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The Meerwein–Ponndorf–Verley–Oppenauer type reaction in supercritical or high-temperature alcohols or acetone without catalyst: Effect of oxidation enthalpy and solvent concentrations on yield

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ABSTRACT

In the traditional Meerwein–Ponndorf–Verley (MPV) reduction, it is known that the yield of the produced alcohol is dependent on the oxidation enthalpy and the concentration of the alcohol used as the reducing reagent. In this study, we investigated the reduction of acetophenone to 1-phenylethanol with alcohols under their supercritical or high-temperature conditions without catalyst to confirm the mechanistic resemblance of the MPV type reduction with supercritical or high-temperature alcohols to the traditional MPV reduction. It was found that the yields of the 1-phenylethanol were dependent on the oxidation enthalpies and the concentrations of the alcohols used as the reducing reagents in common with the traditional MPV reduction. The Oppenauer type oxidation of secondary alcohols afforded the corresponding ketones in around 90% yield with excess amounts of supercritical acetone without catalyst. On the other hand, the Oppenauer type oxidation of primary alcohols to aldehydes resulted in low yields. The low yields were assumed to result from the aldol condensation of the resulting aldehydes with the acetone.

1. Introduction

The Meerwein–Ponndorf–Verley (MPV) reduction of carbonyl compounds to the corresponding alcohols has been one of the standard procedures for the selective reduction of unsaturated carbonyls in laboratories and industries [1–7]. The traditional MPV reduction is carried out in 2-propanol using $Al(O\text{-}^{i}Pr)_3$ as a Lewis-acid catalyst. Much effort has been devoted to the elucidation of the reaction mechanism, and it has been clarified that the reaction goes to equilibrium [8]. The equilibrium position is dependent on the oxidation enthalpy of the alcohol used as the hydrogen source and the concentration ratio of the alcohol/starting carbonyl [1]. This reaction proceeds *via* a cyclic complex that is formed by the coordination of the carbonyl oxygen to the Al^{3+} of the alkoxide used as a catalyst and the approach of the $H^{\delta-}$ on the α-carbon of the alkoxide to the $C^{\delta+}$ of the carbonyl carbon [9,10]. As the catalyst exhibits low activity, almost stoichiometric amounts of the catalyst are usually applied to the reaction. One of the reasons for the low activity of the catalyst is due to aggregation. Nguyen et al. reported *in situ* generation of an active catalyst using an alkylaluminum reagent as a pre-catalyst [11,12]. Their method prevents the catalyst aggregation, and the low aggregation leads to high catalytic activity. The bidentate coordination of the carbonyl oxygen to two aluminum ions also results in the rapid progress of the MPV reduction [13]. Despite the development of these procedures, a tedious post-treatment, *i.e.*, separation of the product and the Lewis-acid catalyst, is still required. The MPV reduction can also be performed with a heterogeneous catalyst [14,15]. Use of a heterogeneous catalyst instead of homogeneous one for the MPV reduction makes it easy to separate the product from the catalyst.

We developed the MPV type reduction without a Lewis-acid catalyst by using supercritical or high-temperature alcohols as the reaction media and reducing reagents [16–18]. The selective reduction of unsaturated aldehydes to unsaturated alcohols is one of the advantages of the MPV type reduction using supercritical or high-temperature alcohols [19]. We have revealed that the reduction of carbonyls using supercritical 2-propanol to the corresponding alcohols proceeded *via* a six-membered cyclic complex analogous to that of the MPV reduction (Scheme 1) [20].

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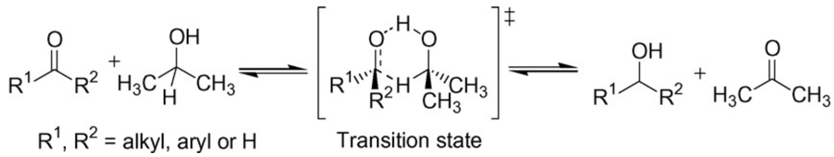

Scheme 1. Proposed reaction mechanism for the reduction of a carbonyl using supercritical 2-propanol.

Table 1
Critical properties[a] and the oxidation enthalpies[b] of alcohols.

Alcohol	Critical temperature (K)	Critical pressure (MPa)	Oxidation enthalpy $\Delta\Delta H$ (kJ/mol)
Methanol	512	8.08	93.0
Ethanol	514	6.13	64.1
1-Propanol	536	5.16	64.2
2-Propanol	508	4.76	55.7
1-Butanol	563	4.41	70.6
2-Butanol	536	4.20	54.5
1-Pentanol	588	3.89	66.2
2-Pentanol	560	3.67	54.7
3-Pentanol	559	–[c]	56.8
Cyclopentanol	619	4.9	45.2
Benzyl alcohol	715	4.3	63.6

[a] Quoted from Refs. [23,24].
[b] Calculated from the standard formation enthalpies of the alcohols and the corresponding carbonyls: see supplementary data.
[c] No available data found.

We now report that the yields of the MPV type reduction of acetophenone by some supercritical or high-temperature alcohols depend on the oxidation enthalpies of the alcohols used as the hydrogen sources and the concentration ratio of the supercritical or high-temperature alcohol/acetophenone. We also attempted the oxidation of several alcohols by supercritical acetone under non-catalytic conditions. This Oppenauer type oxidation [21,22] using the supercritical state was also found to proceed. Critical parameters and the oxidation enthalpies of the alcohols used in this study are listed in Table 1 [23–25].

2. Experimental

2.1. General information and materials

Methanol (99.8%), ethanol (99.5%), 1-propanol (99.5%), 2-propanol (99.5%), 1-butanol (99%), 2-butanol (99%), 1-pentanol (98%), 2-pentanol (98%), 3-pentanol (98%), cyclopentanol (99%), benzyl alcohol (99%), acetophenone (98.5%), acetone (99.5%), 1-phenylethanol (98%), benzhydrol (99%), 2-octanol (98%), 1-octanol (98%), benzyl alcohol (99%), 3-phenyl-2-propen-1-ol (97%) were purchased from Nacalai Tesque, Inc. and used without further purification. GC analyses of reaction mixtures were carried out using a Shimadzu GC-15A equipped with a flame ionization detector. The column used was a 30-m DB-17 capillary column with a 0.32-mm inner diameter and 0.5-μm film thickness (J&W Scientific). The identification of components in the reaction mixture was carried out by comparing the retention times of the authentic samples of each component. The ^{1}H-NMR spectra were also used for the identification.

2.2. General reaction procedure

All reactions were performed in pyrex glass tubes (ca. 2 mm inner diameter, 70 mm length, and 320 μl inner volume). A portion of the reaction mixture (0.25 mol dm^{-3}, 140 μl) was placed in the tube. After replacing the air in the tube with argon, the open end of the tube was sealed by fusing the tube by adjusting the length of the tube to 70 mm. The tube was placed in the vessel (stainless steel, capacity: 30 ml) with methanol to prevent breaking of the tube during the reaction. The vessel was placed in the furnace and then electrically heated to the reaction temperature. The temperature was controlled by a PID temperature control apparatus. Approximately 15 min were required to reach 573 K from room temperature. The reaction time was set to zero when the temperature reached 573 K. The temperature in the stainless vessel was monitored by a thermocouple. After the reaction, the vessel was removed from the furnace and cooled by an air stream to quench the reaction. The reaction mixture in the tube was subjected to a GC analysis to obtain the yield of the product by an internal standard method.

3. Results and discussion

3.1. Reduction of acetophenone using supercritical or high-temperature alcohols

It is well known that the equilibrium constant K of the traditional MPV reduction using RR'CHOH as the reducing reagent [produced alcohol][RR'C=O]/[starting carbonyl][RR'CHOH], reflects the oxidation enthalpy ΔH of RR'CHOH [1]. The lower the oxidation enthalpy of RR'CHOH, the higher the equilibrium constant. In general, the ΔH of a secondary alcohol is lower than that of a primary alcohol (e.g., $\Delta H_{2\text{-propanol}\rightarrow\text{acetone}}$ = 55.7 kJ/mol and $\Delta H_{1\text{-propanol}\rightarrow\text{propanal}}$ = 64.2 kJ/mol) [26]. Therefore, the secondary alcohol is a better reducing reagent for the traditional MPV reduction than the primary alcohol [1,26]. The MPV reduction and the Oppennauer oxidation are equilibrium reactions. According to Le Chatelier's principle, when additional reactant is added to an equilibrium reaction, more product is formed. Thus, when a large excess of alcohol is used as the reducing agent in the MPV reduction, high yields in the reduction can be expected.

The reduction of acetophenone using supercritical or high-temperature alcohols was carried out to confirm that the reduction by supercritical or high-temperature alcohols occurs in the same manner as the traditional catalytic MPV reduction. Fig. 1 shows the time courses of the reduction of acetophenone in methanol, ethanol, 1-propanol, 2-propanol and benzyl alcohol at 573 K. All the examined alcohols act as the reducing reagents during the reduction of acetophenone to 1-phenylethanol. For the reduction with ethanol, 1-propanol or 2-propanol, the yields reach the maximum values at the reaction time of 15 h, and thereafter remain almost unchanged. The attained maximum yields are different for each alcohol; that is, 2-propanol > ethanol > 1-propanol. The dependencies of the reduction yields in the MPV type reduction using supercritical or high-temperature alcohol may be explained on the basis of the oxidation enthalpies of the alcohols used as the hydrogen sources and the concentration of the alcohols during the reaction, in the same manner as in the traditional MPV reduction using a Lewis-acid catalyst. The oxidation enthalpy of 2-propanol ($\Delta H_{2\text{-propanol}\rightarrow\text{acetone}}$ = 55.7 kJ/mol) is much lower than those of ethanol ($\Delta H_{\text{ethanol}\rightarrow\text{ethanal}}$ = 64.1 kJ/mol) and 1-propanol ($\Delta H_{1\text{-propanol}\rightarrow\text{propanal}}$ = 64.2 kJ/mol). Thus, the maximum yield using supercritical 2-propanol is higher than those with ethanol and 1-propanol, although the concentration of the supercritical 2-propanol (5.7 mol dm^{-3}) in the pyrex reactor tube is