Synthesis of Adipic Acid by Oxidation of Cyclohexanol with NO_2 in Supercritical CO_2.

N. Yanagihara[1]*, K. Ohgane[1], Y. Yoshioka[1], N. Abe[1] and M. Yoshida[2]

[1]*Department of Biosciences, Faculty of Science and Engineering, Teikyo University*
1-1 Toyosatodai, Utsunomiya 320-8551
[2]*Department of Applied Chemistry, Faculty of Engineering, Utsunomiya University*
7-2-1 Yoto, Utsunomiya 321-8585

yanagi@koala.mse.teikyo-u.ac.jp

Cyclohexanol was subjected to oxidation with nitrogen dioxide (NO_2) in supercritical carbon dioxide ($scCO_2$). Upon detailed examination of the experimental conditions, it was found that the oxidation reaction was strongly affected by temperature, but not by time, total pressure or amount of NO_2. Consequently, under optimum experimental conditions (for 5 mmol cyclohexanol : 100°C, 1h, 10MPa, 45 mmol NO_2), a maximum total yield of 90% was obtained, in which the product distribution was 76% adipic acid, 10% glutaric acid and 4% succinic acid. Futhermore, after attempting the use of more than 30 commercially available catalysts, it has been revealed that NH_4VO_3 showed the most dramatic effect on the conversion of cyclohexanol to adipic acid (90% yield), with high selectivity (95%).

INTRODUCTION

Adipic acid is an important chemical, whose production is crucial for the manufacture of nylon-6,6, a necessity of modern life. Most industrial adipic acids production processes use nitric acid oxidation of cylcohexanol, cyclohexanone, or both. However, the use of nitric acid leads to the emission of an inevitable stoichiometric waste of nitrous oxide (N_2O), which is commonly thought to cause global warming and ozone depletion. Considering this, many alternative synthetic routes have been developed in recent years, such as the oxidation of six-carbon feedstocks (cyclohexane, cyclohexene, cyclohexanol and cyclohexanone) in the presence of unique catalysts [1].

However, supercritical fluids (SCF), and supercritical CO_2 ($scCO_2$) in particular, have recently attracted a great deal of attention as the fourth chemical phase, in addition to the gas, liquid and solid phases. The physico-chemical characteristics of SCF, such as miscibility with other gases, high mixing rates and relatively weak molecular association, make them unusual media for chemical reactions [2]. Among the SCF, $scCO_2$ seems to be the most attractive because of its low cost, low critical temperature (304 K) and pressure (7.4 MPa), and its non-toxic and non-flammable nature. Furthermore, the separation of CO_2 from the reaction mixture is energy-efficient; hence, the product is obtained directly by simple pressure reduction. Thus, $scCO_2$ shows promise as an environmentally acceptable solvent for a wide range of chemical, analytical, and materials processes, including extraction and materials processing [3], SCF chromatography [4], polymerization [5], and catalytic reactions [6].

Recently, we have succeeded in oxidatively degrading Nylon-6 and -6,6 with NO_2 in sc CO_2; it was found in that study that valuable short-chain α, ω-diacids could be obtained in a good yield under relatively mild conditions [7]. In a continuation of our study seeking a new type of oxidation reaction in $scSO_2$, we describe herein the oxidation of cyclohexanol with NO_2 in $scCO_2$.

MATERIALS AND METHODS

Liquid CO_2 and liquid NO_2 were purchased from Hikari Sanso Co., Ltd. and Takachiho Chemical Ind., Ltd., respectively. Both of their purities were > 99.8%. All other chemicals were purchased from Wako Pure Chemical Ind., Ltd. or Aldrich Chemical Co. with purities >99.9%, and used as received.

All of the reactions were conducted in batch in a 50-cm^3 high-pressure stainless steel reactor with a magnetic stirrer. Ca. 5 mmol of cyclohexanol was placed into the reactor, and the inside of the reactor was purged with a small amount of CO_2. Following by the introduction of appropriate amounts of liquid NO_2 and liquid CO_2, the reactor was heated to the desired reaction temperature using an oil bath and maintained for a set period of time. In this stage, heating rate was critical. The reaction $N_2O_4 \rightleftharpoons 2NO_2$ is extremely exothermic, so the reaction occurs vigorously and can easily get out of control. To prevent this, the heating rate should be lower than 1.5 $^\circ C \cdot min^{-1}$. For example, 1 h was required to leach 100 $^\circ C$ from the ambient temperature. Consequently, the overall reaction time included this heating process time and the following reaction time. However, the preheating times were almost the same for all of the experiments, and also to avoid confusion, *only the reaction time will be denoted hereafter in this paper*. After a certain reaction time, the reactor was put into an ice bath to quench the reaction. When the temperature in the reactor was dropping to the ambient temperature, the vapor space was vented slowly. After almost all of the vapor was vented, the reactor was opened and the reaction product was recovered with acetone.

The reaction product as recovered was qualitatively analyzed by NMR. Additionally, the same product was esterified by diazomethane, and then analyzed by GC-MS and GLC. The separation and quantitative analysis of a mixture of dimethyl esters of the products were carried out at 90$^\circ C$ on a 6 ft. column of silylated diatomaceous earth (NEOSRB-NCS) containing 5(w/w)% SE-30 with helium as a carrier gas. The detector was a FID. The results of GLC analysis were also used to evaluate the yields of each the products. The gases generated during the reaction were also analyzed by GLC equipped with a FID detector, using a 6-ft column of Unibeads-C at 110$^\circ C$.

RESULTS

The final product, which was obtained by the oxidation of cyclohexanol with NO_2 in $scCO_2$, was first subjected to analysis by ^{1}H-NMR. No any nitro-compounds were detected by NMR. Thereafter, upon esterification of the product, GC-MS analysis was also conducted, revealing the clear predominance of three compounds. Although a molecular ion peak was not detectable for all three compounds, by comparing each MS spectrum and its fragamentation pattern with those of the MS spectrum dadabase (NIST Library), the three products were successfully identified as dimethyl succinate, dimethyl glutrate and dimethyl adipate. Therefore, it was concluded that the product of the oxidation of cyclohexanol with NO_2 in

scCO$_2$ was a mixture of short chain aliphatic α, ω-diacids: succinic acid (**SA**), glutaric acid (**GA**) and adipic acid (**AA**). Next, we focused our attention on the yields of the α, ω-diacids, and attempted to verify the effects of varying the experimental conditions, including reaction temperature, time, pressure and quantity of NO$_2$, on their yield.

Effect of experimental factors on the yield of α, ω-diacids

The effect of temperature on the yields was examined, keeping reaction time, pressure and amount of NO$_2$ constant. As can be seen in Fig. 1, it is clear that the main product of cyclohexanol oxidation was **AA**, and that **SA** and **GA** were also present as minor products. The total yields of the acids increased with increasing temperature, and the highest total yield ca. 85% was observed at 100˚C, under which conditions the yield of **AA** was 73% with 86% selectivity. As shown in Fig. 2, the elongation of the reaction time led gradually to a reduction in both the total yield of the diacids and the yield of **AA**.
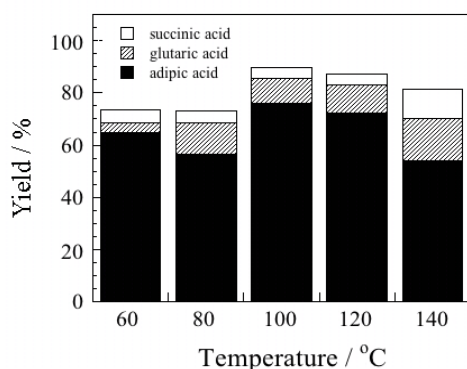

Figure 1. Effect of temperature on the yield of α,ω-diacids obtained by the oxidation of cyclo-hexanol. (sample: 5 mmol, 1 h, 10 MPa, 2.0 g NO$_2$.)
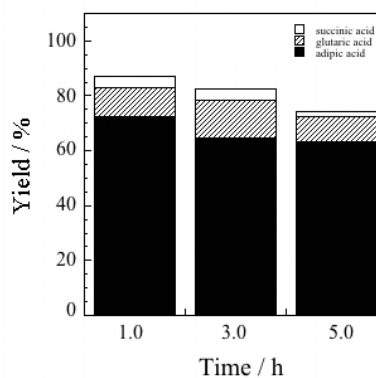

Figure 2. Effect of time on the yield of α,ω-diacids obtained by the oxidation of cyclohexanol. (sample: 5 mmol; 100˚C, 10 MPa, 2.0 g NO$_2$.)

As shown in Fig. 3, when the effect of total pressure was examined, almost no change was observed in the overall yield. However, it is noteworthy that the **AA** conversion was as its maximum (88% of total yield with 80% selectivity for **AA**) at 10MPa. Beyond the maximum, the yield of **AA** tended to decrease drastically. Fig. 4 shows that the amout of NO$_2$ did not affect the total yield. The highest **AA** conversion, however, was obtained with 2 g of NO$_2$, equal to 40 mmol, 8 times more than the amount of cyclohexanol in moles.

Considering the aforementioned results, we concluded that the most promising experimental conditions for obtaining **AA** from the oxidation of cyclohexanol were as
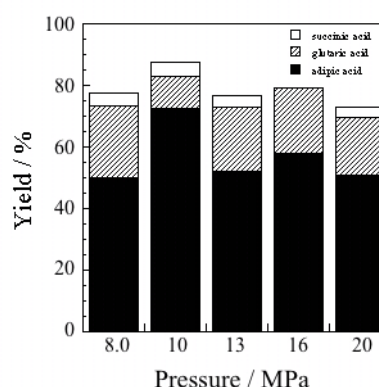

Figure 3. Effect of pressure on the yield of α,ω-diacids obtained by the oxidation of cyclohexanol. (sample: 5 mmol; 1 h, 100 ˚C, 2.0 g NO$_2$.)

follows: reaction time 1 h, 120 °C, 10 MPa and 2.0 g of NO$_2$.

Effect of catalyst on the yield of α, ω-diacids

The product of the oxidation of cylohexanol with NO$_2$ in scCO$_2$ was unfortunately a mixture of α, ω-diacids. Moreover, it was found that the selectivity of **AA** was as only high as 64-89%, a value somewhat lower than expected, although each of the reaction conditions, such as temperature, time, total pressure and amount of NO$_2$, varied widely. Therefore, we attempted to use a catalyst to improve the selectivity of AA in the oxidation reaction of cyclohexanol.

More than 30 commercially available catalysts, almost all of which were transition metal complexes, were first examined. Of those catalysts applied to the reaction, acetyl-acetonate complexes, especially those of V(III) and VO(IV), showed good catalytic behavior on the oxidation of cyclohexanol, as shown in Fig. 5. It is noteworthy that no **SA** was obtained when both of V(III) and VO(IV) complexes were used, despite the fact that the total yield was lower that that recorded in the reaction without a catalyst. However, the selectivity of **AA** was raised from 89% in the case of the non-catalytic reaction to 92% in the VO(acac)$_2$ catalyzed reaction. Howeve decreasing the concentration of VO(acac from 10 mol% to 1 mol% caused both the tot yield and the selectivity to decrease as well.

Since **AA** selectivity was promisingly change when the complexes containing vanadium as catalyst were applied to the present system other vanadium complexes were checke carefully. Finally, we succeeded in findir that NH$_4$VO$_3$ was superior to any oth catalyst studied in the present oxidatic reaction. As shown in Fig. 6, the addition only 1 mol% of NH$_4$VO$_3$ to the syste... greately improved both the total yield and the **AA** selectivity; i.e., while the former value increased to 95% from 88% over the non-catalytic reaction, the **AA** selectivities were
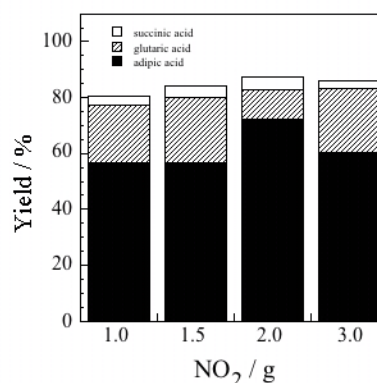

Figure 4. Effect of amount of NO$_2$ on the yield of α,ω-diacids obtained by the oxidation of cyclo-hexanol. (sample: 5 mmol, 1 h, 100 °C, 10 MPa)
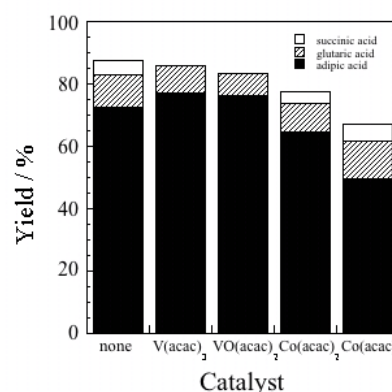

Figure 5. Effect of catalysts on the yield of α,ω -diacids obtained by the oxidation of cyclo-hexanol. (sample: 5 mmol, catalyst : 10 mol%, 1 h, 100 °C, 10 MPa, 2.0 g NO$_2$.)
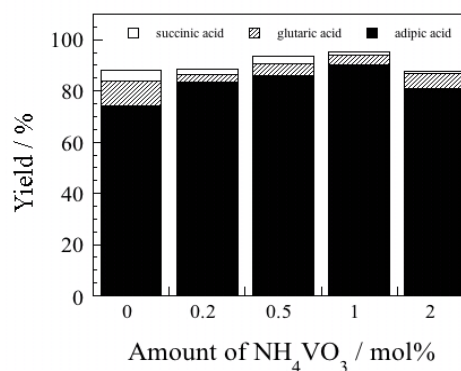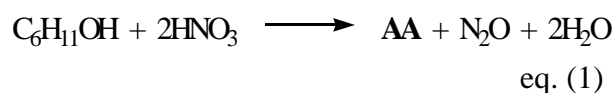

Figure 6. Effect of NH$_4$VO$_3$ on the yield of α,ω-diacids obtained by the oxidation of cyclo-hexanol. (sample: 5 mmol, 1 h, 100 °C, 10 MPa ; 2.0 g NO$_2$.)

95% with the catalyst and 84% without catalyst, respectively. However, there **SA** and **GA** still remained as by-products, with yield of 1.2% and 3.9%, respectively. As shown in Fig. 6, increasing or decreasing the amount of NH_4VO_3 based on the quantity of 1 mol% did not improved the results.

Analysis of N_2O

The conventional method for the production of AA involves the oxidation of a cyclohexanol-cyclohexanone mixture. This process, however, is currently problematic because environmentally harmful N_2O is generated stoichiometrically, as the following equation shows.
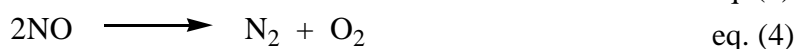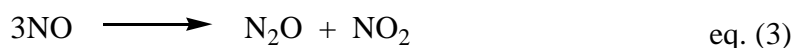
$$C_6H_{11}OH + 2HNO_3 \longrightarrow AA + N_2O + 2H_2O$$

eq. (1)

Figure 7. N_2O yield as a function of time during the oxidation of cyclo-hexanol. (sample: 5 mmol; 1 h; 100 °C ; 10 MPa ; NO_2 : 2.0 g)

In order to improve the traditional method, the toxic reactant HNO_3 was replaced in this study with NO_2 for the production of **AA**, in anticipation of the following environmentally benign reaction.

$$C_6H_{11}OH + 2NO_2 \longrightarrow AA + N_2 + 2H_2O$$

eq. (2)

Unfortunately, contrary to our expectations, we found that N_2O was also generated in our reaction system, as shown in Fig. 7. When cyclohexanol was allowed to react with NO_2 in $scCO_2$ for 2 h, ca. 45% mol (2.3 mmol) of N_2O was found to be produced from an initial amount of 5.0 mmol cyclohexanol. According to the literature [8], N_2O_4 exhibits various conditions-dependent characteristic dissociations as follows: (1) $N_2O_4 \rightleftharpoons NO_2^+ + NO_2^-$ in acidic conditions, (2) $N_2O_4 \rightleftharpoons NO^+ + NO_3^-$ in basic conditions, and (3) $N_2O_4 \rightleftharpoons 2NO_2\bullet$ in heating. Together with our recent study [7], the results of the present study suggest that the overall yield of α, ω-diacids strongly and sensitively depends on the temperature, and radical species of NO_2 presumably play an important role in the oxidation of cyclohexanol with N_2O_4 in $scCO_2$.

However, since NO_2 also exhibits an equilibrium of $N_2O_4 \rightleftharpoons 2NO_2$, in which the equilibrium moves to the right with an increase in temperature, it might be true that a small amount of neutral NO_2 species always exists in the present system. It is known that NO_2 easily decomposes thermally to produce NO: $NO \rightleftharpoons 2NO + O_2$. Thus formed NO successively decomposes to:

$$3NO \longrightarrow N_2O + NO_2 \qquad \text{eq. (3)}$$
$$2NO \longrightarrow N_2 + O_2 \qquad \text{eq. (4)}$$

At relatively low temperatures eq. (3) takes place, and the disproportionation reaction of NO, eq. (4), occurs catalytically at elevated temperatures [9].
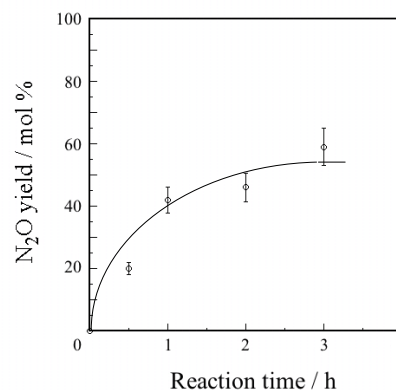
At the present time, it is difficult to explain the generation of N_2O in our reaction system. It is possible that because our system requires an excess of NO_2 to complete the reaction, eq. (3) proceeds via some reaction path, and/or extra NO_2 reacts with H_2O resulting from eq. (2),

CONCLUSION

This study revealed that **AA** can be successfully obtained by the oxidation of cyclohexanol with NO_2 in $scCO_2$ under relatively mild conditions (100˚C, 10 MPa). The oxidation reaction required 1 h of preheating, and was completed within an additional hour with 73% yield, together with more than 85% selectivity under noncatalytic conditions. Moreover, it was revealed that both the yield and the selectivity of **AA** in this reaction can be improved strikingly by the addition of a catalytic amount of vanadium complexes such as $V(acac)_3$, $VO(acac)_2$, and NH_4VO_3. In particular, in the presence of 1.0 mol% of NH_4VO_3, cyclohexanol was 95% converted to **AA** with a selectivity as high as 95%.

At this moment, the mechanism for the oxidation reaction of cyclohexanol with NO_2 in $scCO_2$ can not be proposed. However, we believe that the reaction might have occurred via a radical chain reaction. NO_2 radicals formed upon the thermal decomposition of N_2O_4 attacked the OH group of cyclohexanol, and $C_6H_{11}O$ radicals formed. The *ipso*-proton, located at the bottom of the $C_6H_{11}O$ radical, was then eliminated to form cyclohexanone. In the next stage, it is probable that the *enolic* form of cyclohexanone formed as an intermediate, as cited in the literature [10]. Subsequently, this enol leads to the formation of cyclohexane-1,2-dione as the next intermediate, and upon the cleavage of this cyclic diketone, **AA** was formed as the final product. However, because of the complicated nature of the mechanism of the present reaction, N_2O was generated unexpectedlly.

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