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Controlled Monooxygenation of n- and Isoalkanes with Molecular Oxygen Catalyzed in Nonheme Iron Complex/Hydroquinone Systems

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Linear and branched alkanes are monooxygenated with O_2 in nonheme iron complex/hydroquinone systems. Selectivity to form either alcohols or carbonyl compounds was controlled by the pyridine concentration. Reactivity of different types of C-H bonds was affected by the substituents of hydroquinones, suggesting that hydroquinones are located in the vicinity of an active center in the product formation step.

Monooxygenation of saturated hydrocarbons with activation of molecular oxygen is of current interests and is very important both in the fundamental and industrial chemistry. In the monooxygenase model systems studied so far, very little has been reported on the monooxygenation of open-chained alkanes by nonheme[1-3] and heme[4] iron complexes. Composition of oxygen adducts (alcohols and carbonyl compounds) formed by these model complexes has not been analyzed fully, though that is important for clarifying the mechanisms of monooxygenation and the structures of active species. In the present work, reactivity of saturated C-H bonds in n- and isoalkanes for monooxygenation has been studied by analyzing fully the product composition. The selective formation of alcohols and the selectivity control by the pyridine concentration have been attained. The controlled monooxygenation is important not only for synthetic purpose but also for clarification of mechanisms.

Oxygenations by nonheme tri-iron[1,5] and di-iron[2,6] complexes have been developed in relevance to methane monooxygenases that include two irons. The role of the plural irons for the oxygen activation has not been clarified yet, and there is a possibility that oxygen is activated by a single iron as in the heme iron system. Our interest is to develop the monoiron systems as function models for oxygenases. The importance of a single iron for the oxygen activation even in nonheme iron systems will be clarified by the oxygenation in the similar fashion to oxygenases. Previously we have reported monooxygenation of aromatics[7] and cycloalkanes[8] in the catecholatoiron complex/hydroquinone system. Hydroquinones play both roles of proton and electron donors. The system exhibits the different reactivity from other systems using Zn/acetic acid,[1,5] Zn/hexafluoro-acetylacetonate,[2] and PhNHNHPh/PhCOOH.[3,9] We here found that linear and branched alkanes are catalytically monooxygenated under the mild conditions and that the selectivity depends on the types of hydroquinones.

Reactions of alkanes (n-pentane, n-hexane, n-heptane, and isopentane) were performed by stirring $FeCl_3$ (0.125 mmol), pyrocatechol (Cat, 0.125 mmol), hydroquinones (5.0 mmol), pyridine (py, 0.25 mmol), and alkanes (2.5 cm^3) in acetonitrile (5.0 cm^3) under 1 atm O_2 at 25 °C (n-alkanes) or at 20 °C (isopentane). The reaction was also performed in pyridine (5.0 cm^3, 62 mmol) in place of acetonitrile. $Fe(py)_4Cl_2$ was also used in

place of $FeCl_3$ and pyrocatechol in pyridine. Products were quantitatively analyzed by GLC with a 25 or 50 m capillary column and by GC-MS. Hydroquinones used in this work are 2,5-di-t-butylhydroquinone (DTBHQ), t-butylhydroquinone (TBHQ), methylhydroquinone (MHQ), and hydroquinone (HQ).

Tables 1 and 2 show the results of oxygenation of n-alkanes by using DTBHQ and of isopentane by using various hydroquinones, respectively. The reactions proceeded catalytically both in acetonitrile (at the low pyridine concentration) and in pyridine (at the high pyridine concentration) to give alcohols, ketones, and aldehydes. The further oxidation products (diols, diketones, carboxylic acids) were not detected. The reactivity in acetonitrile was very different from that in pyridine. In acetonitrile, the reaction started without an induction period but after a fairly long induction period in pyridine. The reaction in pyridine, however, started without the induction period in the system using $Fe(py)_4Cl_2$.

As seen in Table 1, oxygenation of n-alkanes formed alcohols selectively in acetonitrile (92%) while carbonyl compounds (68%, ketones>>aldehydes) were the main products in pyridine. The ratio of alcohols to carbonyl compounds (ol:one) was not dependent on the chain length of n-alkanes. The reactivity of carbons was secondary>primary, and the secondary carbons at the inner positions were slightly more reactive than those in the outer. It is expected that the smaller alkanes react in the similar fashion, but different conditions are required for reactions of alkanes that are gaseous at ambient temperature.

Isopentane gave selectively alcohols in acetonitrile and their yields per carbon decreased in the order of 2-ol>3-ol>1-ol≈4-ol. Different from the case of n-alkanes, the yields of the carbonyl compounds formed in pyridine were relatively low (35-49%), reflecting the promoted formation of 2-ol by the hydroxylation of the tertiary C-H bond. The proportion of 2-ol in the all products decreased in the order of DTBHQ>HQ>MHQ>TBHQ. The C^2/C^3 ratio (relative reactivity of the secondary carbon to the tertiary one) decreased also in the order of DTBHQ>HQ>MHQ>TBHQ both in acetonitrile and pyridine. Interestingly, the C^2/C^3 ratio in acetonitrile was similar to that in pyridine irrespective of the product composition. In the case of TBHQ, the ratio was greater than 1, indicating the greater reactivity of the secondary C-H bond than the tertiary one.

In spite of the recent studies,[10,11] the structures of active species and the mechanism of formation of alcohols and carbonyl compounds in the monooxygenation by nonheme iron complexes are far from clarification. The present results indicate that selectivity for the formation of either alcohol or carbonyl compounds is controlled simply by the pyridine concentration and that the selectivity depends on the structure of hydroquinones. These results are not explained by the mechanism involving alkylperoxide intermediates for both products.[10] The solvent effect suggests that different complexes are formed in acetonitrile and pyridine. The acetonitrile solution is blue and involves a catecholatoiron(III) complex as shown previously.[12] Since the reaction proceeds without an induction period, the active species may be formed from this complex. On the other hand, the pyridine solution is yellow, indicating the formation of a different complex. The result that the reaction is catalyzed by $Fe(py)_4Cl_2$ without the induction period suggests that the active species may be formed from a pyridineiron(II) complex. Products are obtained also when $Fe(py)_4Cl_2$ is used in acetonitrile. Compared with the catecholatoiron complex system, the yield is much lower, but the selectivity is similar. Since the acetonitrile solution of $Fe(py)_4Cl_2$ becomes blue in the presence of hydroquinones and oxygen, the structural change of the complex is probable. Spectroscopic studies will be performed to clarify the structures of complexes in the different solvents.

Formation of a high valent iron-oxo species rather than a hydroxyl radical has been proposed on the high NIH shift values in the oxygenation of aromatics[7] and on the high C^2/C^3 values in the oxygenation of adamantane.[8] This is supported by the high C^2/C^3 values obtained with isopentane. As shown in Table 2, the

Table 1. Monooxygenation of n-alkanes by nonheme iron complexes/2,5-di-t-butylhydroquinone/O_2 system[a)]

n-Alkane	Solvent	Yield	Product composition/mol %[c)]								ol:one[d)]
		mol %[b)]	1-ol	2-ol	3-ol	4-ol	ald	2-one	3-one	4-one	
n-Pentane	CH_3CN	418	11	51	30		1	4	3		92:8
	Pyridine	753	3	19	10		3	43	22		32:68
n-Hexane	CH_3CN	410	8	38	46		1	3	4		92:8
	Pyridine	811	1	13	18		11	25	32		32:68
n-Heptane	CH_3CN	348	7	32	34	19	1	3	3	1	92:8
	Pyridine	764	1	11	12	7	10	24	24	11	31:69

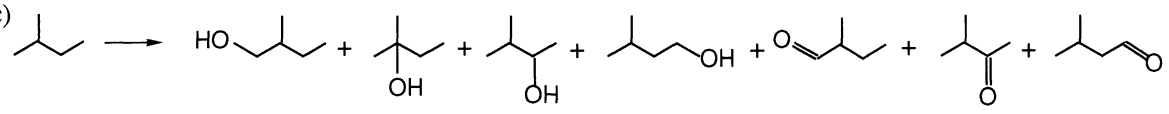
a) $FeCl_3$=0.125 mmol, Fe:Cat:py:DTBHQ=1:1:2:40 in 5 cm^3 of CH_3CN or 1:1:500:40 in 5 cm^3 of pyridine, 2.5 cm^3 of n-alkane, at 25 °C, 24 h. b) Based on [Fe]. c) ol, ald, and one denote alcohol, aldehyde and ketone, respectively, and the numbers represent the positions of the functional groups. d)Mole ratio of alcohols:(aldehydes + ketones).

Table 2. Monooxygenation of isopentane by nonheme iron complexs/hydroquinone/O_2 system[a)]

Solvent	Hydro-	Yield	Product composition/mol %[c)]							ol:one[d)]	C^2/C^3 e)
	quinones	mol %[b)]	1-ol	2-ol	3-ol	4-ol	1-ald	3-one	4-ald.		
CH_3CN	DTBHQ	405	14	50	23	6	3	3	1	92:8	0.52
	TBHQ	132	24	30	28	10	4	3	1	92:8	1.07
	MHQ	67	23	34	28	9	3	2	1	94:6	0.88
	HQ	27	23	38	23	11	2	2	1	95:5	0.64
Pyridine	DTBHQ[f)]	664	6	49	7	3	9	22	4	65:35	0.59
	TBHQ	448	7	33	9	3	13	29	6	51:49	1.18
	MHQ	290	8	41	10	3	7	29	2	61:39	0.96
	HQ	36	6	49	7	2	11	22	3	63:37	0.60

a), b), d) See footnotes in Table 1, except for the reaction temperature at 20 °C.

c)

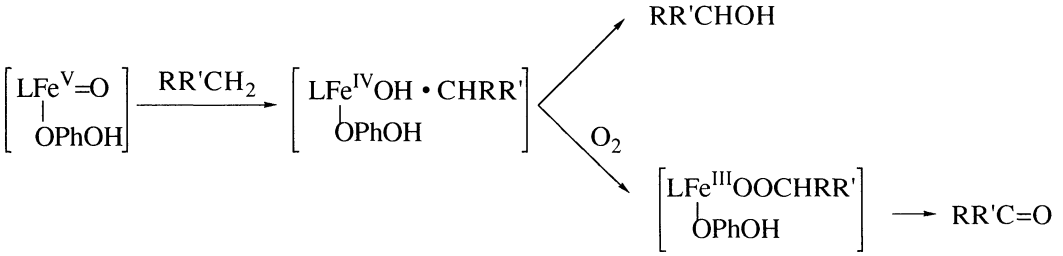


1-ol 2-ol 3-ol 4-ol 1-ald. 3-one 4-ald.

e) Mole ratio of yields, (3-ol + 3-one)/2-ol. f) $Fe(py)_4Cl_2$ (0.125 mmol) was used in place of ($FeCl_3$ + pyrocatechol).

values (0.52 -1.18) are higher than those of the Fenton system (0.43), the free ·OH (0.48), and the bis[(2-carboxy-6-carboxylato)pyridine]Fe^{II}/O_2/PhNHNHPh system (0.29).[3)] The high values of the relative reactivity of the primary C-H bond (C^1/C^3) compared with those of other systems also support the formation of the iron-oxo species. There is no direct evidence for the structure of the iron-oxo species, though different types of iron-oxo species including Fe^{IV}=O and Fe^{V}=O have been proposed. As seen from the correlation of the oxidation potential of hydroquinones with the yield,[7)] the electron transfer from hydroquinone to Fe^{III} is an important process. If Fe^{III}, Fe^{II}, and Fe^{V}=O species are involved in a catalytic cycle, two electron transfer from hydroquinones is required as proposed in the cytochrome P450 system. Reduction of Fe^{III} and formation of the high valent iron-oxo species may proceed in the solvent cage or stepwise *via* a free Fe^{II} species.[6,9)] Supposing LFe^{V}=O as an active species, the effect of ligands on the selectivity may be explained by Scheme 1, in which L

denotes ligands including catecholate, phenolate, pyridine, *etc*. The promoted formation of the *tert*-alcohol from isopentane even in pyridine indicates that the homolytic C-H bond fission with the oxygen species is involved in the formation of alcohols. Alcohols may be formed by a direct reaction of an alkyl radical with ·OH in the solvent cage or by the coupling of the OH and alkyl ligands of a σ-alkyl complex.[10] Carbonyl compounds may be formed after forming an Fe-peroxyalkyl complex with an insertion of oxygen.[10,13] Different ligands may affect the stability of these intermediates, and the results indicate that the formation of carbonyl compounds is promoted by pyridine. The effect of hydroquinones on the selectivity indicates that hydroquinones are located in the vicinity of the active center in the product formation step. The effect on the C^2/C^3 ratio seems to reflect that the stability of σ-alkyl intermediates is affected electronically and sterically by the substituents of hydroquinones. Coordination of a phenolate ligand is probable because the presence of pyridine promotes the deprotonation of hydroquinones. The characteristic reactivity of the DTBHQ system (Table 2) is ascribed to the two *tert*-butyl groups which are strongly electrodonating and may sterically prohibit the coordination of the phenolate ligand. The controlled monooxygenation by the ligand effect will be studied further to develop new monoiron systems.



Scheme 1.

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