to afford normal carbonyl products.

When a dihydrofuran (*para*-**2a**) (100 mg) was irradiated in the presence of catalytic amount of tetraphenylporphin (TPP) in $CH_2Cl_2$ (10 ml) with a 940 W Na lamp under $O_2$ atmosphere at 0 °C for 1 h, a dioxetane (*para*-**3a**) bearing a *p*-aminophenyl group† was selectively produced (Scheme 1), although it decomposed considerably during isolation by chromatography ($SiO_2$) (colorless crystals melted at 83.0 °C, 23% yield). Similar singlet oxygenation of dihydrofurans *para*-**2b** and *para*-**2c** gave dioxetanes *para*-**3b** (*N*-methylamino) and *para*-**3c** (*N*,*N*-dimethylamino),‡ respectively. These dioxetanes (*para*-**3a–c**) decomposed *via* a first-order process to afford the corresponding keto esters (*para*-**4a–c**) exclusively in hot toluene-$d_8$. The decomposition rates were measured at various temperatures (70–110 °C) in toluene-$d_8$ and activation parameters for thermolysis of *para*-**3a–c** were estimated as shown in Table 1, where those for dioxetanes bearing a *p*-methoxyphenyl (*para*-**3d**) and a phenyl moiety (**3e**), which were synthesized similarly, are also cited. Table 1 discloses that (i) the thermal susceptibility of *p*-amino derivatives (*para*-**3a–c**) is prominent, (ii) the order of half-life ($t_{1/2}$) (at 25 °C) is *para*-**3c** < *para*-**3b** < *para*-**3a** << *para*-**3d** < **3e**, and (iii) this order is in good agreement with the order of formal oxidation potential of the parent arenes (**5**) corresponding to dioxetanes (*para*-**3a–e**): **5c** < **5b** < **5a** << **5d** < **5e**.[6] These results are consistent with a report on **1** by Schaap[5] and show that CT-induced decomposition takes place most likely for a dioxetane bearing an aryl moiety with low oxidation potential. However, it should be noted that these marked differences in rates of thermal decomposition of *para*-**3** were not observed for *meta*-analogues (*meta*-**3a**, *meta*-**3d**,[7] **3e**): even *meta*-**3a** is very persistent thermally, as shown in Table 1.



**Scheme 1**

These facts prompted us to next examine thermolysis of *ortho*-analogues of **3a–c**.

An *o*-aminophenyl moiety was first expected to induce decomposition of dioxetanes (*ortho*-**3a–c**) into **4** similarly to *para*-**3a–c**. A dioxetane bearing an *o*-aminophenyl moiety (*ortho*-**3a**) was synthesized from a dihydrofuran (*ortho*-**2a**) similarly to the case of *para*-**3a** (62% isolated yield). Dioxetane (*ortho*-**3a**) was as unexpectedly stable as its *meta*-analogue (*meta*-**3a**), although it decomposed into the normal product (*ortho*-**4a**) exclusively on heating (see Table 1). The result suggests that the CT from an *o*-aminophenyl moiety most likely occurs far less easily than from a *p*-aminophenyl moiety. The significant difference in ease of CT may be attributed mainly not to electronic factors but to the steric characteristics of the aromatic electron donor: the aryl group for *ortho*-**3a** does not rotate around the C–C bond to the dioxetane ring as freely as that for *para*-**3a** because of steric hindrance by the *o*-amino group.§ This tendency was also observed for the *o*-methoxy derivative (*ortho*-**3d**) which is far more persistent than *para*-**3d**, *meta*-**3d** and the parent dioxetane **3e**.

Singlet oxygenation (−78 °C) of an olefin (*ortho*-**2b**) substituted with an *o*-(*N*-methylamino)phenyl group also gave

**Table 1** Activation parameters for the thermolysis of 1-aryl-5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptanes **3**[a]

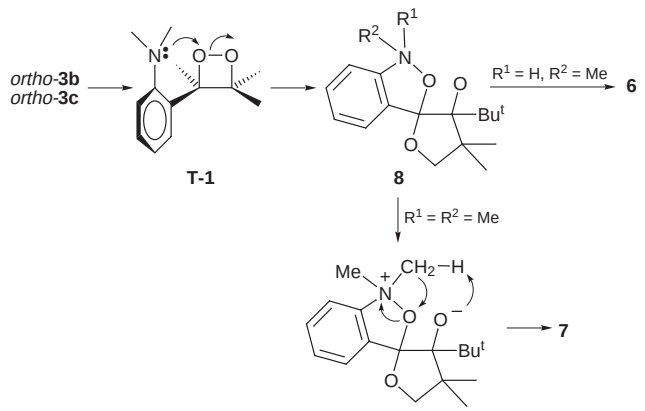
| Dioxetane | $\Delta E_a$/kcal mol$^{-1}$ | log *A* | $t_{1/2}$/years at 25 °C | $E_{1/2}$/V[b] of **5** |
|---|---|---|---|---|
| *para*-**3a** | 28.8 | 12.6 | 4.3 | 0.98 |
| *para*-**3b** | 29.1 | 13.4 | 2.0 | 0.77 |
| *para*-**3c** | 27.7 | 12.5 | 1.4 | 0.73 |
| *para*-**3d** | 30.6 | 13.4 | 27 | 1.76 |
| **3e** | 30.2 | 12.8 | 51 | 2.38 |
| *meta*-**3a** | 29.9 | 12.7 | 33 | |
| *meta*-**3d** | 30.2 | 12.8 | 50 | |
| *ortho*-**3a** | 30.1 | 12.9 | 28 | |
| *ortho*-**3d** | 30.7 | 12.0 | 660 | |

[a] Thermolysis was carried out in toluene-$d_8$ or in *p*-xylene-$d_{10}$. [b] Oxidation half-wave potential (ref. 6); solvent system: $R_4N^+ClO_4^-$. (R = Bu or Pr)/MeCN, reference electrode = SCE, working electrode = Pt.

the corresponding dioxetane (*ortho*-**3b**). The thermal decomposition of *ortho*-**3b** exhibited features completely different from those for the dioxetanes described above. On standing for several hours at room temperature in toluene or $CDCl_3$, *ortho*-**3b** changed into an unusual product (**6**) (pale yellow granules melted at 59.0 °C)† without any detectable amount of the normal product (*ortho*-**4b**) expected initially. Dioxetane *ortho*-**3b** decomposed, however, into *ortho*-**4b** in high yield on heating in refluxing toluene. It should be noted that both products **6** and *ortho*-**4b** are thermally stable and do not change into each other upon heating. Thus, we carried out thermolysis of *ortho*-**3b** at various temperatures in toluene-$d_8$ and measured the product ratio of **6**:*ortho*-**4b**) by 1H NMR spectroscopy: **6**:*ortho*-**4b** = 93:7 at 50 °C, 72:28 at 70 °C, 35:65 at 90 °C, 11:89 at 110 °C. These results suggest that decomposition to *ortho*-**4b** (mode **A**) and unusual decomposition to **6** (mode **B**) take place concurrently in a temperature-dependant manner for dioxetane *ortho*-**3b**.

The decomposition of mode **B** is most likely rationalized by a mechanism similar to the Adam reaction,[9]¶ comprising the intramolecular nucleophilic attack of an *N*-methylamino group at the O–O moiety of the dioxetane and successive O–O bond fission accompanying a proton exchange in an intermediary twitterion (**8**, $R^1$ = H, $R^2$ = Me), as illustrated in Scheme 2. Although the proposed mechanism includes multi-step reactions, the decomposition of *ortho*-**3b** to **6** should be essentially a unimolecular reaction as in the pathway to *ortho*-**4b** (mode **A**). Consequently, the product ratio (**6**/*ortho*-**4b**) described above should be equal to the ratio of rate constants ($k$**B**/$k$**A**) for the corresponding modes at a given temperature. By plotting log(**6**/*ortho*-**4b**) *vs*. 1/$T$, we estimated differences in activation energy $E_a$ and log $A$ between modes **A** and **B** as $\Delta E_a = E_a$ (**A**) − $E_a$ (**B**) = 18.9 kcal mol$^{-1}$ and $\Delta \log A = \log A$ (**A**) − $\log A$ (**B**) = 11.7. The result suggests that the mode **B** requires far a lower activation energy and proceeds through a transition state far more highly ordered than mode **A**. As such in the transition state, one can image a structure where the *o*-aminophenyl moiety lies in or near the plane comprising O–C–C shown as **T-1**.

Finally, we attempted to synthesize a dioxetane (*ortho*-**3c**) bearing an *o*-(*N*,*N*-dimethylamino)phenyl moiety. When singlet oxygenation of a dihydrofuran (*ortho*-**2c**) was carried out similarly to the case of *ortho*-**2a** in $CH_2Cl_2$ at 0 °C, *ortho*-**2c** gave none of the expected dioxetane (*ortho*-**3c**) but gave instead an unprecedented oxygenation product **7** (colorless granules, mp 140.0 °C, 93%)† and a small amount of a keto ester (*ortho*-**4c**) (7%). The low-temperature singlet oxygenation of *ortho*-**2c** gave similar results, so that we could obtain little direct evidence for formation of a dioxetane (*ortho*-**3c**). However, the reaction is reasonably thought to proceed through an unstable dioxetane (*ortho*-**3c**), because both **7** and *ortho*-**4c** are products in which both carbons in the C=C moiety of the starting dihydrofuran (*ortho*-**2c**) are oxygenated. Formation of the unique cyclic aminal **7** is probably attributed to an intramolecular nucleophilic reaction of a dimethylamino group with O–O as in the case of *ortho*-**3b** to **6**; the initially formed zwitterionic intermediate (**8**, $R^1$, $R^2$ = Me) may undergo Stevens-like rearrangement[10] to afford **7** as shown in Scheme 2.¶‖




**Scheme 2**

In conclusion, the present results show that, for dioxetanes bearing a substituted phenyl moiety, a *p*-amino group accelerates significantly decomposition of the dioxetane in the order of H < OMe << $NH_2$ < NHMe < $NMe_2$, while *meta*-analogues are insensitive to this substituent effect. On the other hand, *o*-methylamino and *o*-dimethylamino groups cause preferentially unusual decomposition of dioxetane by their intramolecular nucleophilic attack at O–O of the dioxetane, though their unsubstituted amino analogue decomposes to give the normal carbonyl product.

## Notes and references

† Structures of all products obtained here were characterized by $^1$H NMR , $^{13}$C NMR, IR, and mass spectral analysis. *Selected data* for **6**: $\delta_H$(400 MHz, $CDCl_3$) 0.92 (s, 9H), 1.22 (s, 3H), 1.54 (s, 3H), 3.14 (s, 3H), 3.72 (qAB, $J$ 7.3, 2H), 4.01 (s, 1H), 6.78 (d, $J$ 7.8, 1H), 7.05 (ddd, $J$ 7.8, 7.3, 1.0, 1H), 7.33 (ddd, $J$ 7.8, 7.3, 1.0, 1H), 7.54 (d, $J$ 7.8, 1H); $\delta_C$(100 MHz, $CDCl_3$) 21.4, 25.7, 28.2, 39.4, 46.7, 47.6, 80.7, 88.4, 110.8, 119.5, 122.3, 127.5, 127.5, 129.8, 151.8. For **7**: $\delta_H$(400 MHz, $CDCl_3$) 0.70 (br s, 9H), 1.19 (s, 3H), 1.50 (s, 3H), 2.86 (s, 3H), 3.73 (qAB, $J$ 7.8, 2H), 4.40 (s, 1H), 4.42 (qAB, $J$ 7.3, 2H), 6.76 (d, $J$ 8.3, 1H), 6.86 (m, 1H), 7.26 (m, 1H), 7.75 (dd, $J$ 7.8, 1.5, 1H); $\delta_C$(100 MHz, $CDCl_3$) 22.7, 26.2, 28.2, 35.1, 40.2, 48.0, 78.5, 79.5, 90.6, 108.0, 112.7, 118.6, 125.2, 129.3, 132.0, 148.9.

‡ Dioxetanes *para*-**3b**,**c** were unstable under the chromatographic conditions, so that the crude *para*-**3b**,**c** including little other than a trace amount of keto ester (*para*-**4b**,**c**) was used without purification for thermolysis.

§ The rate of the CT-induced decomposition of a dioxetane bearing a phenoxide anion as an electron donor has been reported to decrease *via* restriction of rotation of the aromatic ring (ref. 8).

¶ Nucleophilic cleavage of a dioxetane with an aromatic amine is unprecedented, although a *sec*-alkylamine has been reported to cause decomposition of a dioxetane to yield *N*,*N*-dialkyl-*O*-(2-hydroxyethyl)hydroxylamine (Adam reaction) (ref. 9). The possibility cannot be ruled out that the reaction of *ortho*-**3b** to give **6** proceeds by a mechanism including attack of a diradical formed initially by homolytic O–O bond cleavage on an amino group, although *ortho*-**3a** should also give an analogue of **6** by this mechanism. The marked difference in decomposition mode between *ortho*-**3a** and *ortho*-**3b** is most likely attributed to a difference in nucleophilicity between $NH_2$ and NHMe: the order of nucleophilicity would be $NH_2$ < NHMe < $NMe_2$. The thermal instability of *ortho*-**3c** might be also rationalized by the high nucleophilicity of the $NMe_2$ group.

‖ Nucleophilic attack of a *tert*-alkylamine on a dioxetane has been reported to lead only to normal carbonyl products through Grob fragmentation (ref. 11) of an intermediary zwitterion (ref. 9). For an intramolecular reaction as presented here, a zwitterion such as **8** might, however, cause predominantly Stevens-like rearrangement, because an oxy anion would lie so close to a methyl of the ammonium ion ($ON^+Me_2$) that the oxy anion is able to easily abstract a methyl proton. The formation of a minor product (*ortho*-**4c**) may be due to Grob fragmentation of **8** and/or direct decomposition of *ortho*-**3c** as in the case of *para*- and *meta*-**3**.


1 A review: C. R. Saha-Moler and W. Adam, *Four-membered Rings with Two Oxygen Atoms* in *Comprehensive Heterocyclic Chemistry II*, ed. A. Padwa, Pergamon, NY, 1996, vol. 1B, pp. 1041–1082.
2 G. B. Schuster, *Acc. Chem. Res*., 1979, **12**, 366.
3 L. H. Catalani and T. Wilson, *J. Am. Chem. Soc*., 1989, **111**, 2633.
4 F. McCapra, *Mechanism in Chemiluminescence and Bioluminescence-Unfinished Business*, in *Bioluminescence and Chemiluminescence*, ed. J. W. Hastings, L. J. Kricka and P. E. Stanley, Wiley, NY, 1996, pp. 7–15.
5 K. A. Zaklika, T. Kissel, A. L. Thayer, P. A. Burns and A. P. Schaap, *Photochem. Photobiol*., 1979, 30, 35; A. P. Schaap, S. D. Gagnon and K. A. Zaklika, *Tetrahedron Lett*., 1982, **23**, 2943.
6 H. Siegerman, *Oxidation and Reduction Half-Wave Potentials of Organic Compounds*, in *Techniques of Electroorganic Synthesis*, ed. N. L. Weinberg, Wiley, NY, 1975, pp. 667–826.
7 M. Matsumoto, N. Watanabe, N. C. Kasuga, F. Hamada and K. Tadokoro, *Tetrahedron Lett*., 1997, **38**, 2863.
8 M. Matsumoto, N. Watanabe, T. Shiono, H. Suganuma and J. Matsubara, *Tetrahedron Lett.*, 1997, **38**, 5825.
9 W. Adam and M. Heil, *J. Am. Chem. Soc*., 1992, **114**, 5591.
10 S. H. Pine, *Org. React*., 1970, **18**, 403.
11 C. A. Grob, *Angew. Chem., Int. Ed. Engl*., 1969, **8**, 535.


*Communication 8/06823B*