Reduction of Dicarboxylic Acid Anhydride with 2-Propanol over Hydrous Zirconium Oxide

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(Received June 15, 1991)

The reduction of dicarboxylic acid anhydrides with 2-propanol proceeded efficiently over hydrous zirconium oxide to give the corresponding lactones and cyclic ethers. Secondary and primary alcohols, with the exception of methanol, are able to act as hydride donors in this reduction. The reduction proceeded as nearly second order concerning the concentration of 2-propanol and minus order concerning that of acid anhydride. These results suggest that the reduction was preferred under lower concentrations of acid anhydride and higher concentrations of 2-propanol. The selectivity of lactone or ether could be changed by the reaction temperature or the molar ratio of dicarboxylic acid anhydride to alcohol.

In previous papers, hydrous zirconium oxide has been reported to have various catalytic activities, such as the amidation[1) of carboxylic acid with amine and the esterification[2) of carboxylic acid with alcohol. The reduction of aldehydes, ketones,[3,4) carboxylic acids,[5) and nitriles[6) with 2-propanol was also catalyzed by hydrous zirconium oxide to give the corresponding alcohol efficiently. Several oxides, such as zeolite[7) and oxide of aluminium,[8) magnesium,[9) silicon,[9) calcium,[9,10) barium,[9) strontium,[9) zirconium,[11) titanium,[11) vanadium,[11) molybdenium,[11) zinc,[11) thorium,[11) and lanthanoid groups,[12) are known to catalyze the reduction of aldehydes and ketones with alcohol as a hydride source. However, no other studies have been reported on the reductions of carboxylic acids or dicarboxylic acid anhydrides with alcohol. In a previous paper,[5) we investigated the catalytic activity of the reduction of cyclohexanecarboxylic acid with 2-propanol over such metal oxides as silica gel, zeolite(A-4), Al_2O_3, MgO, hydrous cerium oxide, hydrous aluminium oxide, hydrous iron oxide, hydrous niobium oxide, and hydrous titanium oxide. However, reduction did not occur in all of the catalysts systems. These results indicated that only hydrous zirconium oxide had catalytic activity for the reduction of carboxylic acid with 2-propanol. We then applied this catalyst system to the reduction of anhydrides of dicarboxylic acids.

Generally, the reduction of anhydride of dicarboxylic acid has been carried out using metal hydrides or by catalytic hydrogenation. These reactions give the corresponding lactone, diol, or cyclic ether. Lithium aluminum hydride,[13) sodium dihydroidobis(2-methoxyethoxy) aluminate,[14) or sodium borohydride[15) has been used for metal hydride reduction. However, these stoichiometric reactions were not suitable for reduction on an industrial scale. In the case of catalytic hydrogenation, a heterogeneous catalyst, such as Ni–Mo,[16) Ni–Mo–Ca,[17) Pd–Re/TiO_2,[18) or Ru–organic phosphine/Zr–organic sulfonic acid,[19) or a homogeneous catalyst, such as $RhCl_2(PPh)_3$,[20) is used. Generally, catalytic hydrogenation must be carried out under high pressure.

The reduction of anhydrides of dicarboxylic acid with 2-propanol as the hydride source over hydrous zirconium oxide has several advantages: 1) the reduction can proceed under atmospheric pressure, 2) the hydrous zirconium oxide is a heterogeneous catalyst and, therefore, the products are easily isolated. Hydrous zirconium oxide comprises hard, translucent granules; it is stable at room temperature in air for as long as 7 years. The oxide has a small amount of strong acid sites as well as strong basicity sites;[21) the reaction of compounds which are unstable under acidic conditions could be performed.[22) The oxide was amorphous,[23) and its specific surface area was 200 to 300 $m^2 g^{-1}$.[24)

In this paper we wish to report that hydrous zirconium oxide catalyzes the reduction of dicarboxylic acid anhydride with alcohol efficiently; these reductions gave the corresponding lactones and/or cyclic ethers. The reactions were carried out in the vapor phase.

Experimental

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

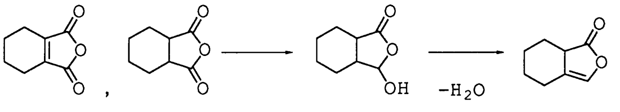
Hydrous Zirconium Oxide. To a solution of zirconium dichloride oxide ($ZrOCl_2 \cdot 8H_2O$) (200 g of a solid in 10 dm^3 of deionized water), we slowly added an aqueous solution of sodium hydroxide (1 mol dm^{-3}) at room temperature. Constant, gentle stirring was maintained, and the addition was continued until the pH of the resulting solution reached 6.80. The resulting product was filtered and washed free of chloride ions. The 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 subsequently heated at 300 °C for 5 h.

General Procedures for Vapor-Phase Reactions. Catalytic reduction was carried out in a glass-flow reactor (6.5 mm in diameter) with a fixed-bed catalyst: The flow rate of nitrogen gas was 60 $cm^3 min^{-1}$; the catalyst was 2.0 g, 24—60 mesh; and the reaction temperature was 250—330 °C. A mixture of a dicarboxylic acid anhydride, an alcohol, and a hydrocarbon as an internal standard was fed into the reactor (5 or 10 $cm^3 h^{-1}$) by means of a microfeeder. In some cases, 1,4-dioxane or tetrahydrofuran was also added in order to dilute the reaction mixture. The conversion and yield of the reaction were determined after steady state had been reached. The products were then analyzed by gas chromatography (a capillary column PEG 20M, 25 m, OV 101 25 m, or a packed column Gaschropack 54, 2 m). The products were identified by a comparison of their retention times with those of authentic samples, GC-MS, or GC-IR.

Procedures in the Autoclave. In a 100 cm^3 autoclave were placed the catalyst (1.0 g), hexahydrophthalic anhydride (10 mmol), 2-propanol (5 ml), and a hydrocarbon as an internal standard. The autoclave was then heated to the reaction temperature (280 °C), which was maintained for 3 h. Analyses of the products were performed in a manner similar to that described above.

Results and Discussion

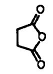
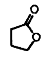
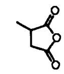
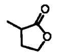
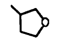
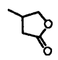
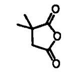
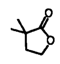
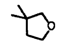
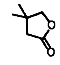
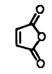
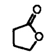
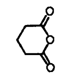
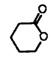
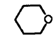
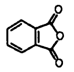
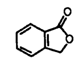
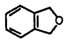
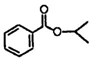
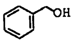
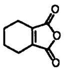
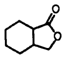
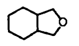
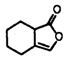
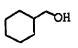
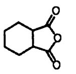
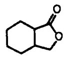
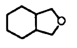
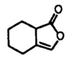
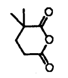
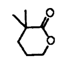
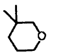
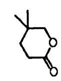
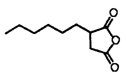
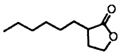
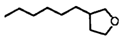
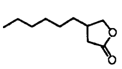
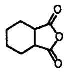
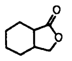
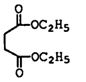
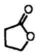
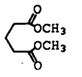
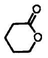
Reduction of Dicarboxylic Acid Anhydride. The results of the reaction of dicarboxylic acid anhydrides with 2-propanol over hydrous zirconium oxide are listed in Table 1. Most of the dicarboxylic acid anhydrides were reduced to give the corresponding lactones and/or cyclic ethers. Succinic anhydride was efficiently reduced to give γ-butyrolactone and tetrahydrofuran. Although α-methyl derivatives of succinic anhydride were also reduced to give the corresponding lactones and cyclic ethers, the steric hindrance lowered the reactivity (Entries 1—3). The regioselectivities of the unsymmetrical acid anhydrides were not good. The conjugated double bonds of maleic anhydride and 3,4,5,6-tetrahydrophthalic anhydride were reduced to give saturated lactones or cyclic ethers (Entries 4 and 7). This result is similar to that regarding the reduction of conjugated carboxylic acid derivatives, such as cinnamonitrile.[6] The anhydride of 1,5-alkanedioic acid, such as glutaric anhydride, was also reduced to give the corresponding lactone and cyclic ether (Entry 5). Phthalic anhydride was reduced to give phthalane in high yield. The reaction of phthalic anhydride also gave small amounts of diisopropyl benzoate and benzyl alcohol by decarboxylation (Entry 6). In the case of the reduction of 3,4,5,6-tetrahydrophthalic anhydride and hexahydrophthalic anhydride, small amounts of unsaturated lactones were detected (Entries 7 and 8). The unsaturated lactone (**3**) is thought to be produced by the dehydration of the half-reduction intermediate (**2**), which is shown in the following scheme:



1 **2** **3**

The steric-hindered anhydrides, such as 2,2-dimethylglutalic anhydride and 2-hexylsuccinic anhydride, resisted reduction (Entries 9 and 10). When

Table 1. Reduction of Anhydride with 2-Propanol[a)]

	Reactant	Conv./%	Yield/%			
1		100		20		62
2		100		28		28
				29		
3		73		25		2
				32		
4		100		42		30
5		100		57		11
6[b)]		100		0		80
				2		14
7[b)]		86		22		20
				10		3
8[b)]		61		15		5
				16		
9[b)]		41		4		6
				4		
10[b)]		59		7		9
				4		
11[c)]		94		34		
12		100		10		61
13		100		59		17

a) Catalyst; hydrous zirconium oxide 2.0 g, temperature; 280° C, reactant; 0.05 mmol cm^{-3} in 2-propanol, reactant: 2-propanol=1:260, sample feed; 10 cm^3 h^{-1}. b) Temperature; 320° C. c) Reaction in the autoclave, catalyst; hydrous zirconium oxide; 1.0 g, temperature; 280 °C, 3 h, reactant 10 mmol in 2-propanol (5 ml).

Table 2. Reduction of Succinic Anhydride with Several Alcohols[a)]

Entry	Alcohol	Conversion/%	Yield/%		
			Lactone	THF	Diester
1	Methanol	100	1	0	80
2	Ethanol	100	39	0	31
3	1-Propanol	100	50	0	41
4	1-Butanol	100	56	3	30
5	2-Propanol	100	52	15	8
6[b)]	2-Propanol	100	39	1	8
7[b)]	Cyclohexanol	100	20	0	17

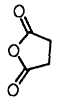
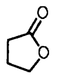
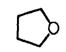
a) Catalyst; hydrous zirconium oxide 2.0 g, temperature; 285 °C, carrier gas; N_2 60 $cm^3\ min^{-1}$, succinic anhydride; 0.1 mmol cm^{-3} in alcohol and 1,4-dioxane(succinic anhydride:alcohol=1:65), sample feed; 10 $cm^3\ h^{-1}$. b) Succinic anhydride 0.2 mmol cm^{-3} in alcohol and 1,4-dioxane (succinic anhydride: alcohol=1:30), sample feed; 5 $cm^3\ h^{-1}$.

the reduction of hexahydrophthalic anhydride with 2-propanol was carried out in an autoclave, the corresponding lactone was given in higher yield than the vapor-phase reaction (Entry 11).

Reduction of Diester. The results of the reduction of diethyl succinate and dimethyl glutarate are also shown in Table 1 (Entries 12 and 13). Diesters as well as the dicarboxylic acid anhydrides were efficiently reduced to the corresponding lactones or cyclic ethers, suggesting that the reduction of diesters proceeds via a similar reaction pass way as that of dicarboxylic acid anhydride.

Dependence on Alcohol as a Hydrogen Donor. The reductions of succinic anhydride were carried out with several kinds of alcohols over hydrous zirconium oxide; the results are shown in Table 2. Although the reaction with methanol mainly gave the diester, on the other hand, reactions with other primary alcohols mainly gave γ-butyrolactone (Entries 1—4). In a previous paper[3)] we reported that primary alcohols did not work as hydride donors in the reduction of hexanal. However, they could act as hydride donors in this reaction. The reducing power of secondary alcohols was superior to that of primary ones, since the total yield of γ-butyrolactone and tetrahydrofuran when using secondary alcohols was higher than that when using primary alcohols (Entry 5). The reduction with 2-propanol, whose steric hindrance is the least among secondary alcohols, gave γ-butyrolactone and tetrahydrofuran in the highest yield (Entries 6 and 7). 2-Propanol was the most suitable as the hydride donor for this reduction.

Table 3. Reduction of Anhydride with 2-Propanol[a)]

	Reactant	Conv./%	Yield/%	
	 : 2-propanol			
1	1:130	100	63	19
2	1:195	100	47	35
3	1:260	100	20	62

a) Catalyst; hydrous zirconium oxide 2.0 g, temperature; 280 °C, reactant; 0.05 mmol cm^{-3} in 2-propanol and 1,4-dioxane, sample feed; 10 $cm^3\ h^{-1}$.

Variation of the Selectivity for the Lactone or Cyclic Ether. In order to investigate the variation of the selectivity for the lactone or cyclic ether, the reduction was carried out under various conditions. In the first place, we tried changing the molar ratio of the dicarboxylic acid anhydride to the alcohol. Table 3 shows the dependence on the molar ratio of succinic anhydride to 2-propanol in the reduction of succinic anhydride. In all cases, the total yields of both γ-butyrolactone and tetrahydrofuran were the same. However, when the molar ratio of succinic anhydride to 2-propanol was 1 : 130, the yield of γ-butyrolactone was 63%. An increase in the molar ratio of 2-propanol to succinic anhydride caused the yield of tetrahydrofuran to increase, and the reduction gave tetrahydrofuran in 62% yield in the ratio 1 : 260. This suggests that the selectivity of the lactone or cyclic ether can be changed by the molar ratio of the dicarboxylic acid anhydride to the alcohol.

We then tried to change the reaction temperature. The reduction of succinic anhydride with 2-propanol in 1,4-dioxane as a diluent was carried out under the following conditions: The concentration of succinic anhydride, that of 2-propanol, the rate of sample feed, and the temperature range were 0.1 mol dm^{-3}, 6.5 mol dm^{-3}, 10 $cm^3\ h^{-1}$, and 250—330 °C, respectively. The results are given in Fig. 1. The reaction of the succinic anhydride with 2-propanol mainly led to esterification below 270 °C. However the reduction became dominant over the esterification and gave γ-butyrolactone and tetrahydrofuran above 280 °C. The main product of the reduction was γ-butyrolactone in the range of about 280 to 300 °C, and the succinic anhydride was further reduced to tetrahydrofuran as a main product at temperatures above 305 °C. This temperature dependence is similar to that of the reduction of carboxylic acid[5)] and nitrile.[6)]

On the other hand, reduction of methylsuccinic anhydride was carried out at 280 and 300 °C. α-

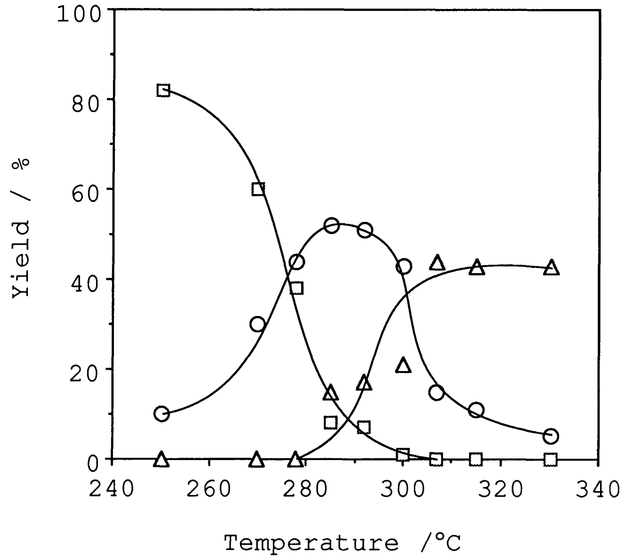


Fig. 1. Temperature dependence of the reduction of succinic anhydride with 2-propanol in 1,4-dioxane. ○: γ-Butyrolactone, △: Tetrahydrofuran, □: Diisopropyl succinate. Catalyst; hydrous zirconium oxide 2.0 g, carrier gas; N_2 60 cm^3 min^{-1}, succinic anhydride; 0.1 mmol cm^{-3} in 2-propanol and 1,4-dioxane (succinic anhydride:2-propanol=1:65), sample feed; 10 cm^3 h^{-1}.

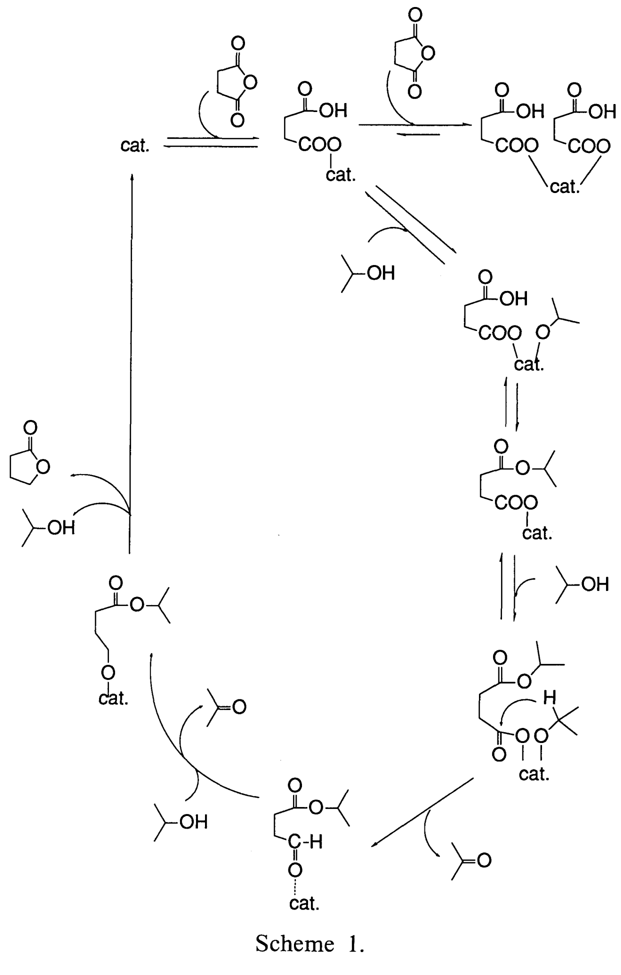
Methyl-γ-butyrolactone, β-methyl-γ-butyrolactone, and 3-methylterahydrofuran were obtained in 28, 29, and 28% yields, respectively, at 280 °C; they were obtained in 2.1, 1.6, 76% yields, respectively, at 300 °C. The selectivity was also changed by the reaction temperature in this case.

The reduction over hydrous zirconium oxide gave the lactone at a relatively lower temperature, and mainly gave the ether at higher temperatures. We have described above that the selectivity of the lactone or cyclic ether could be changed by the molar ratio of anhydride to alcohol in the reduction of dicarboxylic acid anhydride; it could also be controlled by the reaction temperature.

Kinetic Discussion. In order to determine the order of alcohol concentration, the reduction rates of succinic anhydride with 2-propanol were measured under the following conditions: At a reaction temperature of 278 °C and a constant concentration of succinic anhydride of 0.1 mol dm^{-3}, the concentration of 2-propanol was varied in the range from 4.00 to 8.50 mol dm^{-3}, and 1,4-dioxane was added as a diluent to keep the volume of the reaction mixture constant. In all cases, the reactions under these conditions gave only γ-butyrolactone as the reduction product. The correlation between the natural logarithm of the concentrations of 2-propanol and that of the specific rate indicated that the estimated order in alcohol concentration was estimated is +1.8.

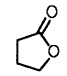
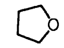
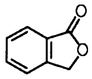
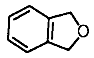
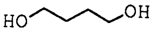
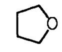
Similarly, we investigated the order of the succinic anhydride concentration under the following conditions: A constant concentration of 2-propanol of 6.5 mol dm^{-3}, and varying concentrations of succinic anhydride in the range from 0.1 to 0.22 mol dm^{-3}. The reaction rate was estimated to be dependent on the concentration of succinic anhydride to an order of −1.2. The minus order dependence on the concentration of succinic anhydride suggests that succinic anhydride inhibits the reaction by adsorption on the surface of the hydrous zirconium oxide.

The mechanism for esterification over hydrous zirconium oxide has been reported to proceed as first-order on the alcohol concentration and minus first order on carboxylic acid.[1] The order on succinic anhydride concentration is the same as that on acetic acid in esterification with ethanol. The first step in the reduction of acid anhydride is considered to proceed by a similar mechanism on the esterification and gave the half ester. The half ester was reduced by 2-propanol to give a derivative of aldehyde; further reduction gave lactone. We postulate that the rate-determining step is a hydride transfer from 2-propanol to the half ester, since it has been reported[2] that the rate-determining step for the reduction of aldehydes is a hydride transfer from 2-propanol. These mechanism are shown in Scheme 1. Based on this proposed scheme, the second-order for alcohol and the minus first-order for succinic anhydride



Scheme 1.

Table 4. Reduction of Lactone with 2-Propanol[a)]

	Reactant	Conv./%	Yield/%
1		100	 77
2[b)]		100	 95
3		100	 86

a) Catalyst; hydrous zirconium oxide 2.0 g, temperature; 300 °C, reactant; 0.2 mmol cm^{-3} in 2-propanol, sample feed; 5 cm^3 h^{-1}. b) Catalyst; hydrous zirconium oxide 2.0 g, temperature; 320 °C, reactant; 0.05 mmol cm^{-3} in 2-propanol, sample feed; 10 cm^3 h^{-1}.

would be obtained by the use of a stationary-state method. These results agreed with the experimental data.

The reduction proceeded in nearly second order for the concentration of 2-propanol and in a minus order for that of acid anhydride. These results suggested that the reduction was preferred under lower concentrations of acid anhydride and higher concentrations of 2-propanol.

Although the reduction of dicarboxylic acid anhydride gave the corresponding lactone and cyclic ether, we could not find the corresponding diol. We had assumed that this reduction would give the corresponding diol, since the reduction of carboxylic acid ester gave the corresponding alcohol, as was reported in our previous paper.[5)] In order to clarify why the diol was not detected, the reaction of 1,4-butanediol over hydrous zirconium oxide was carried out. The results are shown in Table 4. 1,4-Butanediol converted into tetrahydrofuran efficiently. The reaction of lactones was also carried out under the same conditions; they were reduced to the corresponding ethers in high yields, as shown in Table 4. In a previous paper[2)] we described that esters were reduced to give the corresponding alcohols efficiently. Lactones could therefore be converted to the corresponding diols. We consider that the reaction of dicarboxylic acid anhydride gives the ether by way of the diol.

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