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THE OXIDATION OF ADAMANTANE WITH AN IRON SALEN COMPLEX MODELLING ω-HYDROXYLASE

Iwao Tabushi,* Toshio Nakajima, and Kiyotomo Seto

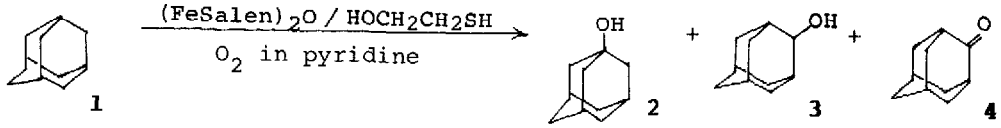
Department of Synthetic Chemistry, Faculty of Engineering

Kyoto University, Yoshida, Kyoto 606, Japan

An interesting regioselectivity (high secondary selectivity) was observed in the oxidation of adamantane in the presence of $(FeSalen)_2O$, 2-mercaptoethanol, pyridine, and oxygen, giving 1-adamantanol (67 % based on the catalyst used), 2-adamantanol (162 %) and 2-adamantanone (51 %) for a typical example. The yield of each product was dependent on the reaction conditions especially on the mercaptan concentration. This high secondary selectivity (product ratio, 3.2 : 1) and the predominant formation of 2-adamantanol is unique and quite different from those (ca 1 : 1 mostly adamantanone/1-adamantanol) of autoxidation. This is the first successful ω-hydroxylase model.

ω-Hydroxylase[1] catalyzes the hydroxylation of n-alkane regiospecifically at the ω-carbon atom. However, the active site of this enzyme has not yet been clarified. Moreover, nonheme oxidase model studies[2] on n-alkanes have not been very successful and the oxidation products were obtained only in poor yields (less than 70 % based on the catalyst used even for the best substrate, cyclohexane). We have found interesting regioselectivity in the oxidation of saturated hydrocarbons with molecular oxygen in the presence of μ-oxobis[N,N'-ethylenebis(salicylideneiminato)iron(III)] (abbreviated as $(FeSalen)_2O$), 2-mercaptoethanol, and pyridine and wish to report here this ω-hydroxylase model.

In the presence of $(FeSalen)_2O$ (3.8×10^{-4} M) and 2-mercaptoethanol (0.032—1.3 M), adamantane (0.18 M) was oxidized with molecular oxygen (1 atm) in pyridine (20 ml) to give 1-adamantanol (**2**) (0.70—1.47 mg), 2-adamantanol (**3**) (0.10—1.90 mg), and adamantanone (**4**) (0.42—0.85 mg) (eq 1) with satisfactory yields (110—360 % based on the catalyst used, see Table I). Although the yield of the oxidation products reached to a saturation after about 6 hours, further



(1)

Table Oxidation of Adamantane with $(FeSalen)_2O$ and 2-Mercaptoethanol[a)]

2-Mercaptoethanol	1.3 M	0.64 M	0.32 M	0.16 M	0.064 M	0.032 M
Yield (%)[b)]						
1-Adamantanol (**2**)	67	71	65	110	129	60
2-Adamantanol (**3**)	162	163	106	92	56	8
Adamantanone (**4**)	51	36	59	158	135	42
Total (**2** + **3** + **4**)	280	270	230	360	320	110
BR/BH[c)]	1.05	0.93	0.86	0.75	0.50	0.29

a) Other components and conditions were $Fe(Salen)_2O$ (3.8×10^{-4} M), adamantane (**1**) (0.18 M), and oxygen (1 atm) in pyridine (20 ml); for 4 hours at room temperature. b) Based on $(FeSalen)_2O$ used. c) See text.

oxidation started on addition of 2-mercaptoethanol, resulting in the continuous increase of the yield (Figure 1). This effect of 2-mercaptoethanol demonstrates that the saturation of the yield is attributable to a consumption of 2-mercaptoethanol by the action of oxygen.

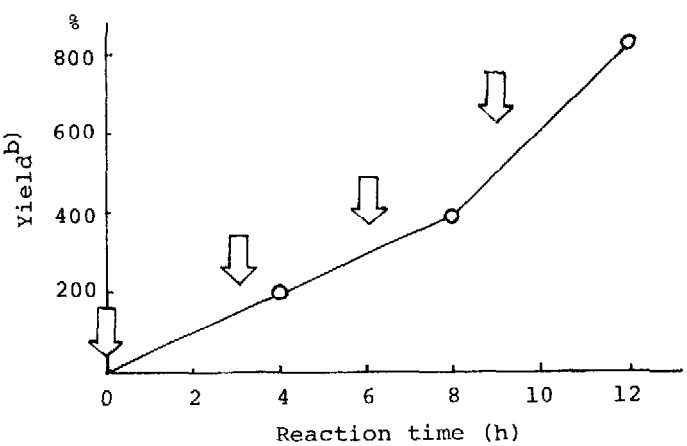


Fig. 1. Effect of successive addition of 2-mercaptoethanol.[a)]
(⇩ mark means the addition of 2-mercaptoethanol (200 mg each).)

a) At room temp.; $[(FeSalen)_2O] = 7.6 \times 10^{-4}$M, [adamantane] = 0.18 M, $[O_2]$ = 1 atm in pyridine (20 ml). b) Total yield of the oxidation products (**2**, **3** and **4**).

In the autoxidation of adamantane, the relative reactivity of secondary to tertiary carbon (BR/BH[3] with statistical correction for numbers of hydrogens) was reported in the range from 0.18 to 0.42.[4] In the present oxidation, the relative reactivity (BR/BH) was dependent on the 2-mercaptoethanol concentration and it was unusually high (BR/BH = 1.05 as the highest) at the high mercaptane concentration as shown in Table I. This concentration dependence suggests that at least two routes should be involved in the oxidation, (i) the hydroxylase model reaction with the high secondary selectivity and (ii) autoxidation leading to mostly adamantanone and 1-adamantanol with BR/BH ratio of 0.2—0.3 as described above. Increase in the secondary selectivity with increasing the mercaptan concentration seems to be due to increase in an active oxidant promoting the route (i) oxidation and also to the more efficient quenching of the autoxidation. Similarly, ascorbic acid promoted the oxidation to some extent, but it did not affect the RB/RH values markedly (0.28—0.42, see Table II) (vide infra).

Table II. Oxidation of Adamantane with $(FeSalen)_2O$ and Ascorbic Acid[a)]

Ascorbic acid	0.025 M	0.13 M	0.51 M
Yield (%)[b)]			
1-Adamantanol (**2**)	104	238	220
2-Adamantanol (**3**)	not detected	94	161
Adamantanone (**4**)	85	139	115
Total (**2** + **3** + **4**)	189	471	496
BR/BH[c)]	0.28	0.33	0.42

a) Other components and conditions were $(FeSalen)_2O$ (6.7×10^{-4} M), adamantane (**1**) (0.18 M), and oxygen (1 atm) in pyridine (20 ml); for 4 hours at room temperature. b) Based on $Fe(Salen)_2O$ used. c) See text.

When 2-mercaptoethanol was added to the pyridine solution of $(FeSalen)_2O$ under the anaerobic condition, the biphasic change of the electronic spectrum was observed (Figure 2), the first step of which was over within 10 seconds, followed by a slow second change ($t_{1/2} \sim 2$ min at 15°C) with two isosbestic points at 343 nm and 390 nm. For ascorbic acid, however, the spectral change

was monophasic (Figure 3). Thus a conclusion may be drawn that the thiol coordination plays an important role in the formation of the present active oxidizing species.

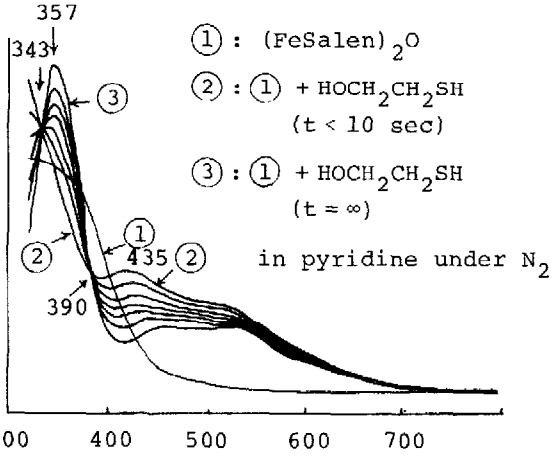


Fig. 2. Electronic spectral change of iron species on the 2-mercapto-ethanol addition.

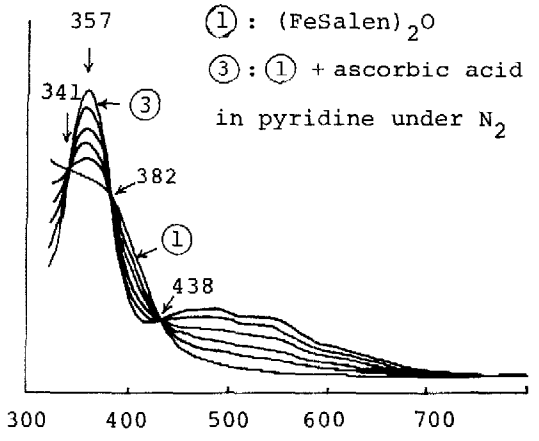


Fig. 3. Electronic spectral change of iron species on the ascorbic acid addition.

Efficient turn-over of the present catalyst and the remarkably increased secondary selectivity are significant and noteworthy but the detailed mechanism is not yet clear in this stage. Our results, however, provide a possibility constructing an artificial catalyst for the selective ω-hydroxylation of n-alkane.

REFERENCES AND NOTE

1. E. J. McKenna and M. J. Coon, J. Biol. Chem., **245**, 3882 (1970); R. T. Ruettinger, S. T. Olson, R. F. Boyer, and M. J. Coon, Biochem. Biophys. Res. Commun., **57**, 1011 (1974).
2. U. Formmer and V. Ullrich, Z. Naturforsch., B, **26**, 322 (1971); G. A. Hamilton, R. J. Workman, and L. Woo, J. Am. Chem. Soc., **86**, 3390 (1964).
3. The reactivity ratio, bridge hydrogen to bridgehead hydrogen; see I. Tabushi, J. Hamuro, and R. Oda, J. Am. Chem. Soc., **89**, 7127 (1967); J. Org. Chem., **33**, 2108 (1968).
4. G. W. Smith and H. D. Williams, J. Org. Chem., **26**, 2207 (1961).

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