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

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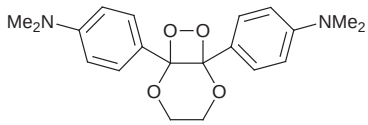
A dioxetane (*ortho*-3a) decomposes thermally to give the normal carbonyl product while dioxetanes (*ortho*-3b–c) decompose at low temperature to afford heterocycles 6 and 7 in high yields.

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



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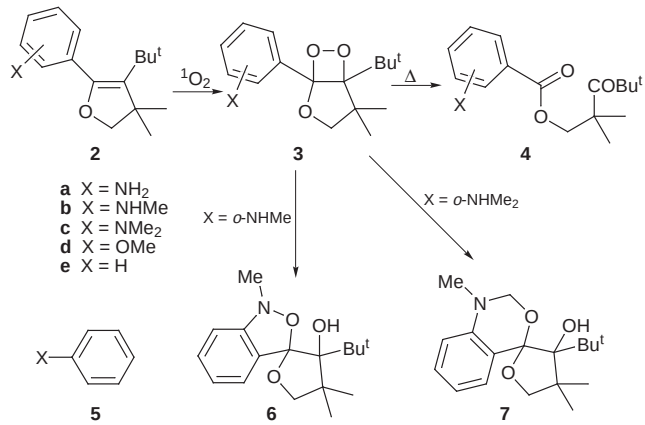
bearing *p*-(*N*,*N*-dimethylamino)phenyl groups (**1**) is a typical example of species that undergo CT-induced decomposition.[5] In the course of our investigations on highly efficient chemiluminescent substrates, we found that dioxetanes (*ortho*-**3b–c**) bearing a phenyl substituted with an *N*-methylamino 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]

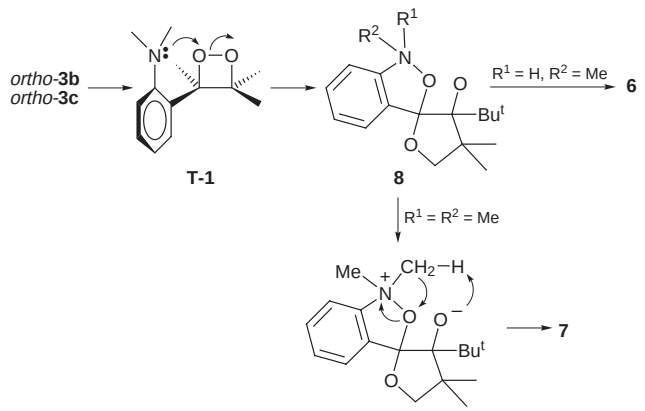
Dioxetane	ΔE_a/kcal mol^{-1}	log *A*	$t_{1/2}$/years at 25 °C	$E_{1/2}$/V[b] of **5**
para-**3a**	28.8	12.6	4.3	0.98
para-**3b**	29.1	13.4	2.0	0.77
para-**3c**	27.7	12.5	1.4	0.73
para-**3d**	30.6	13.4	27	1.76
3e	30.2	12.8	51	2.38
meta-**3a**	29.9	12.7	33	
meta-**3d**	30.2	12.8	50	
ortho-**3a**	30.1	12.9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

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