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Novel Photo-fragmentation of 3,3,6,6-Tetra(*p*-methoxyphenyl)-1,2-dioxane through a C-O Bond Cleaved 1,6-Diradical Intermediate

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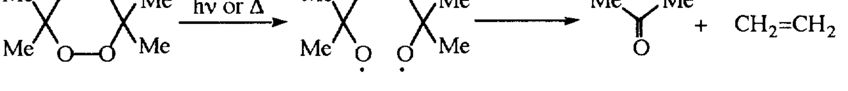
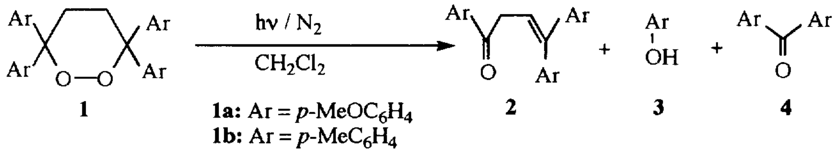
Abstract: Photolysis and thermolysis of 3,3,6,6-tetraaryl-1,2-dioxanes were investigated. The photolysis of 3,3,6,6-tetra(*p*-methoxyphenyl)-1,2-dioxane afforded 1,4,4-tri(*p*-methoxyphenyl)-3-buten-1-one and *p*-methoxyphenol through a novel C-O bond cleaved 1,6-diradical intermediate, while the thermolysis mainly afforded the expected decomposition product 4,4'-dimethoxybenzophenone through an O-O bond cleaved 1,6-dioxy diradical intermediate. Copyright © 1996 Elsevier Science Ltd

Cyclic peroxides have attracted much attention from the synthetic and mechanistic viewpoints.[1] Studies on such compounds are further stimulated by the recent discovery of antimalarial 1,2,4-trioxanes, such as qinghaosu and its derivatives.[2] For example, in the Fe(II)-mediated reduction of qinghaosu and related analogs studied by Posner[3] and Bloodworth[4], the reductive O-O bond cleavage is a key step to promote an oxy radical rearrangement involving 1,5-hydrogen atom transfer. Photolysis and thermolysis are the more common methods to induce O-O bond cleavage of peroxy compounds.[5] Therefore, photo- and thermal reactions of cyclic peroxides are of considerable interest since the atom transfer rearrangements of generated oxy radicals are also expected. About 20 years ago, however, Adam and coworkers reported that both the photolysis and thermolysis of 3,3,6,6-tetramethyl-1,2-dioxane quantitatively produce simple fragmentation products, such as acetone and ethylene, through a 1,6-dioxy diradical (eq 1).[6] Their observations and our experience in the preparation of related cyclic peroxides[7] stimulated us to investigate the reactivities of the dioxy diradical species generated from aryl substituted cyclic peroxides, such as 3,3,6,6-tetraary-1,2-dioxanes **1**, since little is known about the reactivities of aryl substituted 1,2-dioxanes[8] in contrast to those of aliphatic ones.[5] If the reactions of **1** proceed similarly to equation 1, diarylketones and ethylene would be the expected products. However, the photolysis of 3,3,6,6-tetra(*p*-methoxyphenyl)-1,2-dioxane **1a** afforded unprecedented fragmentation products. We now wish to report our preliminary but novel results for the photolysis and thermolysis of **1**.



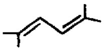
(eq. 1)

Cyclic peroxides **1** were prepared from the corresponding 1,1-diarylethylenes by the modified procedure of literature.[8b, 9] When a nitrogen purged CH_2Cl_2 solution of **1a** (0.20 mmol) was irradiated with a 400 W high pressure Hg lamp in a Pyrex tube for 10 h, 1,4,4-tri(*p*-methoxyphenyl)-3-buten-1-one **2a** (0.132 mmol, 66%) and *p*-methoxyphenol **3a** (0.144 mmol, 72%) were isolated along with a small amount of the expected 4,4'-dimethoxybenzophenone **4a** (0.020 mmol, 10 %) (entry 1 in Table 1).[10] To elucidate the generality of this fragmentation reaction, 3,3,6,6-tetra(*p*-methylphenyl)-1,2-dioxane **1b** was subjected to the photolysis. In contrast to the case of **1a**, 4,4'-dimethylbenzophenone **4b** (15%) was obtained as the major



1a: Ar = p-MeOC$_6$H$_4$
1b: Ar = p-MeC$_6$H$_4$

Table 1. Photolysis of 3,3,6,6-Tetraaryl-1,2-dioxanes **1**.[a]

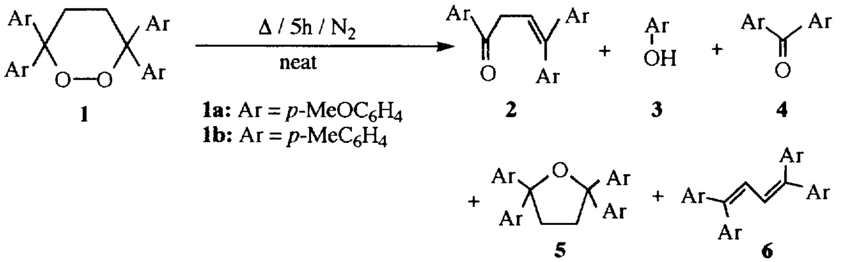
entry	**1**	additive	time/h	conv./ %	yield/%[b]		
					2	**3**	**4**
1	**1a**	none	10	100	66	72	10
2	**1a**	 [c]	10	4	0	0	7
3	**1a**	 [d]	10	14	0	0	9
4	**1b**	none	10	16	0	0	15
5	**1b**	none	20	36	0	0	29

[a] 400W high pressure mercury lamp; Pyrex cut; 20°C; **1** = 0.2 mmol; CH$_2$Cl$_2$ = 10 ml.

[b] Isolated yields by silica gel TLC.

[c] 2,5-Dimethyl-2,4-hexadiene (2.0 mmol); E_T = 58.7 kcal mol^{-1}.

[d] 1,3-Cyclohexadiene (2.0 mmol); E_T = 52.4 kcal mol^{-1}.



1a: Ar = p-MeOC$_6$H$_4$
1b: Ar = p-MeC$_6$H$_4$

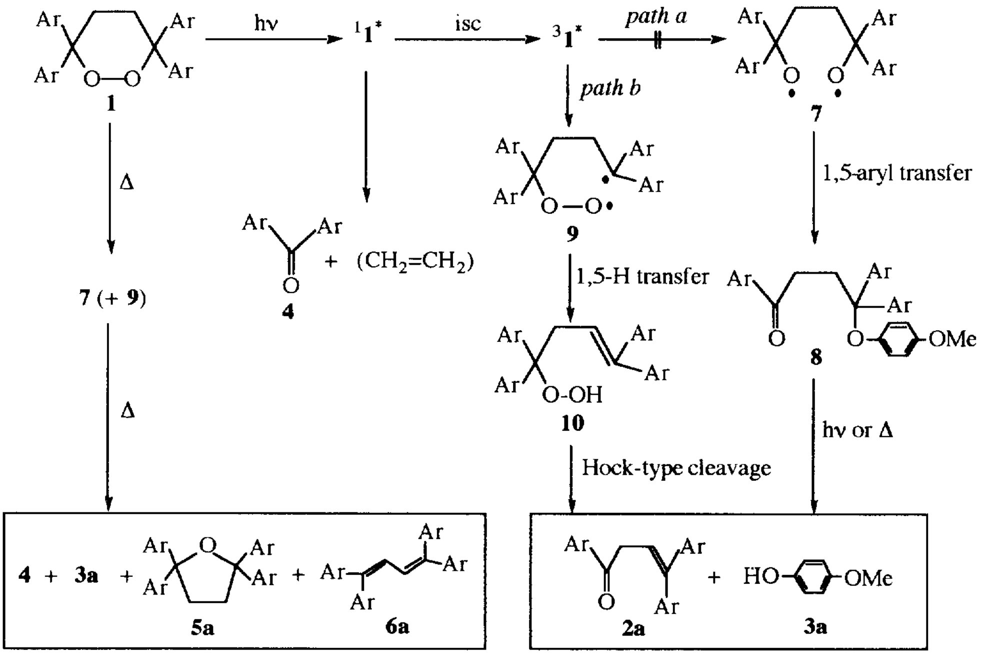
Table 2. Thermolysis of 3,3,6,6-Tetraaryl-1,2-dioxanes **1**.[a]

entry	**1**	temp./°C	conv./ %	yield/%[b]				
				2	**3**	**4**	**5**	**6**
1	**1a**	180	20	0	0	8	0	0
2	**1a**	200	100	0	22	95	9	10
3	**1b**	200	34	0	0	42	0	0

[a] Heated under nitrogen atmosphere; **1** = 0.2 mmol.

[b] Isolated yields by silica gel TLC.

product at low conversion (entry 4). Neither enone **2b** nor *p*-cresol **3b** was obtained even after prolonged irradiation (entry 5). To determine the multiplicity of the responsible excited states, quenching experiments were carried out by using triplet quenchers such as 2,5-dimethyl-2,4-hexadiene and 1,3-cyclohexadiene. The formations of **2a** and **3a** were completely suppressed by the addition of quenchers, while that of **4a** was not significantly affected (entry 2, 3). Triplet sensitization experiments of **1a** and **1b** were also carried out by using a 2 kW Xe lamp (λ>340 nm). While the formations of **2a** and **3a** were significantly accelerated by the addition of benzophenone, **2b** and **3b** were still not obtained. Next, we conducted the thermolysis of **1**. When **1a** was heated at 200°C for 5 h under nitrogen atmosphere, **4a** (95%) and **3a** (22%) were obtained as major products along with small amounts of 2,2,5,5-tetra(*p*-methoxyphenyl)tetrahydrofuran **5a** (9%) and 1,1,4,4-tetra(*p*-methoxyphenyl)-1,3-butadiene **6a** (10%, entry 2 in Table 2).[11] Likewise, the thermolysis of **1b** predominantly produced the ketone **4b** (entry 3).[8] No enones **2** were obtained in either of these reactions. In addition, enone **2a** was found to decompose to complex products under the thermal conditions.



Scheme 1

Based on the above results, we propose a reaction mechanism as shown in Scheme 1. From the results of the triplet quenching and the triplet sensitization experiments, diarylketones **4** could be formed from the excited singlet state of **1**. Two different pathways are plausible for the formation of **2** and **3** from the excited triplet state of **1**. One is the formation of O-O bond cleaved 1,6-dioxy diradical **7**, which undergoes 1,5-aryl transfer to produce keto ether **8**[13] followed by fragmentation to give **2** and **3** (*path a*). The other is the formation of C-O bond cleaved 1,6-diradical **9**, which undergoes 1,5-hydrogen transfer to produce hydroperoxide **10** followed by Hock-type cleavage[2c,14] to afford **2** and **3** (*path b*). Although attempts to isolate the rearranged products **8** and **10** were unsuccessful, 1,4,4-tri(*p*-methoxyphenyl)-4-phenylthiobutanone

11a (68%)[15] and *p*-methoxyphenol **3a** (90%) were produced upon irradiation of **1a** in the presence of thiophenol (10 equiv.). This result indicates that the diradical **9** is involved in the photolysis and is probably responsible for the formation of **2a** (*path b*). The lack of **2b** and **3b** could be attributed to the low efficiency of the intersystem crossing from S1 to T1 in **1b** and the poor formation of the triplet state of **1b**. On the other hand, thermal activation of **1** mainly generates the 1,6-dioxy diradical **7** (partly including **9**). The diradical **7** produces diarylketones **4** and ethylene (not isolated) as major products. Although a concerted mechanism can not be completely excluded for the thermolysis, the isolation of **5a** and **6a** would be more consistent with the intervention of such diradical species.

In summary, we have found that the photolysis of the *p*-methoxyphenyl substituted 1,2-dioxane undergoes the novel fragmentation through the C-O bond cleaved 1,6-diradical. We are conducting further studies on the fragmentation of other cyclic peroxides to elucidate the generality of this novel reaction.

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8. a) The flash vacuum pyrolysis (540°C / 0.01 mmHg) of **1b** has been reported to produce 4,4'-dimethylbenzophenone **4b** (90%) along with 1,1-di(*p*-methylphenyl)ethylene (4%) and ethylene.[8b] b) Haynes, R. K.; Probert, M. K. S.; Wilmot, I. D. *Aust. J. Chem.* **1978**, *31*, 1737-1746.
9. Gollnick, K.; Schnatterer, A. *Tetrahedron Lett.* **1984**, *25*, 185-188; 2735-2738. The UV absorption maxima of **1a** and **1b** in CH_2Cl_2 are 275 nm (ε 7400) and 265 nm (ε 2000), respectively. For each compound the absorption at wavelength greater than 300 nm is decreased significantly. Their extinction coefficients at 325 nm are 32 for **1a** and 7 M^{-1} cm^{-1} for **1b**, respectively.
10. All products were isolated by silica gel TLC and characterized by their spectral data. **2a**: mp 100-101°C (C_2H_5OH), IR ($CHCl_3$) 1675 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.75 (d, 2H, J = 7.2 Hz), 3.77 (s, 3H), 3.82 (s, 6H), 6.25 (t, 1H, J = 7.2 Hz), 6.72-6.96 (m, 6H), 7.06-7.25 (m, 4H), 7.77-7.90 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 39.62 (t), 55.17 (q), 55.38 (q), 113.34 (d), 113.58 (d), 113.65 (d), 119.51 (d), 128.58 (d), 129.64 (s), 130.48 (d), 130.92 (d), 132.02 (s), 135.14 (s), 143.39 (s), 158.72 (s), 158.90 (s), 163.36 (s), 196.93 (s).
11. The structures of **3a**, **4a**, **5a**,[9a] and **6a**[12] were determined by their authentic spectral data.
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13. We have found that 1,3-diaryl-3-hydroxypropanone *p*-methoxyphenyl ethers similar to **8** are obtained in the photolysis of 3-(*p*-methoxyphenyl)-3,5-diaryl-1,2-dioxolanes. The details will be reported elsewhere.
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15. **11a**: IR ($CHCl_3$)1672 cm^{-1}, ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.54 (dd, 2H, J = 7.0 Hz, 5.1 Hz), 2.97 (dd,2H, J = 7.0 Hz, 5.1 Hz), 3.77 (s, 6H), 3.81 (s, 3H), 6.70-7.02 (m, 8H), 7.05-7.14 (m, 2H), 7.15-7.35 (m, 5H), 7.76-7.87 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 33.59 (t), 34.36 (t), 55.10 (q), 55.30 (q), 62.37 (s), 112.94 (d),113.50 (d), 128.18 (d), 128.75 (d), 129.61 (d), 129.95 (s), 130.16 (d), 131.12 (s), 137.08 (d), 137.27 (s), 157.98 (s), 163.25 (s), 198.46 (s).

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