

Oxidation of Secondary Alcohols over Hydrous Zirconium(IV) Oxide

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(Received March 8, 1990)

The oxidation of secondary alcohols with ketones was carried out by catalysis with hydrous zirconium(IV) oxide. In the batch reaction system, the oxidation proceeded efficiently to give the corresponding ketones, except for some secondary alcohols. On the other hand, all of the secondary alcohols were efficiently converted to the corresponding ketones in the flow oxidation system. The influence of the hydrogen acceptor on the oxidation rate was investigated by the use of several ketones, and the oxidation rate was influenced by the electron density and steric hindrance around the carbonyl group. The dependence on the reaction temperature was also investigated in the flow reaction system.

Ketones and aldehydes can be reduced by the use of metal alkoxides and alcohols (Meerwein-Ponndorf-Verley reduction). The reverse reaction, which is known as Oppenauer oxidation, has been used for the oxidation of alcohols. In previous papers,^{1,2} we have reported that the Meerwein-Ponndorf-Verley type reduction of aldehydes, ketones, and carboxylic acid proceeded efficiently over hydrous zirconium(IV) oxide. Generally, oxidation has been carried out by the use of a metal alkoxide catalyst, and aluminium isopropoxide has been found to be the best reagent for this oxidation.³ However, this method calls for not only the addition of a large amount of aluminium isopropoxide, but also for the neutralization of alkoxide salt with acid. Therefore, it has several disadvantages, such as the need for tedious purification and the unreusability of the catalyst.

Heterogeneous catalysts for the oxidation are known; silica,⁴ magnesia,⁴ and aluminium oxide⁵ have been reported to be successful catalysts. These methods have several advantages in the isolation of products. However, they need to be carried out in the vapor phase and require a high reaction temperature.

In this paper we report that the oxidation of secondary alcohols with ketones proceeded efficiently over hydrous zirconium oxide in our batch reaction system, and that it was found that the majority of alcohols were converted to the corresponding ketones in a high yield. By using this method the following advantages are expected: (1) easy product isolation (2) the lack of a need to maintain water-free conditions (3) reusability of the catalyst, and (4) durability of the catalytic activity. The oxidation of several secondary alcohols also proceed efficiently by using a flow reaction system. The flow reaction system can control the contact period with the catalyst and expand the range of reaction temperatures. As a result, a number of secondary alcohols could be efficiently converted to the corresponding ketones.

Further, we also report the effect of the hydrogen acceptor and the dependence on the reaction temperature in the oxidation of secondary alcohols with ketones catalyzed by the hydrous zirconium oxide.

Experimental

Materials. Commercial reagents were used for the reaction without any further purification.

Hydrous Zirconium(IV) Oxide. To a solution of zirconium dichloride oxide ($\text{ZrCl}_2\text{O} \cdot 8\text{H}_2\text{O}$) (200 g of a solid in 10 dm³ of deionized water), we slowly added an aqueous solution of sodium hydroxide (1 mol dm⁻³) at room temperature. Constant gentle stirring was maintained and the addition was continued until the pH of the resulting solution reached 6.80. The solution was allowed to stand for 48 h at room temperature. The resulting product was filtered and washed free of chloride ions. A gel was spread on a glass plate and dried in air at room temperature for 10 h and then at 80 °C for 2 h. Fifty four grams of hydrous zirconium oxide were obtained in the form of granules, which were heated at 300 °C for 5 h.

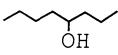
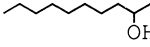
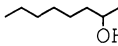
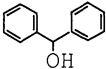
General Procedure in the Batch Reaction System. In a 20 cm³ round-bottomed flask equipped with a reflux condenser were placed hydrous zirconium oxide (24–60 mesh; 1.0 g), a benzene or toluene solution (10 cm³) of an alcohol (0.25 mmol), a ketone (14.6 mmol), and a hydrocarbon (0.20 mmol) as an internal standard. The contents were then heated at 80 or 110 °C. The reaction mixture products were analyzed by gas chromatography (a capillary column PEG 20M 30 m and OV101 30 m) and GC-MS (Shimadzu QP1000).

General Procedure in the Flow Reaction System. Catalytic oxidation was carried out in a glass-flow reactor (6.5 mm in diameter) with a fixed-bed catalyst: flow rate of nitrogen = 60 cm³ min⁻¹; catalyst = 1.0 g, 24–60 mesh; reaction temperature = 55–115 °C. A mixture of an alcohol (1.25 mmol), a ketone (50 cm³), and a hydrocarbon (1.25 mmol) as an internal standard was fed into the reactor (5 cm³ h⁻¹) by means of a microfeeder. The activity and yield of the reaction were determined after the steady states had been reached. The products were then analyzed in a similar manner to that described above.

Results and Discussion

Oxidation of Secondary Alcohols in the Batch Reaction System. Table 1 shows the oxidation of various alcohols with acetone catalyzed by the hydrous zirconium(IV) oxide. The majority of these alcohols were converted to the corresponding ketones in high

Table 1. Oxidation of Secondary Alcohols over Hydrous Zirconium(IV) Oxide in the Batch Reaction System^{a)}

Reactant	Time/h	Conv./%	Yield/%	k/s^{-1}
	8.0	100.0	100.0	3.33×10^{-5}
	8.0	100.0	91.9	6.39×10^{-5}
	4.0	100.0	99.6	8.89×10^{-5}
	1.5	100.0	87.4	2.31×10^{-4}
	1.5	68.7	48.1	—
	8.0	100.0	87.9	6.11×10^{-5}
	10.0	100.0	92.7	4.01×10^{-5}
	8.0	100.0	100.0	3.89×10^{-5}
	8.0	19.2	19.2	2.78×10^{-6}
	6.0	100.0	98.6	8.33×10^{-5}
	8.0	100.0	100.0	3.06×10^{-5}

a) Catalyst; 1.0 g, alcohol; 0.25 mmol, acetone; 1.0 cm³, benzene; 9.0 cm³, temperature; 80 °C. b) Maximum yield.

yields. In particular, it is noteworthy that borneol was converted to camphor in a 100% yield. Camphor resisted reduction with 2-propanol over hydrous zirconium oxide due to its steric hindrance.¹⁾ Generally, the Oppenauer oxidation is often accompanied by side reactions, for instance aldol condensation. In fact, the oxidation of alcohols with a large amount of acetone over hydrous zirconium oxide mainly gives aldol condensation products. However, oxidation using the diluted ketone proceeded efficiently without any side reactions, except in the case of cyclohexanol. The oxidation of cyclohexanol gave a low yield of cyclohexanone and aldol products with acetone were obtained. On the other hand, 2-methyl and 2-ethylcyclohexanol were oxidized efficiently. These results indicate that the α -alkyl group on the cyclohexane ring has a pronounced effect in interfering with the aldol condensation with acetone.

The rate constants of the oxidation of the alcohols are dependent on the steric circumstances around the

Table 2. Effect of Hydrogen Acceptor for the Specific Rate Constant in the Oxidation of 2-Octanol^{a)}

Hydrogen acceptor	k/s^{-1}	Electron density	
		C ^{b)}	O ^{c)}
Acetone	2.89×10^{-4}	3.776	6.293
Diethyl ketone	2.50×10^{-4}	3.778	6.287
Diisopropyl ketone	7.78×10^{-5}	3.771	6.289
Cyclohexanone	2.44×10^{-4}	3.769	6.292
Benzophenone	3.08×10^{-4}	3.691	6.281

a) Catalyst; 1.0 g, 2-Octanol; 0.25 mmol, toluene; 10.0 cm³, hydrogen acceptor; 3.0 mol%, reaction temperature; 110 °C. b) Carbonyl carbon. c) Carbonyl oxygen.

hydroxyl group. In fact, the rate constants of 2-octanol, 2-methylcyclohexanol, and 2-phenylethanol are larger than those of 4-octanol, 2-ethylcyclohexanol, and diphenylmethanol, respectively. The slow rate in the case of menthol may be explained by its steric hindrance.

Effect of Hydrogen Acceptor in the Batch Reaction System. In order to elucidate the dependence on the variety of hydrogen acceptors, the oxidation of 2-octanol with several ketones was carried out at 110 °C. This results are listed in Table 2. The rate constant of the oxidation using benzophenone was larger than those of the others. The result can be attributed to the electron density at the carbonyl group. The electron densities at the carbonyl carbon and oxygen of the ketones are listed in Table 2. These values were calculated by using computational chemistry. The method used was as follows; the most stable conformation of each ketone was calculated by a molecular mechanics program called CHARMm,⁶⁾ and its molecular orbital was calculated by AMPAC.⁷⁾ From these results it turned out that the electron density at the carbonyl carbon of benzophenone was much lower in comparison with that of the other ketones. The low electron density at the carbonyl carbon was a dominant factor in accelerating oxidation. In previous papers,¹⁾ we reported the reduction of aldehydes and ketones with 2-propanol over hydrous zirconium oxide; the rate-determining step was proposed to be a step involving hydride transfer from 2-propanol to a carbonyl compound. Further, a Hammett relationship was found in the reduction of substituted benzaldehyde.⁸⁾ These results can be explained if the reactivity is dependent on the electron density of the carbonyl carbon. An agreement of this explanation with the reactivity in the oxidation suggested that these oxidations would also proceed by a similar mechanism.

However, the reduction of benzophenone with 2-propanol proceeded slowly.¹⁾ This conflict was interpreted in terms of the relatively low electron density at the carbonyl oxygen of benzophenone, as shown in Table 2. Carbonyl compounds coordinate to

the catalyst by donating an electron pair. The adsorption of benzophenone was relatively slow in comparison with other ketones because of the relatively low electron density of the carbonyl oxygen atom. Because of the low concentration of benzophenone in the reduction, the length of time required for this adsorption had a greater effect on the reaction rate than the hydride transfer. In contrast, for oxidation when a large excess of benzophenone was used, the adsorption rate was not an important factor regarding the reaction rate.

On the other hand, the oxidation rate in diisopropyl ketone was much slower than those of other ketones, although this ketone was almost equal to acetone and diethyl ketone with regard to the electron density at both of the carbonyl carbon and oxygen. These results can be explained as being caused by a steric hindrance around the carbonyl group.

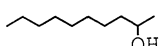
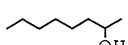
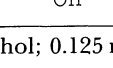
Oxidation of Alcohols in the Flow Reaction System. The results of the oxidation of secondary alcohols in the flow reaction system are listed in Table 3. The majority of these alcohols were converted to the

corresponding ketones in high yields. In particular, it was noteworthy that menthol is efficiently converted to menthone in comparison with the yield from the batch reaction system. Although the sterically hindered ketones could be oxidized by use of the flow reaction system, cyclohexanol was not efficiently converted to cyclohexanone. In order to achieve a high oxidation yield, we changed the hydrogen acceptor from acetone to 30 mol% of diethyl ketone with benzene. As a result, cyclohexanol was converted to cyclohexanone in a 84.6% yield.

Dependence on Reaction Temperature. In order to investigate the dependence on the reaction temperature, the oxidation of 2-decanol and menthol was carried out in the range of 55 to 115 °C. The natural logarithm of the rate, r , vs. the reciprocal of the absolute temperature (the Arrhenius plot), is shown in Fig. 1. As can be seen from Fig. 1, very straight lines are obtained. From the slope of the lines, the activation energies of these oxidations were calculated as being 4.34 kcal mol⁻¹ (2-decanol) and 3.13 kcal mol⁻¹ (menthol). The activation energy of 2-decanol has almost the same value as that of menthol.

Effect of Hydrogen Acceptor in the Flow Reaction System. The influence of various hydrogen acceptors was investigated for the oxidation of 2-octanol. The results are listed in Table 4. In the case of acetone and diethyl ketone, 2-octanol was efficiently converted to 2-octanone. On the other hand, when using diisopropyl ketone or cyclohexanone, the oxidation of 2-octanol did not proceed with a high yield. These four ketones are almost equal in the electron densities around the carbonyl group. Accordingly, it was considered that the main factor of these results could

Table 3. Oxidation of Secondary Alcohols over Hydrous Zirconium(IV) Oxide in the Flow Reaction System

Reactant	Cat./g	Temp./°C	Yield/%
	1.0	100	94.5
	1.0	100	93.6
	1.0	100	95.7
	1.0	100	41.6
	1.0	100	92.7
	1.0	100	92.0
	2.0	100	68.7
	2.0	115	86.5
	1.0	100	88.1
	1.0	150	100.0
	1.0	150	92.3

Alcohol; 0.125 mmol h⁻¹, Acetone; 5 cm³ h⁻¹.

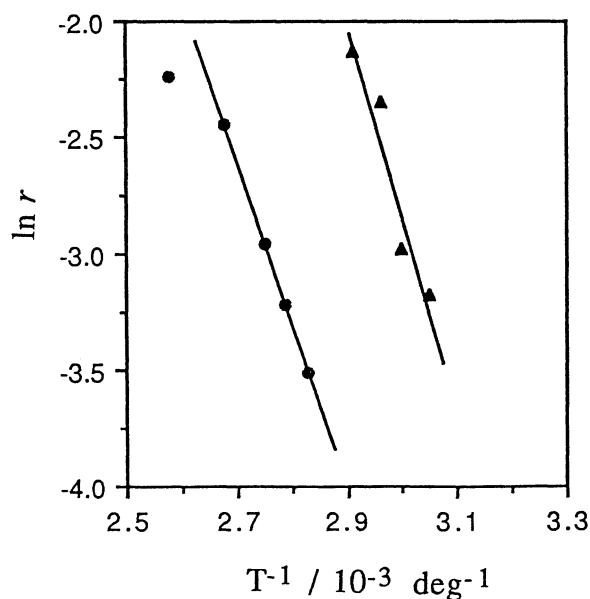


Fig. 1. Arrhenius Plot. ●; Menthol (cat. 2.0 g), ▲; 2-Decanol (cat. 1.0 g), Conditions: Alcohol 1.25×10⁻¹ mmol h⁻¹, Acetone 5 cm³ h⁻¹.

Table 4. Effect of Hydrogen Acceptor in the Oxidation of 2-Octanol (Flow Reaction System)^{a)}

Hydrogen acceptor	Yield/%	Electron density	
		C ^{b)}	O ^{c)}
Acetone	94.5	3.776	6.293
Diethyl ketone	95.1	3.778	6.287
Diisopropyl ketone	9.2	3.771	6.289
Cyclohexanone	13.5	3.769	6.292

a) Catalyst; 1.0 g, 2-Octanol; 0.125 mmol h⁻¹, hydrogen acceptor; 5.0 cm³ h⁻¹, reaction temperature; 100°C.

b) Carbonyl carbon. c) Carbonyl oxygen.

be attributable to a hindrance around the carbonyl carbon. This is similar to the results from the batch reaction system.

Catalytic Activity of Several Catalysts in the Oxidation. In order to compare the catalytic activities, the oxidation of 2-octanol with acetone was carried out over several catalysts. The results are listed in Table 5. Except for hydrous zirconium oxide and aluminium oxide, oxidation proceeded with a low yield. Aluminium oxide has been reported as being a heterogeneous catalyst in the Oppenauer oxidation.⁶⁾ However, hydrous zirconium(IV) oxide was superior to aluminium oxide with regard to both activity and selectivity. Consequently, it can be elucidated that hydrous zirconium oxide is the best catalyst for the oxidation of secondary alcohol with acetone among these catalysts.

Table 5. Comparison of the Catalytic Activity of Several Catalysts in the Oxidation of 2-Octanol with Acetone^{a)}

Catalyst	Conversion/%	Yield/%
Hydrous zirconium(IV) oxide	100.0	99.6
Hydrous titanium(IV) oxide	tr.	tr.
Hydrous tin(V) oxide	tr.	tr.
Al ₂ O ₃	51.7	29.9
SiO ₂	tr.	tr.
Aluminium silicate	29.4	9.5
Zeolite, A-4	3.6	3.6

a) Catalyst; 1.0 g, 2-octanol; 0.25 mmol, acetone; 1.0 cm³, benzene; 9.0 cm³, temperature; 80°C.

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