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ENDOPEROXIDATION OF 9,10-BIS(1-HYDROXYALKYL)-ANTHRACENES AND SUCCESSIVE FORMATION OF 9,10-ANTHRAQUINONE UNDER GRIGNARD REACTION CONDITIONS

Shigeyasu Kuroda,* Mitsunori Oda,* Hir oki Syumiya, Shah M. I. Shaheen, Ryuta Miyatake, Teruhiko Nishikawa, Akiko Yoneda, Tokiko Tanaka, Masaru Mouri, and Mayumi Kyogoku
Department of Applied Chemistry, Faculty of Engineering, Toyama University,
Gofuku 3190, Toyama 930-8555, Japan
E-mail address: kuro@eng.toyama-u.ac.jp

Abstract-The reaction of anthracene-9,10-carboaldehyde with various Grignard reagents under ambient conditions gave 9,10-bis(1-hydroxyalkyl)anthracene-9,10-peroxides and 9,10-anthraquinone as the first example. The endoperoxidation of 9,10-bis(1-hydroxyalkyl)anthracenes was assisted by the lone paired electron of oxygen in the side chain, and the endoperoxides were transformed to anthraquinone by the Grignard reagents.

INTRODUCTION

The endoperoxidation of anthracene and its derivatives by molecular oxygen ($^1O_2$) has been widely and actively investigated from the viewpoint of their utility as synthetic substrates and photosensitizers.[1, 2] The endoperoxides rearranged to various types of compounds under photochemical, ionic, and thermal conditions,[3] though the formation of 9,10-anthraquinone under the Grignard reaction conditions has not been reported so far. During the course of our research on the synthesis of new conjugated aromatic compounds containing an anthracene moiety, we found that the new reactions of anthracene-9,10-carboaldehyde (**1**) with Grignard reagents under ambient conditions gave 9,10-anthraquinone (**4**) along

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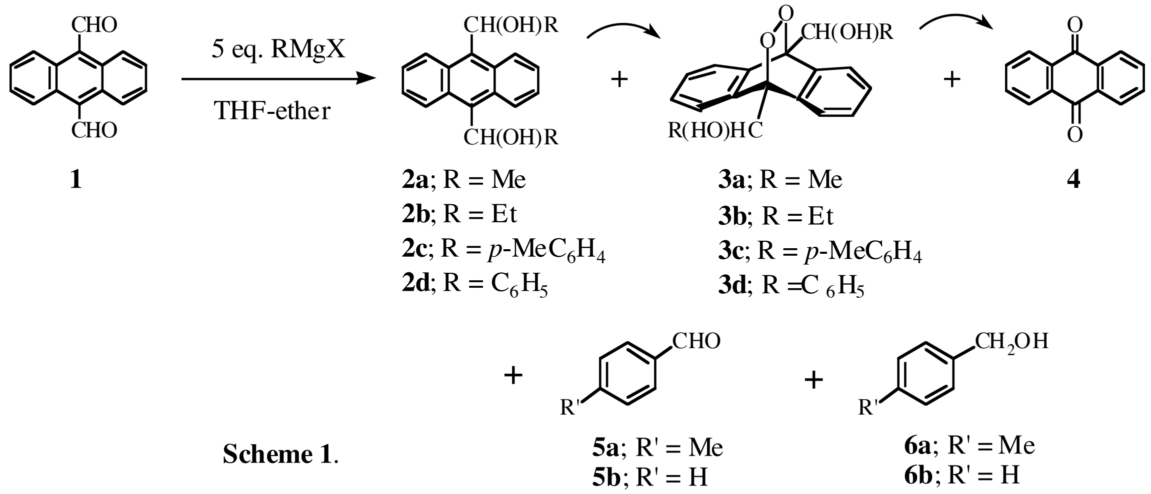
*) Dedicated to Prof. Dr. L. A. Paquette on occasion of his 70th birthday

with 9,10-bis(1-hydroxyalkyl)anthracenes (**2**) and 9,10-bis(1-hydroxyalkyl)anthracene-9,10-endoperoxides (**3**) in excellent yields. The mechanistic studies on the quinone formation revealed that the lone paired electron of oxygen in the side chain assists the endoperoxidation to themselves, and the quinone (**4**) was formed by the action of the Grignard reagents on endoperoxides.



Scheme 1.

Table 1. The Grignard reaction conditions and yields.

Entry No. and Grignard reagent	Condition			Yield (%)				
	atmosphere	light	time	**2**	**3**	**4**	**5**	**6**
				2a	**3a**			
1. R = Me	air	room light	2 h	62	18	12	0	0
2. R = Me	O_2	room light	18 h	42	25	25	0	0
3. R = Me	N_2	room light	2 h	92	0	0	0	0
4. R = Me	N_2	dark	18 h	quant.	0	0	0	0
				2b				
5. R = Et	air	room light	18 h	60[a)]	0	34[a)]	0	0
6. R = Et	N_2	dark	18 h	43	0	0	0	0
				2c			**5a**[b)]	**6a**[b)]
7. R = p-MeC_6H_4	O_2	lamp[c)]	18 h	46	0	51	41	45
8. R = p-MeC_6H_4	O_2	lamp	60 h	41	0	52	47	51
				2d			**5b**[b)]	**6b**[b)]
9. R = Ph	O_2	lamp	18 h	24	0	52	46	49

a) Crude yields.

b) The relative ratio is given compared to **4**, which was determined by ^1H NMR spectra.

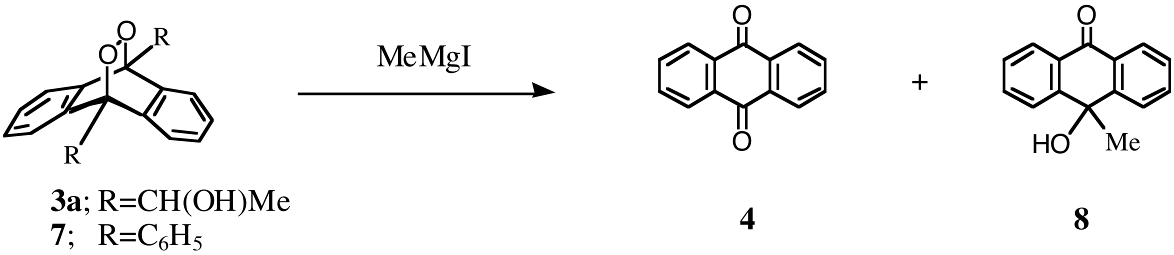
c) The reaction mixture in flask was irraditated with a 100W tungsten lamp from a distance of 20 cm.

RESULTS AND DISCUSSION

The reaction of **1** with freshly prepared 5 equiv. of methylmagnesium iodide in dry ether-THF solution at rt for 18 h gave diol (**2a**), [2,4] endoperoxidized diol (**3a**), and 9,10-anthraquinone (**4**). The reaction of **1** with the Grignard reagents such as ethyl-, *p*-tolyl- or phenylmagnesium bromide gave a mixture of diols (**2b-d**) and (**4**), respectively (Table 1), though endoperoxides (**3b-d**)[4] could not be detected. While the isolated diols (**2a-d**) were endoperoxideized to give (**3a-d**) under the room light at room temperature. It suggests that the endoperoxides as (**3b~d**) formed in the Grignard reaction were transformed to quinone under the conditions. The reaction of **2a** under the similar conditions as above in the presence of diazabicyclo[2.2.2]octane (dabco) [5] gave no endoperoxide (**3a**) supporting the formation of singlet oxygen as a reactant. Furthermore, the endoperoxidation reactions of (**2a-d**) with chemically induced singlet oxygen[1e] gave the corresponding endoperoxides (**3a-d**) along with a small amount of **4**. Since the formation of endoperoxides (**3a**) and (**4**) formed via (**3a-d**) under ambient conditions is so far unprecedented, the generality and the reaction mechanism were examined by various conditions shown in Table 1, and the experiments revealed the following.

Endoperoxidation: (a) The endoperoxidation of **2** was observed under no extra irradiation of light in the laboratory, but it was not observed under darkness and under nitrogen atmosphere. (b) The preliminary experiments described as above revealed that the rates of the endoperoxidation of **2a-d** bearing hydroxyalkyl groups at the 9- and 10-positions[6] was faster than that of compound bearing phenyl group at the 9- and 10-positions, which is known as the Steering effect.[7~9] And this endoperoxidation proceeded under Grignard conditions provides an evidence effected by the role of the lone paired electron of oxygen in the side chain rather than by the hydrogen bonding in the Steering effect.[8] (c) The reaction of **1** with large excess of the Grignard reagent (10~15 mol equiv.) under the same conditions as with the use of 5 equiv. of MeMgI exclusively gave **2a~d** quantitatively, suggesting that oxygen existing in the solution was consumed by the excess Grignard reagents.[10] (d) The pathway from diols (**2a**, **2b**) to quione (**4**) by autoxidation was excluded, because the standing of (**2a**, **2b**) or (**3a**, **3b**) dissolved in solvents such as CH_2Cl_2, ether, THF, and AcOEt in the dark at room temperature for 18 h recovered the starting materials. (f) The light-induced dissociation of the O-O bond of the endoperoxides also did not proceed, since **3a** did not change under the irradiation of light.

Quinone formation: The roles of the Grignard reagent and the hydroxyl groups in the side chain for the quinone formation were revealed as follows. (a) The reaction of **3a** with 2.0 or more equiv. of MeMgI for 2 h gave **4** along with a small amount of **8**, which may be formed from **4** (Table 2). The reaction of



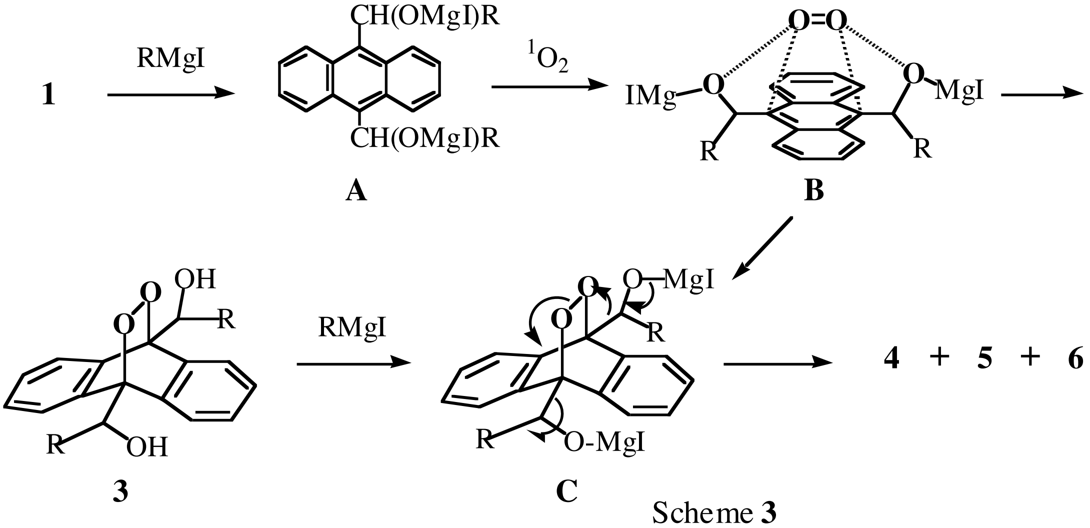
Scheme 2

Table 2 The reaction of **3a** and **7** with various molar ratios of MeMgI

Entry	Substrate	Conditions (molar ratio of MeMgI)	Yield (%)		
			3a (recovered)	**4**	**8**
1	**3a**	10 equiv.	0	81	4
2	**3a**	2 equiv.	0	82	3
3	**3a**	0.5 equiv.	56	37	0
4	**3a**	0.2 equiv.	75	12	0
			7 (recovered)	**4**	**8**
5	**7**	2 equiv.	100	0	0

9,10-diphenylanthracene-9,10-endoperoxide (**7**) with MeMgI under the same conditions gave no products. This suggests that the hydroxyl groups on the side chain at the 9- and 10-positions are necessary for the O-O bond fission. The reaction of **1** with *p*-Me-C_6H_4MgBr gave no endoperoxide (**3c**) or (**3d**), but it gave **2c**, **4**, *p*-methylbenzaldehyde (**5a**), and *p*-methylbenzyl alcohol (**6a**). Similarly, benzaldehyde (**5b**) and benzyl alcohol (**6b**). were obtained by the use of PhMgBr. These afford significant information on the role of the Grignard reagent and the reaction sequence of the quinone formation.[9] (d) It should be noted that the endoperoxide (**3a**) was also transformed quantitatively to quinone (**4**) by PhMgBr. Although the reaction of **3a** with activated magnesium (Mg*)[11] obtained by using 1,2-dibromoethane as entrainer also gave **4** quantitatively, that with Mg* prepared by other methods[11, 12] gave no product. It suggests that some amount of Grignard reagent as 2-bromoethylmagnesium bromide exists in the former reaction mixture.

Mechanism: Taking the above results into account, the overall plausible mechanism is proposed as shown in Scheme 3. First, the Grignard reagent added to formyl groups to form intermediate (**A**). Subsequently, the room light-induced singlet oxygen ($^1O_2$) sensitized by anthracene derivatives reacted at the 9,10-positions of (**A**) which was assisted by the interactions of the lone paired electron of oxygen in the side chain (intermediate **B**) to form an intermediate (**C**). Additionally, PM3 calculation showed a little greater electron density of the HSOMO of 9- and 10-positions of **2a** than those of HOMO of 9,10-dimethylanthracene (**9**). It suggests the greater interaction of **2a** with oxygen than that of **9**. Then, the O-O bond of endoperoxide was broken by the action of the Grignard reagents to give quinone, aldehydes, and alcohols.



Scheme **3**

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4. The data of the endoperoxides. **3a**: colorless crystals, mp 97˚C (benzene-hexane), IR(KBr) □ $_{max}$ 3410brm, 3020w, 2891w, 2872w, 1460m, 1378m, 1252w, 1158w,1112m, 997w, 929m, 907m, 760s, 668w, 639w cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) □= 7.81 (br, 2H), 7.42 (br, 2H), 7.23 (br, 4H), 5.14 (br, 2H), 2.28 (br s, 2H), 1.75 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) □= 139.8, 139.7, 127.0, 126.9, 126.8, 126.7, 124.2, 123.9, 122.3, 122.0, 83.6, 83.6, 66.6, 66.5, 19.4; UV-VIS □max (MeOH) 361 (log □=1.80), 270 (3.08), 250sh (3.43), 223 nm (3.86); MS *m/z* 298 (M^+, 1%), 208 (M^+-2xCH(OH)CH_3, 77%), 180 (M^+-{2xCH(OH)CH_3 + CO}, 91%), 152 (M^+-{2xCH(OH)CH_3 + 2xCO}, 100%). Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.26; H, 5.99.

   3b: Pale yellow crystals, mp 79˚C (benzene-hexane); IR (KBr) □ $_{max}$ 3450brs, 3060w, 3040w, 2960s, 2930s, 2870s, 1460s, 1400w, 1240w, 1150w, 1110m, 1060w, 1040w, 980m, 920m, 890w, 760s, 710w, 700w, 640w cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) □=7.81 (m, 2H), 7.31 (m, 2H), 7.22 (m, 4H), 4.79 (t, *J* = 9.2Hz, 2H, -CH-), 2.23 (m, 2H, -CH_2-), 2.00 (m, 2H, -CH_2-), 1.90 (m, 2H, -OH), 1.28 (m, 6H, 2x -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) □=140.1, 140.0, 126.9, 126.9, 126.7, 124.5, 123.9, 122.2, 121.8, 83.9, 83.8, 72.4, 31.6, 26.1, 11.5; UV-VIS □max (MeOH) 260sh (log □= 3.30), 250sh (3.37), 217nm (4.53); MS *m/z* 326 (M^+, 0.2%), 208 (M^+ -2xCH(OH)Et, 100%), 180 (M^+-{2xCH(OH)Et + CO}, 86%), 152 (M^+-{2xCH(OH)Et + 2xCO}, 67%); Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.59; H, 6.90.

   3c: Pale yellow powder, mp 135˚C (decomp) (CH_2Cl_2-hexane); IR (KBr) □$_{max}$ 3399brs, 3031w, 2920w, 1655m, 1613m, 1512s, 1458s, 1387s, 1186s, 1060s, 1017s, 918s, 818s, 758vs, 723m, 696m, 642m cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN-TMS) □=7.94 (m, 2H), 7.59 (d, *J*=7.99, 4H), 7.42 (m, 2H), 7.18 (m, 2H), 7.17 (d, *J*=7.99, 4H), 7.09 (m, 2H), 5.96 (m, 2H), 4.08 (brs, 2H, -OH), 2.30 (s, 6H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) □=142.0, 141.1, 138.5, 138,0, 130.0, 129.4, 127.2, 127.0, 126.9, 125.2, 125.1, 123.8, 123.7, 83.9, 83.8, 73.0, 72.9, 20.9; UV-VIS □max (MeOH) 259 (log □=4.80), 333 (3.50), 355 (2.59), 374 (1.62), 395 nm (1.58); MS *m/z* 330 (M^+ -*p*-Me-C_6H_4CHO, 54%), 296 (100%), 208 (anthraquinone, 17%), 180 (12%); Anal. Calcd for $C_{20}H_{22}O_4$: C, 78.41; H, 5.92.

Found: C, 78.88; H, 5.97.

3d: Pale yellow powder, mp 90°C (decomp) (CH_2Cl_2-hexane); IR (KBr) □ $_{max}$ 3393brs, 3065m, 3030m, 2921m, 2850w, 1698m, 1589m, 1455s, 1317m, 1204m, 1171s, 1121s, 1090m, 1042m, 932m, 828m, 747s, 648m, 613m cm^{-1}; ^1H NMR (400 MHz, CD_3CN-TMS) □=7.96 (m, 2H), 7.72 (d, *J*=7.99, 2H), 7.42 (m, 2H), 7.36 (m, 4H), 7.30 (m, 2H), 7.19 (m, 2H), 7.11 (m, 2H), 6.00 (m, 2H), 4.18 (brs, 2H, -OH); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) □=142.3, 141.3, 141.2, 130.4, 129.1, 128.9, 127.6, 127.3, 127.2, 125.5, 125.4, 124.1, 124.0, 84.1, 73.5; UV-VIS □max (MeOH) 230 (log □=4.92), 260 (4.38), 356 (3.48), 376 (2.57), 395 nm (2.55); MS *m/z* 316 (M^+ -C_6H_5CHO, 3%), 299 (4%), 208 (100%), 180 (83%), 67%); Anal. Calcd for $C_{20}H_{22}O_4$: C, 79.60; H, 5.25. Found: C, 79.40; H, 5.55.

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