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Catalytic Monooxygenation of Saturated Hydrocarbons with O_2 by a Nonheme Mono-Iron Complex Using Hydroquinones as Reductants

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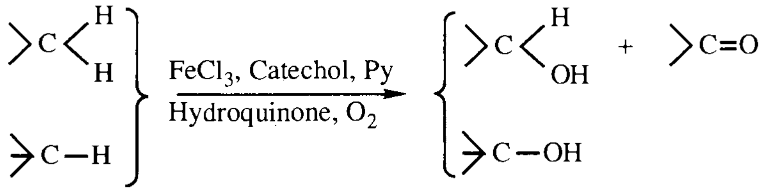
Saturated C-H bonds in hydrocarbons are readily monooxygenated with O_2 to alcohols and ketones by a catecholatoiron complex in acetonitrile in the presence of pyridine and hydroquinones as reductants. The pyridine concentration was found to be important for controlling the reactivity and selectivity of products, promoting the formation of alcohols and ketones in the low and high pyridine concentrations, respectively.

Activation of saturated C-H bond and monooxygenation of saturated hydrocarbons with molecular oxygen in mild conditions is one of the recent important topics. Some transition metal complexes such as a palladium complex[1)] have been developed, but iron complexes have extensively been studied not only for the synthetic importance but also for development of the biomimetic catalysts. Barton et al.[2)] have developed the Gif system which involves a tri-iron cluster complex ($Fe_3O(OAc)_6Pyr_{3.5}$), acetic acid (AcOH), pyridine, and Zn. Di-iron complexes have also been studied in relation to dinuclear iron biomolecules such as methanemonooxygenases.[3,4)] Mono-iron complexes have also been used as catalysts in the system using hydrazobenzene[5,6)] or orthophenylene diamine.[5)] We now developed a new simple mono-iron system for the monooxygenation of saturated hydrocarbons. In relation to our studies on the dioxygenation of catechols in which catecholatoiron species are proposed as intermediates, we have used a pyrocatecholatoiron complex, which is not oxygenatively cloven.[7)] Hydroquinones are used as reductants and as proton donors. Reaction proceeds in the homogeneous phase, different from the Gif system, and the reactivity is controlled by the types of hydroquinones and the pyridine concentration.

The reactions reported here are represented by the following equation.



Reactions were performed at 45 °C, under 1 atm O_2 by stirring $FeCl_3$ (20 mg, 0.125 mmol), pyrocatechol (14 mg, 0.125 mmol), and hydroquinones (5.0 mmol), substrate (2.5 mL), pyridine (20 μL, 0.25 mmol), and acetonitrile (5.0 mL). Reactions were also performed in pyridine (5 mL). In the case of adamantane, adamantane (0.68 g, 5 mmol) and acetonitrile (7.5 mL) were used. Products were quantitatively analyzed by g.l.c. with 25 m capillary columns.

Figure 1 shows the effect of hydroquinones on the catalytic activity. The yield of products is much greater in pyridine than in acetonitrile, but is affected similarly by the alkyl substituent on hydroquinones. The yield decreases in the order of TBHQ (t-butylhydroquinone) > DTBHQ (di-t-butylhydroquinone) > MHQ (methylhydroquinone) > HQ (hydroquinone). The order of TBHQ>MHQ>HQ is parallel to the increasing order of the oxidation potential of hydroquinones. The reactivity of the DTBHQ reflects the steric effect of two t-butyl groups at the *ortho*-positions.

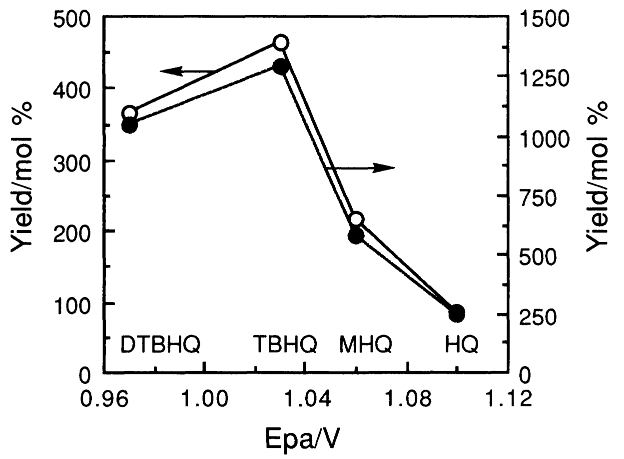


Fig. 1. Effect of hydroquinones on the yield of oxygenation of cyclohexane by the $FeCl_3$/catechol/pyridine catalyst. (Epa:first oxidation potential vs. SCE in acetonitrile)
○ : In acetonitrile ● : In pyridine

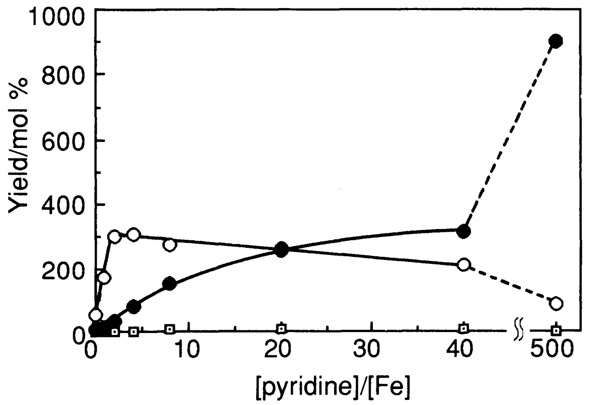
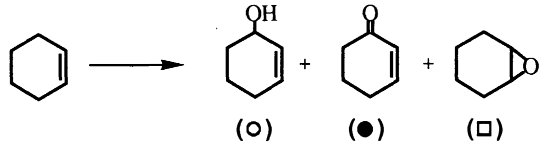


Fig. 2. Effect of pyridine concentration on the oxygenation of cyclohexene in the TBHQ system.



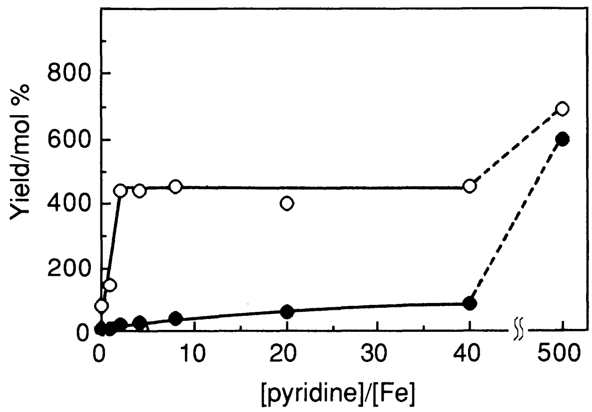
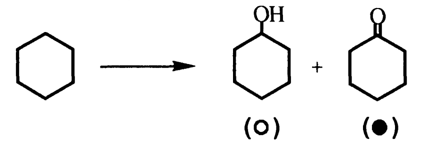


Fig. 3. Effect of pyridine concentration on the oxygenation of cyclohexane in the TBHQ system.



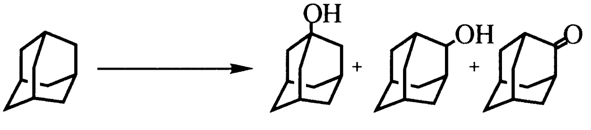
Figures 2 and 3 show the effect of the pyridine concentration on the yield and the selectivity of products in the oxygenation of cyclohexene and cyclohexane in the TBHQ system. It is clear that alcohols are selectively formed in the absence of the excess pyridine and the fraction of ketones increases with the pyridine concentration. The effect of pyridine is more remarkable with cyclohexene than cyclohexane, forming selectively cyclohexenone in pyridine. Cyclohexene oxide is hardly formed similarly to the other nonheme iron systems.[2,3,5] Cyclohexene oxide is converted to alcohol and ketone in the reaction condition, but the reactivity has indicated that the saturated C-H bond is directly oxygenated without *via* cyclohexene oxide. In the reaction of cyclohexane, the alcohol:ketone ratio in pyridine is 54:46 and 72:28 in the TBHQ and DTBHQ systems, respectively, indicating the effect of hydroquinones on the selectivity. Cyclooctane gives alcohol and ketone in the ratio of 72:28 in pyridine in the TBHQ system. Alcohols are not converted to ketones, indicating the different reaction processes for these two products.

Table 1 shows the results of oxygenation of adamantane. Compared with the other substrates, yield of products is much smaller. One reason for this result is the lower concentration of the solid reactant in the solution. Table 1 also shows the results obtained by using the different kinds of reductants, PhNHNHPh[5,6] and Zn/AcOH[2], for comparison. Total yield of products in the hydroquinone system is not so different from others, but the yield of 1-adamantanol is smaller in the hydroquinone system. The promoting effect of pyridine for formation of ketones is also observed in these systems. The difference is also found in the C^2/C^3 ratio, the ratio of the monoxygenation at the secondary to tertiary carbons. It is noteworthy that the ratio is high in the hydroquinone system both in acetonitrile and pyridine, specially in the TBHQ and MHQ systems. The different C^2/C^3 ratio between di-substituted DTBHQ and mono-substituted TBHQ and MHQ indicates that alkyl substituents on hydroquinones affect the reactivity not only electronically by modifying the redox potential but also sterically.

Table 1. Monooxygenation of adamantane by $FeCl_3$/pyrocatechol/pyridine/hydroquinones[a]

Reductant[b]	Py/Fe[c]	Solv[d]	Yield/mol %[e]	Composition/%[f] (1-OH : 2-OH : 2-(=O))			C^2/C^3 [g]
DTBHQ	2	AN	66	20	67	13	4.0
	≈500	Py	323	20	51	28	3.9
TBHQ	2	AN	50	6	84	10	15
	≈500	Py	293	11	41	48	8.0
MHQ	2	AN	33	7	92	2	14
	≈500	Py	178	9	63	29	11
PhNHNHPh	2	AN	48	35	56	9	1.9
	≈500	Py	510	39	44	17	1.6
Zn/AcOH	2	AN	30	62	21	17	0.6
	≈500	Py	223	32	12	55	2.1

a)$FeCl_3$:0.125 mmol, Fe:Cat:Red:Adamantane=1:1:40:40. b)TBHQ, DTBHQ, MHQ: see Text; Fe:Zn:AcOH=1:40:80. c)Mole ratio. Py: pyridine. d)AN: acetonitrile, e)Yield based on [Fe]. f)Mole ratio: g)Ratio of (2-OH + 2-(=O))/(1-OH).



1-OH 2-OH 2-(=O)

The C^2/C^3 ratio is referred to the characterization of the active oxygen species.[2] The small value of C^2/C^3 (<1) is expected for the active species with the radical character, *e.g.* •OH, and iron-oxygen species such as oxoiron species, Fe=O, has been proposed in the case of the large value of the ratio.[2)] Large values have been reported in the Gif system,[2)] but in the other cases small values have been reported[4,6)]. In the present system, the ratio is high irrespective of the solvent, supporting the iron-oxygen species as an active species. This seems reasonable in the system using hydroquinones which are often used as radical inhibitors. However, the low yield of epoxide from olefins suggests that the iron-oxygen species may be different form the Fe=O species proposed in the heme-iron model systems.[8)]

The present system is the most simple system for monoxygenation of saturated hydrocarbon with oxygen. Hydroquinones play both roles of reductants and proton donors in place of Zn and acetic acid in the Gif system. We believe that the hydroquinone-quinone redox reactions which play important roles in the biological redox system can become useful in the biomimetic and synthetic systems by modification of the reaction conditions. Repeated use of the reductant is possible since quinones are readily reduced to hydroquinones at least in the separate system. Effect of the presence of excess pyridine is correlated to the change of the iron complex by coordination of pyridine from the five coordinated complex in acetonitrile to the six coordinated complex in pyridine.[9)] Further studies on the reaction mechanism and on the development of the present system to useful oxygenation process are in progress.

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