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Novel photo-rearrangement of 1,5-di(*p*-methoxyphenyl)-6,7-dioxabicyclo[3.2.2]nonane through an *O*-neophyl-type 1,2-aryl shift: evidence for a 1,6-dioxyl diradical intermediate

Masaki Kamata* and Ken-ichi Komatsu

Department of Chemistry, Faculty of Education and Human Science, Niigata University, Ikarashi, Niigata 950-2181, Japan

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Abstract—Photolysis and thermolysis of 1,5-diaryl-6,7-dioxabicyclo[3.2.2]nonane **1a–c** (**a**: Ar = *p*-$MeOC_6H_4$, **b**: Ar = *p*-MeC_6H_4, **c**: Ar = Ph) were investigated. (*p*-Methoxyphenyl)-substituted **1a** underwent a novel photo-initiated *O*-neophyl-type 1,2-aryl shift to afford 1-(*p*-methoxyphenyl)oxy-5-(*p*-methoxyphenyl)-8-oxabicyclo[3.2.1]octane **7a** along with a small amount of 1-(*p*-methoxyphenyl)-3-(2-(4′-methoxyphenyl)tetrahydrofuran-2-yl)propan-1-one **4a** through an 1,6-dioxyl diradical intermediate, while the thermolysis mainly afforded the 1,5-di(*p*-methoxyphenyl)pentan-1,5-dione **5a** and 1,4-di(*p*-methoxyphenyl)butan-1,4-dione **8a**.
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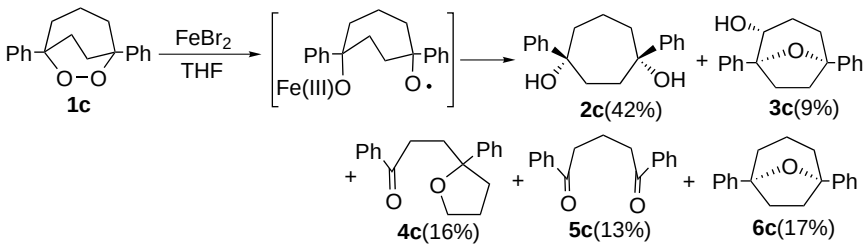
Cyclic peroxides have attracted much attention from synthetic and mechanistic viewpoints.[1–7] In particular, the fragmentation mechanisms for 1,2-dioxolanes and 1,2-dioxanes have been intensively investigated to explore the reactivities of oxyl radical species[8–10] and to clarify potent antimalarial intermediates.[11–15] Posner and co-workers reported that structurally simple and easily prepared 1,5-diaryl-6,7-dioxabicyclo[3.2.2]-nonanes **1a** and **1c** are potent antimalarials.[16,17] They also demonstrated that the reaction of 1,5-diphenyl derivative **1c** with $FeBr_2$, in which the reductive O–O bond cleavage is a key step to promote a mono-oxyl radical rearrangement involving 1,5-hydrogen atom transfer, afforded various rearrangement products and fragmentation products **2c–6c** (Scheme 1).[16,17]

On the other hand, photolysis and thermolysis are the more common methods to induce O–O bond cleavage of peroxy compounds.[18–20] Bloodworth and co-workers reported that structurally simple 6,7-dioxabicyclo[3.2.2]nonane **1d** photochemically and thermally underwent the fragmentation through an O–O bond cleaved 1,6-dioxyl diradical (Scheme 2).[21] In this respect, we reported that photochemical and thermal behaviors of arylated monocyclic peroxides, such as 3,3,5,5-tetraary-1,2-dioxolanes[22] and 3,3,6,6-tetraary-1,2-dioxanes[23] are significantly different from that of the related aliphatic peroxides.[8–10] These contrastive results have strongly prompted us to study the reactivities of 1,6-dioxyl diradical species generated from the 1,5-diaryl-6,7-dioxabicyclo[3.2.2]nonanes **1.** Herein, we



Scheme 1.

* Corresponding author. Tel./fax: +81-25-262-7150; e-mail: kamata@ed.niigata-u.ac.jp

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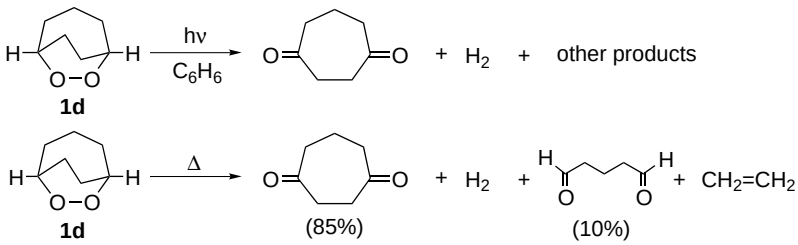
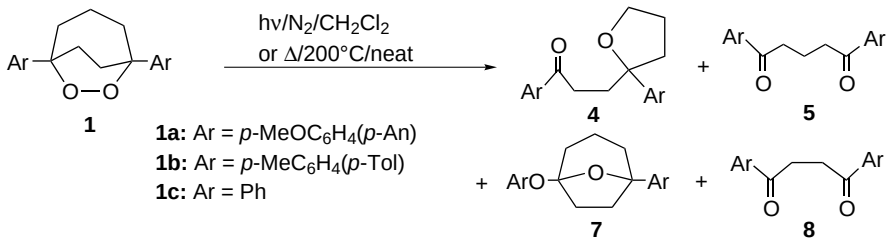


Scheme 2.

wish to report our preliminary but novel results that the 1,6-dioxyl diradical intermediate generated by photolysis of (*p*-methoxyphenyl)-substituted **1a** underwent rearrangement to afford 1-(*p*-methoxyphenyl)oxy-5-(*p*-methoxyphenyl)-8-oxabicyclo[3.2.1]octane **7a** through a novel *O*-neophyl type 1,2-aryl shift.[24†]

When a nitrogen-purged CH_2Cl_2 solution of **1a**[25‡] (0.20 mmol) was irradiated by a 400 W high-pressure Hg lamp in a Pyrex tube for 5 h, novel cyclic acetal **7a** (80%) and 1-(*p*-methoxyphenyl)-3-(2-(4′-methoxyphenyl)tetrahydrofuran-2-yl)propan-1-one **4** (2%) were obtained as rearrangement products along with small amounts of expected fragmentation products, such as 1,5-di(*p*-methoxyphenyl)pentan-1,5-dione **5a** (5%) and 1,4-di(*p*-methoxyphenyl)butan-1,4-dione **8a** (2%, Scheme 3; entry 1 in Table 1).[§] On the other hand, when *p*-methylphenyl derivative **1b** was subjected



Scheme 3.

Table 1. Photolysis of 1,5-diaryl-6,7-dioxabicyclo[3.2.2]nonanes 1[a]

Entry	1	Additive	Time (h)	Conv. (%)	Yield (%)[b]			
					4	5	7	8
1	**1a**	None	5	100	2	5	80	2
2	**1a**	O_2	5	100	<1	<1	82	2
3[c]	**1a**	$Ph_2C{=}O$[d] ($\lambda>340$ nm)	5	100	18	22	32	4
4[c]	**1a**	None ($\lambda>280$ nm)	5	67	<1	3	51	2
5	**1b**	None	10	68	6	13	<1	5
6	**1c**	None	10	74	19	13	0	4

[a] 400 W high-pressure mercury lamp; Pyrex cut (λ>280 nm); 20–24°C; **1** = 0.2 mmol; CH_2Cl_2 = 10 ml.
[b] Isolated yields by silica gel TLC.
[c] 2 kW Xe lamp.
[d] 0.2 mmol; E_T = 69.2 kcal mol^{-1}.

† The first example of an *O*-neophyl-type 1,2-aryl shift has been reported by Workentin who conducted the electrochemical reduction of 9,10-diphenyl-9,10-epidioxyanthracene.

‡ The UV absorption maxima of **1a**–**c** in CH_3CN are 274.5 nm (ε 3500), 270 nm (ε 900), and 257 nm (ε 510), respectively. For each compound the absorption at wavelength greater than 300 nm is decreased significantly. Their extinction coefficients at 313 nm are 64 for **1a**, 23 for **1b**, and 11 M^{-1} cm^{-1} for **1c**, respectively.

§ All products were isolated by silica gel TLC and characterized by their spectral data. The structures **5** and **8** were determined by their authentic spectral data. Selected data for **7a**: mp 109–110°C; IR (KBr, cm^{-1}) 3050, 3020, 2980, 2960, 2890, 2860, 1618, 1590, 1521, 1510. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.52–2.28 (m, 10H), 3.76 (s, 3H), 3.80 (s, 3H), 6.75–6.92 (m, 4H), 7.13–7.24 (m, 2H), 7.28–7.38 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.60 (t, 1C), 32.44 (t, 1C), 34.07 (t, 1C), 34.90 (t, 1C), 37.53 (t, 1C), 55.22 (q, 1C), 55.46 (q, 1C), 84.19 (s, 1C), 109.51 (s, 1C), 113.40 (d, 2C), 113.92 (d, 2C), 123.31 (d, 2C), 125.37 (d, 2C), 138.96 (s, 1C), 147.95 (s, 1C), 155.64 (s, 1C), 158.21 (s, 1C). Anal. C, 74.01; H, 7.11, requires C, 74.09; H, 7.11; MS (EI) 340 (M$^+$, 21), 217 (100), 135 (19), 121 (15). Selected data for **4a**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3050, 3020, 2970, 2950, 2890, 2850, 1675 (C=O), 1603, 1580, 1512; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.71–2.06 (m, 2H), 2.08–2.35 (m, 4H), 2.48–2.67 (m, 1H), 2.95–3.13 (m, 1H), 3.79 (s, 3H), 3.82 (s, 3H), 3.88–4.02 (m, 2H), 6.82–6.92 (m, 4H), 7.28–7.35 (m, 2H), 7.78–7.88 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.53 (t, 1C), 33.59 (t, 1C), 36.38 (t, 1C), 39.32 (t, 1C), 55.14 (q, 1C), 55.32 (q, 1C), 67.57 (t, 1C), 85.81 (s, 1C), 113.42 (d, 4C), 126.26 (d, 2C), 129.97 (s, 1C), 130.17 (d, 2C), 138.04 (s, 1C), 158.07 (s, 1C), 163.12 (s, 1C), 198.99 (s, 1C). Anal. C, 73.81; H, 7.26, requires C, 74.09; H, 7.11; MS (CI) 341 (M$^+$+1, 100).

to the photolysis, only a trace amount of **7b** (<1%) was produced along with **4b** (6%), **5b** (13%), and **8b** (5%) at 68% conversion (entry 5). Likewise, the photolysis of **1c** afforded **4c** (19%), **5c** (13%), and **8c** (4%) at 74% conversion, but **7c** was not produced (entry 6). Diol **2**, hydroxyfuran **3**, and furan **6** were not produced in this study, which is significantly different from the results of the Fe(II)-mediated fragmentation of **1c** (Scheme 1).[16,17]

In order to determine the multiplicity of the responsible excited states, a quenching experiment was carried out by using oxygen as a triplet quencher. The yields of **4a** and **5a** were decreased by the addition of oxygen while those of **7a** and **8a** were not significantly affected (entry 2). A triplet sensitization experiment of **1a** was also carried out by using benzophenone (λ>340 nm). While the yields of **4a** and **5a** were increased, those of **7a** and **8a** were not increased (entry 3, 4). In contrast to the photoreactions, **5a** (58%) and **8a** (13%) were obtained as major products along with small amounts of **4a** (4%) and **7a** (3%) when **1a** was heated at 200°C for 1 h under nitrogen atmosphere (entry 1 in Table 2). Likewise, the thermolysis of **1b** and **1c** afforded similar product distributions (entry 2, 3 in Table 2). No acetals **7b–c** were obtained in either case.

Table 2. Thermolysis of 1,5-diaryl-6,7-dioxabicyclo-[3.2.2]nonanes **1**[a]

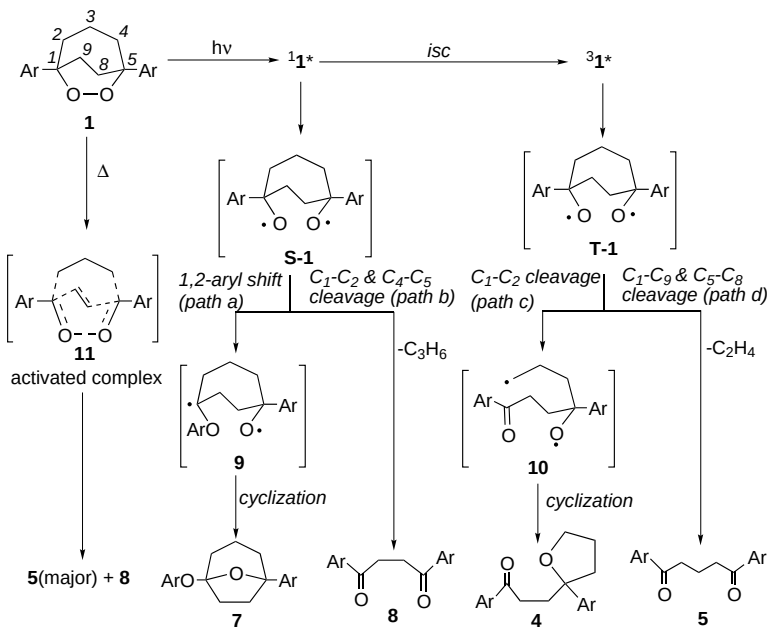
Entry	1	Temp. (°C)	Conv. (%)	Yield (%)[b]			
				4	5	7	8
1	**1a**	200	100	4	58	3	13
2	**1b**	200	87	6	57	0	12
3	**1c**	200	93	5	53	0	10

[a] Heated under nitrogen atmosphere; **1** = 0.2 mmol.
[b] Isolated yields by silica gel TLC.

On the basis of the above results, we propose a plausible mechanism as shown in Scheme 4. From the results of the triplet quenching and the triplet sensitization experiments, acetal **7** and 1,4-diketone **8** are considered to be generated from the singlet 1,6-dioxyl diradical **S-1**. Ketofuran **4** and 1,5-diketone **5** are considered to be generated from the triplet 1,6-dioxyl diradical **T-1**. Two different pathways are plausible for the product formation from **S-1**. One is the formation of the intermediate **9** through an *O*-neophyl type 1,2-aryl shift in **S-1** followed by cyclization to afford actal **7** (*path a*). The 1,2-aryl shift would be promoted by electron-donating aromatic substituents (*p*-An>*p*-Tol>Ph). The other is the formation of 1,4-diketone **8** through simultaneous C_1–C_2 and C_4–C_5 bond cleavages in **S-1** followed by elimination of propene or cyclopropane (*path b*). On the other hand, two different pathways are also plausible for the product formation from **T-1**. One is the formation of the intermediate **10** through the C_1–C_2 bond cleavage in **T-1** followed by cyclization to afford ketofuran **4** (*path c*). The other is the formation of 1,5-diketone **5** through stepwise C_1–C_9 and C_5–C_8 bond cleavages in **T-1** followed by elimination of ethylene (*path d*).

On the contrary, thermolysis of **1** mainly generates the activated complex **11** (partly including an 1,6-dioxyl diradical intermediate).[9,10] The complex **11** affords 1,5-diketone **5** and ethylene (not isolated) through simultaneous O–O, C_1–C_9, and C_5–C_8 bond cleavages, and affords 1,4-diketone **8** and propene (or cyclopropane) via simultaneous O–O, C_1–C_2, and C_4–C_5 bond cleavages. The isolation of acetal **7a** and ketofuran **4** would indicate the intervention of a 1,6-dioxyl diradical species.

In summary, we have found that the photolysis of the *p*-methoxyphenyl substituted [3.2.2]cyclic peroxide **1a**



Scheme 4.

undergoes a novel *O*-neophyl-type 1,2-aryl shift through the O–O bond cleaved 1,6-dioxyl diradical intermediate. We are conducting further studies on the fragmentation of other cyclic peroxides to elucidate the generality of this novel reaction.

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