

Oxidative Ring Cleavage of 3,5-Di-*t*-butyl-catechol and -*o*-benzoquinone by Base-Catalyzed Oxygenation

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(Received May 8, 1976)

Synopsis. The oxygenation of 3,5-di-*t*-butyl-catechol and -*o*-benzoquinone in *t*-BuOH with *t*-BuOK leads to the direct oxidative cleavage of the C₁–C₂ bond affording 2,4-di-*t*-butyl-4-carboxymethyl-2-buten-4-olide, a muconic acid derivative. The reaction is rationalized by assuming the reaction of 3,5-di-*t*-butyl-*o*-benzosemiquinone with oxygen.

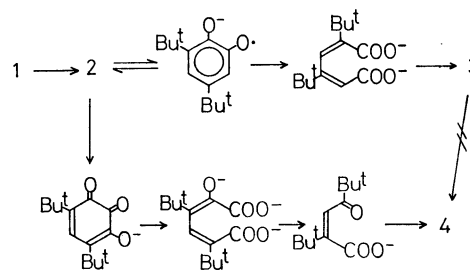
Oxidative ring cleavage of catechols by molecular oxygen is of interest in connection with the biological oxygenation of catechols.^{1–4} It has been shown that photooxygenation¹ and oxygenation with copper(I) chloride–pyridine complex² lead to the direct oxidative cleavage of the C₁–C₂ bond of catechols giving rise to muconic acid derivatives. No such direct cleavage has been observed in the base-catalyzed oxygenation of 3,5-di-*t*-butylcatechol in MeOH³ or in DMF,⁴ where products were always accompanied by further introduction of oxygen function to the molecules.

In the present paper it is reported that the oxygenation of 3,5-di-*t*-butylcatechol (**1**) or 3,5-di-*t*-butyl-*o*-benzoquinone (**2**) in *t*-BuOH containing *t*-BuOK causes the direct oxidative cleavage of the C₁–C₂ bond to give 2,4-di-*t*-butyl-4-carboxymethyl-2-buten-4-olide (**3**), a muconic acid derivative. When oxygen was bubbled through a solution of **1** in *t*-BuOH containing *t*-BuOK at room temperature for 8 h, compound **3**, 2,4-di-*t*-butyl-4-hydroxy-2-buten-4-olide (**4**), and 2,4-di-*t*-butyl-3-(3,5-di-*t*-butyl-2-hydroxyphenoxy)-2-buten-4-olide (**5a**) were obtained in 41, 14, and 21% yields, respectively.⁵ The structure of **5a** was determined from its elemental analysis and spectral data, and also by the fact that the acetylation of **5a** gave 2,4-di-*t*-butyl-3-(2-acetoxy-3,5-di-*t*-butylphenoxy)-2-buten-4-olide (**5b**). Since compound **3** is quite stable under the reaction conditions, it should not be an intermediate for the

formation of **4**. These products, therefore, must be formed *via* different reaction path.

Oxygenation of 3,5-di-*t*-butyl-*o*-benzoquinone (**2**), on the other hand, in *t*-BuOH with *t*-BuOK resulted in the preferential formation of **3** (Table 1). Since the quinone **2** gave the corresponding semiquinone anion under the reaction conditions and oxygen was not significantly reduced in *t*-BuOH containing *t*-BuOK, it is believed that the formation of **3** results from the reaction of the semiquinone anion with molecular oxygen. On the other hand, 2,4-di-*t*-butyl-4-(carboxyhydroxymethyl)-2-buten-4-olide (**6**) has been found to be the sole product on the oxidation of the quinone **2** by H₂O₂³ and compound **4** is easily obtained on the *t*-BuOK-catalyzed oxygenation of **6**.⁴

It is therefore concluded that the reaction of the *o*-benzosemiquinone with molecular oxygen leads to the direct oxidative cleavage of the C₁–C₂ bond, whereas the reaction of **2** with hydrogen peroxide or its anionic species gives rise to the formation of **4** as depicted in the following scheme.



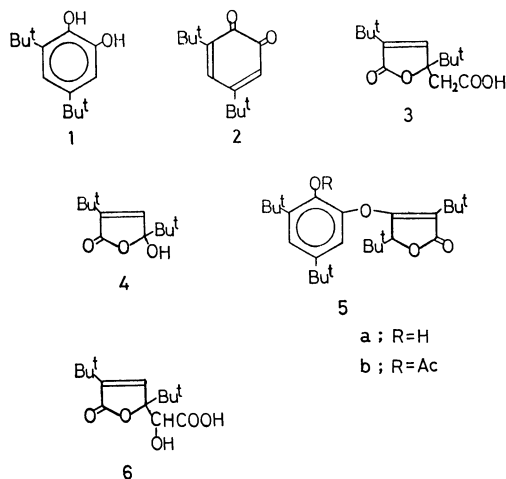
Scheme 2.

The formation of a small amount of **4** in the oxygenation of **2** may be attributed to the reduction of oxygen by an anionic species of **1** resulting from disproportionation of the semiquinone.

TABLE 1. BASE-CATALYZED OXYGENATION OF **2** IN VARIOUS SOLVENTS AT ROOM TEMPERATURE

Solvent	<i>t</i> -BuOK/2 (mol ratio)	Reaction time (h)	Conversion (%)	Product (%) ^a	
				3	4
MeOH	4.5	8	100	—	41
<i>t</i> -BuOH	4.5	8	100	64	7
NHEt ₂	4.5	8	100	62	6
NEt ₃	4.5	8	100	51	18
DMF	4.5	8	100	24	36
DMSO	4.5	8	100	35	25
HMPA	4.5	8	100	58	7
DME	4.5	8	100	62	6

a) Yields were determined by NMR.



Scheme 1.

The dimeric compound **5a** was not formed on the oxygenation of **2**, suggesting that the formation of **5a** in the oxygenation of **1** is considered to result from the combination of the phenolate anion of **1** with **2** but not from the coupling of the semiquinone with each other.

Similar results were obtained in other solvents (Table 1). Compound **3** was not isolable on the reaction in MeOH, where only **4** was isolated. In this system the reaction of **2** with H_2O_2 takes place predominantly because the quinone **2** is reduced to **1** in MeOH in the presence of base. Comparable amounts of **3** and **4** were obtained in DMF and in DMSO.⁶⁾ When luminol is added to a solution of *t*-BuOK in DMF or DMSO under O_2 bubbling, chemiluminescence is observed. This is indicative of the formation of superoxide anion.⁷⁾ Superoxide anion is well-known to form O_2 and H_2O_2 through its dismutation.⁸⁾ Therefore, the results in the oxygenation of **2** in DMF and DMSO indicate that there is a competition between the reaction of the semiquinone with O_2 and that of the quinone **2** with H_2O_2 in these solvents. A similar competition reaction has been reported for the oxidation of **1** with KO_2 , where compounds **3** and **6** are main products.⁹⁾ It is suggested by Moro-oka and Foote⁹⁾ that the formation of **3** and **6** is attributed to the different type of decomposition of a common peroxide intermediate resulting from the combination of the semiquinone and superoxide anion. This mechanism is also possible for the formation of **3** and **4** in the present oxygenation.

Experimental

Oxygenation of 1 in *t*-BuOH-*t*-BuOK. Oxygen was bubbled through a soln of **1** (0.274 g) in *t*-BuOH (15 ml) containing *t*-BuOK (0.5 g) at 40 °C for 8 h. The reaction mixture was acidified with dil. HCl and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was triturated with hexane to give **3** (0.14 g, 41%), identical with the product in the photooxygenation¹⁾ of **1** (IR, NMR, and mp). The organic soln. after removal of **3** was chromatographed on a silica gel plate (developed by CHCl_3) to give **4** (0.53 g, 14%), identical with the reported product⁴⁾ (IR, NMR, mp), and **5a** (0.05 g, 21%), colorless

needles (hexane), mp 199–200 °C; IR (Nujol): 3380 (OH), 1715 ($\text{C}=\text{O}$) cm^{-1} ; NMR (CDCl_3): δ 1.07 (*t*-Bu), 1.28 (*t*-Bu), 1.35 (*t*-Bu), 1.43 (*t*-Bu), 5.30 (1H, s, $=\text{C}-\text{CH}-\text{O}$), 5.74 (OH), 6.90 (1H, s, ArH), 7.21 (1H, s, ArH).

Found: C, 74.93; H, 9.58%. Calcd for $\text{C}_{26}\text{H}_{40}\text{O}_4$: C, 74.96; H, 9.68%.

Acetylation of 5a. A soln of **5a** (0.1 g) in acetic anhydride (10 ml) containing pyridine (4 ml) was allowed to stand at room temperature for 3 h. The reaction mixture was poured into a large excess of water to afford **5b** (0.11 g), colorless needles (hexane), mp 190–191 °C; IR (Nujol): 1780 (AcO), 1740 ($\text{C}=\text{O}$) cm^{-1} ; NMR (CDCl_3): δ 1.07 (*t*-Bu), 1.28 (*t*-Bu), 1.38 (*t*-Bu), 1.44 (*t*-Bu), 2.35 (AcO), 5.05 (1H, s, $=\text{C}-\text{CH}-\text{O}$), 6.90 (1H, d, $J=2.0$ Hz, ArH), 6.97 (1H, d, $J=2.0$ Hz, ArH).

Found: C, 73.24; H, 8.97%. Calcd for $\text{C}_{28}\text{H}_{42}\text{O}_5$: C, 73.32; H, 9.23%.

Oxygenation of 2. A procedure similar to that in the oxygenation of **1** described above was applied: **2** (1 mmol) in various solvents (15 ml). The results are summarized in Table 1.

The present work was financially supported by the Ministry of Education.

References

- 1) T. Matsuura, H. Matsushima, S. Kato, and I. Saito, *Tetrahedron*, **28**, 5119 (1972).
- 2) J. Tsuji and H. Takayanagi, *J. Am. Chem. Soc.*, **96**, 7349 (1974); *Tetrahedron Lett.*, **1975**, 1245.
- 3) R. R. Grinstead, *Biochemistry*, **3**, 1308 (1964).
- 4) A. Nishinaga, T. Itahara, and T. Matsuura, *Bull. Chem. Soc. Jpn.*, **47**, 1811 (1974).
- 5) A. Nishinaga, T. Itahara, and T. Matsuura, *Tetrahedron Lett.*, **1974**, 4481.
- 6) In a previous paper⁴⁾ only the product **4** was mentioned, but a detailed re-examination of the oxygenation in DMF or DMSO confirmed the existence of **3** in the reaction mixture.
- 7) A similar chemiluminescence is observed when luminol is added to a solution of KO_2 in DMF or DMSO.
- 8) A. U. Kahn, *Science*, **168**, 476 (1970).
- 9) Y. Moro-oka and C. S. Foote, *J. Am. Chem. Soc.*, **98**, 1510 (1976).