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OXYGENATION OF 4-ALKYNYL-2,6-DI-t-BUTYLPHENOLS

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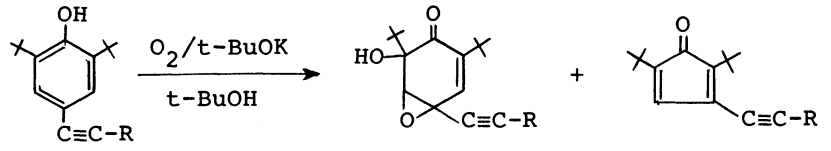
The oxygenation of 4-alkynyl-2,6-di-t-butylphenols (1) promoted by Co(Salpr) resulted in the dioxygen incorporation predominantly into the side chain, whereas in the oxygenation of 1 with t-BuOK in t-BuOH dioxygen was incorporated exclusively into the ortho position. The results are rationalized by a radical process in the former reaction and a nonradical process in the latter oxygenation.

Oxygenations of organic compounds with transition metal complexes capable of binding dioxygen are of particular interest in connection with new approach in organic syntheses and the understanding of biological oxidations.[1, 2] Co(Salpr), a five coordinate cobalt(II) Schiff base complex, has been shown to promote oxygenations of 4-alkyl- and 4-aryl-2,6-di-t-butylphenols resulting in the regioselective formation of peroxyquinolato cobalt(III) complexes, where the regioselectivity is the same as that observed in the base promoted oxygenation of these phenols.[3] The proposed mechanism involves phenolato cobalt(III) species, into which dioxygen is incorporated by a nonradical process.[3]
In this communication, we report that different regioselectivities were observed between the oxygenations of 4-alkynyl-2,6-di-t-butyl-phenols with t-BuOK in t-BuOH and with Co(Salpr) in dichloromethane. The results can be understood in terms of a nonradical process for the dioxygen incorporation into the ortho position and a radical process for the side chain oxidation promoted by Co(Salpr).

Although 4-alkynyl-2,6-di-t-butylphenols (1) were not susceptible to the oxygenation with t-BuOK in N,N-dimethylformamide where the phenolate anion is in a free state, they were readily oxygenated with t-BuOK in t-BuOH to give 4-alkynyl-2,6-di-t-butyl-4,5-epoxy-6-hydroxy-2-cyclohexenones (2)[4] and 3-alkynyl-

2,5-di-t-butylcyclopentadienones (3)[5] resulting eventually from the dioxygen incorporation into the ortho position (Table 1). These results are quite similar to those obtained in the oxygenation of 4-aryl-2,6-di-t-butylphenols promoted by the same base.[6] In the base promoted oxygenation of 4-aryl-2,6-di-t-butylphenols,



1 2 3

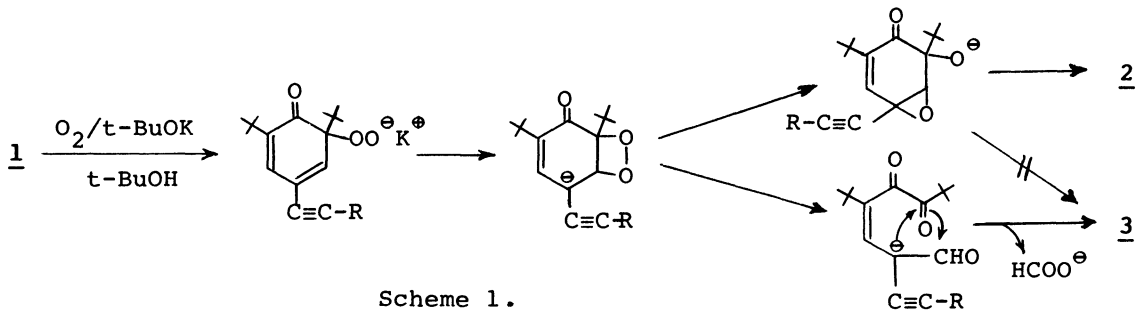
a; R = Ph b; R = n-Bu c; R = t-Bu

Table 1. Oxygenation of Phenols 1

1	Method[a]	Reaction Time / h[b]	Product yield / %[c] 2	3	4	5
1a	A	6.0	64	16	-	-
1a	B	1.0	-	-	63(68)[d]	(32)[d]
1b	A	2.0	77	-[e]	-	-
1b	B	1.0	-	-	70	-
1c	A	2.0	76	14	-	-
1c	B	1.0	-	-	56(58)[d]	40(42)[d]

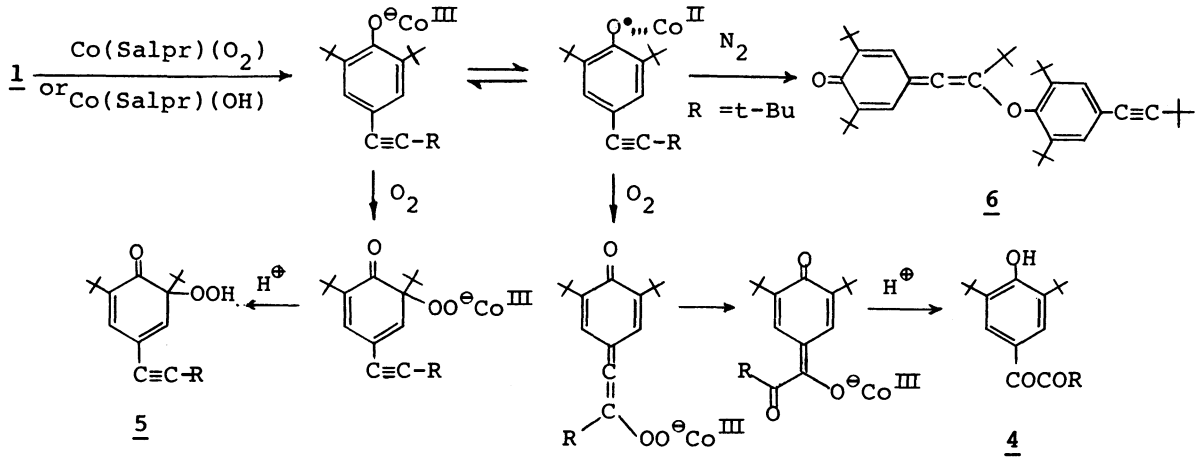
a) Method A: 1 (0.5 mmol)/t-BuOK (2.5 mmol)/t-BuOH (10 ml)/n-C_6H_{14} (5 ml) at room temperature. Method B: 1 (0.5 mmol)/Co(Salpr) (0.6 mmol)/CH_2Cl_2 (15 ml) at 0 °C. b) Time required for completion of the reaction. c) Isolation yield. d) Values in parenthesis are determined by ^1H NMR of the reaction mixture, in which no other products were detected(TLC). e) Not isolated but detected by TLC of the reaction mixture.

cyclopentadienones of type 3 are derived from the epoxy-o-quinols of type 2 under the reaction conditions.[6] Interestingly, however, treatment of 2 with t-BuOK in t-BuOH did not give 3 even at high temperatures, where 2 was recovered quantitatively. Therefore, 2 can not be the intermediate of 3 contrary to the case with 4-aryl derivatives. The results are rationalized by assuming a dioxetane intermediate, from which compounds 2 and 3 are formed separately (Scheme 1).



Scheme 1.

The oxygenation of 1 with Co(Salpr), contrary to the Co(Salpr) promoted oxygenation of 4-aryl-2,6-di-t-butylphenols where dioxygen is incorporated exclusively into the ortho position to give peroxy-o-quinols,[3] resulted in the dioxygen incorporation predominantly into the side chain to give 4-acylcarbonyl-2,6-di-t-butylphenols (4)[7] along with 4-alkynyl-2,6-di-t-butyl-6-hydroperoxy-2,4-cyclohexadienones (peroxy-o-quinols) (5)[8] (Table 1). Similar results were obtained when Co(Salpr)(OH) was used in place of Co(Salpr). On the other hand, when 1c was treated with an equimolar amount of Co(Salpr)(OH) in dichloromethane under nitrogen at room temperature for 6.5 h, the radical dimer 6[9] was obtained quantitatively, indicating that the phenolato Co(Salpr) undergoes homolysis. Further, the oxygenation of 1c with Co(Salen) or with Co(Salen)(OH), by which phenolato complexes formed undergo homolysis efficiently to give phenoxy radicals, did not give 5c at all, but a mixture of 4c and 6 isolated in 43% and 30% yield, respectively. These results suggest that the formation of 4 results from the reaction between the phenoxy radical (1·) and O_2 while compounds 5 are formed by dioxygen incorporation into the phenolate species, Co^{III}(Salpr)(1^-). Taking into account the findings that 4-aryl-2,6-di-t-butylphenoxy radicals are reduced by Co(Salpr) to phenolate species,[3] and the reactions of 4-acyl-, 4-alkoxycarbonyl-, 4-aryl-, and 4-cyano-2,6-di-t-butylphenoxy radicals with superoxo cobalt(III) complexes gave exclusively peroxy-p-quinols,[10] whereas the oxygenation of the parent phenols of these radicals with Co(Salpr) gave only peroxy-o-quinols,[3, 11] the mechanism of the present oxygenation can reasonably be understood as Scheme 2.



Scheme 2.

Thus, an important conclusion may be reached on the basis of the present results as follows: the regioselectivity in the Co(Salpr) promoted dioxygen incorporation into 2,6-di-t-butylphenols is governed by the magnitude of the equilibrium between phenolato Co^{III} and phenoxy radical Co^{II} complexes and of the rate constant of the dioxygen incorporation into each component.

References

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3) A. Nishinaga, H. Tomita, K. Nishizawa, T. Matsuura, S. Ooi, and K. Hirotsu, J. Chem. Soc.,Dalton Trans., 1981, 1504.
4) Compounds 2 were obtained as pale yellow liquid and gave satisfactory analytical results. 2a: ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 9H), 1.23 (s, 9H), 4.02 (s, 1H, OH), 4.02 (d, 1H, J = 1.4 Hz), 6.80 (d, 1H, J = 1.4 Hz), 7.2-7.6 (m, 5H); IR (Film) 3520, 2225, 1678 cm^{-1}. 2b: ^{1}H NMR ($CDCl_3$) δ 1.03 (S, 9H), 1.22 (s, 9H), 1.0-1.5 (m, 7H), 2.0-2.3 (m, 2H), 3.86 (d, 1H, J = 1.4 Hz), 4.02 (s, 1H, OH), 6.68 (d, 1H, J = 1.4 Hz); IR (Film) 3542, 2233, 1676 cm^{-1}. 2c: ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 9H), 1.23 (s, 9H), 1.29 (s, 9H), 3.84 (d, 1H, J = 1.4 Hz), 3.97 (s, 1H, OH), 6.67 (d, 1H, J = 1.4 Hz); IR (Film) 3519, 2225, 1678 cm^{-1}.
5) Compound 3a was obtained as orange needles from methanol, mp 81-82 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 9H), 1.36 (s, 9H), 6.38 (s, 1H), 7.2-7.5 (br s, 5H). Anal: C, ± 0.2%; H,±0.1%. Compound 3c was obtained as an orange oil; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 9H), 1.25 (s, 18H), 6.12 (s, 1H). MS: 272.21437; error, 0.3%.
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7) Compounds 4 were obtained as colorless prisms from hexane and gave satisfactory analytical results. 4a: mp 105-106 °C; ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 18H), 5.94 (s, 1H, OH), 7.2 (m, 5H), 7.85 (s, 2H); IR (Nujol) 3638, 1675, 1655 cm^{-1}. 4b: mp 187-188 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 18H), 0.9-1.4 (m, 7H), 2.6-3.0 (t, 2H, J = 7 Hz), 5.89 (s, 1H, OH), 7.85 (s, 2H); IR (Nujol) 3631, 1745, 1655 cm^{-1}. 4c: mp 136-137 °C; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 18H), 1.31 (s, 9H), 5.87 (s, 1H, OH), 7.69 (s, 2H); IR (Nujol) 3617, 1696, 1659 cm^{-1}.
8) Compounds 5 were not isolated in pure form but their ^{1}H NMR data in $CDCl_3$ are in good agreement with the structure. 5a: 0.99 (s, 9H), 1.26 (s, 9H), 6.63 (d, 1H, J = 1.4 Hz), 6.75 (d, 1H, J = 1.4 Hz). 5c: 0.98 (s, 9H), 1.25 (s, 9H), 1.31 (s, 9H), 6.56 (d, 1H, J = 1.4 Hz), 6.60 (d, 1H, J = 1.4 Hz), 8.60 (s, 1H, OOH).
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