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MECHANISM OF REGIOSELECTIVE HYDROPEROXYLATION OF 2,4,6-TRI-t-BUTYLPHENOL BY BASE-CATALYZED OXYGENATION

A. Nishinaga,* T. Shimizu, and T. Matsuura

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto, Japan

The hydroperoxylation of 2,4,6-tri-t-butylphenol (1) by base-catalyzed oxygenation displays the regioselectivity depending on the solvent used: para oxygenation takes place in alcoholic (except tertiary alcohols) and aprotic polar solvents whereas ortho oxygenation is observed in tertiary alcohols.[1] The mechanism of this interesting ortho selective hydroperoxylation has not been clarified. We now wish to report the mechanism of the ortho selectivity which is caused by the effective migration of hydroperoxy group of p-hydroperoxide primarily formed to the ortho position. The oxygenation of 1 in t-BuOH/t-BuOK at 40 °C quantitatively gives 6-hydroxy-2,4,6-tri-t-butyl-4,5-epoxy-2-cyclohexenone (4) which has been found to result from the intramolecular decomposition of 6-hydroperoxy-2,4,6-tri-t-butyl-2,4-cyclohexadienone (3) selectively formed under the reaction conditions.[1] It is found that the oxygenation of 1 at 0 °C in t-BuOH/t-BuOK mainly gives 4-hydroperoxy-2,4,6-tri-t-butyl-2,5-cyclohexadienone (2) and that with increase of the reaction temperature the amount of 2 decreases while the amounts of 3 and 4 increase (Table).

Table. Effect of Reaction Temperature on Product Distribution in the Oxygenation of 1.[a)]

Reaction Temperature (°C)	[t-BuOK]/[1]	Reaction Time (min)	Conversion (%)	Product (%)[b)] 2	3	4
0	5	30	68	86	14	-
10	5	20	85	69	31	-
20	5	15	97	53	47	-
30	5	10	98	27	65	8
40	5	10	98	3	59	39

a) 1 (5 mmol) in t-BuOH (50 ml) and hexane (50 ml) which is added to avoid freezing. b) No other product was detected and the yields were determined by NMR.

The time course of the oxygenation of 1 with t-BuOK in t-BuOH/hexane (1:1) at 20 °C shows that in the initial step 2 is formed with the same rate as that for the consumption of 1 and in the following step 3 is formed at the expense of 2 (Figure). These results clearly indicate that the

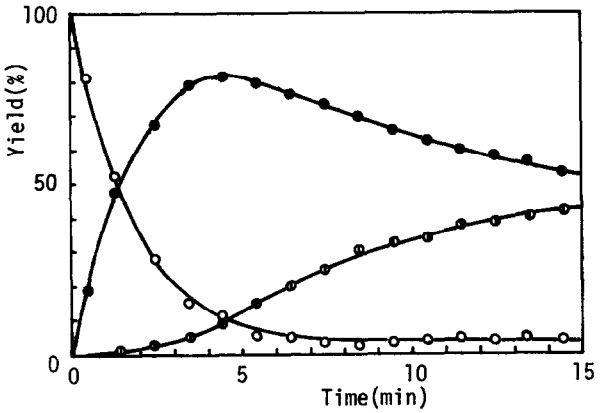
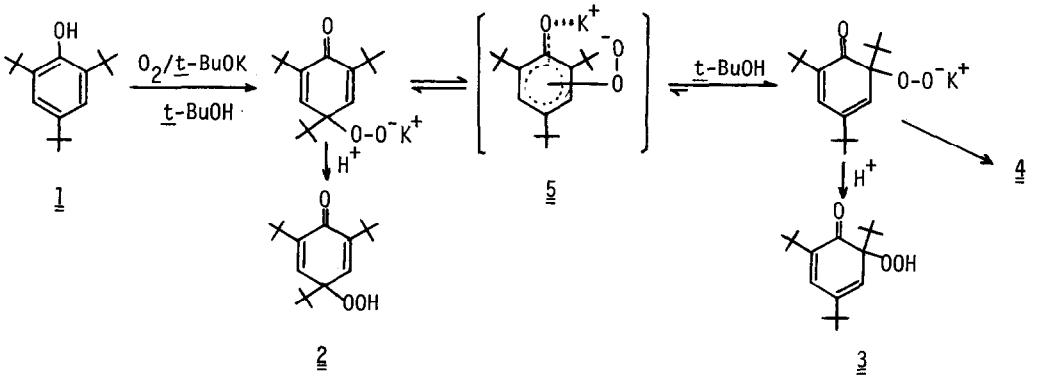


Figure. Time Course of Oxygenation of 1 (5 mM) in t-BuOH-Hexane Containing t-BuOK (25 mM) at at 20 °C. ○; 1 ●; 2 ⊕; 3

ortho selectivity is caused by the effective migration of the hydroperoxy group in 2 to the ortho position. Actually, 2 undergoes the migration to 3 irreversibly by the base catalysis. The migration follows first order kinetics with a rate constant of 3.14 X $10^{-3}sec^{-1}$ at 30 °C indicating the migration is an intramolecular reaction.

Mechanism of the migration involving phenoxy radical and superoxide anion can be ruled out because the reaction of the phenoxy radical from 1 and KO_2 results only in the electron transfer from the superoxide anion to the phenoxy radical to give molecular oxygen and 1.[2] Therefore, a non-radical π-complex transition state 5 is reasonably proposed for the migration. No migration takes place without the base. Hydroperoxides 2 and 3 are considered to be



1 2 5 3

in equilibrium.[3] The exclusive migration of 2 to 3 in t-BuOH/t-BuOK is rationalized by assuming chelate formation in the transition state depicted in the scheme.

References and Notes

1) A. Nishinaga, T. Itahara, T. Shimizu, and T. Matsuura, J. Am. Chem. Soc., 100, 1820 (1978).
2) A. Nishinaga, T. Shimizu, and T. Matsuura, Chem. Lett., 547 (1977).
3) In EtOH containing KOH, 2 or 3 gives a mixture (1:1) of these hydroperoxides, indicating that they are in equilibrium in basic medium. Similar argument on the equilibrium has been made by A.F.Bickel and H.R.Gersmann (J. Chem. Soc., 2711 (1959)) without descisive evidence.

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