Preparation of Industrially Important Hydroxy Acids and Diacids from 2,2-Disubstituted Propane-1,3-Diols and Linear Primary Diols by Green Chemistry Methods

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ACADEMIC DISSERTATION

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PREFACE

The experimental work for this thesis was carried out at the Laboratory of Organic Chemistry of the University of Helsinki. The supervisor of this investigation was Professor Tapio Hase. M.Sc. Jukka Hietala advised on the special aspects of this work.

The high performance liquid chromatograms and the gas chromatograms of this work were in part run at Fortum Oil and Gas Oy. Dr. Risto Koivula from the Laboratory of Radiochemistry of the University of Helsinki carried out the radioisotope X-ray fluorescence measurements. The scanning electron micrographs were recorded at the Electron Microscopy Unit in the Institute of Biotechnology of the University of Helsinki.

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Helsinki, January 2008
Jari Karppanen

ABSTRACT

Environmentally benign and economical methods for the preparation of industrially important hydroxy acids and diacids were developed. The carboxylic acids, used in polyesters, alkyd resins, and polyamides, were obtained by the oxidation of the corresponding alcohols with hydrogen peroxide or air catalyzed by sodium tungstate or supported noble metals. These oxidations were carried out using water as a solvent. The alcohols are also a useful alternative to the conventional reactants, hydroxyaldehydes and cycloalkanes.

The oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide catalyzed by sodium tungstate afforded 2,2-disubstituted 3-hydroxypropanoic acids and 1,1-disubstituted ethane-1,2-diols as products. A computational study of the Baeyer-Villiger rearrangement of the intermediate 2,2-disubstituted 3-hydroxypropanals gave in-depth data of the mechanism of the reaction.

Linear primary diols having chain length of at least six carbons were easily oxidized with hydrogen peroxide to linear dicarboxylic acids catalyzed by sodium tungstate.

The Pt/C catalyzed air oxidation of 2,2-disubstituted propane-1,3-diols and linear primary diols afforded the highest yield of the corresponding hydroxy acids, while the Pt, Bi/C catalyzed oxidation of the diols afforded the highest yield of the corresponding diacids. The mechanism of the promoted oxidation was best described by the ensemble effect, and by the formation of a complex of the hydroxy and the carboxy groups of the hydroxy acids with bismuth

atoms. The Pt, Bi/C catalyzed air oxidation of 2-substituted 2-hydroxymethylpropane-1,3-diols gave 2-substituted malonic acids by the decarboxylation of the corresponding triacids.

Activated carbon was the best support and bismuth the most efficient promoter in the air oxidation of 2,2-dialkylpropane-1,3-diols to diacids. In oxidations carried out in organic solvents barium sulfate could be a valuable alternative to activated carbon as a non-flammable support.

In the Pt/C catalyzed air oxidation of 2,2-disubstituted propane-1,3-diols to 2,2-disubstituted 3-hydroxypropanoic acids the small size of the 2-substituents enhanced the rate of the oxidation. When the potential of platinum of the catalyst was not controlled, the highest yield of the diacids in the Pt, Bi/C catalyzed air oxidation of 2,2-dialkylpropane-1,3-diols was obtained in the regime of mass transfer. The most favorable pH of the reaction mixture of the promoted oxidation was 10. The reaction temperature of 40°C prevented the decarboxylation of the diacids.

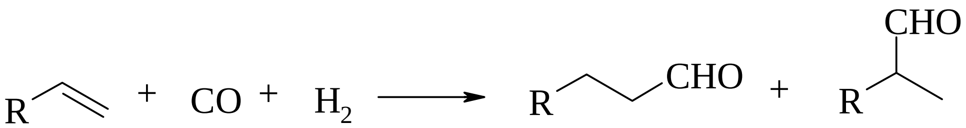
CONTENTS

ABBREVIATIONS

A	pre-exponential factor
Ac	acetyl
atm.	atmosphere
C	conversion
COMPASS	Condensed-phase Optimized Molecular Potentials for Atomistic Simulation Studies
DFT	density functional theory
DND	double numerical plus d-functions
E_a	apparent activation energy
ee	enentiomeric excess
equiv.	equivalent
FID	flame ionization detector
GC	gas chromatography
HPLC	high performance liquid chromatography
IUPAC	The International Union of Pure and Applied Chemistry
k	rate constant
k_k	kinetic factor
k_{mt}	mass transfer factor
lit.	literature
MMSI	medium metal-support interaction
mp.	melting point
MS	mass spectrometry
NMR	nuclear magnetic resonance
P	Pearson product moment correlation coefficient
pI	isoelectric point
r	rate
R	gas constant
Ref.	reference
rpm	revolutions per minute
S	selectivity
SEM	scanning electron microscopy
SMSI	strong metal-support interaction
t	time
T	temperature
TON	turn over number
w	weight
WMSI	weak metal-support interaction
XRF	radioisotope X-ray fluorescence
Y	yield

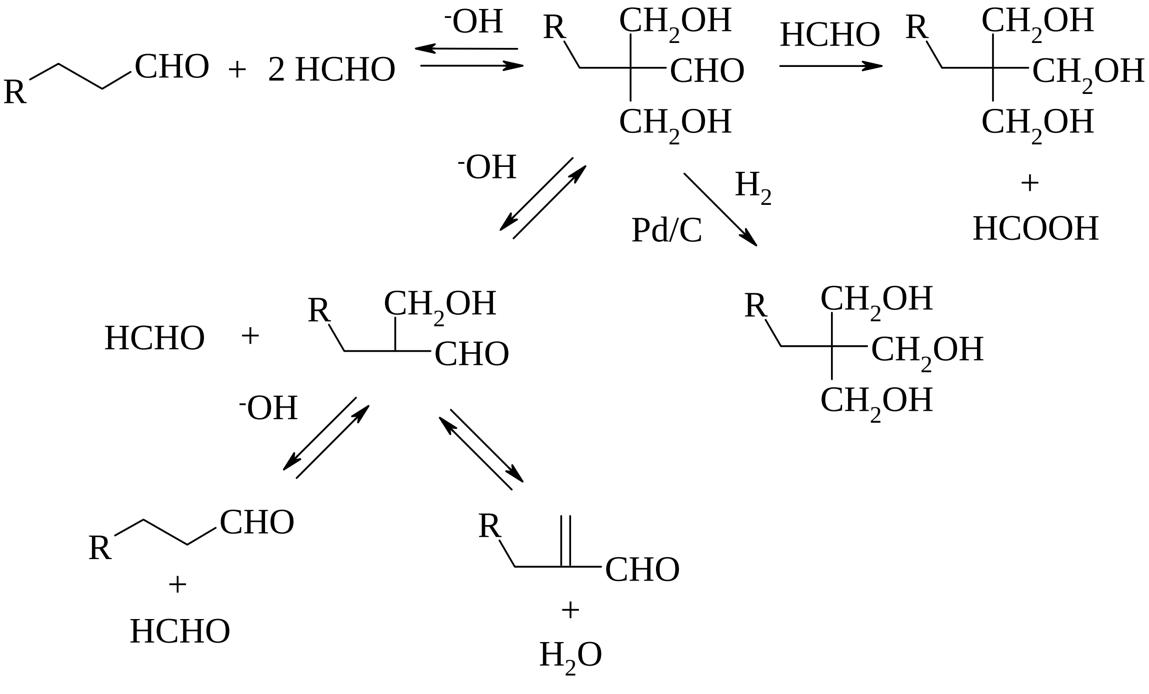
1 INTRODUCTION

In the industry the present process for the production of 2,2-disubstituted propane-1,3-diols and the corresponding hydroxy acids starts with the oxo synthesis in which alkenes are hydroformylated with synthesis gas (Scheme 1).[1]



Scheme 1. Hydroformylation of terminal alkenes.

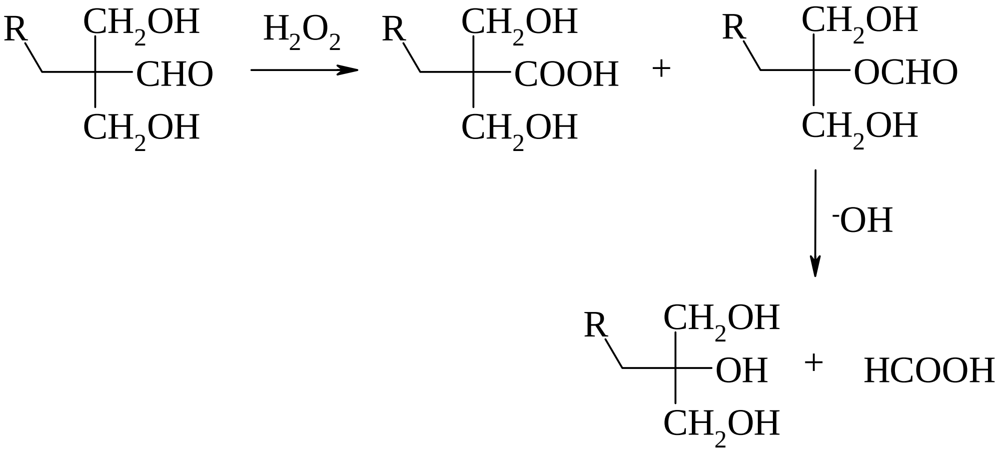
The aldehydes from the oxo synthesis and acetaldehyde react with formaldehyde in a base catalyzed mixed aldol reaction affording hydroxyaldehydes as presented in Scheme 2 for the straight chain aldehydes.[2a]



Scheme 2. Preparation of polyols from straight chain aldehydes.

With hydroxide ion catalysis an equilibrium is obtained, in which the hydroxyaldehydes undergo also a retrograde aldol reaction.[2b] The retrograde aldol reaction side-products may further dehydrate to unsaturated aldehydes. When using one equivalent excess of formaldehyde the aldol reaction continues by a crossed Cannizzaro reaction (Tollens' reaction) giving 2,2-disubstituted propane-1,3-diols as products. In addition, 2,2-disubstituted propane-1,3-diols can be obtained by catalytic hydrogenation of the hydroxyaldehydes from the aldol reaction.

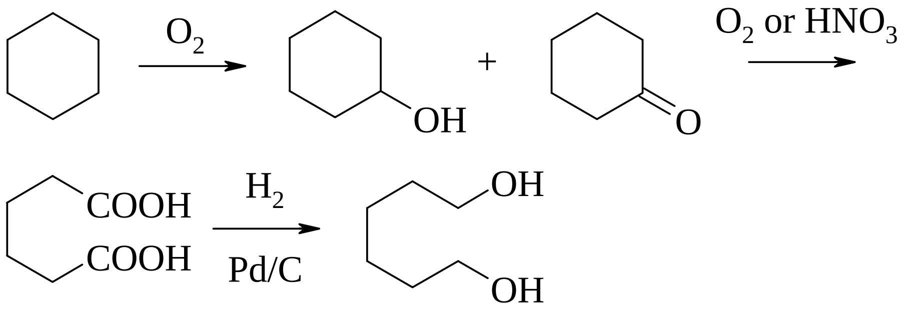
2,2-Disubstituted 3-hydroxypropanoic acids are easily obtained from the hydroxyaldehydes by an oxidation with hydrogen peroxide without any catalysts (Scheme 3).[3] The oxidation, followed by a hydrolysis of the formyloxy group of the other oxidation product, affords also alcohols having a tertiary hydroxy group as co-products.



Scheme 3. Oxidation of hydroxyaldehydes with hydrogen peroxide.

2,2-Disubstituted propane-1,3-diols and 2,2-disubstituted 3-hydroxypropanoic acids are raw materials of polyesters and alkyd resins.[2a] Steric hindrance of the neopentyl type structure impedes the ester formation, but makes the esters when formed particularly stable toward hydrolysis. The alcohols having a tertiary hydroxy group are potential raw materials for polymers used in coatings, because the tertiary hydroxy group may increase the adhesion of the polymers to surfaces.[4]

Linear diacids and linear primary diols are commercially prepared by various methods.[5,6] The most important process is the oxidative cleavage of cyclohexane to adipic acid followed by the reduction of adipic acid or its dimethyl ester to hexane-1,6-diol. (Scheme 4).[6]



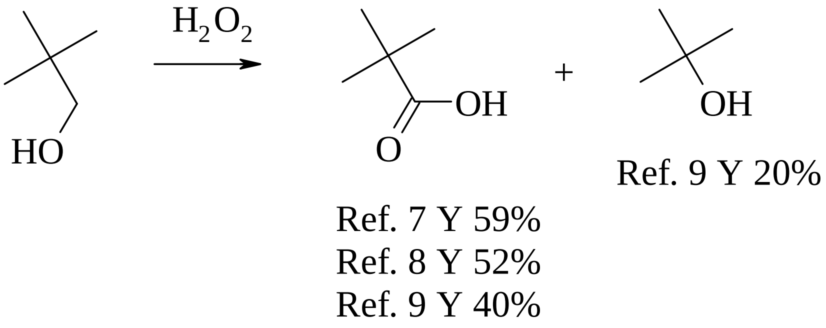
Scheme 4. Preparation of adipic acid from cyclohexane.

Linear diacids are raw materials of polyamides used for the manufacture of synthetic fibers such as Nylon 6,6.[6] The diacids and linear primary diols are also components in polyesters, alkyd resins, lubricants, and plastic materials.

Hydrogen peroxide or air as oxidants and water as a solvent in preparing 2,2-disubstituted and linear hydroxy acids and diacids from the corresponding alcohols would give an environmentally benign and economical alternative to their present manufacturing processes. 2,2-Disubstituted propane-1,3-diols and linear primary diols are valuable starting materials in cases where the conventional reactants, such as the hydroxyaldehydes and cycloalkanes, are not available.

1.1 Oxidation of 2,2-disubstituted propane-1,3-diols to hydroxy acids with hydrogen peroxide; migration of tertiary groups in the Baeyer-Villiger rearrangement

In the literature there are no reports on the oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide. However, 2,2-dimethylpropanol has been oxidized to 2,2-dimethylpropanoic acid and 2-methyl-2-propanol with hydrogen peroxide catalyzed by sodium tungstate[7,8] or methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate[9] (Scheme 5).



Scheme 5. Oxidation of 2,2-dimethylpropanol with hydrogen peroxide catalyzed by sodium tungstate[7,8] or methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate[9]. Yields (Y) of the products with references (Ref.) are also presented.

Although hydrogen peroxide can oxidize aldehydes to carboxylic acids without any catalyst.[3,10], the oxidation of primary alcohols to aldehydes requires an activation of hydrogen peroxide for example with transition metals.[11] Many transition metal compounds with d^0 metal electronic structure in their highest oxidation level, such as sodium tungstate and sodium molybdate, activate hydrogen peroxide by the formation a reactive diperoxo complex[12] or its dimer[13] (Figure 1).

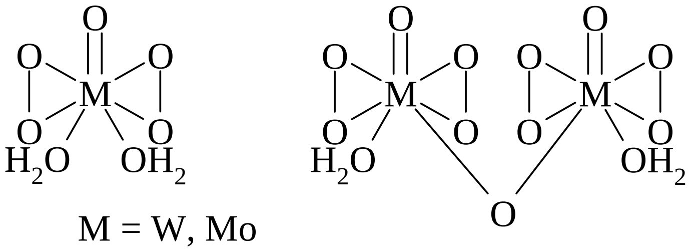
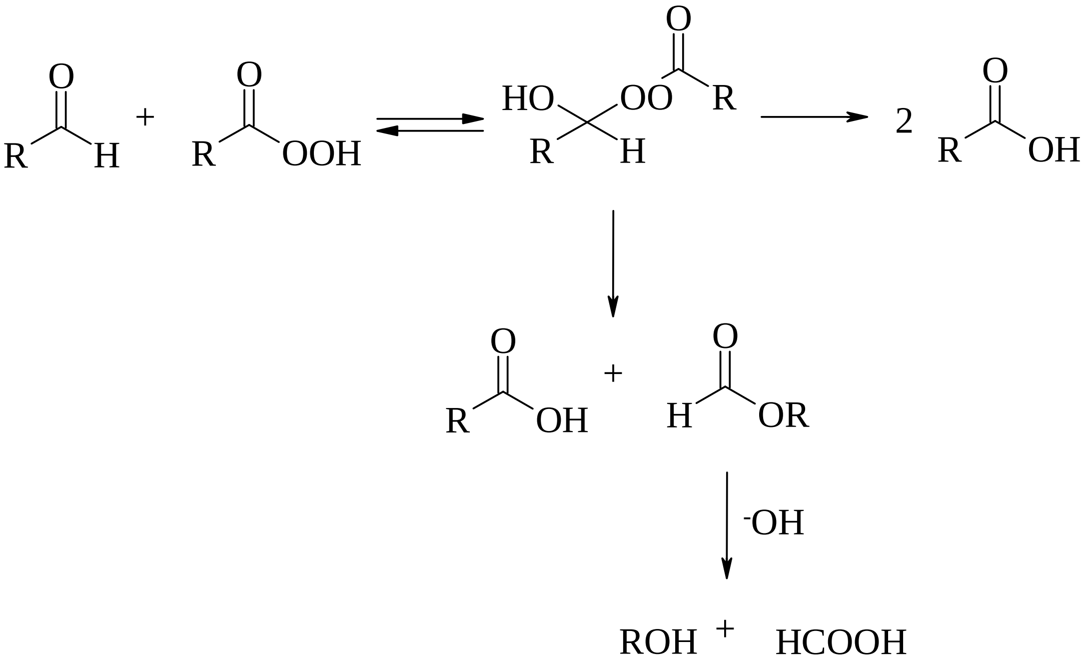


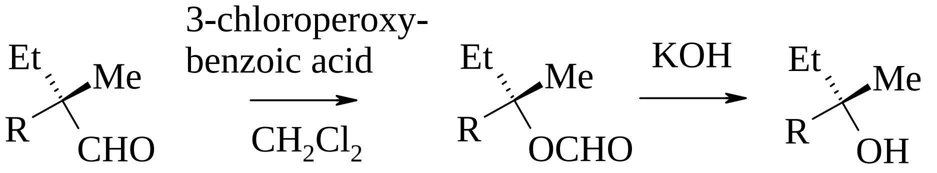
Figure 1. Diperoxo complex and its dimer of tungsten and molybdenum.

In the oxidation of primary alcohols to carboxylic acids the intermediate aldehydes are known to undergo an acid catalyzed Baeyer-Villiger rearrangement with peroxy acids, hydrogen peroxide or other peroxy compounds (Scheme 6).[14]



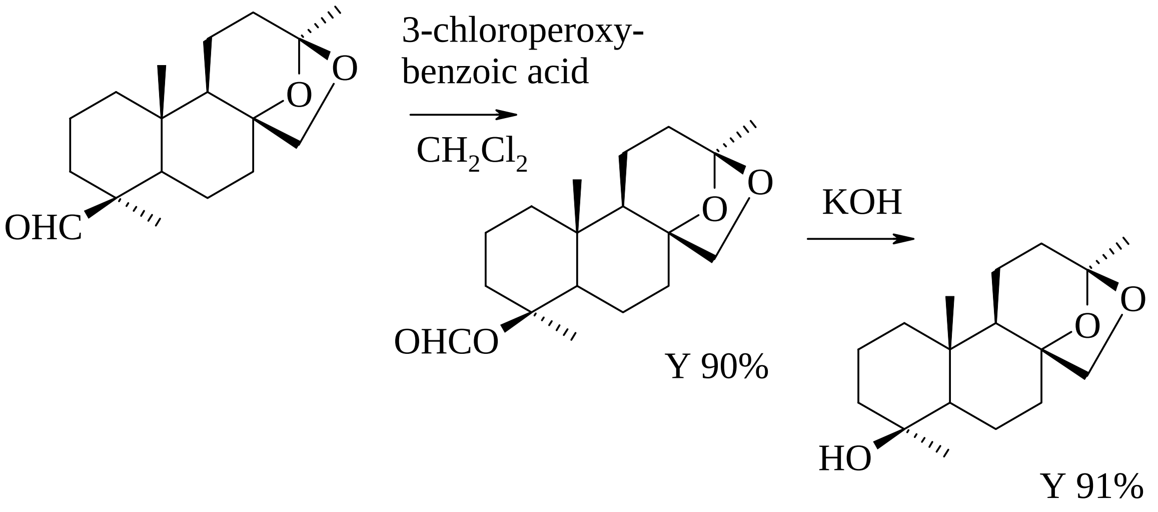
Scheme 6. Baeyer-Villiger rearrangement of aldehydes with peroxy acids.

First the aldehyde and the peroxy acid form a Criegee intermediate.[15] The decomposition of the intermediate to the formic acid ester and the carboxylic acid increases when the group R in the aldehyde is more substituted in the order methyl < primary < secondary < tertiary.[16] However, in aldehydes the migration of hydrogen is preferred to the migration of tertiary groups. The formic acid ester may subsequently be hydrolyzed to an alcohol and formic acid. In the literature there are some reports concerning the Baeyer-Villiger rearrangement of aliphatic aldehydes when the migrating group is a tertiary group. Leuser *et al.*[17] prepared chiral tertiary alcohols with high enantioselectivity (Scheme 7), and Barrero and Alvarez-Manzaneda *et al.*[18] applied the Baeyer-Villiger rearrangement to ring A functionalized terpenoids (Scheme 8).



R = $(CH_2)_4CH_3$, Y 76%, ee 92%
R = $(CH_2)_5CH_3$, Y 68%, ee 93%

Scheme 7. Baeyer-Villiger rearrangement of chiral aliphatic aldehydes and yields and enantiomeric excesses (ee) of the alcoholic products.[17]



Scheme 8. Example of the Baeyer-Villiger rearrangement of a ring A functionalized terpenoid.[18]

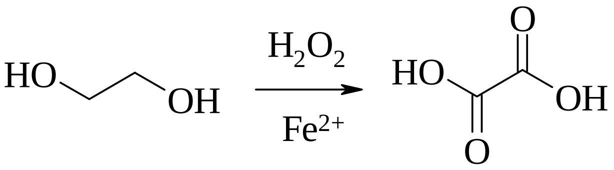
In these oxidations with 3-chloroperoxybenzoic acid the possible formation of carboxylic acid products by the migration of the aldehydic hydrogen was not mentioned, and the rearrangement of the aldehydes to formic acid esters occurred mainly under anhydrous reaction conditions.

In the oxidation of 2,2-dimethylpropanol the use of aqueous hydrogen peroxide as an oxidant enabled the formation of the carboxylic acid product, but the comparatively low yield of 2,2-dimethylpropanoic acid was also caused of the migration of the tertiary group of the intermediate aldehyde affording a formic acid ester which was subsequently hydrolyzed to 2-methyl-2-propanol (Scheme 5).[7-9]

According to the examples in the literature[7-9] 2,2-disubstituted propane-1,3-diols can be oxidized at least to 2,2-disubstituted 3-hydroxypropanoic acids with hydrogen peroxide catalyzed by various tungsten catalysts. The oxidations may also afford formic acid 1,1-disubstituted 2-hydroxyethyl esters or 1,1-disubstituted ethane-1,2-diols, the corresponding alcohols having a tertiary hydroxy group, as co-products. The formation of dicarboxylic acids in the oxidations of 2,2-disubstituted propane-1,3-diols and other primary diols with hydrogen peroxide is discussed in the next chapter. In the review of Sheldon *et al.* the oxidation of primary alcohols to carboxylic acids with hydrogen peroxide catalyzed for instance by various tungsten and molybdenum catalysts is expected to be used especially in the fine chemical industry in the future due to environmental regulations.[19]

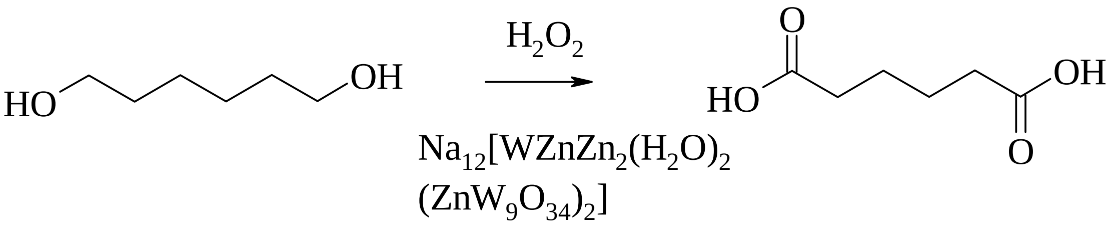
1.2 Oxidation of primary diols to dicarboxylic acids with hydrogen peroxide

In the literature there are only a few reports concerning the oxidation of primary diols to dicarboxylic acids with hydrogen peroxide. McGinnis *et al.* reported on the oxidation of ethylene glycol to oxalic acid with hydrogen peroxide catalyzed by Fenton's reagent. Hydrogen peroxide was decomposed homolytically by the catalyst generating reactive HO$^{\cdot}$ radicals (Scheme 9).[20]



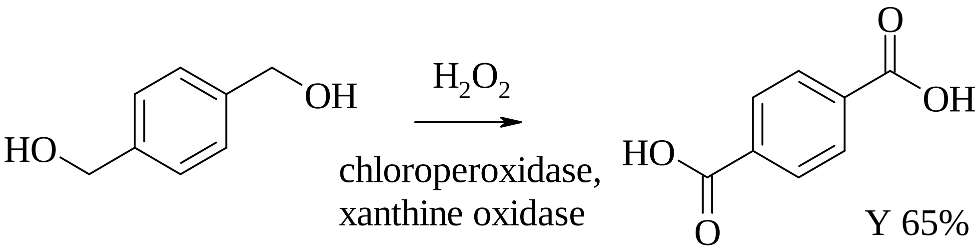
Scheme 9. Oxidation of ethylene glycol with hydrogen peroxide catalyzed by Fenton's reagent.

The oxidation of hexane-1,6-diol to adipic acid with hydrogen peroxide catalyzed by the "sandwich" type polyoxometalate $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ involving a heterolytic decomposition of hydrogen peroxide was reported by Sloboda-Rozner *et al.* (Scheme 10).[21]



Scheme 10. Oxidation of hexane-1,6-diol with hydrogen peroxide catalyzed by a polyoxometalate.

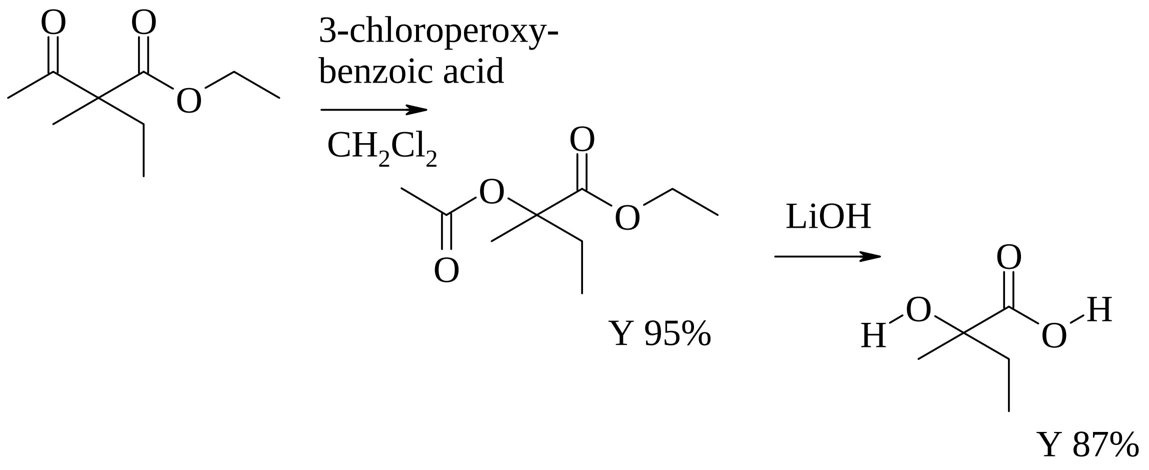
In addition, Morgan *et al.* oxidized (4-hydroxymethylphenyl)methanol to terephthalic acid with hydrogen peroxide catalyzed by chloroperoxidase and xanthine oxidase (Scheme 11).[22]



Scheme 11. Oxidation of (4-hydroxymethylphenyl)methanol with hydrogen peroxide catalyzed by enzymes.

These oxidations give an example of all the main mechanisms of the oxidations with hydrogen peroxide. The $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ catalyzed oxidation of hexane-1,6-diol to adipic acid shows that sodium tungstate may be active at least in the oxidation of linear primary diols to dicarboxylic acids. In addition, this kind of oxidation may be applicable in the industry as described in Chapter 1.1.[19]

As described in Chapter 1.1 there are no reports on the oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide in the literature. However, many 2,2-disubstituted 3-oxocarboxylic acid esters have been oxidized with 3-chloroperoxybenzoic acid to 2,2-disubstituted 2-acyloxycarboxylic acid esters.[23] For example Cristau *et al.*[23b] oxidized ethyl 2-ethyl-2-methyl-3-oxobutanoate to ethyl 2-(acetyloxy)-2-methylbutanoate (Scheme 12). The acetyloxy group was subsequently hydrolyzed affording 2-hydroxy-2-methylbutanoic acid as the final product. The oxidations of 2,2-disubstituted 3-oxocarboxylic acid esters indicate that after the oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide to the corresponding monocarboxylic acids the second hydroxymethyl group of the hydroxy acid may also be oxidized to a formyloxy group via an intermediate formyl group. Thus obtained 2,2-disubstituted 2-formyloxyacetic acids may subsequently be hydrolyzed to 2,2-disubstituted 2-hydroxyacetic acids. In addition, the hydroxy acids may also be oxidized to dicarboxylic acids, which may subsequently undergo the well-known decarboxylation of malonic acids.[24]

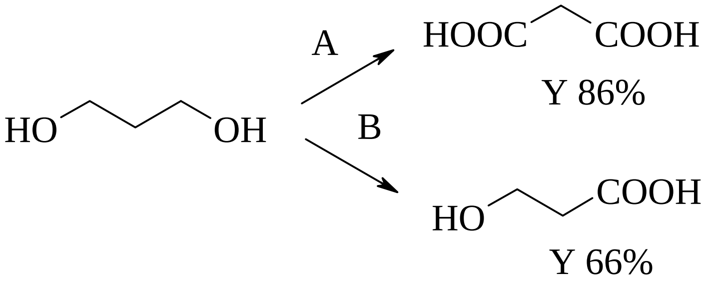


Scheme 12. Oxidation of ethyl 2-ethyl-2-methyl-3-oxobutanoate with 3-chloroperoxybenzoic acid.

1.3 Oxidation of primary diols with air or oxygen catalyzed by supported noble metals

The supported noble metal catalyzed air oxidation of primary alcohols and carbohydrates is an industrially interesting method as reviewed also by Kluytmans *et al.*[25] The reports in the literature concerning the oxidation of aliphatic primary diols and polyols to dicarboxylic acids with oxygen or air catalyzed by supported noble metals are summarized in Table 1.

Behr *et al.* reported the oxidation of propane-1,3-diol to malonic acid with air catalyzed by Pd/C (Scheme 13).[26] The catalyst was used in a quantity corresponding to 2.8% by the weight of palladium, based on propane-1,3-diol.



Scheme 13. Oxidation of propane-1,3-diol with air catalyzed by Pd/C. A: Pd/reactant (w/w) = 0.028, B: Pd/reactant (w/w) = 0.0024.

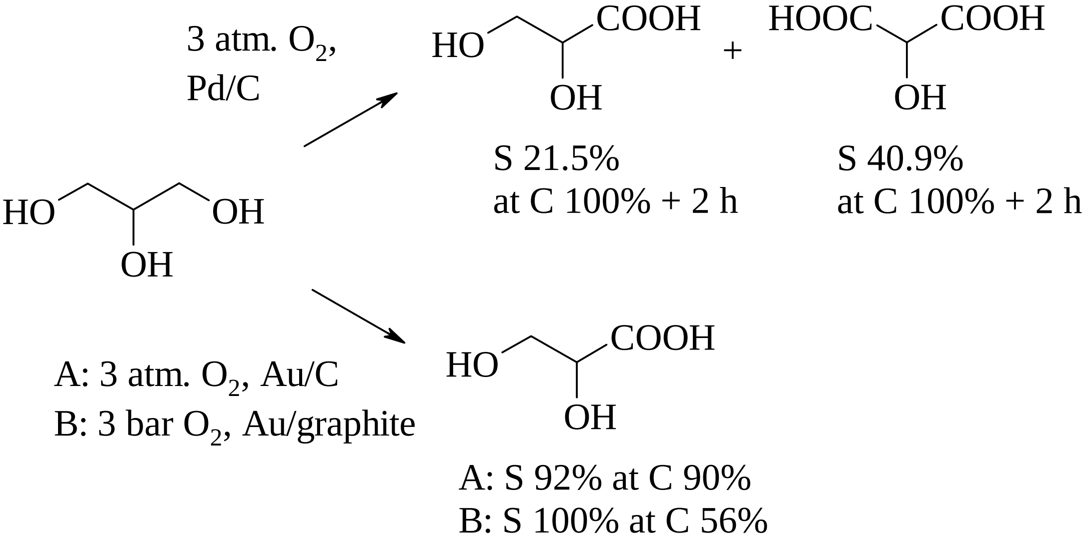
Akada *et al.* oxidized propane-1,3-diol and butane-1,4-diol to the corresponding diacids with oxygen catalyzed by a Pd/C + $Pb(OAc)_2$ catalyst, where Ac denotes acetyl[27] In most noble metal catalyzed oxidations of glycerol the major product is 2,3-dihydroxypropanoic acid.[28]

Table 1. Oxidation of aliphatic primary diols and polyols to hydroxy acids and diacids with oxygen or air catalyzed by supported noble metals.[a]

Diol or polyol	Catalysts	Hydroxy acid	Diacid	Ref.
Ethylene glycol[b]	Pd/C, Pt/C, Au/C, Au/Al_2O_3	Glycolic acid		29, 32, 33
Propane-1,3-diol[c]	Pd/C; Pd/C + $Pb(OAc)_2$		Malonic acid	26, 27
Propane-1,3-diol[d]	Pd/C; Pd, Pt, Bi/C; Au/C; Au/TiO_2	3-Hydroxy-propanoic acid		29, 34
Glycerol[e]	Pd/C, Pt/C, Au/C, Au/graphite	2,3-Dihydroxy-propanoic acid	2-Hydroxy-malonic acid	28, 35, 36
Butane-1,4-diol	Pd/C + $Pb(OAc)_2$		Succinic acid	27
2-(2-Hydroxy-ethoxy)ethanol[f]	Au/TiO_2, Au/C	(2-Hydroxy-ethoxy)-acetic acid	Carboxy-methoxy-acetic acid	29
2,2-Disubstituted propane-1,3-diols	Pt/C, Pd/C	Hydroxy acids		37, 38
Carbohydrates and their derivatives[g]	Pt/C, Pt/C or Pt/Al_2O_3 + hexamethylene-tetramine	Hydroxy acids	Diacids	30, 31, 39, 40

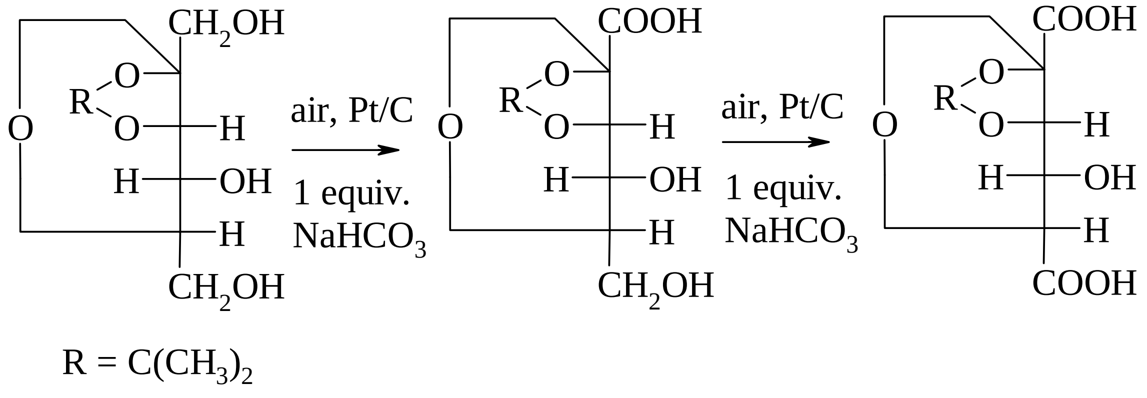
[a] Ref. = the references in Chapter 5.
[b] O_2 was used at normal or 2 to 3 atm. pressure.
[c] With Pd/C Pd/propane-1,3-diol (w/w) was 0.028.
[d] With Pd/C Pd/propane-1,3-diol (w/w) was 0.0024. With Au-catalysts O_2 was used at 3 atm. pressure.
[e] At normal pressure only Pd/C afforded the diacid. With Au-catalysts O_2 was used at elevated pressure.
[f] O_2 was used at 3 atmospheric pressure (atm.). Au/C afforded only the hydroxy acid.
[g] Only Pt/C with two equivalents of $NaHCO_3$ afforded the diacids.

However, the best selectivity of hydroxymalonic acid in the oxidation of glycerol was obtained with oxygen at elevated pressure catalyzed by Pd/C catalysts (Scheme 14).[28b]



Scheme 14. Selectivities (S) of the products in the oxidation of glycerol with oxygen catalyzed by supported noble metals.[28] Conversions (C) of glycerol are also presented.

Biella *et al.* oxidized 2-(2-hydroxyethoxy)ethanol (diethylene glycol) with oxygen at three atmospheres pressure catalyzed by Au/TiO_2 to (2-hydroxyethoxy)acetic acid and carboxymethoxyacetic acid in 55% and 45% selectivity, respectively.[29] Two primary hydroxy groups of galactitol (dulcitol)[30] and a sorbose derivative[31] were oxidized with oxygen and air, respectively, to the corresponding diacids under Pt/C catalysis (Scheme 15). In these oxidations two equivalents of sodium hydrogen carbonate were added to the reaction mixtures.



Scheme 15. Selectivity achieved by one or two equivalents (equiv.) of sodium hydrogen carbonate in the oxidation of a sorbose derivative with air catalyzed by Pt/C.

According to these examples the selectivity toward dicarboxylic acids in the oxidation of aliphatic primary diols and polyols with oxygen or air is favored by Pd/C catalysts or by elevated pressure of oxygen. However, some carbohydrates are readily oxidized to dicarboxylic acids by Pt/C catalysts even at atmospheric pressure.

In the literature the oxidation of aliphatic primary diols and polyols to hydroxy acids with oxygen or air catalyzed by supported noble metals is reported more frequently than similar oxidations of aliphatic primary diols and polyols to dicarboxylic acids (Table 1). The best selectivities of glycolic acid in the oxidation of ethylene glycol with oxygen or air were obtained by Au/C and Au/Al_2O_3 catalysts.[29,32,33] The formation of oxalic acid was not reported. Even with Pd/C with oxygen at three or two atmospheres pressure glycolic acid was obtained in 77% selectivity.[48,33b] Behr *et al.* oxidized propane-1,3-diol to 3-hydroxypropanoic acid with air, catalyzed by Pd/C (Scheme 13) and Pd, Pt, Bi/C.[34] Compared to the oxidation[26] of propane-1,3-diol to malonic acid less Pd/C was used. Au/C afforded the corresponding hydroxy acids in the oxidations of propane-1,3-diol and 2-(2-hydroxyethoxy)ethanol (diethylene glycol) with oxygen even though the oxidations were performed at elevated pressure.[29] As mentioned in the previous paragraph glycerol is oxidized usually to 2,3-dihydroxypropanoic acid and hydroxymalonic acid the monocarboxylic acid being the major product.[28,35,36] Thus the best selectivities of 2,3-dihydroxypropanoic acid were obtained with oxygen catalyzed by Au/C and Au/graphite (Scheme 14).[36] The oxidations of two 2,2-disubstituted propane-1,3-diols, 2,2-bis-(hydroxymethyl)propane-1,3-diol[37] and 2-hydroxymethyl-2-methylpropane-1,3-diol[38], with oxygen catalyzed by Pt/C and with an oxygen-containing gas catalyzed by Pd/C, respectively, afforded the corresponding hydroxy acids. The formation of the diacids was not reported. L-Sorbose[39] and a D-fructose derivative (methyl α-D-fructofuranoside)[40] were oxidized to the corresponding monoacids with oxygen catalyzed by Pt/C. In addition, the Pt/C catalyzed air oxidation[31] of a sorbose derivative mentioned in the previous paragraph was interrupted yielding the monoacid, when just one equivalent of sodium hydrogen carbonate was added to the reaction mixture (Scheme 15).

According to these examples the selectivity toward hydroxy acids in the oxidation of aliphatic primary diols and polyols with oxygen or air is mainly achieved by Pt/C catalysts or by various supported Au catalysts at elevated pressure. However, in the Pd/C catalyzed oxidations of ethylene glycol[29] and 2-hydroxymethyl-2-methylpropane-1,3-diol[38] to the corresponding hydroxy acids the formation of some dicarboxylic acids is still probable, because the formation of the diacids is usually favored by Pd/C catalysts according to the examples in the previous paragraph. In addition, in the oxidations of propane-

1,3-diol, increasing the amount of Pd/C changed the selectivity of the reaction from the hydroxy acid toward the diacid.[26,34]

According to the oxidations of propane-1,3-diol, 2,2-bis-(hydroxymethyl)propane-1,3-diol, and 2-hydroxymethyl-2-methylpropane-1,3-diol, linear primary diols and 2,2-disubstituted propane-1,3-diols can be oxidized at least to the corresponding hydroxy acids with air or oxygen catalyzed by supported palladium or platinum. In addition, the oxidations of propane-1,3-diol and butane-1,4-diol indicate that linear primary diols can be oxidized even to the corresponding diacids with oxygen at elevated pressure catalyzed by Pd/C or with air catalyzed by a high proportion of Pd/C.

The selectivity toward the diacids in the oxidations of 2,2-disubstituted propane-1,3-diols and linear primary diols may also be achieved by promoted catalysts. Literature reviews on the promotion of supported noble metal catalysts discuss the enhancement of the selectivity and the formation of the desired products in oxidations with oxygen and oxygen-containing gases.[41] In fact, the oxidations of propane-1,3-diol and butane-1,4-diol to the diacids with oxygen may have been a result of the promotion of Pd/C with $Pb(OAc)_2$.[27] On the other hand the Pd, Pt, Bi/C catalyzed oxidation of propane-1,3-diol afforded the corresponding hydroxy acid.[34] The many reports in the literature of the mechanisms of the promoted reactions help also to predict the mechanism of the oxidation of 2,2-disubstituted propane-1,3-diols and linear primary diols to their corresponding diacids.

1.4 Effect of supports on the noble metal catalyzed oxidation of primary alcohols with air or oxygen

According to the literature the most common supports are activated carbon and alumina (aluminum oxide) in the supported noble metal catalyzed oxidations of primary alcohols with oxygen or oxygen-containing gas as shown also for aliphatic primary diols and polyols in Table 1.[41] Even though propane-1,3-diol and 2-(2-hydroxyethoxy)ethanol have been oxidized with oxygen catalyzed by Au/TiO_2,[29] noble metals supported on titanium dioxide are usually used as photocatalysts due to the semiconductor nature of titanium dioxide.[42] Although titanium silicalite (TS-1) was originally designed for industrial oxidation reactions with hydrogen peroxide,[43] noble metals supported on titanium silicalite may also be suitable catalysts for the oxidations of primary alcohols with oxygen or oxygen-containing gas. An example of the use of noble metals supported on titanium silicalite is the epoxidation of propene with hydrogen peroxide catalyzed by Pd, Pt/TS-1,[44] In addition, noble metals supported on barium sulfate may be active catalysts in the oxidations of primary alcohols. Currently catalysts supported on barium sulfate are mainly used in catalytic hydrogenations of double and triple bonds.[45]

A large surface area of active species, for example of noble metals, in heterogeneous catalysts is obtained by supports.[46] For maximizing the active surface area small particle size and porosity are the most significant characteristics of the supports. In addition, for preventing the agglomeration of the active species into large entities, the strength of the interaction of the small active species with the support should be strong enough.

Activated carbons, which have carboxy and phenolic surface groups, are porous materials.[46] They are usually neutral at acidic pH values, and with metals they have only a weak metal-support interaction (WMSI). The most common form of alumina used as a support is the porous γ-alumina, which has hydroxy surface groups. α-Alumina, which is another form of alumina, is non-porous, and it has almost no surface hydroxy groups. Isoelectric points (pI) of the both forms of alumina, at which they are neutral, lie at pH values of about 9 to 9.5. In addition, with metals alumina has only a weak metal-support interaction. The most common crystal form of titanium dioxide used as a support is the porous anatase. Anatase has also surface hydroxy groups, and its pI lies at slightly acidic pH values. Titanium dioxide has a strong metal-support interaction (SMSI) with metals, when reduced by hydrogen at high temperatures. Titanium silicalite is a porous material composed of TiO_4 and SiO_4 units, which are arranged in a MFI zeolite type framework.[47] With metals zeolites have a medium metal-support interaction (MMSI). The composition of titanium silicalite is $x\ TiO_2 \cdot (1-x)\ SiO_2$, in which x lies between 0.0001 and 0.04.[43]

1.5 Effect of promoters on the noble metal catalyzed oxidation of primary alcohols with air or oxygen

In the literature many interpretations of the role of promoters in noble metal catalysts are proposed.[41] According to the recommendations of The International Union of Pure and Applied Chemistry (IUPAC) the use of the word promoter implies that an additive of a catalyst improves some particular property of the catalyst e. g. the activity of the catalyst or the selectivity of a reaction.[41d] When Kimura *et al.* oxidized a special primary alcohol (Emulgen 108) with oxygen catalyzed by Pd/C promoted with many *p*-block elements they found that each promoter had an optimum loading with which the highest yield of the carboxylic acid product was obtained.[48] Most studies of the promoters in the oxidations of alcohols catalyzed by promoted noble metals concern the role of bismuth and lead as promoters due to their high promoting efficiency. However, in the literature there are hardly any comparative studies of many promoters handling the oxidations of alcohols. The main promoting mechanism of bismuth and lead in the oxidations of alcohols is the ensemble effect. According to the ensemble effect the promoting elements are thought to decrease the size of the active site ensembles thus preventing the adsorption of the long chain poisoning species formed by polymerization.[49,50] In addition, the hydroxy and carboxy groups of the alcohols and hydroxy acids may form a complex with the promoter atoms.[51] The promoted catalysts were also briefly discussed in Chapter 1.3 as means to enhance the selectivity toward the diacids in the oxidations of 2,2-disubstituted propane-1,3-diols and linear primary diols.

1.6 Kinetics of the oxidation of primary alcohols with air or oxygen catalyzed by supported noble metals

As in the general kinetics of the heterogeneous catalysis the kinetics of the noble metal catalyzed oxidations of primary alcohols with oxygen or oxygen-containing gas can also be divided into two regimes.[52] When there are negligible concentration and temperature external gradients surrounding the catalyst particles and negligible concentration and temperature internal gradients in the pores of the catalyst, the rate of the reaction is determined only by the rate of the chemical reaction on the surface of the catalyst. Under these reaction conditions the reaction is said to operate in the kinetic regime. When the rate of the reaction is influenced by the external or internal concentration or temperature gradients existing in the reaction mixture or in the pores of the catalyst, the reaction operates in the regime of external or internal mass or heat transfer. The noble metal catalyzed oxidations of primary alcohols to carboxylic acids can be considered as consecutive irreversible multiple-stage first-order reactions.[53] The rates of the noble metal catalyzed oxidations of primary alcohols can also be expressed by the Langmuir-Hinshelwood type rate laws.[54] Kluytmans *et al.* have discussed especially the engineering aspects of the kinetics of noble metal catalyzed oxidations of alcohols.[25a]

In the literature there are some reports concerning the effect of the amount of the catalyst on the rate of the oxidation of alcohols. Nicoletti and Whitesides oxidized propan-2-ol to acetone with oxygen.[55] In the Pt/C catalyzed oxidation the initial rate of the reaction increased linearly with the amount of the catalyst, while in the Pt/SiO_2 catalyzed oxidation the initial rate of the oxidation was probably limited by the mass transfer of oxygen. Ali Khan *et al.* obtained also a linear relationship between the amount of Pt/C and the initial rate of the oxidation of ethylene glycol.[56]

The effect of pH of the reaction mixture on the rate of the oxidation of alcohols has been studied in the oxidation of glycerol,[35] L-sorbose,[57] glucose[58] and methyl α-D-glucopyranoside[59]. In all the oxidations the raise of pH especially to the basic values enhanced the rate of the oxidations. The dependence of the rate of the oxidation of 2,2-dimethyl-3-hydroxypropanal on the temperature was studied by Zhizhkun *et al.*[60] The Zhizhkun group oxidized the aldehyde to the corresponding hydroxy acid and to the diacid with oxygen catalyzed by Pd/Al_2O_3. The reaction was proved to operate in the kinetic regime by several experiments.

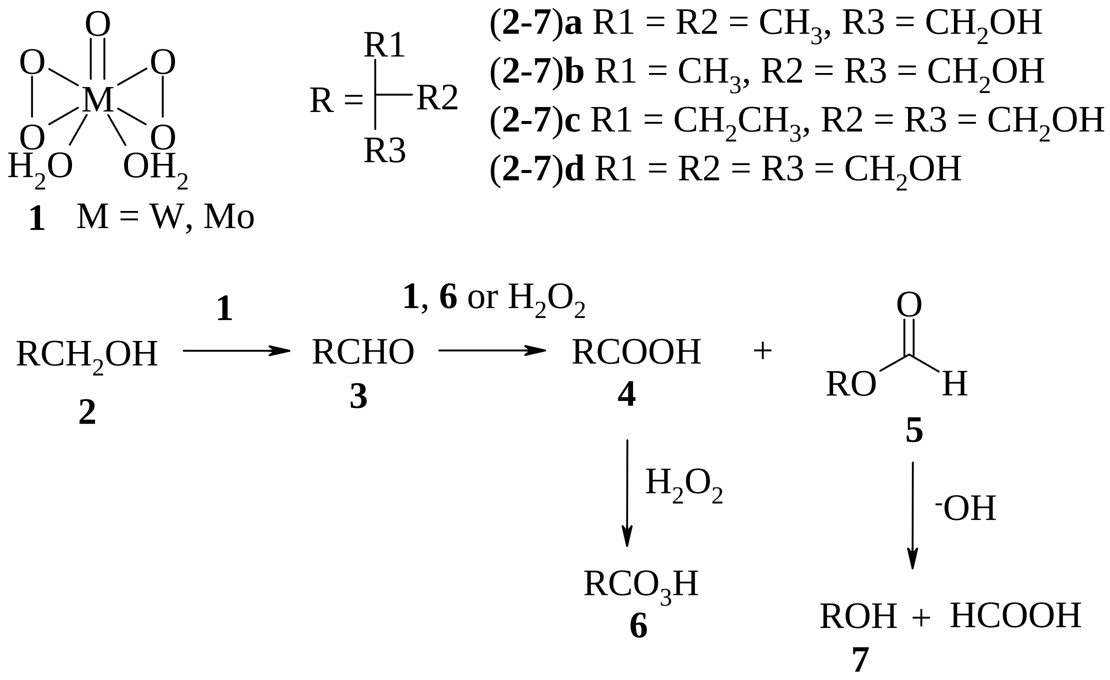
2 AIMS OF THE STUDY

The aim of the present study was to investigate the preparation of industrially important hydroxy acids and diacids from 2,2-disubstituted propane-1,3-diols and linear primary diols by green chemistry methods. The preparation of the hydroxy acids and the diacids, which are used as raw materials of polyesters, alkyd resins or polyamides, was studied by the oxidation of the diols with hydrogen peroxide and air using water as a solvent. These methods would give environmentally benign and economical alternatives to their present manufacturing processes. In addition, 2,2-disubstituted propane-1,3-diols and linear primary diols as reactants would be valuable alternatives in cases in which the conventional reactants, such as 2,2-disubstituted 3-hydroxypropanals and cycloalkanes, are not available.

3 RESULTS AND DISCUSSION

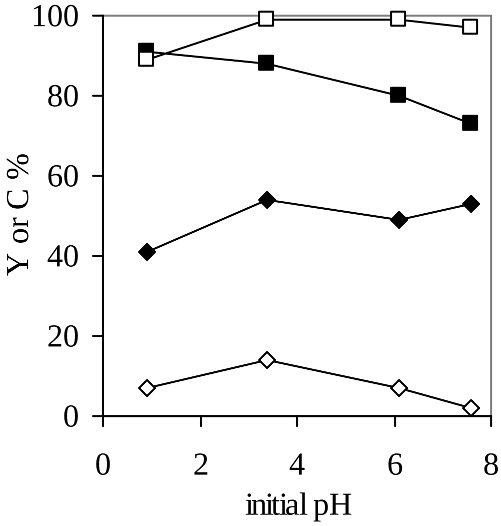
3.1 Oxidation of 2,2-disubstituted propane-1,3-diols to hydroxy acids with hydrogen peroxide catalyzed by sodium tungstate and sodium molybdate; Baeyer-Villiger rearrangement of the intermediate aldehydes

To study the preparation of 2,2-disubstituted 3-hydroxypropanoic acids four 2,2-disubstituted propane-1,3-diols were oxidized with hydrogen peroxide catalyzed by sodium tungstate and sodium molybdate (Scheme 16).



Scheme 16. Oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide catalyzed by sodium tungstate and sodium molybdate.

According to the literature sodium tungstate is an efficient catalyst in the oxidation of 2,2-dimethylpropanol with hydrogen peroxide,[7-9] so it was also expected to be active in the oxidation of 2,2-disubstituted propane-1,3-diols. In addition, the activity of sodium molybdate was tested in the same reaction because of the similar d^0 metal electronic structure of molybdenum and tungsten in their highest oxidation state. As a comparative preliminary experiment 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**) was oxidized at various initial pH values catalyzed by sodium tungstate (Figure 2) and sodium molybdate (Figure 3).



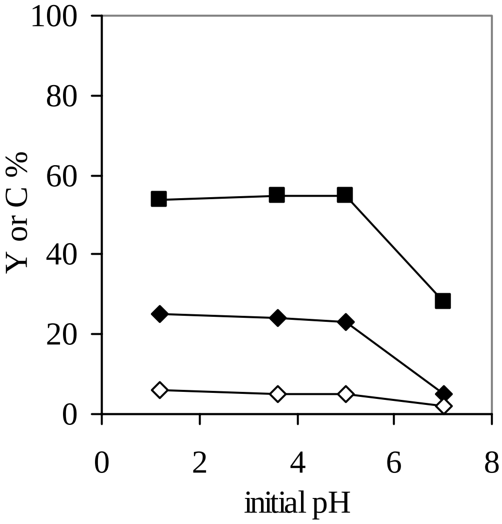
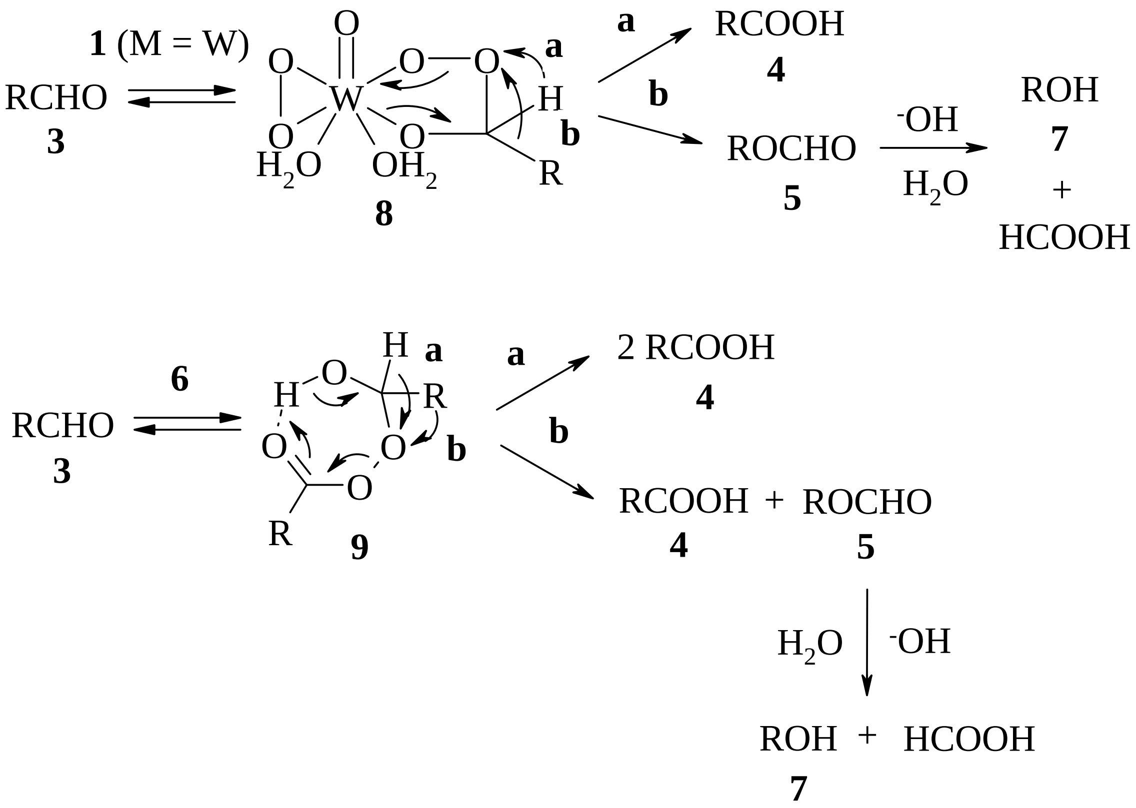


Figure 2. Na_2WO_4 catalyst, reaction time 3 hours (h). ■ = **2b** C, □ = H_2O_2 C, ♦ = **4b** Y, ◊ = **5b** Y.

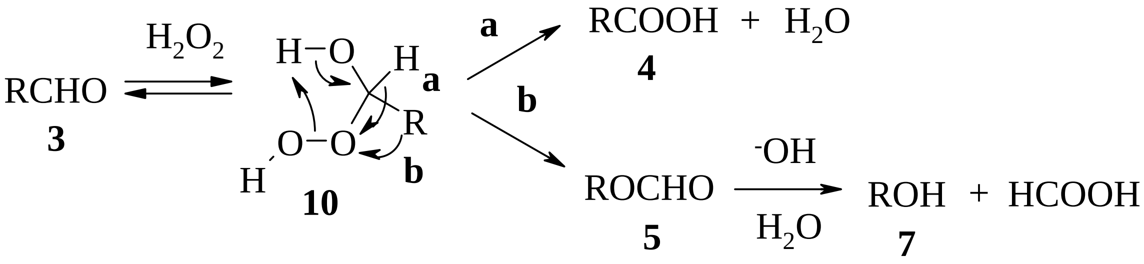
Figure 3. Na_2MoO_4 catalyst, reaction time 3 h. ■ = **2b** C, ♦ = **4b** Y, ◊ = **5b** Y.

At all the examined initial pH values the conversion of **2b** and the yields of 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**) and formic acid 2-hydroxy-1-hydroxymethyl-1-methylethyl ester (**5b**) in sodium tungstate catalyzed oxidations were higher than in sodium molybdate catalyzed oxidations. This result is also similar to the result reported by Arcoria *et al.* The Arcoria group stated that the neutral form of the diperoxo complex of tungsten at acidic pH values is a more effective oxidant than the corresponding peroxo compound of molybdenum.[61] Usually the less dissociated diperoxo complex is the better oxidant. In organic solvents the diperoxo complex of molybdenum has been found to be less dissociated and more reactive than the diperoxo complex of tungsten due to the higher acidity of the tungsten compound. However, at acidic pH values the tungsten compound is neutralized and more reactive.

Because of the high activity of sodium tungstate it was chosen as a catalyst for the further experiments of the oxidations of the alcohols **2**(**a-d**) with hydrogen peroxide. In these oxidations the effect of the Baeyer-Villiger rearrangement on the distribution of the products was explored in more detail. The Baeyer-Villiger rearrangement of the Criegee intermediate type complexes (Scheme 6) of the aldehydes **3**(**a-d**) with the diperoxo complex of tungsten **1** (M = W), with the peroxy acids **6**(**a-d**) and with hydrogen peroxide is presented in Scheme 17.



Scheme 17. Baeyer-Villiger rearrangement of aldehydes **3**(**a-d**). Pathway **a**: H-migration and pathway **b**: R-migration.



Scheme 17, continued.

According to the strength of the conjugate acid of the peroxy compounds the reactivity order of the intermediates is probably **8** > **9** > **10**.[14] In the Baeyer-Villiger rearrangement of aldehydes the migration of hydrogen in the intermediates **8**, **9**, and **10** (pathway **a**) is most favored[16], but electron-donating groups in the group R increase the formation of the ester **5** (pathway **b**)[14]. This relationship was also recognized in the oxidations of 2,2-dimethylpropane-1,3-diol (**2a**) (Figure 4), 2-ethyl-2-hydroxymethylpropane-1,3-diol (**2c**) (Figure 5), and 2,2-bis-(hydroxymethyl)propane-1,3-diol (**2d**) (Figure 6) at various initial pH values.

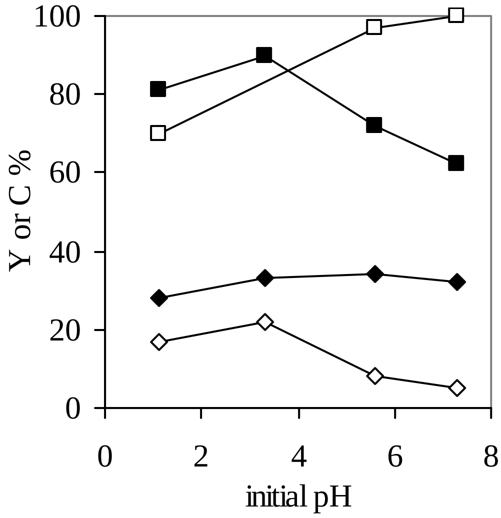


Figure 4. Na_2WO_4 catalyst, reaction time 3 h. ■ = **2a** C, □ = H_2O_2 C, ♦ = **4a** Y, ◊ = **5a** Y.

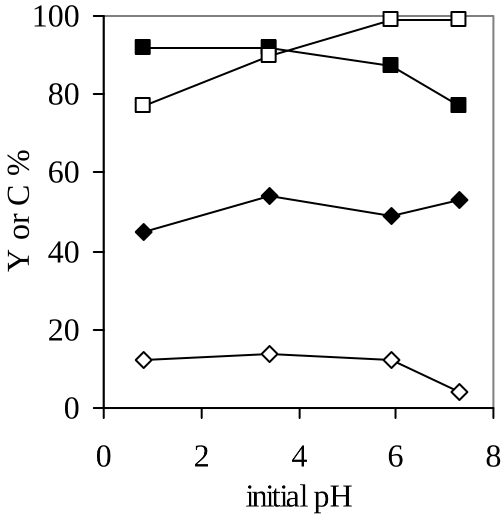


Figure 5. Na_2WO_4 catalyst, reaction time 3 h. ■ = **2c** C, □ = H_2O_2 C, ♦ = **4c** Y, ◊ = **5c** Y.

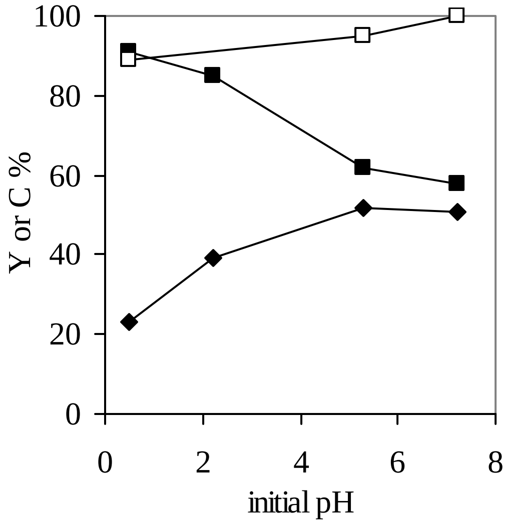


Figure 6. Na_2WO_4 catalyst, reaction time 3 h. ■ = **2d** C, □ = H_2O_2 C, ♦ = **4d** Y.

At all the examined initial pH values the main product in the oxidations of **2**(**a**-**d**) was the acid **4**; 3-hydroxy-2,2-dimethylpropanoic acid (**4a**), 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**), 2,2-bis-(hydroxymethyl)butanoic acid (**4c**), and 3-hydroxy-2,2-bis-(hydroxymethyl)propanoic acid (**4d**), respectively; indicating the preference of the pathway **a** over the pathway **b**. The unhydrolyzed co-products were formic acid 2-hydroxy-1,1-dimethylethyl ester (**5a**), formic acid 2-hydroxy-1-hydroxymethyl-1-methylethyl ester (**5b**), and formic acid 1,1-bis-(hydroxymethyl)propyl ester (**5c**), respectively. The oxidations of **2**(**b-d**) having two or three electron-withdrawing hydroxymethyl groups in the group R gave the best yields of the acids **4**(**b-d**). In the oxidation of **2a** the two electron-donating methyl groups in R enhanced the yield of the unhydrolyzed co-product **5a** compared to the acid **4a**. The highest combined yields of **4** and **5** were obtained at the pH range 3 to 4.

The selectivities of **4**(**a**-**d**) and **5**(**a**-**c**) in the oxidations of **2**(**a**-**d**) at various initial pH values are presented in Figures 7 and 8.

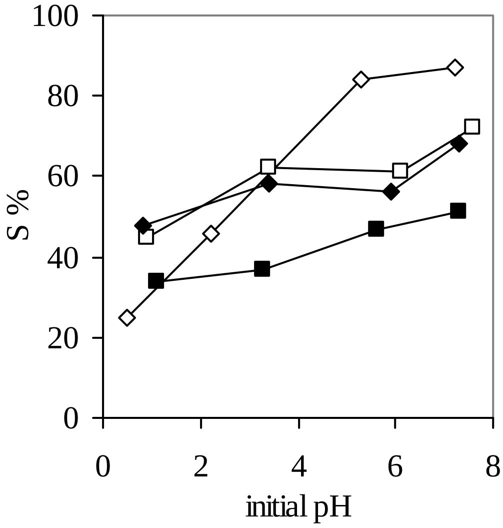


Figure 7. Selectivities of **4**(**a**-**d**). Na$_2$WO$_4$ catalyst, reaction time 3h. ■ = **4a**, □ = **4b**, ♦ = **4c**, ◊ = **4d**.

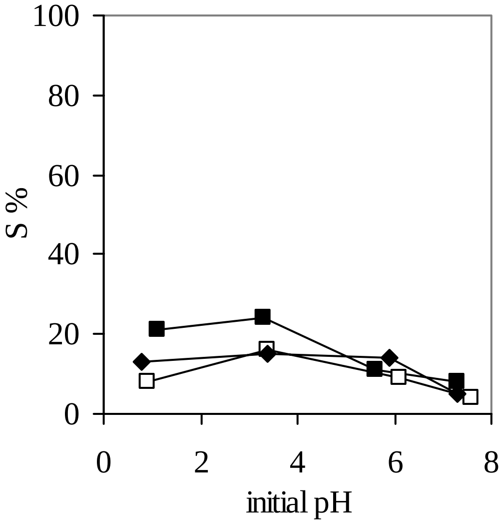


Figure 8. Selectivities of **5**(**a**-**c**). Na$_2$WO$_4$ catalyst, reaction time 3h. ■ = **5a**, □ = **5b**, ♦ = **5c**.

According to Figure 7 the selectivities of **4**(**a**-**d**) are directly proportional to the initial pH values in the oxidations of **2**(**a**-**d**). The highest selectivities of **4**(**a**-**d**) were obtained at neutral or slightly basic initial pH values. The two or three electron-withdrawing hydroxymethyl groups in the group R in **2**(**b**-**d**) increased more the selectivity of the hydroxy acids compared to **2a** which has two electron-donating methyl groups in R. The selectivities of the co-products **5**(**a**-**c**) are inversely proportional to the initial pH values in the oxidations of **2**(**a**-**c**), although the selectivities were not very high at any examined pH values (Figure 8).

According to the literature the use of organic solvents and peroxy acids as oxidants would enhance the formation of the formic acid esters **5** in the Baeyer-Villiger rearrangements (Scheme 7 and 8).[17,18] Thus the proportion of the unhydrolyzed co-products **5** would have also been higher in anhydrous reaction conditions. In addition, because 2,2-disubstituted 3-oxocarboxylic acid esters do not usually afford the corresponding dicarboxylic acid esters when oxidized with peroxy acids,[23] the amount of dicarboxylic acids were also probably negligible in the oxidations of 2,2-disubstituted propane-1,3-diols **2**. The possibly formed dicarboxylic acids may have also undergone the well-known decarboxylation of malonic acids at the reaction temperature of 90°C.[24]

The isolated yields of the products **4**(**a-d**) and **7**(**a-c**) of the oxidations of **2**(**a-d**) are summarized in Table 2.

Table 2. Oxidation of 2,2-disubstituted propane-1,3-diols with H_2O_2 catalyzed by Na_2WO_4.[a]

Entry	H_2O_2, equiv.	Reactant	Product	Y, %	Product	Y, %
1	2	**2a**	**4a**	30	**7a**[b]	
2	2	**2b**	**4b**	49	**7b**[b]	
3	2	**2c**	**4c**	43	**7c**[b]	
4	2	**2d**	**4d**	47	**7d**[b]	
5	4	**2a**	**4a**[b]		**7a**	23
6	4	**2b**	**4b**[b]		**7b**	14
7	4	**2c**	**4c**[b]		**7c**	15

[a] The yields of **4** and **7** are isolated yields, see Experimental. pH was 2.0 and the reaction time 6 h. In Entries 5-7 4.0 equiv. of H_2O_2 was used to obtain a complete conversion of **2**.

[b] Not isolated.

The ratios of the isolated yields **4a**/**7a**, **4b**/**7b**, and **4c**/**7c** are 1.4, 3.0, and 2.8, respectively. The low ratio of **4a**/**7a** indicates the effect of the two electron-donating methyl groups of the aldehyde **3a** on the migration of the tertiary group in the Baeyer-Villiger rearrangement (pathway **b**) thus increasing the proportion of the co-product **7a**.

The turn over numbers (TON) of the oxidations of **2**(**a-d**) are summarized in Table 3.

Table 3. Turn over numbers (TON) of **4** and **5** in the oxidation of **2** with H_2O_2 catalyzed by Na_2WO_4.[a]

Entry	pH	2	C, %	4	Y, %	TON	5	Y, %	TON
1	4.4	**a**	80	**a**	31	388	**a**	28	350
2	3.4	**b**	67	**b**	33	413	**b**	8	100
3	3.4	**c**	69	**c**	32	400	**c**	9	113
4	3.9	**d**	78	**d**	37	463	**d**		

[a] TON is the molar ratio **4**/Na_2WO_4 and **5**/Na_2WO_4, when the molar ratio **2**/Na_2WO_4 was 1250. The reaction time was 24 h.

The highest combined TON of **4** and **5** (738) was obtained in the oxidation of **2a**. All the TON values of the oxidation of 2,2-disubstituted propane-1,3-diols were much higher compared to the TONs of the oxidation of 2,2-dimethylpropanol in References 7 and 8 in which the TONs of 2,2-dimethylpropanoic acid were only 12 and 25, respectively. On the other hand the molar ratios of 2,2-dimethylpropanol to sodium tungstate in References 7 and 8 were also quite low, only 20 and 49, respectively. A more comparable TON in Reference 8 is the value 3000 for octanoic acid obtained in the sodium tungstate catalyzed oxidation of octan-1-ol with hydrogen peroxide. The ratio octan-1-ol/Na_2WO_4 was 20 000:1. The higher TON of octanoic acid is related to the higher yields in the oxidations of linear primary alcohols compared to the yields in the oxidations of 2,2-disubstituted primary alcohols. For instance the yield of octanoic acid was 87% in the oxidation of octan-1-ol with 2.5 equivalents of hydrogen peroxide and catalyzed by 0.02 equivalents of sodium tungstate.[8]

In the literature there are two examples in which 2,2-dimethyl-3-hydroxypropanal was oxidized with hydrogen peroxide without any catalyst affording 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) in 74% and 69% yields.[3a,3c] In addition, in the literature there is an example in which 3-hydroxy-2-hydroxymethyl-2-methylpropanal was oxidized in the same way affording 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**) in an 84% yield.[3e] The formation of 2-methylpropane-1,2-diol (**7a**) or 2-methylpropane-1,2,3-triol (**7b**) were not reported. Compared to these examples the yields of the acids **4a** and **4b** in Figures 4 and 2 and in Table 2 were approximately 50% lower. However, because the combined yields of the acids **4** and the co-products **5** or **7** in Figures 4 and 2 and in Table 2 lie between 37% and 68%, the oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide catalyzed by sodium tungstate is an industrially valuable alternative for the preparation of 2,2-disubstituted 3-hydroxypropanoic acids and 1,1-disubstituted ethane-1,2-diols, the co-product alcohols having a tertiary hydroxy group.[19]

3.1.1 Experimental

Materials. 30% Aqueous hydrogen peroxide was purchased from Riedel-de Haën and 2-ethyl-2-hydroxymethylpropane-1,3-diol from Fluka. 2,2-Dimethylpropane-1,3-diol was obtained from Neste Chemicals. Sodium tungstate dihydrate and sodium molybdate dihydrate were purchased from Merck, and 2-hydroxymethyl-2-methylpropane-1,3-diol and 2,2-bis-(hydroxymethyl)propane-1,3-diol from Sigma-Aldrich. All the chemicals were used as obtained from the suppliers.

Analyses of the reaction mixtures and the isolated products. The concentration of hydrogen peroxide and the conversion of hydrogen peroxide in the reaction mixtures were determined by iodometric titration.[62] The conversion of the reactants and the yield of the products in the reaction mixtures were determined by ^{1}H nuclear magnetic resonance (NMR) (200 MHz) with a Varian Gemini 2000 spectrometer in D_2O using 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt and sodium acetate dihydrate as the internal standards. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra of the isolated products were also recorded in the same way. Mass spectrometry (MS) spectra were obtained using JEOL JMS-SX102 mass spectrometer operating at an ionization potential of 70 eV.

3-Hydroxy-2,2-dimethylpropanoic acid (4a). The synthesis of **4a** is presented as a general procedure. Sodium tungstate dihydrate (0.063 g, 0.19 mmol, 0.02 equiv.) and 2,2-dimethylpropane-1,3-diol (**2a**) (1.000 g, 9.6 mmol, 1.0 equiv.) were dissolved in 29% (w/w) aqueous hydrogen peroxide (2.0 mL, 19.2 mmol, 2.0 equiv.). pH of the mixture was adjusted to 2.0 with 1 M H_2SO_4, and the mixture was stirred at 300 revolutions per minute (rpm) with a magnetic stirrer, and heated at 90^{o}C for 6 hours. pH of the reaction mixture was adjusted to 12 with 50% NaOH, and the product was isolated by passing the mixture through a Dowex 2X8 ion exchange column. The column was eluted with 1 M HCl, and the eluate was evaporated. **4a** (0.349 g, 3.0 mmol, 30%) was obtained as white crystals. Melting point (mp.) 122-125^{o}C (water), (literature (lit.)[3c] 125-126^{o}C). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[63]

2-Methylpropane-1,2-diol (7a). **2a** was oxidized with 4.0 equiv. of 29% (w/w) aqueous hydrogen peroxide as described for **4a**. After adjusting pH of the reaction mixture to 12 with 50% NaOH the product was isolated by passing the mixture through a Dowex 2X8 ion exchange column. The eluate was concentrated and extracted with diethyl ether. The organic phase was dried with anhydrous Na_2SO_4 and evaporated. **7a** (0.196 g, 2.2 mmol, 23%) was obtained as colorless oil. ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[64]

3-Hydroxy-2-hydroxymethyl-2-methylpropanoic acid (4b). 2b was oxidized, and the product was isolated as described for **4a**. **4b** (0.547 g, 4.1 mmol, 49%) was obtained as white crystals. mp. 179-180°C (water), (lit.[65] 180-183°C). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[63]

2-Methylpropane-1,2,3-triol (7b). 2b was oxidized with 4.0 equiv. of 29% (w/w) aqueous hydrogen peroxide as described for **4a**. The product was isolated as described for **7a**. **7b** (0.118 g, 1.1 mmol, 14%) was obtained as colorless oil. ^{1}H NMR and MS spectra were in agreement with those in the literature.[66] ^{13}C NMR (50 MHz, D_2O): δ 22.4, 68.5, 76.1.

2,2-Bis-(hydroxymethyl)butanoic acid (4c). 2c was oxidized, and the product was isolated as described for **4a**. **4c** (0.478 g, 3.2 mmol, 43%) was obtained as white crystals. mp. 102-104°C (water), (lit.[65] 107-110°C). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[63]

2-Ethylpropane-1,2,3-triol (7c). 2c was oxidized with 4.0 equiv. of 29% (w/w) aqueous hydrogen peroxide as described for **4a**. The product was isolated as described for **7a**. **7c** (0.132 g, 1.1 mmol, 15%) was obtained as colorless oil. ^{1}H NMR and MS spectra were in agreement with those in the literature.[66a] ^{13}C NMR (50 MHz, D_2O): δ 9.2, 28.1, 66.3, 77.7.

3-Hydroxy-2,2-bis-(hydroxymethyl)propanoic acid (4d). 2d was oxidized, and the product was isolated as described for **4a**. **4d** (0.520 g, 3.5 mmol, 47%) was obtained as white crystals. mp. 206°C (propan-2-ol), (lit.[67] 210-213°C). ^{1}H NMR (200 MHz, D_2O): δ 3.78 (s, 6H). ^{13}C NMR spectrum was in agreement with that in the literature.[68] MS: m/z 120, 102, 84 (100), 73, 55, 39.

3.1.2 Computational studies

The Baeyer-Villiger rearrangement of the intermediate 2,2-disubstituted 3-hydroxypropanals in the oxidation of 2,2-disubstituted propane-1,3-diols was also studied by a computational modeling. The most favorable spatial arrangement for the migrating hydrogen or group R in the Criegee intermediate type complexes **8**, **9**, and **10** (Scheme 17) is antiperiplanar to the peroxide bond. In this case the torsion angle between the peroxide bond and the migrating hydrogen or group R should be from ±150° to 180°.[14] In addition, the bond angle formed of the peroxide oxygen, the aldehyde carbon, and the migrating hydrogen or group R should be close to 90° (Figure 9).[69] According to Noyori *et al.* one of the nonbonding electron pairs in the aldehydic hydroxy oxygen should be antiperiplanar to the migrating hydrogen or group R.[70]

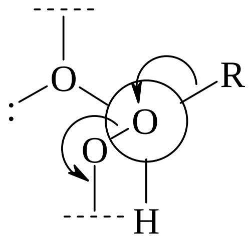
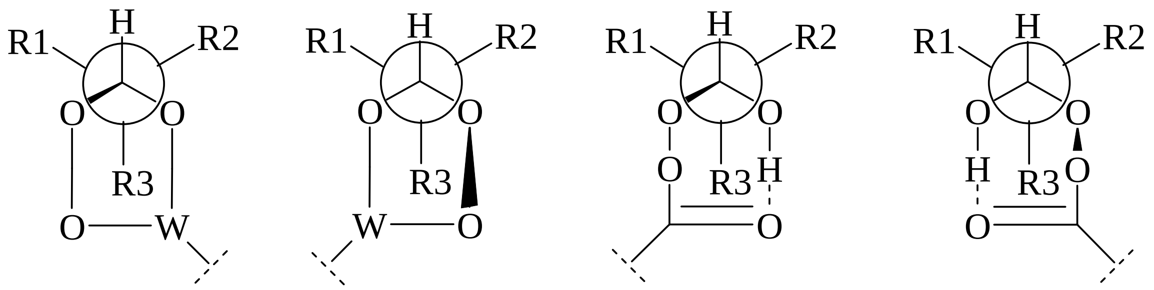


Figure 9. The spatial arrangement for the migrating of the group R in Criegee intermediate type complexes.

In the computational studies energies and structures of conformations of the most reactive intermediates **8** and **9** in the Baeyer-Villiger rearrangement of 2,2-dimethyl-3-hydroxypropanal (**3a**) and 3-hydroxy-2-hydroxymethyl-2-methylpropanal (**3b**) were calculated (Figure 10, Tables 4 and 5). According to the strength of the conjugate acid of the peroxy compounds the conformations of the least reactive intermediate **10** were not explored.[14] The calculations of the intermediate **8** were carried out with the Dmol^3 program[71] employing methods of density functional theory (DFT). The local functional used was PWC with the basis set of double numerical plus d-functions (DND). The calculations of the intermediate **9** were carried out with the Discover program[72] using Condensed-phase Optimized Molecular Potentials for Atomistic Simulation Studies (COMPASS) *ab initio* force field.



8(H) **8(R)** **9(H)** **9(R)**

Figure 10. Conformations of the intermediates **8** and **9**. **H** = hydrogen is migrating and **R** = R is migrating.

Table 4. Energies and torsion angles (α) of the conformations of the intermediates **8** and **9**.[a]

Entry	**8**, **9**	R1	R2	R3	Energy[b] Ha/mol or kJ/mol	α M deg.	α m deg.
1	**8a(H)**	CH_3	CH_2OH	CH_3	-16153.47275	-157.9	86.1
2	**8a(H)**	CH_3	CH_3	CH_2OH	-16153.47204	-161.0	83.8
3	**8a(H)**	CH_2OH	CH_3	CH_3	-16153.47410	-159.3	85.0
4	**8a(R)**	CH_3	CH_2OH	CH_3	-16153.47763	-173.3	65.7
5	**8a(R)**	CH_3	CH_3	CH_2OH	-16153.47462	-176.4	65.3
6	**8a(R)**	CH_2OH	CH_3	CH_3	-16153.47844	-172.6	67.3
7	**8b(H)**	CH_3	CH_2OH	CH_2OH	-16228.20589	-161.4	82.3
8	**8b(H)**	CH_2OH	CH_3	CH_2OH	-16228.22000	-161.6	83.7
9	**8b(H)**	CH_2OH	CH_2OH	CH_3	-16228.20502	-163.6	79.9
10	**8b(R)**	CH_3	CH_2OH	CH_2OH	-16228.20922	-166.7	73.6
11	**8b(R)**	CH_2OH	CH_3	CH_2OH	-16228.20728	-176.3	63.6
12	**8b(R)**	CH_2OH	CH_2OH	CH_3	-16228.20553	-176.8	62.7
13	**9a(H)**	CH_2OH	CH_3	CH_3	154.89846	-174.4	68.6
14	**9a(H)**	CH_3	CH_2OH	CH_3	160.11560	-175.7	66.8
15	**9a(H)**	CH_3	CH_3	CH_2OH	169.80670	-169.8	73.5
16	**9a(R)**	CH_2OH	CH_3	CH_3	168.12683	176.5 (-183.5)	57.3
17	**9a(R)**	CH_3	CH_2OH	CH_3	158.74850	-177.5	63.4
18	**9a(R)**	CH_3	CH_3	CH_2OH	180.08108	172.8 (-187.2)	54.1
19	**9b(H)**	CH_2OH	CH_2OH	CH_3	84.01608	-175.2	68.4
20	**9b(H)**	CH_3	CH_2OH	CH_2OH	128.91160	-167.0	76.8
21	**9b(H)**	CH_2OH	CH_3	CH_2OH	108.79209	-163.1	80.2
22	**9b(R)**	CH_2OH	CH_2OH	CH_3	59.08023	179.3 (-180.7)	60.8
23	**9b(R)**	CH_3	CH_2OH	CH_2OH	75.08731	-165.1	74.2
24	**9b(R)**	CH_2OH	CH_3	CH_2OH	111.45517	167.8 (-192.2)	48.2

[a] For the structures, see Figure 10. **H** = hydrogen is migrating and **R** = R is migrating. α = O-O-$C_{aldehyde}$-M or m. M = the migrating hydrogen or group R and m = the non-migrating hydrogen or group R. Angles are given in degrees (deg.).

[b] In Entries 1-12 energies are given in Ha/mol, and in Entries 13-24 in kJ/mol. 1 Hartree (Ha)/mol = 2625.5 kJ/mol.

Table 5. Bond angles (β) and hydrogen bonds of the conformations of the intermediates **8** and **9**.[a]

Entry	**8**, **9**	R1	R2	R3	β M deg.	β m deg.	hydrogen bonds[b] nm
1	**8a(H)**	CH_3	CH_2OH	CH_3	101.6	114.1	
2	**8a(H)**	CH_3	CH_3	CH_2OH	102.1	113.6	
3	**8a(H)**	CH_2OH	CH_3	CH_3	101.8	114.6	
4	**8a(R)**	CH_3	CH_2OH	CH_3	108.1	109.6	
5	**8a(R)**	CH_3	CH_3	CH_2OH	109.2	108.6	
6	**8a(R)**	CH_2OH	CH_3	CH_3	107.1	109.9	
7	**8b(H)**	CH_3	CH_2OH	CH_2OH	102.2	115.6	0.1711 0.2376
8	**8b(H)**	CH_2OH	CH_3	CH_2OH	103.1	112.7	0.1520
9	**8b(H)**	CH_2OH	CH_2OH	CH_3	102.1	114.3	0.1554
10	**8b(R)**	CH_3	CH_2OH	CH_2OH	106.5	110.1	0.1826
11	**8b(R)**	CH_2OH	CH_3	CH_2OH	108.4	109.4	0.1971
12	**8b(R)**	CH_2OH	CH_2OH	CH_3	109.3	108.9	0.1896
13	**9a(H)**	CH_2OH	CH_3	CH_3	105.5	113.3	0.2028
14	**9a(H)**	CH_3	CH_2OH	CH_3	105.9	113.6	0.1921
15	**9a(H)**	CH_3	CH_3	CH_2OH	105.5	113.3	0.2057
16	**9a(R)**	CH_2OH	CH_3	CH_3	110.1	107.8	0.2178
17	**9a(R)**	CH_3	CH_2OH	CH_3	109.0	108.0	0.2166
18	**9a(R)**	CH_3	CH_3	CH_2OH	109.2	108.1	0.2042
19	**9b(H)**	CH_2OH	CH_2OH	CH_3	105.3	114.3	0.1908
20	**9b(H)**	CH_3	CH_2OH	CH_2OH	104.4	115.8	0.2230
21	**9b(H)**	CH_2OH	CH_3	CH_2OH	105.5	113.5	0.1891
22	**9b(R)**	CH_2OH	CH_2OH	CH_3	109.9	107.0	
23	**9b(R)**	CH_3	CH_2OH	CH_2OH	108.4	108.1	0.1768 0.1917
24	**9b(R)**	CH_2OH	CH_3	CH_2OH	112.7	107.5	0.2095

[a] For the structures, see Figure 10. **H** = hydrogen is migrating and **R** = R is migrating. β = O_{OO}-$C_{aldehyde}$-M or m. M = the migrating hydrogen or group R and m = the non-migrating hydrogen or group R. Angles are given in degrees (deg.).

[b] Hydrogen bonds in Entry 7 are OH_{R3}---O_{OO}W (0.1711 nm) and OH_{R3}---O_{OO}C (0.2376 nm), in Entry 8 HO_{R3}---HOH, in Entry 9 HO_{R2}---HOH, in Entry 10 OH_{R3}---O=W, in Entry 11 OH_{R3}---O_{OO}W, in Entry 12 OH_{R2}---O_{OO}W, in Entries 13-21 and 24 the hydrogen bond in the 7-membered ring and in Entry 23 HO_{R3}---$HOC_{aldehyde}$ (0.1768 nm) and OH_{R3}---O=W (0.1917 nm).

According to the experimental results the most probably intermediates in the Baeyer-Villiger rearrangement of 2,2-dimethyl-3-hydroxypropanal (**3a**) are the complexes **8a(R)** and **9a(R)** and in the Baeyer-Villiger rearrangement of 3-hydroxy-2-hydroxymethyl-2-methylpropanal (**3b**) the complexes **8b(H)** and **9b(H)**. The oxidations of 2,2-dimethylpropane-1,3-diol (**2a**) and 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**) to the corresponding aldehydes **3a** and **3b** are necessarily sodium tungstate or sodium molybdate catalyzed reactions, but the Baeyer-Villiger rearrangements of **3a** and **3b** may also occur only through the intermediates **9** and **10**. Thus interesting questions are do the results of the computational studies in the Tables 4 and 5 give further evidence for the supposed mechanisms of the Baeyer-Villiger rearrangements of the aldehydes **3a** and **3b** and do the intermediates **8a** and **8b** take part in the Baeyer-Villiger rearrangements.

In all conformations of the intermediates **8** and **9** the migrating hydrogen or group R is antiperiplanar to the peroxide bond, while the non-migrating hydrogen or group R being synclinal to the peroxide bond (Table 4). In addition, in most conformations of the intermediates **8** and **9** the bond angle formed of the peroxide oxygen, the aldehyde carbon, and the migrating hydrogen or group R is closer to 90° than the same angle for the non-migrating hydrogen or group R (Table 5).

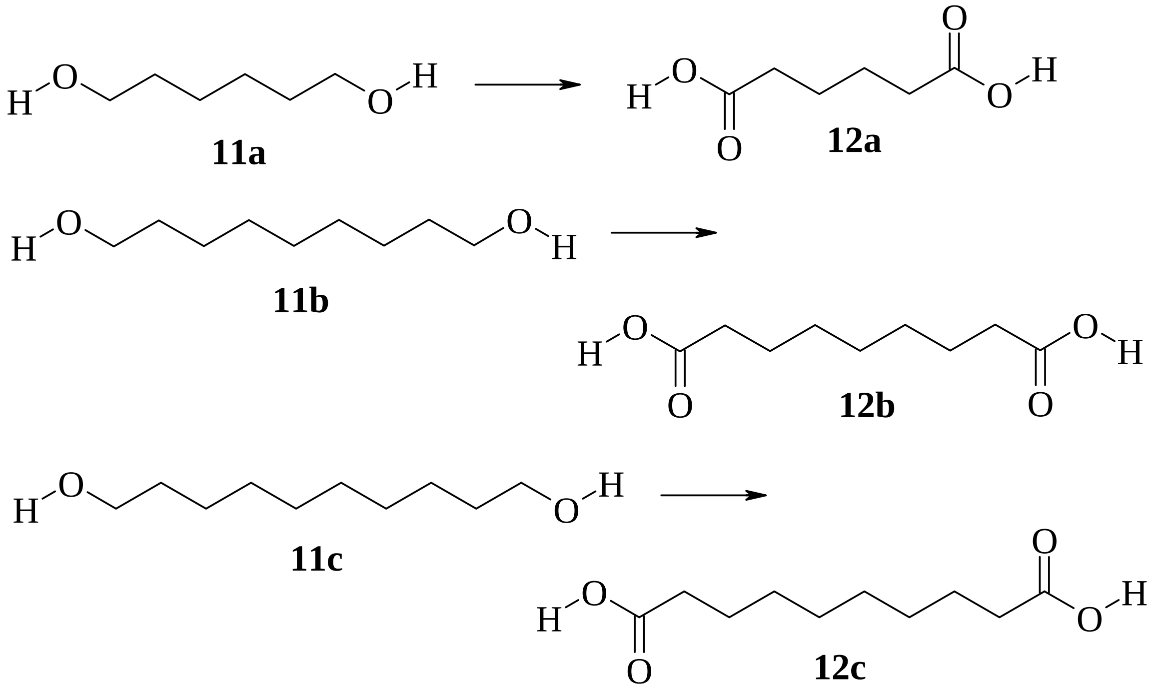
According to the energy values all the conformations of **8a(R)** are more stable than the conformations of **8a(H)**, while the most stable conformation of **9a** is the conformation **9a(H)** in Entry 13. The torsion angles α of the conformations **8a(R)** are also 11.6 to18.5 degrees closer to 180° than the torsion angles of the conformations of **8a(H)**, but the mean value of the torsion angles α of the conformations **9a(H)** are only 2.3° smaller than the mean value of the torsion angles of the conformations **9a(R)**. Although the stable **9a(H)** (Entry 13) would favor the migration of hydrogen, a moderate proportion of the Baeyer-Villiger rearrangement of the aldehyde **3a** occurs through the intermediates **8a(R)** thus favoring the migration of the group R. The most stable conformation of **8a(R)** is 11.4 kJ/mol more stable than the most stable conformation of **8a(H)**, while the conformation **9a(H)** in Entry 13 is only 3.9 kJ/mol more stable than the most stable conformation of **9a(R)** in Entry 17. In addition to the experimental results these computational results make the participation of the intermediate **8a** obvious to the Baeyer-Villiger rearrangement of the aldehyde **3a**. The bond angles β and the lengths of the hydrogen bonds of the conformations of **8a** and **9a** do not have any significant correlation to the other results. In all conformations of **9a** one of the nonbonding electron pairs in the aldehydic hydroxy oxygen seems to be antiperiplanar to the migrating hydrogen or group R.[70]

Among the conformations of the intermediate **8b** the most stable one is the conformation of **8b(H)** in Entry 8, which is 28.3 kJ/mol more stable than the most stable conformation of **8b(R)** in Entry 10. The conformations of **8b** are also in part stabilized by hydrogen bonds, so the most stable conformations have the shortest hydrogen bonds. Because the conformations of **9b(R)** in Entries 22 and 23 do not have the hydrogen bond, which exists in the seven-membered ring of the normal intermediate **9**, the most relevant conformation of **9b(R)** is the one in Entry 24. The energy level of this conformation is 27.4 kJ/mol higher than the energy level of the most stable conformation of **9b(H)** in Entry 19. In **9b(H)** in Entry 19 the torsion angle α is also closer to 180° and the hydrogen bond shorter than in **9b(R)** in Entry 24. From these findings it can be concluded that the most stable conformations of the intermediates **8b(H)** and **9b(H)** take part to the Baeyer-Villiger rearrangement of the aldehyde **3b** thus enabling the migration of hydrogen. The favorable bond angles β of the conformations of **8b** and **9b** enhance also the migration of hydrogen. In all conformations of **9b** one of the nonbonding electron pairs in the aldehydic hydroxy oxygen seems also to be antiperiplanar to the migrating hydrogen or group R.[70]

The computational studies show also that in the reports in which 2,2-dimethyl-3-hydroxypropanal[3a,3c] and 3-hydroxy-2-hydroxymethyl-2-methylpropanal[3e] were oxidized with hydrogen peroxide without any catalyst the acids **4a** and **4b** were obtained in higher yields than presented in Figures 4 and 2 and in Table 2 due to the absent of the intermediates **8a(R)** or **8b(R)** which seem to favor the migration of the group R.

3.2 Oxidation of primary diols to dicarboxylic acids with hydrogen peroxide catalyzed by sodium tungstate

Taking example by Sloboda-Rozner's *et al.* report[21] in which hexane-1,6-diol was oxidized to adipic acid with hydrogen peroxide catalyzed by $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ sodium tungstate was chosen as a catalyst for the experiments of the oxidation of linear primary diols with hydrogen peroxide to the corresponding dicarboxylic acids (Scheme 18).



Scheme 18. Oxidation of linear primary diols.

The results of the oxidation of hexane-1,6-diol (**11a**), nonane-1,9-diol (**11b**), and decane-1,10-diol (**11c**) are presented in Table 6.

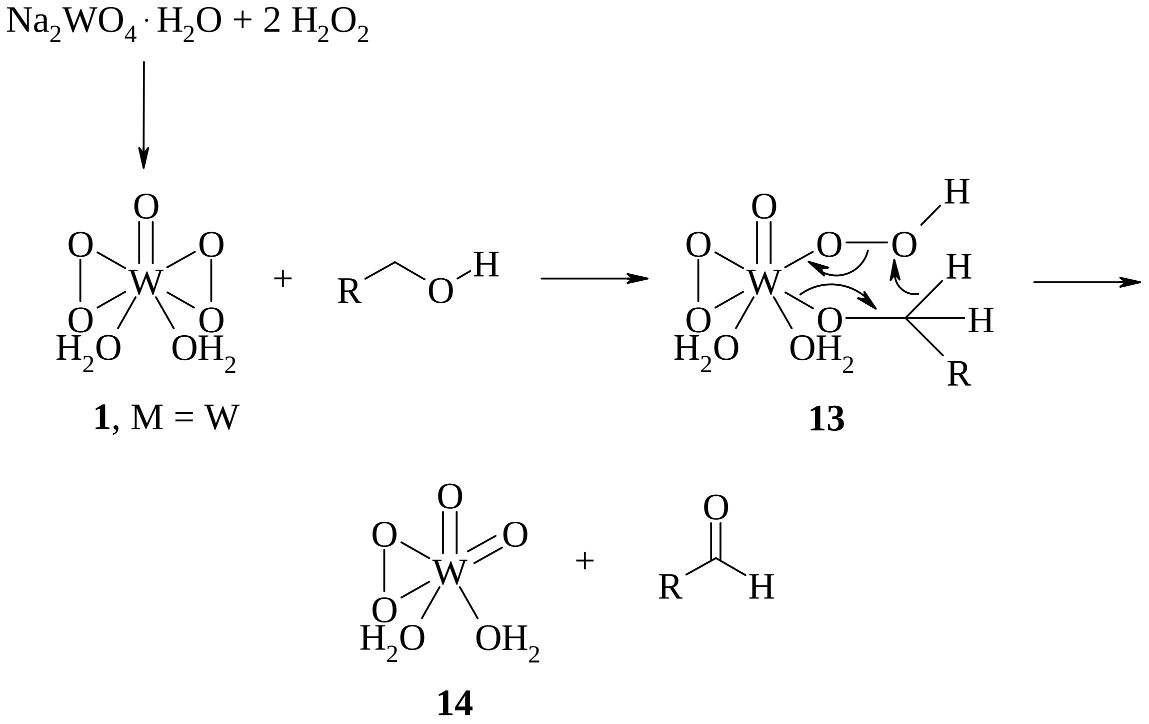
Table 6. Oxidation of linear primary diols to dicarboxylic acids with hydrogen peroxide catalyzed by sodium tungstate.[a]

Entry	Diol	C, %	Diacid	Y, %
1	Hexane-1,6-diol (**11a**)	86[c]	Adipic acid (**12a**)	80[b], 83[c]
2	Nonane-1,9-diol (**11b**)		Nonanedioic acid (**12b**)	78[b]
3	Decane-1,10-diol (**11c**)		Decanedioic acid (**12c**)	82[b]

[a] pH was 2.0 and the reaction time 24 h. 4.0 equiv. of H_2O_2 was used. In Entries 2 and 3 0.04 equiv. of Aliquat 336 was added to the reaction mixture.
[b] Isolated yield.
[c] The reaction mixture was analyzed by ^{1}H NMR.

The results show that linear primary diols having chain length of at least six carbons are easily oxidized with hydrogen peroxide to dicarboxylic acids catalyzed by sodium tungstate. The yields of the diacids are also higher than the yields of the monocarboxylic acids in the oxidation of 2,2-disubstituted propane-1,3-diols (Chapter 3.1).

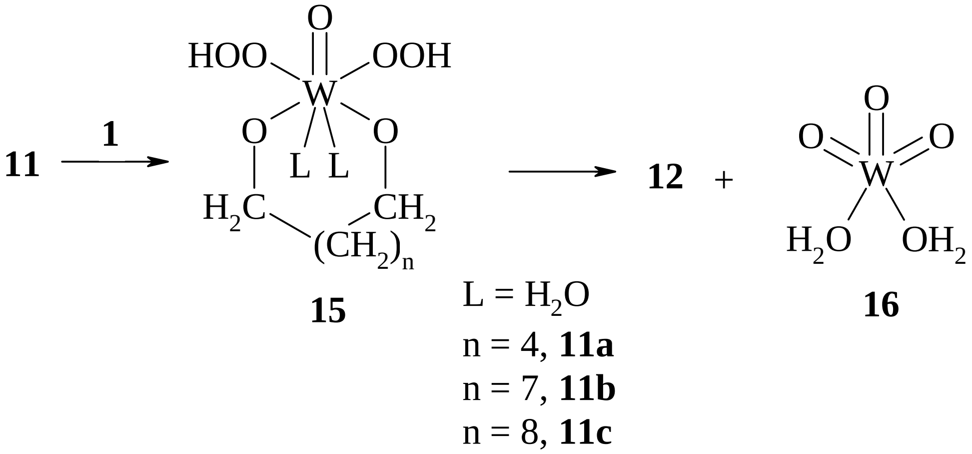
As described in Chapters 1.1 and 3.1 sodium tungstate and sodium molybdate form a diperoxo complex with hydrogen peroxide (**1**, Scheme 16). According to the mechanism of the oxidation of secondary alcohols to ketones with the diperoxo complex of tungsten **1** (M = W) suggested by Jacobson *et al.*[73] the mechanism of the sodium tungstate catalyzed oxidation of primary alcohols to aldehydes with hydrogen peroxide is presented in Scheme 19.



Scheme 19. Mechanism of the sodium tungstate catalyzed oxidation of primary alcohols with hydrogen peroxide.

For the linear primary diols **11** the structure of the **13** type intermediate may consist of a ring formed by an interaction of both the hydroxy groups of the diol with the peroxy groups of the diperoxo complex of tungsten **1** (**15**, Scheme 20). The structure of this intermediate is based on Jacobson's *et al.*[73]

suggestion that both the peroxo groups of the diperoxo complex of tungsten are reactive. In their experiment 1.7 moles of a secondary alcohol was oxidized to a ketone by one mole of the diperoxo complex. The analysis of the reduced oxidant **16** showed only metal oxo bonds and no peroxo bonds.



15

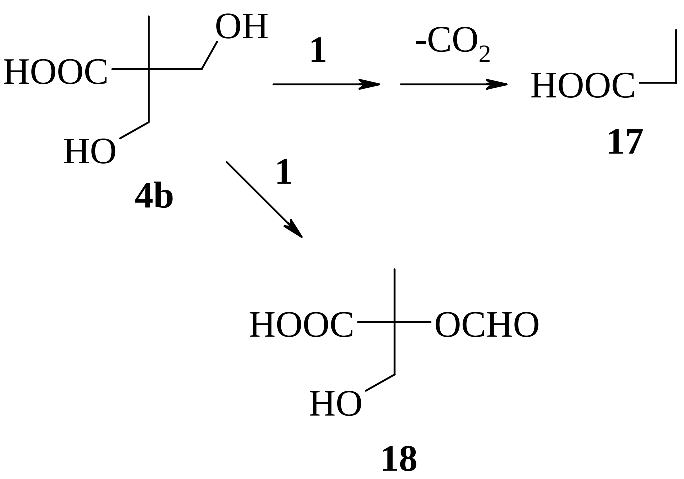
16

L = H_2O
n = 4, **11a**
n = 7, **11b**
n = 8, **11c**

Scheme 20. Mechanism of the sodium tungstate catalyzed oxidation of the linear primary diols **11** with hydrogen peroxide.

A further evidence for the supposed mechanism of the oxidation of the linear primary diols was obtained from ^{1}H NMR analysis of the oxidation of hexane-1,6-diol (Entry 1 in Table 6). In the ^{1}H NMR spectra of this oxidation no signals of the monocarboxylic acid were detected.

The oxidation of 2,2-disubstituted propane-1,3-diols with hydrogen peroxide to dicarboxylic acids was investigated by the sodium tungstate catalyzed oxidation of 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**) (Scheme 21 and Entry 1 in Table 7).



Scheme 21. Oxidation of 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid with hydrogen peroxide catalyzed by sodium tungstate.

Table 7. Oxidation of 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid and a mixture of *cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol with hydrogen peroxide catalyzed by sodium tungstate.[a]

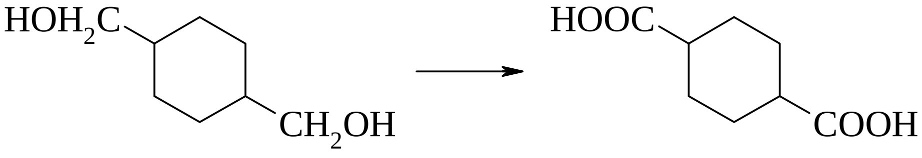
Entry	Reactant	C, %	Product	Y, %
1	3-Hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**)	38[b]	2-formyloxy-3-hydroxy-2-methylpropanoic acid (**18**)	3[b]
2[a]	*cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol (**19**)		*trans*-cyclohexane-1,4-dicarboxylic acid (**20**)	56[c]

[a] pH was 2.0 and the reaction time 24 h. In Entry 1 2.0 equiv. and in Entry 2 4.0 equiv. of H_2O_2 was used. The molar percentages of *cis* and *trans* isomers in **19** were 46% and 54%.
[b] The reaction mixture was analyzed by ^{1}H NMR.
[c] Isolated yield. *cis*-**20** could not be isolated as a pure isomer.

2,2-Disubstituted propane-1,3-diols are easily oxidized with hydrogen peroxide catalyzed by sodium tungstate to 2,2-disubstituted 3-hydroxypropanoic acids and formic acid 1,1-disubstituted 2-hydroxyethyl esters as presented in Chapter 3.1. However, in the oxidation of 2,2-

disubstituted propane-1,3-diols the formation of the **15** type intermediates (Scheme 20) are not favored, because the strain of the rings formed of 2,2-disubstituted propane-1,3-diols and diperoxo complex of tungsten would be substantial. Thus as in the oxidation of one hydroxymethyl group of 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**, Scheme 16 in Chapter 3.1) to carboxylic and formyloxy groups the other two hydroxymethyl groups of 3-hydroxy-2-hydroxymethyl-2-methylpropanoic (**4b**) may be oxidized in the same way, but, in addition, the dicarboxylic acid products may undergo the decarboxylation typical for malonic acids.[24] So the supposed final products in the oxidation of **4b** are propanoic acid (**17**) and 2-formyloxy-3-hydroxy-2-methylpropanoic acid (**18**) (Entry 1 in Table 7). According to the literature the reaction temperature of 90°C was enough high for the decarboxylation of the dicarboxylic acid products, because it is reported that the heating of an aqueous solution of malonic acid above 70°C results in a decomposition of the acid to carbon dioxide and acetic acid.[24a] Because the conversion of **4b** was 38%, but no signals of **17** were detected by ^{1}H NMR, it is probably that propanoic acid had evaporated from the reaction mixture. According to the examples in the literature, in which many 2,2-disubstituted 3-oxocarboxylic acid esters have been oxidized with 3-chloroperoxybenzoic acid to 2,2-disubstituted 2-acyloxycarboxylic acid esters (Chapter 1.2),[23] the formation of **18** is also possible in the oxidation of **4b**. Thus the only signals in addition to the signals of **4b** detected by ^{1}H NMR should be the signals of **18**. The rate the oxidation of **4b** was much lower than the rate the oxidation of **2b** to **4b**, because the carboxy group of **4b** will co-ordinate to the metal of the complex **1** more readily than the hydroxy group of **4b**.

As a comparative experiment a mixture of *cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol was oxidized in the same way as the linear primary diols **11**(**a**-**b**) and the 2,2-disubstituted hydroxy acid **4b** (Scheme 22 and Entry 2 in Table 7).



19 **20**

Scheme 22. Oxidation of (4-hydroxymethylcyclohexyl)methanol.

As the diols **11**(**a**-**b**), *cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol have also some characteristic of linearity due to the chain of six carbons between the hydroxy groups of them. In addition, the ring structure of *cis*- and *trans*-cyclohexane-1,4-dicarboxylic acid starting from the β-position of the hydroxy groups gives an impression of a 2,2-disubstituted structure as in **4b**. As expected the yield of *trans*-cyclohexane-1,4-dicarboxylic acid (**20**) in the oxidation of **19** was not as high as the yields of the diacids **12**(**a**-**b**) in the oxidation of **11**(**a**-**b**). Because the cyclic structure of **19** is more rigid than the acyclic carbon chains of **11**(**a**-**b**), an obvious reason for the lower yield of *trans*-**20** is that the structure of the **15** type intermediate (Scheme 20) of **19** is more unfavorable than the structures of the intermediates **15** of **11**(**a**-**b**). The oxidation of *cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol shows also that the β-branching of the diols is not as determinative as the sufficient length of the carbon chain of the diols in the oxidation of primary diols to the corresponding diacids.

The results of the sodium tungstate catalyzed oxidation of primary diols to dicarboxylic acids with hydrogen peroxide show that this procedure can offer an industrially applicable alternative for the preparation of the linear dicarboxylic acids, especially when the usual reactants, cycloalkanes, are not available.[19] In addition, according to the results the oxidation of 2,2-disubstituted 3-hydroxy-propanoic acids does not afford dicarboxylic acids as final products due to the decarboxylation of the diacids at the reaction temperature of the procedure. Finally, the results show that with primary diols a carbon chain of a sufficient length, at least six carbons, seems to be the most significant characteristic of the diols in their sodium tungstate catalyzed oxidation to dicarboxylic acids with hydrogen peroxide.

3.2.1 Experimental

Materials. Nonane-1,9-diol was purchased from EGA-Chemie. Hexane-1,6-diol and tricaprylylmethylammonium chloride (Aliquat 336) were purchased from Fluka, 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid and a mixture of *cis*- and *trans*-(4-hydroxymethylcyclohexyl)methanol from Sigma-Aldrich, and decane-1,10-diol from Merck. The other chemicals used are described in Chapter 3.1.1. All the chemicals were used as obtained from the suppliers.

Analyses of the reaction mixtures and the isolated products. The concentration of hydrogen peroxide, the conversion of the reactants, and the yield of the products in the reaction mixtures were determined as described in Chapter 3.1.1. NMR and MS spectra of the isolated products were also recorded as described in Chapter 3.1.1, except NMR spectra in $(CD_3)_2SO$, in which the solvent was used as the internal standard.

Adipic acid (12a). The synthesis of **12a** is presented as a general procedure. Sodium tungstate dihydrate (0.056 g, 0.17 mmol, 0.02 equiv.) and hexane-1,6-diol (**11a**) (1.000 g, 8.5 mmol, 1.0 equiv.) were dissolved in 29% (w/w) aqueous hydrogen peroxide (3.6 mL, 33.9 mmol, 4.0 equiv.). pH of the mixture was adjusted to 2.0 with 1 M H_2SO_4 and the mixture was stirred at 300 rpm with a magnetic stirrer and heated at 90°C for 24 hours. The reaction mixture was cooled to 0°C, and the product was isolated by filtering the precipitate. The precipitate was washed with ice water. **12a** (0.990 g, 6.8 mmol, 80%) was obtained as white crystals. mp. 151-153°C (water), (lit.[74] 152-153°C). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[75]

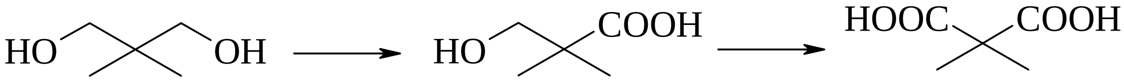
Nonanedioic acid (12b). Nonane-1,9-diol (**11b**) was oxidized as described for **12a**. In addition, tricaprylylmethylammonium chloride (Aliquat 336) (0.04 equiv.) was added to the two-phased mixture due to the insolubility of **11b**. The reaction mixture was stirred at 750 rpm. After cooling the reaction mixture to ambient temperature the product was isolated by filtering the precipitate. The precipitate was washed with ice water. **12b** (0.917 g, 4.9 mmol, 78%) was obtained as white crystals. mp. 94-97°C (water), (lit.[76] 91-97°C). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[75c]

Decanedioic acid (12c). Decane-1,10-diol (**11c**) was oxidized as described for **12a**. In addition, tricaprylylmethylammonium chloride (Aliquat 336) (0.04 equiv.) was added to the two-phased mixture due to the insolubility of **11c**. The reaction mixture was stirred at 750 rpm. After cooling the reaction mixture to ambient temperature the product was isolated by filtering the precipitate. The precipitate was washed with ice water. **12c** (0.950 g, 4.7 mmol, 82%) was obtained as white crystals. mp. 125-129°C (water), (lit.[77] 129-131°C). ^{1}H NMR (200 MHz, $(CD_3)_2SO$): δ 1.28-1.44 (m, 8H), 1.48-1.71 (m, 4H), 2.28 (t, 4H, ^3J=7.40 Hz). ^{13}C NMR (50 MHz, $(CD_3)_2SO$): δ 28.5, 32.5, 37.7, 178.5. At δ 32.5 two peaks are probably overlapping. MS spectrum was in agreement with that in the literature.[75c]

***trans*-Cyclohexane-1,4-dicarboxylic acid (*trans*-20).** A mixture of *cis*- and *trans*-(4-hydroxymethylcyclohexyl)-methanol (**19**) was oxidized as described for **12a**. The molar percentages of *cis* and *trans* isomers in **19** were 46% and 54%, respectively, determined by ^{1}H NMR. The *trans*-isomer of the product was isolated as described for **12a**. *trans*-**20** (0.359 g, 2.1 mmol, 56%) was obtained as white crystals, and its yield is based on *trans*-**19**. mp. 311-313°C (water), (lit.[78] 313°C). ^{1}H NMR (200 MHz, $(CD_3)_2SO$): δ 1.71-1.81 (m, 4H), 2.34-2.37 (m, 4H), 2.95-2.97 (m, 2H), 12.27 (s, 2H). ^{13}C NMR and MS spectra were in agreement with those in the literature.[75c] Even though *cis*-**20** was detected by ^{13}C NMR of the reaction mixture it could not be isolated as a pure isomer.

3.3 Oxidation of 2,2-disubstituted propane-1,3-diols and linear primary diols with air catalyzed by noble metals supported on activated carbon

The oxidation of 2,2-disubstituted propane-1,3-diols to hydroxy acids and diacids with air was studied by the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) catalyzed by palladium, platinum, and gold supported on activated carbon (Scheme 23).



2a **4a** **21**

Scheme 23. Oxidation of 2,2-dimethylpropane-1,3-diol.

The oxidations of 2,2-dimethylpropane-1,3-diol catalyzed by self-made noble metal catalysts are presented in Figure 11. The same oxidation catalyzed by a commercial Pd/C and Pt/C is presented in Figures 12 and 13. The lowest conversion of **2a** and the lowest yields of 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) and dimethylmalonic acid (**21**) were obtained in the Au/C catalyzed oxidation of **2a** (Figure 11). However, the conversion of **2a** and the yields of the products may be higher when performing the oxidation of **2a** with air at elevated pressure, because in the literature[29,32,33,36] most gold catalyzed oxidations of diols and polyols are reported to be performed with oxygen at two or three atmospheres pressure (Chapter 1.3). The highest yields of **21**, though below 20%, were obtained by both the self-made and commercial Pd/C (Figures 11 and 12). These results indicate that the formation of the corresponding dicarboxylic acid may have also been possible in the Pd/C catalyzed oxidation[38] of 2-hydroxymethyl-2-methylpropane-1,3-diol with an oxygen-containing gas, even though the formation of any diacids was not reported (Chapter 1.3).

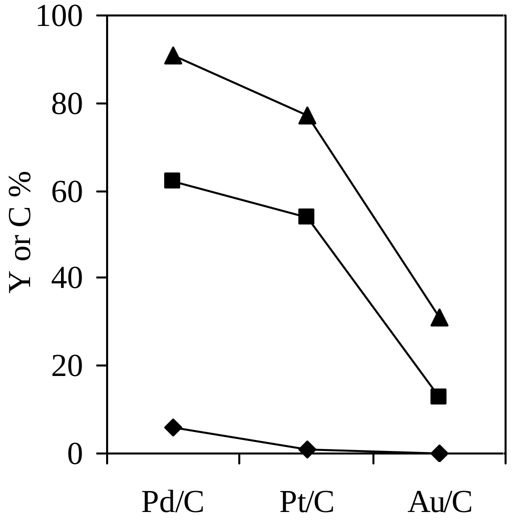


Figure 11. The theoretical metal percentage of the self-made catalysts was 5%. The reaction time was 2 h. ▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y.

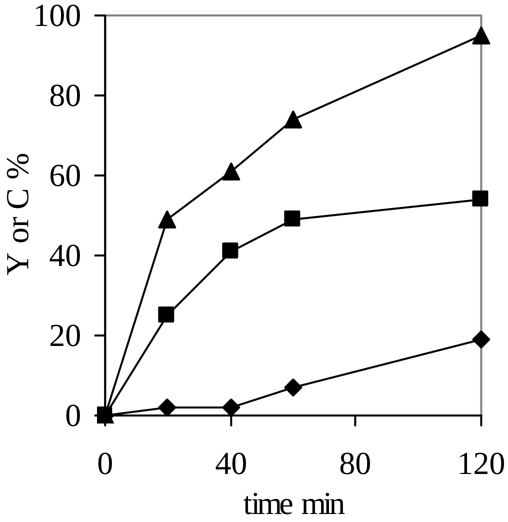


Figure 12. Commercial 5% Pd/C catalyst. Before the reaction was started the reaction mixture was stirred under H_2 for 10 min to activate the catalyst. ▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y.

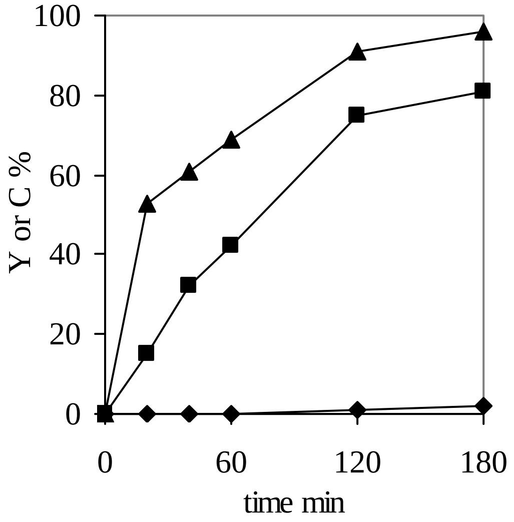
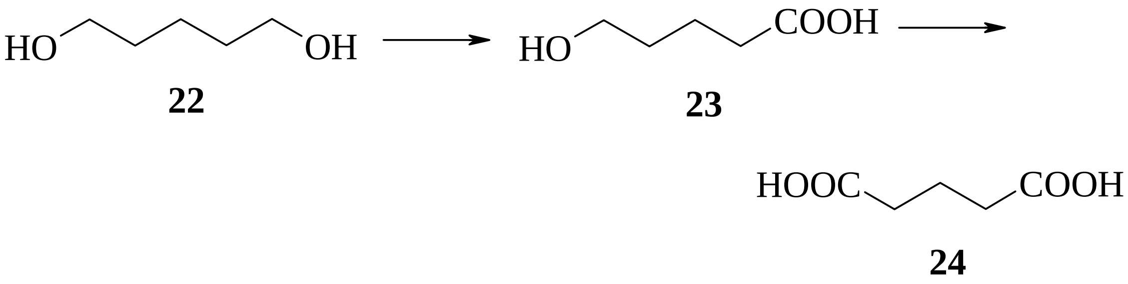


Figure 13. Commercial 5% Pt/C catalyst. ▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y.

The highest yield of **4a**, 81%, was obtained in the commercial Pt/C catalyzed 180 minutes' oxidation of **2a** (Figure 13). Although the yield of **4a** was higher in the self-made Pd/C catalyzed oxidation of **2a**, compared to the self-made Pt/C catalyzed oxidation, the 70% selectivity of **4a** in the self-made Pt/C catalyzed oxidation is still higher than the 68% selectivity of **4a** in the self-made Pd/C catalyzed oxidation. In addition, the selectivity of **4a**, 82%, is also higher in the commercial Pt/C catalyzed 120 minutes' oxidation of **2a**, compared to the 57% selectivity of **4a** in the commercial Pd/C catalyzed oxidation.

The oxidation of linear primary diols to hydroxy acids and diacids with air was studied by the oxidation of pentane-1,5-diol (**22**) catalyzed by palladium and platinum supported on activated carbon (Scheme 24, and Figures 14 and 15).



Scheme 24. Oxidation of pentane-1,5-diol.

The Pd/C catalyzed oxidation of pentane-1,5-diol afforded a higher yield of glutaric acid (**24**), though only 5% in an 120 minutes' oxidation, compared to the Pt/C catalyzed oxidation of **22**. The corresponding hydroxy acid, 5-hydroxypentanoic acid (**23**), was obtained in a 58% yield and in an 82% selectivity in the Pt/C catalyzed oxidation of **22**. In the Pd/C catalyzed oxidation of **22** the yield of **23** was slightly lower, 50%, but the selectivity of **23** was only 65%.

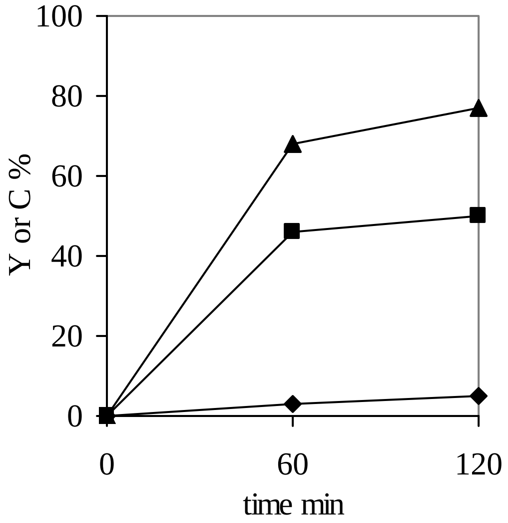


Figure 14. Commercial 5% Pd/C catalyst. Before the reaction was started the reaction mixture was stirred under H_2 for 10 min to activate the catalyst. ▲ = **22** C, ■ = **23** Y, ♦ = **24** Y.

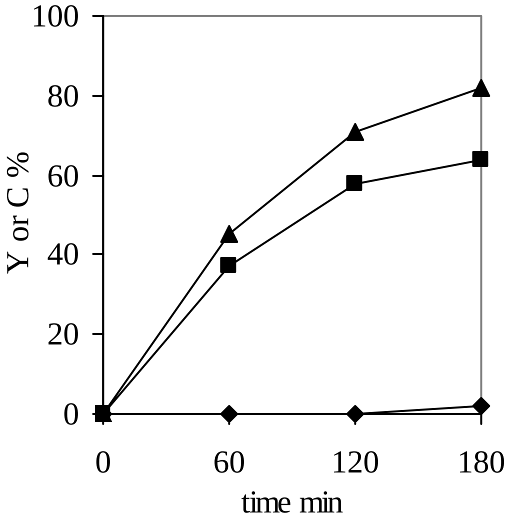


Figure 15. Commercial 5% Pt/C catalyst. ▲ = **22** C, ■ = **23** Y, ♦ = **24** Y.

The higher yields of the diacids **21** and **24** in the Pd/C catalyzed oxidations of **2a** and **22**, respectively, compared to the yields of the hydroxy acids **4a** and **23** in the Pt/C catalyzed oxidations, may be a consequence of an enhanced adsorption of the hydroxy acids to the surface of palladium. At least palladium is known to have a lower stability toward an oxygen poisoning, compared to platinum, and this phenomenon may also cause the enhanced oxidation of the hydroxy acids to the diacids.[79]

The lower rates of the oxidations of pentane-1,5-diol, compared to the rates of the oxidations of 2,2-dimethylpropane-1,3-diol, are probably caused of the long carbon chain of pentane-1,5-diol. When Druz oxidized straight chain primary C_2-C_8 monoalcohols, he found that the poisoning effect of the products was directly proportional to the molecular weight of the corresponding alcohol.[80] Although 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol have the same molecular weight, it is probable that the linear glutaric acid will adsorb more readily to the catalyst than the branched dimethylmalonic acid.

The noble metal catalyzed air oxidations of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol show that this kind of oxidation is best suitable for the preparation of 2,2-disubstituted 3-hydroxypropanoic acids and linear hydroxy acids by Pt/C as a catalyst. As described in Chapter 1.3 this method can also be industrially valuable.[25] However, in a basic reaction medium the intermediate 2,2-disubstituted 3-hydroxypropanals, formed from 2,2-disubstituted propane-1,3-diols, may undergo also a retrograde aldol reaction (Chapter 1, Scheme 2). Although this side reaction is a reversible reaction, the aldehydic products of the reaction may irreversibly oxidize to undesired carboxylic acids thus lowering somewhat the yields of the desired hydroxy acids of the main reaction.

3.3.1 Experimental

Materials. Pentane-1,5-diol, potassium tetrachloroplatinate(II), sodium borohydride, 5% Pd/C and 5% Pt/C were purchased from Aldrich. Hydrogen tetrachloroaurate(III) tetrahydrate and activated carbon (Charcoal) were purchased from Merck and palladium(II) acetate from Ega-Chemie. The other chemicals used are described in Chapter 3.1.1. Solvents of HPLC grade were used for the analyses of the products. All the chemicals were used as obtained from the supplier.

Preparation of the catalysts. For the preparation of 5% Pd/C palladium(II) acetate (0.011 g, 0.05 mmol) dissolved in 0.5 mL of water was added dropwise into a suspension of activated carbon (0.178 g) in 2 mL of water in 15 minutes. Sodium borohydride (0.002 g, 0.05 mmol) dissolved in 0.5 mL of water was added dropwise into the mixed slurry in 15 minutes. The catalyst was filtered, washed until neutral with water, and used as a wet powder. 5% Pt/C and 5% Au/C were prepared similarly.

Characterization of the catalysts. Characteristics of activated carbon (Charcoal) are iodine adsorptive capacity (81 mL/g of 0.05 mol I_2/L), methylene blue adsorption (14 mL/0.1 g of 0.15% solution), and particle size (about 90% of <100 μm and about 30 μm of Cilas (d50)). The morphological investigations of the commercial Pt/C were performed by scanning electron microscopy (SEM) using a Zeiss DSM 962 scanning electron microscope.

Analyses of the reaction mixtures.

The conversion of the reactants in the reaction mixtures of the oxidations of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol were determined by gas chromatography (GC) using a Hewlett Packard 6890 gas chromatograph. The temperature of the injector was 200ºC and the flame ionization detector (FID) 250ºC. The column was a HP-5 30 m x 0.32 mm fused-silica capillary column with a 0.25-μm film thickness. The initial column temperature was 30ºC (1 min) followed by the temperature-programmed rate of 10ºC min^{-1} (7 min) and the final temperature of 100ºC (1 min). The total run time was 9 minutes. The initial pressure of the helium carrier gas was 1.286 bar, and the gas was used at a flow rate of 2.0 mL min^{-1}. The exact amount of the reactant present in the reaction mixtures was determined using 1-methoxy-2-[2-(2-methoxyethoxy)ethoxy]ethane (triglyme) as an internal standard.

The yield of the carboxylic acid products in the reaction mixtures of the oxidations of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol were determined by high performance liquid chromatography (HPLC) using a system consisting of a Waters 600 Controller and Pump, a Waters 996 Photodiode Array Detector and a Waters 717 plus Autosampler. The detection wavelength was 210 nm and the column a Merck LiCrospher 100 RP-18 with a 5-µm particle size. The eluent was 8% CH_3CN in water and pH of the eluent was adjusted to 2.3 with phosphoric acid. The flow rate of the eluent was 1 mL min^{-1}. The exact amounts of the products present in the reaction mixtures were determined using an external standard method.[81]

Oxidation procedure. The Pd/C catalyzed oxidation of 2,2-dimethylpropane-1,3-diol is presented as a general oxidation procedure. 2,2-Dimethylpropane-1,3-diol (**1**) (0.500 g, 4.8 mmol) was dissolved in 20 mL of water in a 100 mL glass batch reactor equipped with syringes for a gas and a base solution inlet, a pH electrode with a thermometer (Metrohm Pt 1000), and a reflux condenser. After suspending 5% Pd/C (0.187 g, 0.01 equiv. of Pd) in the mixture argon was bubbled 200 mL min^{-1} through the mixture for 5 minutes. The reaction was started by bubbling air 200 mL min^{-1} through the mixture. The reaction mixture was stirred 1000 rpm with a magnetic stirrer. The reaction temperature was 40ºC, and pH of the reaction mixture was kept at 10 by adding 10% NaOH via a pump controlled by a pH meter (Metrohm 744).

3.4 Oxidation of 2,2-disubstituted propane-1,3-diols and linear primary diols to diacids with air catalyzed by noble metals supported on activated carbon and promoted with bismuth

As a preliminary experiment the activity of palladium, platinum, and gold supported on activated carbon and promoted with bismuth, prepared by the method A, was studied by the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**, Scheme 23 in Chapter 3.3) with air (Figure 16).

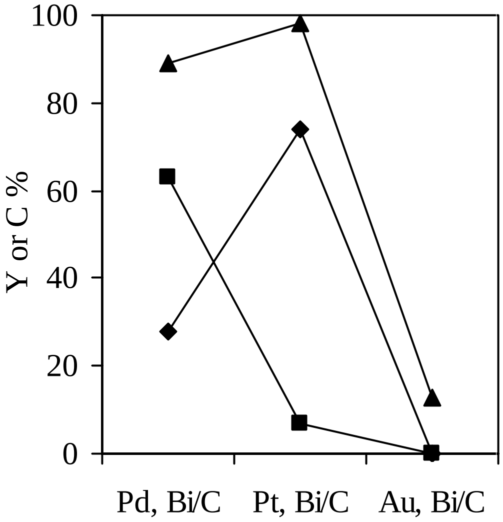


Figure 16. The metal percentages of the self-made catalysts (method A) were 5%. The reaction time was 3 h. ▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y.

In a three hours' oxidation of **2a** Pt, Bi/C afforded the highest yield of the diacid **21**. In addition, because platinum has a higher stability toward the oxygen poisoning, compared to palladium,[79] it was chosen for the investigation of the promoted catalysts, although the yields of the diacids **21** and **24** were higher in the Pd/C catalyzed oxidations of **2a** and **22**, respectively, compared to the Pt/C catalyzed oxidations (Chapter 3.3). The stability of platinum compensates also the lower price of palladium.[79]

Bismuth as a promoter was supposed to prevent the adsorption of poisoning species on the surface of platinum thus directing the reaction to the desired products.[49]

The air oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) catalyzed by a self-made Pt, Bi/C (method B) is presented in Figure 17. Compared to the commercial Pt/C catalyzed oxidation of **2a** (Chapter 3.3, Figure 13), the effect of the promotion is clearly seen. In the Pt, Bi/C catalyzed oxidation no 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) was left after a 180 minutes' reaction, and dimethylmalonic acid (**21**) was obtained in an 81% yield.

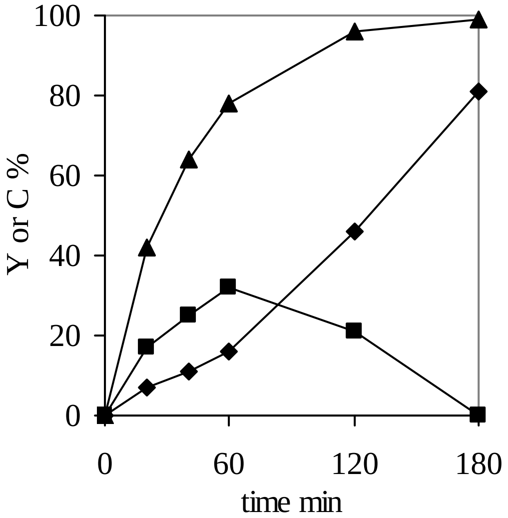


Figure 17. The catalyst was a self-made 5% Pt, 5% Bi/C (method B).
▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y.

The other experiments concerning the Pt, Bi/C (method B) catalyzed oxidations are presented in Table 8.

Table 8. Air oxidations of 2,2-disubstituted propane-1,3-diols catalyzed by 5% Pt, 5% Bi/C.[a]

Entry	Time, h	Reactant	C, %	Hydroxy acid	Y,%	Diacid	Y, %
1a[a]	2	**2a**	81	**4a**	57	**21**	4
1b[a]	3	**2a**	37[b]	**4a**	27[b]	**21**	5[b]
2[c]	3	**2a**	21	**4a**	4	**21**	0
3[d]	3	**21**				**21**	96[b]
4[e]	2	**2a**	65	**4a**	38	**21**	11
5[f]	3	**2a**	100	**4a**	22	**21**	50
6	1	**4a**	89			**21**	83
7	7	**2b**	100[b]	**4b**	16[b]	**27**	63[b], 51[g]

[a] 5% Pt, 5% Bi/C was prepared by the method B described in Experimental, except in Entry 1a in which the catalyst was a commercial 10% Pt/C (0.094 g) and $BiCl_3$ (0.015 g, 0.048 mmol) and in Entry 1b in which the catalyst was a commercial 5% Pt/C (0.165 g) and Bi_2O_3 (0.0184 g, 0.040 mmol). In Entry 1b air was bubbled 800 mL min^{-1} through the reaction mixture.

[b] The reaction mixture was analyzed by ^1H NMR.

[c] At the beginning of the reaction, **21** (0.635 g, 4,8 mmol, 1.0 equiv.) was added to the reaction mixture. The added amount of **21** was subtracted from its yield.

[d] Air was not bubbled through the reaction mixture.

[e] pH was adjusted to 10 with a solution containing 10% of NaOH and 13% of **2a**. In the solution the amount of **2a** was 0.5 equivalents compared to NaOH. The added amount of **2a** (0.392 g) was included to the conversion of **2a** and the yields of **4a** and **21**.

[f] The catalyst was used six times in an oxidation described in Entry 1.

[g] Isolated yield.

The promoter can also be added as a salt or as an oxide to the reaction mixture.[82] However, as seen in Entry 1a and 1b this procedure gave only a low yield of the diacid in the oxidation of **2a** and the yield of the hydroxy acid was even less than in the commercial 5% Pt/C catalyzed oxidation of **2a** (Figure 13 in Chapter 3.3).

The carboxylic acid products are known to deactivate supported platinum catalysts by adsorption on the metal in the oxidation of primary alcohols.[83]

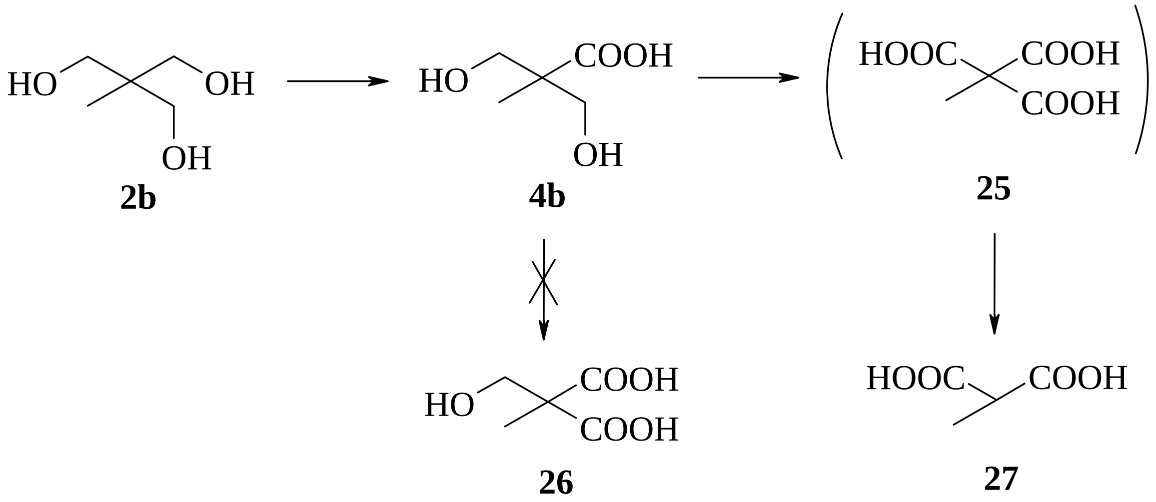
Dimethylmalonic acid had also the same effect on the oxidation of **2a**. When one equivalent of **21** was added to the reaction mixture at the beginning of the reaction both the yields of the hydroxy acid and the diacid were decreased considerably (Entry 2). Because the weight ratio of Pt, Bi/C to dimethylmalonic acid was quite high, 0.3, the diacid was probably also slightly adsorbed on the activated carbon support of the catalyst (Entry 3). One solution to overcome the deactivation of the catalyst is to perform the reaction in a continuous flow reactor, in which the products are isolated by conducting the reaction mixture through an ion exchange resin.[84]

When 2,2-dimethylpropane-1,3-diol was added to the reaction mixture at half the rate as sodium hydroxide was consumed, calculated as moles, the consumption of **2a** was 21% higher than the consumption of **2a** in the 120 minutes' oxidation in Figure 17 (Entry 4). In addition, the combined production of **4a** and **21** was also 25% higher than their production in the 120 minutes' oxidation of **2a** in Figure 17. This indicates that the reactant does not have a significant influence on the deactivation of Pt, Bi/C. In fact, alcohols are reported to reduce over-oxidized supported platinum catalysts thus enabling even the increase of the reaction rates.[85]

The deactivation of Pt, Bi/C was also studied by using the same catalyst in seven oxidations of **2a** (Entry 5). Nevertheless the yield of dimethylmalonic acid was still moderate. In addition, the combined selectivity of **4a** and **21** remained quite high, 72%, compared to their 82% combined selectivity after the first oxidation of **2a** (Figure 17). The increase of the yield of the hydroxy acid was probably caused of the dissolving of bismuth from the catalyst.[86]

To evaluate quantitatively the proportion of the retrograde aldol reaction (Chapters 1 and 3.3) and other side reactions in the oxidation of 2,2-dimethylpropane-1,3-diol to 3-hydroxy-2,2-dimethylpropanoic acid (**4a**), **4a** was oxidized to dimethylmalonic acid (**21**) in the same way as 2,2-dimethylpropane-1,3-diol in Figure 17. By comparing Figure 17 and Entry 6 it can be evaluated that the decrease of the selectivity is about 10% due to the retrograde aldol reaction and other side reactions in the oxidation of 2,2-dimethylpropane-1,3-diol to the hydroxy acid, because the selectivity of **21** was very high, 93%, in the oxidation of **4a** to **21**.

In the Pt, Bi/C catalyzed air oxidation of 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**) the intermediate 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**) oxidized further to ethane-1,1,1-tricarboxylic acid (**25**) which decarboxylated giving methylmalonic acid (**27**) as the final product (Entry 7, Scheme 25).



Scheme 25. Pt, Bi/C catalyzed air oxidation of 2-hydroxymethyl-2-methylpropane-1,3-diol.

2-Hydroxymethyl-2-methylmalonic acid (**26**) was not obtained, although it should be quite stable toward the decarboxylation under the mild reaction conditions used, because even dimethyl-malonic acid did not suffer any significant decarboxylation in the similar oxidation of 2,2-dimethylpropane-1,3-diol (Figure 17). Thus the oxidation of **2b** indicates that the Pt, Bi/C catalyzed air oxidations of 2-substituted 2-hydroxymethylpropane-1,3-diols are not suitable for the preparation of the corresponding dicarboxylic acids.

The activity of promoted catalysts in the air oxidation of linear primary diols to dicarboxylic acids was studied by the oxidation of pentane-1,5-diol (**22**, Scheme 24 in Chapter 3.3) with air catalyzed by Pt, Bi/C, prepared by the method B, (Figure 18).

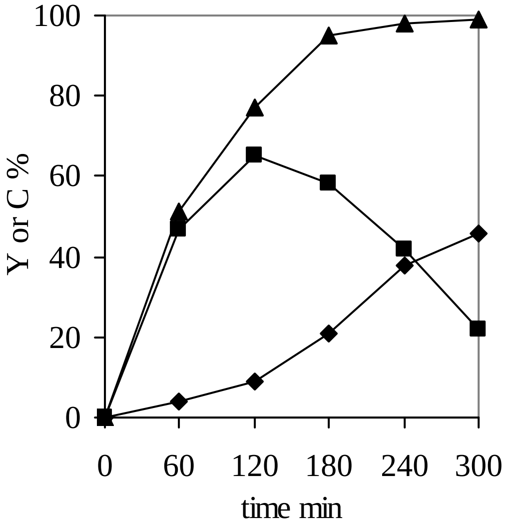


Figure 18. The catalyst was a self-made 5% Pt, 5% Bi/C (method B). ▲ = **22** C, ■ = **23** Y, ♦ = **24** Y.

The rate of the Pt, Bi/C catalyzed oxidation of pentane-1,5-diol was much lower compared to the rate of the oxidation of 2,2-dimethylpropane-1,3-diol (Figure 17). The conversion of **22** in a 60 minutes’ oxidation was only 51%, while the conversion of **2a** in a 60 minutes’ oxidation was 78%. The long carbon chain of pentane-1,5-diol is obviously the reason for its low rate of oxidation in the same way as in its Pt/C catalyzed oxidation (Figure 15).[80]

The air oxidation of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol catalyzed by Pt, Bi/C indicates that the promotion of Pt/C with bismuth affords an effective catalyst for the preparation of 2,2-dialkylmalonic acids and linear dicarboxylic acids. This method can also be industrially valuable especially in the preparation of 2,2-dialkylmalonic acids.[25b]

3.4.1 Mechanism and steric conditions of the promoted oxidation of 2,2-disubstituted propane-1,3-diols and linear primary diols

In the literature many interpretations of the role of promoters in noble metal catalysts are proposed.[41] The well-known ensemble effect is also the most relevant of them in the oxidation of primary diols to diacids.[49] Bismuth is thought to decrease the size of the active site ensembles thus preventing the adsorption of the long chain poisoning species formed by polymerization. However, the diols and the hydroxy acids can still be adsorbed on the smaller active site ensembles. In addition, the hydroxy and the carboxy groups of the hydroxy acids may form a complex with bismuth atoms in Pt, Bi/C, which leads to the loss of the two hydrogen atoms of the primary hydroxy group (Figure 19).[51] The formation of this complex can in part enhance the rate of the oxidation of the hydroxy acids to the diacids. The enhanced reaction rate became also apparent from the oxidation of 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) to dimethylmalonic acid (**21**) (Table 8, Entry 6) compared to the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) to the hydroxy acid **4a** (Figure 13). In a 60 minutes' oxidation of **4a** dimethylmalonic acid was obtained in a 83% yield, while at the same time in the oxidation of **2a** the hydroxy acid was obtained only in a 42% yield. In addition, Figure 19 indicates that the optimal loading of bismuth in Pt, Bi/C would be higher in the oxidation of linear primary diols than in the oxidation of 2,2-disubstituted propane-1,3-diols.

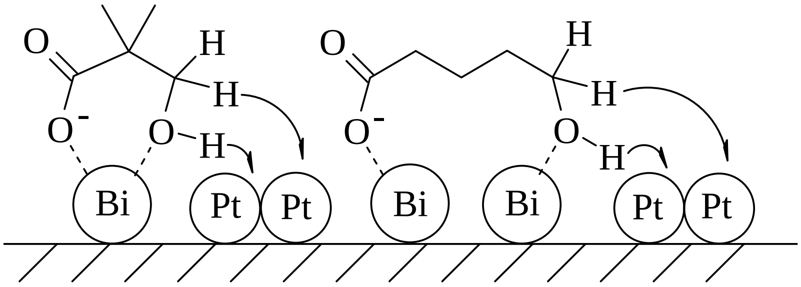


Figure 19. The formation of a complex of the hydroxy and the carboxy groups of 3-hydroxy-2,2-dimethylpropanoic acid and 5-hydroxypentanoic acid with bismuth atoms in Pt, Bi/C.

A further insight into the nature of the promoted oxidation of primary diols can be obtained from the structures of both unpromoted and promoted catalysts. Scanning electron microscopy (SEM) investigation shows platinum crystallites and agglomerated crystallites of various size and shape on activated carbon for the commercial 5% Pt/C (Figure 20).

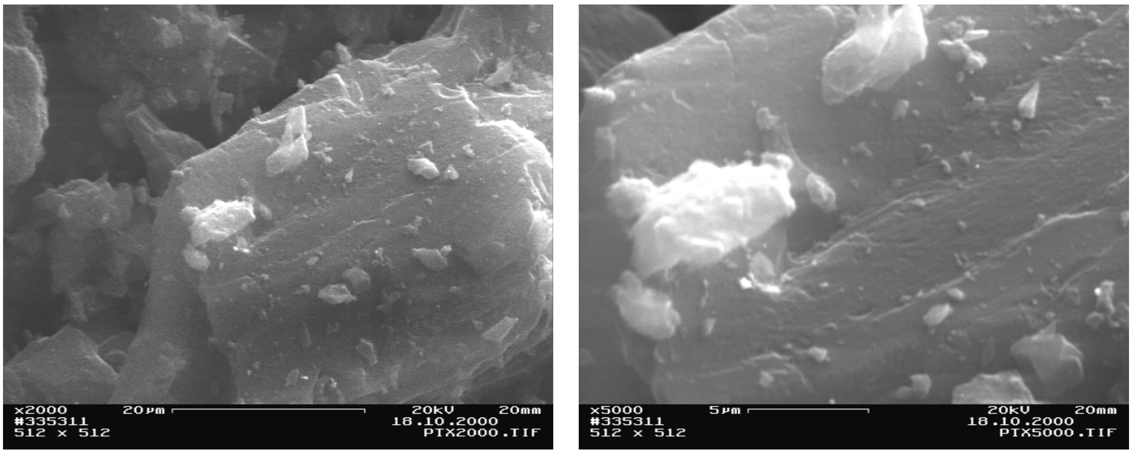


Figure 20. SEM micrographs of the commercial 5% Pt/C.

Because in structure insensitive reactions the dispersion of the noble metal does not affect much the reaction rates, calculated per a unit area of the active sites,[87] the structure of the commercial Pt/C with many different kinds of platinum crystallites is suitable also for the oxidation of primary diols to hydroxy acids.

Mallat *et al.* and Anderson *et al.* proposed that an ideal surface geometry for the promoter element is a submonolayer or especially isolated single atoms on the surface of the noble metal.[88] This kind of structure was also possible to obtain for the self-made Pt, Bi/C (method B) by slow adding of the promoter metal salt solutions and the reducing agent into the catalyst slurry (Chapter 3.4.2). The SEM micrographs show quite the similar crystallite structures for the self-made 5% Pt, 5% Bi/C (Figure 21) as the crystallites in Figure 20 for the commercial Pt/C, even though the exact surface geometry of bismuth at atomic level could not be verified by the SEM investigations.

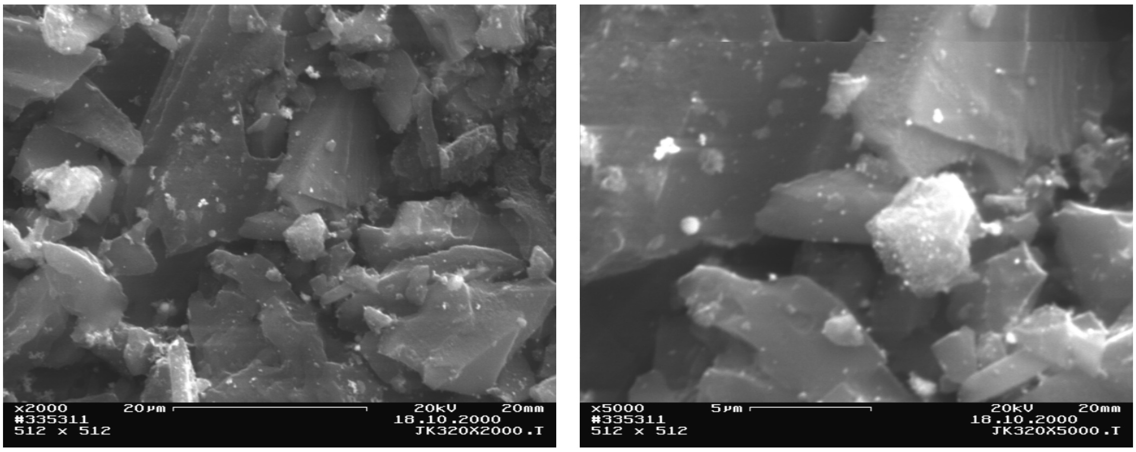


Figure 21. SEM micrographs of the self-made 5% Pt, 5% Bi/C (method B).

But because the yields and the selectivities of the diacids were quite high in the Pt, Bi/C catalyzed oxidation of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol, it is obvious that a sufficient part of bismuth is also in quite small crystallites on the surface of platinum in the self-made Pt, Bi/C.

3.4.2 Experimental

Materials. 3-Hydroxy-2,2-dimethylpropanoic acid and dimethylmalonic acid were obtained from Neste Chemicals. Hydrogen hexachloroplatinate(IV) hydrate and 10% Pt/C were purchased from Aldrich, bismuth(III) chloride from Hopkin & Williams, ≥36.5% formaldehyde from Riedel-de Haën, and bismuth(III) oxide from Merck. The other chemicals used are described in Chapters 3.1.1 and 3.3.1. All the chemicals were used as obtained from the supplier.

Preparation of the catalysts.

Method A: For the preparation of 5% Pd, 5% Bi/C palladium(II) acetate (0.063 g, 0.28 mmol) and bismuth(III) chloride (0.084 g, 0.26 mmol) dissolved in 5 mL of 6 M HCl were added dropwise into a suspension of activated carbon (1.000 g) in 20 mL of water in an hour. After mixing the slurry and adjusting its pH to 12 with 50% NaOH in 30 minutes ≥36.5% formaldehyde (5.654 g, 68.8 mmol) was added dropwise into the slurry in 30 minutes at the same time maintaining its pH at 12 with 50% NaOH. The catalyst was filtered, washed until neutral with water, and dried *in vacuo*. The yield of 5% Pd, 5% Bi/C was 1.110 g (100%). 5% Pt, 5% Bi/C and 5% Au, 5% Bi/C were prepared similarly in 1.107 g (100%) and 1.119 g (100%) yields, respectively.

Method B: For the preparation of 5% Pt, 5% Bi/C hydrogen hexachloroplatinate(IV) hydrate (2.190 g, 4.23 mmol) dissolved in 30 mL of water and bismuth(III) chloride (1.260 g, 4.00 mmol) dissolved in 60 mL of 5 M HCl were added dropwise into a suspension of activated carbon (15.000 g) in 300 mL of water in 30 minutes. After mixing the slurry and adjusting its pH to 12 with 30% NaOH in an hour ≥36.5% formaldehyde (36.270 g, 0.44 mol) was added dropwise into the slurry in 30 minutes at the same time maintaining its pH at 12 with 30% NaOH. The catalyst was filtered, washed until neutral with water, and dried *in vacuo*. The yield of 5% Pt, 5% Bi/C was 16.334 g (100%).

Characterization of the catalysts. The characteristics of activated carbon are described in Chapter 3.3.1. The exact metal composition of Pt, Bi/C (method B) was 5.0% Pt, 5.3% Bi/C measured using radioisotope X-ray fluorescence (XRF). The X-ray spectra were collected by Canberra Ultra-LEGe detector (GUL0035P) in a set-up where ^{109}Cd was used as an excitation source. The X-ray spectra, Pt $L_{\alpha1}$(9.434 keV) and Bi $L_{\alpha1}$(10.828 keV), were analyzed using Canberra Packard's WinAxil program. The sample measurements were compared to external standard series made from identical activated carbon and metal chemicals in order to avoid uncontrolled attenuation of X-rays. The morphological investigations of Pt, Bi/C (method B) were performed as described for the commercial Pt/C in Chapter 3.3.1.

Analyses of the reaction mixtures and the isolated methylmalonic acid.

The reaction mixtures of the oxidations of 2,2-dimethylpropane-1,3-diol and pentane-1,5-diol were analyzed by HPLC and GC as described in Chapter 3.3.1.

The reaction mixture of the oxidation of 2-hydroxymethyl-2-methylpropane-1,3-diol was analyzed by ^{1}H NMR, ^{13}C NMR, and MS as described in Chapter 3.1.1.

Oxidation procedure. The general oxidation procedure is described in Chapter 3.3.1.

Methylmalonic acid (27). 2-Hydroxymethyl-2-methylpropane-1,3-diol (**2b**) was oxidized according to the general oxidation procedure except that the triol (1.000 g, 8.3 mmol) was dissolved in 20 mL of water, and argon and air were bubbled 800 mL min^{-1} through the reaction mixture. After adjusting pH to 12 with 50% NaOH the product was isolated by passing the reaction mixture through a Dowex 2X8 ion exchange column. The column was eluted with 1 M HCl, and the eluate was evaporated. **27** (0.502 g, 4.3 mmol, 51%) was obtained as white crystals. mp 127ºC (ethyl acetate), (lit.[89] 131-132ºC). ^{1}H NMR, ^{13}C NMR, and MS spectra were in agreement with those in the literature.[90]

3.5 Effect of supports on the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed Pt, Bi/C

The effect of various supports on the air oxidation of 2,2-dialkylpropane-1,3-diols was studied by the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**, Scheme 23 in Chapter 3.3) catalyzed by platinum promoted with bismuth and supported on activated carbon, alumina (Al_2O_3), titanium dioxide (TiO_2), titanium silicalite (TS-1), and barium sulfate ($BaSO_4$) (Figure 22). In these oxidations the conversions of 2,2-dimethylpropane-1,3-diol (**2a**) indicate that the rates of the consumption of **2a** follow the first-order rate law

$$\ln([\mathbf{2a}]/[\mathbf{2a}]0) = -kt, \qquad \text{Equation 1}$$

in which [**2a**]0 is the initial concentration of **2a**, k is the rate constant for the consumption of **2a**, and t is the reaction time in seconds. Thus according to Equation 1 straight lines are obtained when ln([**2a**]/[**2a**]0) is plotted as a function of the time (Figure 23).

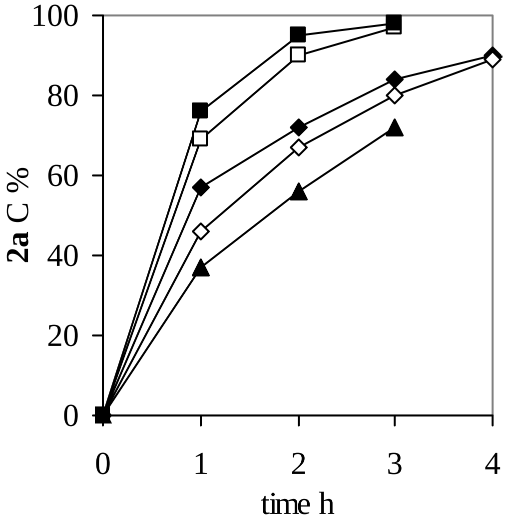


Figure 22. ■ = activated carbon, □ = $BaSO_4$, ♦ = Al_2O_3, ◊ = TiO_2, ▲ = TS-1.

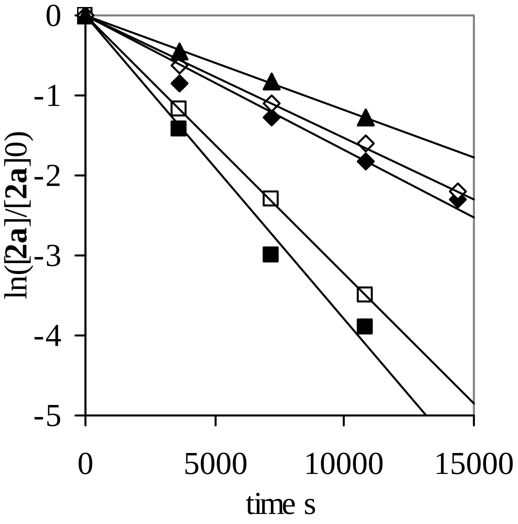


Figure 23. ■ = activated carbon, □ = $BaSO_4$, ♦ = Al_2O_3, ◊ = TiO_2, ▲ = TS-1.

According to Scheme 23 2,2-dimethylpropane-1,3-diol is oxidized to 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) and dimethylmalonic acid (**21**). The yields of these acids in air oxidations catalyzed by the various supported Pt, Bi/C are presented in Figures 24 and 25. For the interpretation of the results in Figures 22-25 some characteristics of the supports affecting the oxidation of **2a** are summarized in Table 9. In Figure 23 the slope of the straight lines is the opposite number of the rate constant k for the consumption of **2a** (Equation 1).

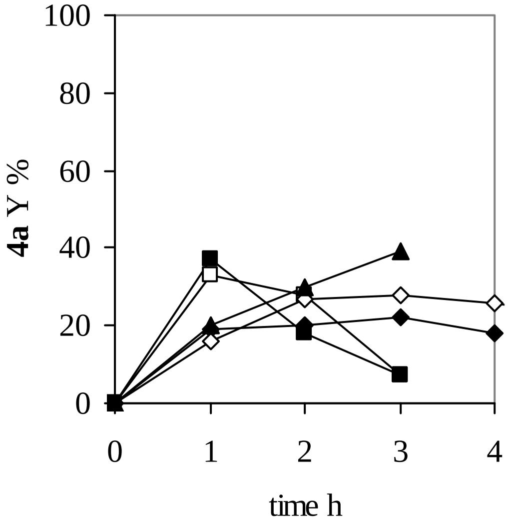


Figure 24. ■ = activated carbon, □ = $BaSO_4$, ♦ = Al_2O_3, ◊ = TiO_2, ▲ = TS-1.

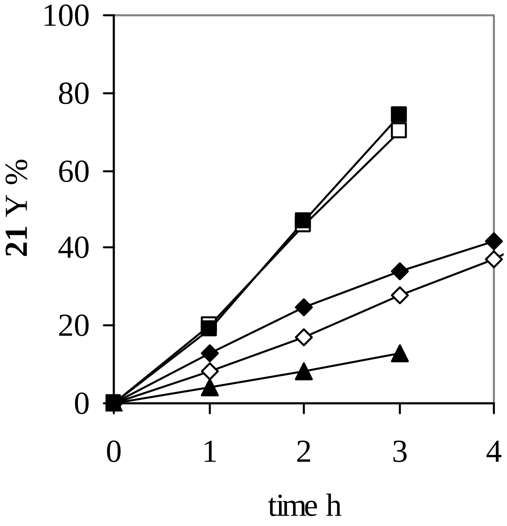


Figure 25. ■ = activated carbon, □ = $BaSO_4$, ♦ = Al_2O_3, ◊ = TiO_2, ▲ = TS-1.

The results of the oxidations of 2,2-dimethylpropane-1,3-diol show that the favorable characteristics of activated carbon for a catalyst support enable in part the high rate of the oxidation, the moderate yield of dimethylmalonic acid, and the high 83% combined selectivity of 3-hydroxy-2,2-dimethylpropanoic acid and dimethyl-malonic acid. Because the isoelectric point of activated carbon lies at an acidic pH, the carboxylate anions of the products do not adsorb too strongly to the surface of the support. However, at a multiple use of the same catalyst the weak metal-support interaction may cause the agglomeration of the metals into large entities, and the decrease of the activity of the catalyst.

Table 9. Characteristics of the supports in the air oxidations of 2,2-dimethylpropane-1,3-diol catalyzed by Pt, Bi/support.

Support	k,[a] 10^{-4} 1/s	Surface area,[b] m^2/g	Pore diameter,[b] nm	pI,[b] pH	Metal-support interaction[b]	Notes
Activated carbon	3.80	300-1500	porous	acidic	WMSI	charcoal[c]
Barium sulfate	3.23		probably non-porous			
Alumina	1.68	0.1-5	non-porous	9.5	WMSI	α-alumina
Titanium dioxide	1.53	40-200	15-50	5.9	SMSI	anatase
Titanium silicalite	1.18		micro-porous		MMSI	MFI[d]

[a] See Figure 23 and Equation 1.

[b] Reference 46. pI = isoelectric point. For the metal-support interaction, see Chapter 1.4.

[c] For the other characteristics, see Experimental.

[d] For the zeolite framework type, see Reference 47 and Chapter 1.4.

In the Pt, Bi/$BaSO_4$ catalyzed oxidation of **2a** the rate of the oxidation and the yields of the products were almost as high as in the Pt, Bi/C catalyzed oxidation of **2a**, even though barium sulfate is probably non-porous, and its surface area is not as high as the surface area of activated carbon. Because the combined selectivity of the products was also high, 79%, barium sulfate may offer an alternative to activated carbon as a catalyst support in some oxidations of 2,2-dialkylpropane-1,3-diols or other primary diols to the corresponding dicarboxylic acids. In oxidations performed in organic solvents barium sulfate may be a non-flammable alternative for a catalyst support.

Although the characteristics of alumina and titanium dioxide are quite different, the rates of the oxidation and the yields of the products in the Pt, Bi/Al_2O_3 and Pt, Bi/TiO_2 catalyzed oxidations of **2a** were almost the same.

Because the isoelectric point of α-alumina is at pH of 9.5, it may adsorb the carboxylate anions of the products more than titanium dioxide. The combined selectivities of the products for alumina and titanium dioxide were also at the same level, 67% and 70%, respectively.

The rate of the oxidation and the yields of the products in the Pt, Bi/TS-1 catalyzed oxidation of **2a** were the lowest of the catalysts studied. However, the combined selectivity of the products in the Pt, Bi/TS-1 catalyzed oxidation was slightly higher, 72%, than the selectivities in the Pt, Bi/Al_2O_3 and Pt, Bi/TiO_2 catalyzed oxidations.

The air oxidations of 2,2-dimethylpropane-1,3-diol show that, of the catalyst supports studied, platinum promoted with bismuth and supported on activated carbon is the most efficient catalyst in the air oxidation of 2,2-dialkylpropane-1,3-diols or other primary diols. In oxidations performed in organic solvents barium sulfate may also be a valuable alternative to activated carbon as a non-flammable support.

3.5.1 Experimental

Materials. Alumina was purchased from BDH, titanium dioxide from Kemira, and barium sulfate from J. T. Baker. The other chemicals used are described in Chapters 3.1.1, 3.3.1, and 3.4.2. All the chemicals were used as obtained from the supplier.

Preparation of the catalysts. For the preparation of 5% Pt, 5% Bi/C potassium tetrachloroplatinate(II) (0.121 g, 0.28 mmol) and bismuth(III) chloride (0.084 g, 0.26 mmol) dissolved in 5 mL of 6 M HCl were added dropwise into a suspension of activated carbon (1.000 g) in 20 mL of water in an hour. After mixing the slurry and adjusting its pH to 12 with 50% NaOH in 30 minutes ≥36.5% formaldehyde (5.654 g, 68.8 mmol) was added dropwise into the slurry in 30 minutes at the same time maintaining its pH at 12 with 50% NaOH. The catalyst was filtered, washed until neutral with water, and dried *in vacuo*. The yield of 5% Pt, 5% Bi/C was 1.107 g (100%). 5% Pt, 5% Bi/$BaSO_4$, 5% Pt, 5% Bi/Al_2O_3, 5% Pt, 5% Bi/TiO_2, and 5% Pt, 5% Bi/TS-1 were prepared similarly in 1.107 g (100%), 1.114 g (100%), 1.109 g (100%), 1.100 g (99%), and 1.115 g (100%) yields, respectively.

Characteristics of the catalysts. The characteristics of activated carbon are described in Chapter 3.3.1. The form of alumina was α-alumina, and the crystal form of titanium dioxide was anatase.

Analyses of the reaction mixtures. The reaction mixtures of the oxidation of 2,2-dimethylpropane-1,3-diol were analyzed by HPLC and GC as described in Chapter 3.3.1.

Oxidation procedure. The general oxidation procedure is described in Chapter 3.3.1.

3.6 Effect of promoters on the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed by Pt, Bi/C

The effect of various promoters on the air oxidation of 2,2-dialkylpropane-1,3-diols was studied by the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) catalyzed by platinum supported on activated carbon and promoted with bismuth, lead, thallium, tellurium, antimony, tin, and selenium (Figure 26).

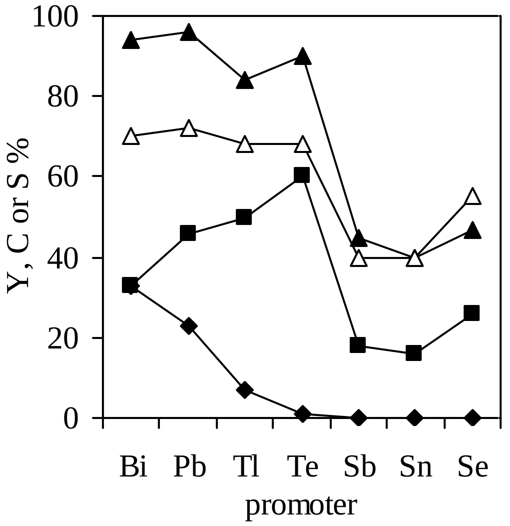


Figure 26. Self-made Pt, promoter/C catalyst, reaction time 2 h. ▲ = **2a** C, ■ = **4a** Y, ♦ = **21** Y, Δ = (**4a** + **21**) S.

In the catalysts the theoretical molar ratios of Pt/promoters were 1:1, because in the study of Kimura *et al.* it was found that the optimum loading of the promoters in weight percents was usually directly proportional to the atomic weight of the promoter element.[48] Figure 26 indicates that the Pt, Bi/C catalyzed oxidation of **2a** afforded the highest yield of dimethyl-malonic acid (**21**), while the Pt, Te/C catalyzed oxidation afforded the highest yield of 3-hydroxy-2,2-dimethylpropanoic acid (**4a**). The highest combined selectivities of **4a** and **21** were obtained by the heaviest promoters. Compared to the self-made Pt/C catalyzed oxidation of **2a** in Chapter 3.3 (Figure 11) the promotion of Pt/C with tellurium did not enhance remarkably the conversion of **2a** and the yield and the selectivity of **4a**. Antimony, tin, and selenium had even an inhibiting effect on the oxidation of **2a**. In addition, the results presented in Figure 26 are similar to the comparative studies of promoters concerning the oxidation of primary alcohols reported in the literature.[48,91] When Kimura *et al.* oxidized a special primary alcohol (Emulgen 108) with oxygen catalyzed by 2% Pd/C promoted with bismuth, lead, and tin each at a 2% loading, they found that the highest yield of the carboxylic acid product was obtained in the Pd, Bi/C catalyzed oxidation.[48]

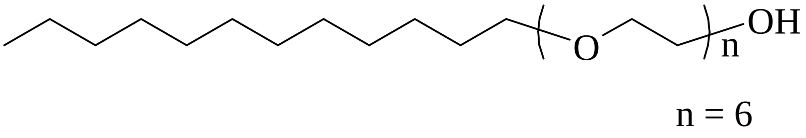


Figure 27. 2-[2-(2-{2-[2-(2-Dodecyloxyethoxy)ethoxy]ethoxy}ethoxy)-ethoxy]ethanol (Emulgen 108).

The Pt, Bi/C catalyzed oxidation afforded also the highest selectivity of 2-keto-gluconic acid in the oxidation of fructose with oxygen in a series of experiments in which the promoting effect of bismuth, lead, antimony, and tin were compared.[85]

The air oxidation of 2,2-dimethylpropane-1,3-diol shows that the highest yields of dicarboxylic acids in the air oxidation of 2,2-dialkylpropane-1,3-diols can be obtained by Pt, Bi/C as a catalyst. The promotion of Pt/C did not bring any remarkable advantage to the air oxidation of 2,2-dimethylpropane-1,3-diol to the corresponding hydroxy acid.

3.6.1 Experimental

Materials. Tin(II) chloride dihydrate, selenium(IV) chloride, antimony(III) chloride, and tellurium(I) chloride were purchased from Merck, lead(II) nitrate from J. T. Baker, and thallium(I) carbonate from Riedel-de Haën. The other chemicals used are described in Chapters 3.1.1, 3.3.1, and 3.4.2. All the chemicals were used as obtained from the supplier.

Preparation of the catalysts. For the preparation of 5% Pt, 5% Bi/C potassium tetrachloroplatinate(II) (0.020 g, 0.05 mmol) and bismuth(III) chloride (0.015 g, 0.05 mmol) dissolved in 0.5 mL of water and 6 M HCl was added dropwise into a suspension of activated carbon (0.168 g) in 2 mL of water. Sodium borohydride (0.005 g, 0.05 mmol) dissolved in 0.5 mL of water was added dropwise into the mixed slurry. The catalyst was filtered, washed until neutral with water, and used as a wet powder. 5% Pt, 2% Se/C was prepared similarly except that the platinum and the selenium salts were dissolved in 0.5 mL of water. 5% Pt, 3% Te/C, 5% Pt, 3% Sn/C, and 5% Pt, 3% Sb/C were also prepared similarly except that the platinum and the promoter salts were dissolved in 0.5 mL of 6 M HCl. In addition, 5% Pt, 5% Tl/C and 5% Pt, 5% Pb/C were prepared similarly except that potassium tetrachloroplatinate(II) dissolved in 0.25 mL of water and thallium(I) carbonate and lead(II) nitrate dissolved in 0.25 mL of water were added separately into the suspension of activated carbon in water to avoid the precipitation of thallium(I) chloride and lead(II) chloride.

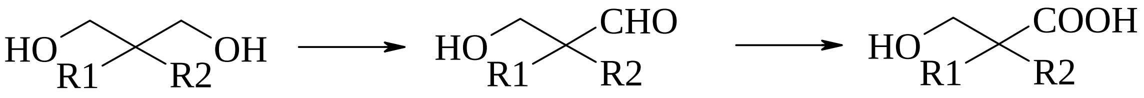
Characteristics of the catalysts. The characteristics of activated carbon are described in Chapter 3.3.1. The theoretical molar ratios of Pt/promoters/2,2-dimethylpropane-1,3-diol of the catalysts and the reactant in the oxidations were 0.01/0.01/1.

Analyses of the reaction mixtures. The reaction mixtures of the oxidation of 2,2-dimethyl-propane-1,3-diol were analyzed by HPLC and GC as described in Chapter 3.3.1.

Oxidation procedure. The general oxidation procedure is described in Chapter 3.3.1.

3.7 Kinetics of the air oxidation of 2,2-disubstituted propane-1,3-diols catalyzed by noble metals supported on activated carbon

To obtain useful kinetic data of the oxidation of 2,2-disubstituted propane-1,3-diols the kinetic experiments were performed in a non-steady state batch reactor operated at an integral mode.[92] The air oxidation of primary alcohols to carboxylic acids catalyzed by supported noble metals is assumed to be a consecutive irreversible two-stage reaction.[53] As a preliminary comparative experiment 2,2-dimethylpropane-1,3-diol (**2a**), 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**), 2-ethyl-2-hydroxymethylpropane-1,3-diol (**2c**), and 2,2-bis-(hydroxymethyl)propane-1,3-diol (**2d**) were oxidized with air catalyzed by a commercial 5% Pt/C (Scheme 26 and Figures 28 and 29).

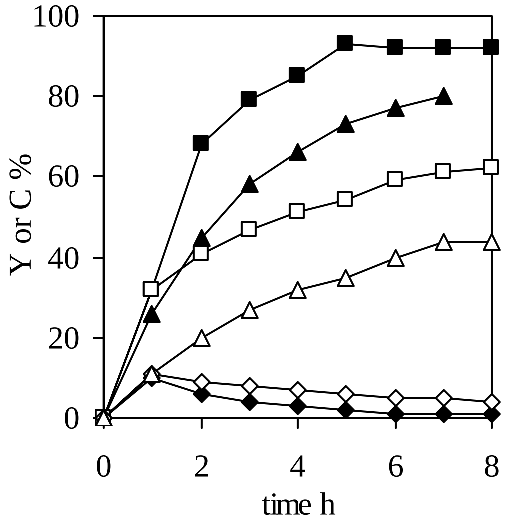


2 **3** **4**

(**2-4**)**a** R1 = R2 = CH_3
(**2-4**)**b** R1 = CH_3, R2 = CH_2OH
(**2-4**)**c** R1 = CH_2CH_3, R2 = CH_2OH
(**2-4**)**d** R1 = R2 = CH_2OH

Scheme 26. Oxidation of 2,2-disubstituted propane-1,3-diols.

The highest conversion was obtained in the oxidation of 2,2-dimethylpropane-1,3-diol possibly due to the small methyl R1 and R2 substituents. In addition, the highest yield of the hydroxy acid was also obtained in the oxidation of **2a**. The conversions of the reactants and the yields of the hydroxy acids show that the inhibiting effect of the substituents R1 and R2 on the rate of the reaction increases in the order CH_3, CH_3 < CH_3, CH_2OH < CH_2OH, CH_2OH < CH_2CH_3, CH_2OH.



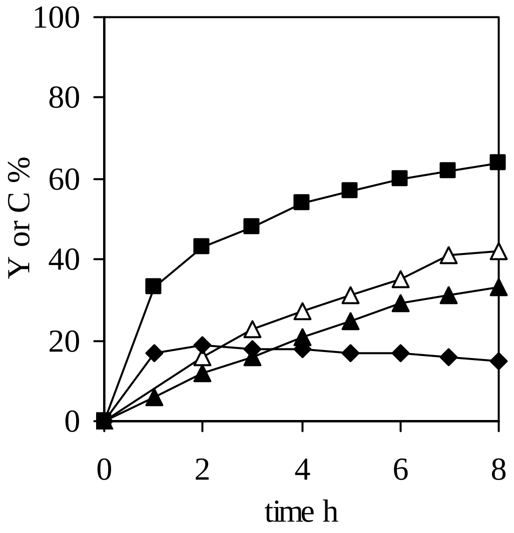


Figure 28. Commercial 5% Pt/C catalyst, reaction temperature 20ºC. pH of the reaction mixture was kept at 8. ■ = **2a** C, ♦ = **3a** Y, ▲ = **4a** Y, □ = **2b** C, ◊ = **3b** Y, Δ = **4b** Y.

Figure 29. Commercial 5% Pt/C catalyst, reaction temperature 20ºC. pH of the reaction mixture was kept at 8. ■ = **2c** C, ♦ = **3c** Y, ▲ = **4c** Y, Δ = **4d** Y. **2d** and **3d** could not be analyzed.

In a 7 or 8 hours' oxidation the selectivities of 3-hydroxy-2,2-dimethylpropanoic acid (**4a**), 3-hydroxy-2-hydroxymethyl-2-methylpropanoic acid (**4b**), and 2,2-bis-(hydroxymethyl)butanoic acid (**4c**) were 86%, 71%, and 52%, respectively, which indicates also the different effects of the substituents R1 and R2 on the rate of the main reaction. The low selectivity of the hydroxy acids is probably caused of the retrograde aldol reaction of the intermediate hydroxyaldehydes (Chapter 3.3 and Scheme 2 in Chapter 1). In fact, the highest yield of the hydroxyaldehyde was obtained in the oxidation of 2-ethyl-2-hydroxymethylpropane-1,3-diol. This oxidation gave also the lowest selectivity of the hydroxy acid. Despite the molar ratio of Pt/**2** was quite high, 0.02, the considerably retarding rate of the reactions is an indication of the deactivation of the catalyst. After an eight hours' oxidation the consumption of all the alcohols **2** and the production of all the hydroxy acids **4** were almost stopped. Because the air flow rate through the reaction mixtures of the oxidations of the alcohols **2** was quite high, 800 mL min^{-1}, the over-oxidation of the active surface sites of platinum was probably one reason for the deactivation of catalyst. In addition, the catalyst may have also been deactivated in part by the adsorption of long chain poisoning species formed by polymerization (Chapter 3.4.1).[49]

To study the effect of the air flow rate through the reaction mixtures in the oxidations of alcohols **2** 2-hydroxymethyl-2-methylpropane-1,3-diol (**2b**) was oxidized with various air flow rates catalyzed by a commercial 5% Pd/C (Figure 30). In addition, to enhance further the rate of the oxidation of **2b** compared to the Pt/C catalyzed oxidations of **2**(**a-d**) the reaction temperature was raised to 40ºC, and pH of the reaction mixture was kept at 10. On the other hand the molar ratio of Pd/**2b** was only 0.01.

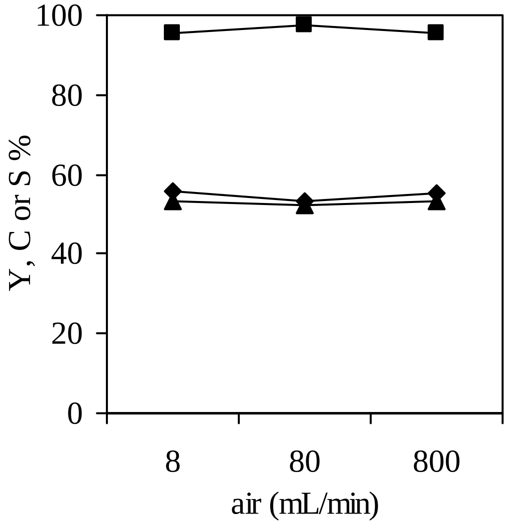
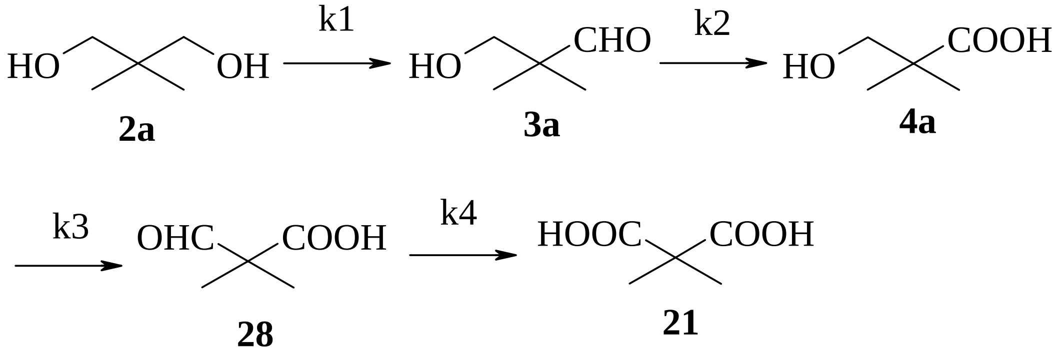


Figure 30. Commercial 5% Pd/C catalyst, reaction time 3 h. ■ = **2b** C, ▲ = **4b** Y, ♦ = **4b** S.

Figure 30 indicates that even with an air flow rate of 8 mL min^{-1} the adsorption of oxygen on the surface of palladium was not a limiting factor on the rate of the reaction, because the conversion of **2b** and the yield and the selectivity of **4b** were almost the same with all the air flow rates studied. At the reaction temperature of 40ºC and at pH 10 of the reaction mixture the consumption of **2b** did not stop even though palladium is known to have a lower stability toward an oxygen poisoning compared to platinum.[79] A more optimum rate for the air input during the oxidations of the alcohols **2** can be obtained by controlling the oxidation state of the active metals of the catalysts by measuring the potential of the metals according to the Nernst equation.[79,93]

The kinetics of the oxidation of 2,2-dialkylpropane-1,3-diols to diacids was studied by the oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) with air catalyzed by a self-made 5% Pt, 5% Bi/C (Scheme 27).



Scheme 27. Oxidation of 2,2-dimethylpropane-1,3-diol.

The oxidation of **2a** catalyzed by various amounts of the catalyst is presented in Figures 31 and 32. The reaction temperature and pH of the reaction mixtures were the same as in the Pd/C catalyzed oxidation of **2b** (Figure 30). The air flow rate was decreased to 200 mL min^{-1} in order to decrease the over-oxidation of the catalyst.

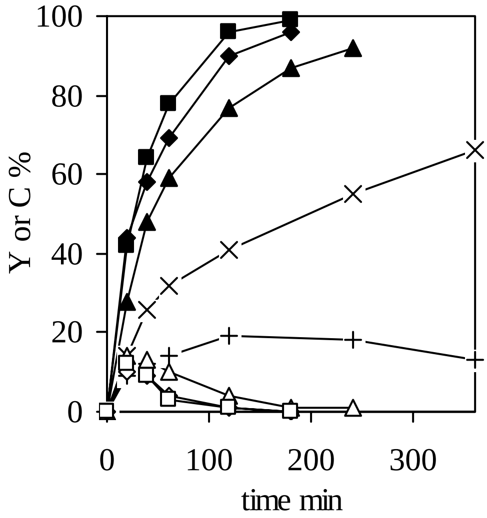


Figure 31. Self-made Pt, Bi/C catalyst. The molar ratios of Pt/(**2-3**)**a** were for **2a** C: ■ = 0.0100, ♦ = 0.0050, ▲ = 0.0025, x = 0.0010, and for **3a** Y: □ = 0.0100, ◊ = 0.0050, Δ = 0.0025, + = 0.0010.

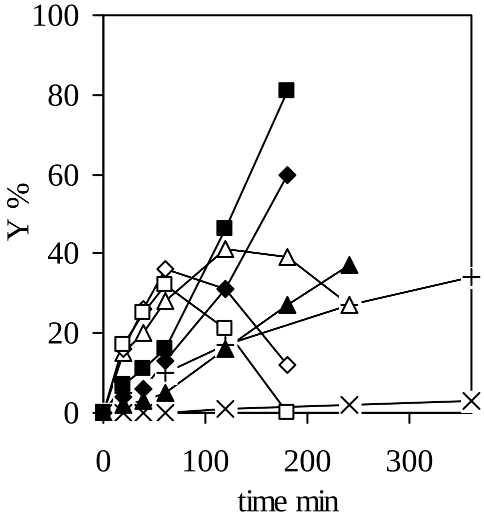


Figure 32. Self-made Pt, Bi/C catalyst. The molar ratios of Pt/(**2-3**)**a** were for **4a** Y: □ = 0.0100, ◊ = 0.0050, Δ = 0.0025, + = 0.0010, and for **21** Y: ■ = 0.0100, ♦ = 0.0050, ▲ = 0.0025, x = 0.0010.

The conversions of 2,2-dimethylpropane-1,3-diol (**2a**) indicate that the rates of the consumption of **2a** follow the first-order rate law

$$\ln([\mathbf{2a}]/[\mathbf{2a}]0) = -(k1)t, \qquad \text{Equation 2}$$

in which [**2a**]0 is the initial concentration of **2a**, k1 is the rate constant for the consumption of **2a**, and t is the reaction time in seconds. Thus according to Equation 2 straight lines are obtained, when ln([**2a**]/[**2a**]0) is plotted as a function of the time (Figure 33).

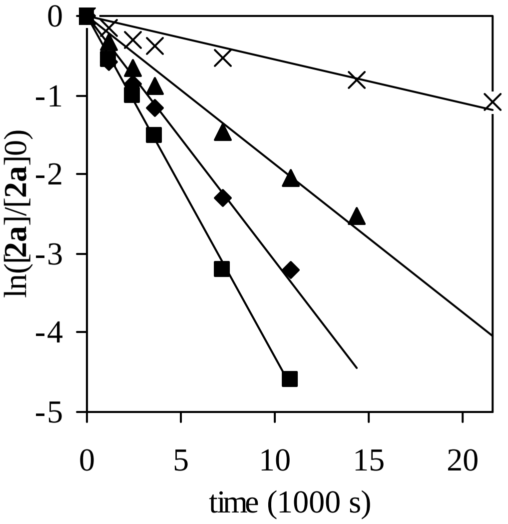


Figure 33. The molar ratios of Pt/**2a** were ■ = 0.0100, ♦ = 0.0050, ▲ = 0.0025, x = 0.0010.

In Figure 33 the slope of the straight lines is the opposite number of the rate constant k1 for the consumption of **2a** (Table 10).

Table 10. Rate constants for the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed by various amounts of Pt, Bi/C.[a]

Molar ratio of Pt/**2a**	k1, 10^{-4} 1/s	P^2
0.0100	4.32	0.9988
0.0050	3.09	0.9883
0.0025	1.87	0.9717
0.0010	0.55	0.8299

[a] P^2 is the square of the Pearson product moment correlation coefficient.

Figures 31 and 32 and the rate constants k1 show that the oxidation of **2a** operated mainly in the regime of mass or heat transfer at the highest molar ratio of Pt/**2a** while the kinetic regime was dominant at the low molar ratios of Pt/**2a**. The low squares of the correlation coefficients P^2 of the rate constant k1 at the low molar ratios of Pt/**2a** indicate that the catalyst was probably in part deactivated at the end of the oxidation. The main reason for the linear relationships between the amount of the catalyst and the rates of the oxidation of alcohols reported in the literature is the much smaller amount of the catalyst compared to the air oxidations of **2a** catalyzed by Pt, Bi/C.[55,56]

In the oxidation of 2,2-dimethylpropane-1,3-diol to dimethyl-malonic acid the intermediate 2-formyl-2-methylpropanoic acid (**28**) could not be analyzed due to its very high rate of oxidation to dimethylmalonic acid.[60] Thus the concentration of **28** was supposed to maintain constant and close to zero during the conversion of 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) to dimethylmalonic acid. Because the rate constant k4 is also assumed to be much higher than the rate constant k3, the kinetic reaction scheme of the oxidation of **2a** can be reduced according to the steady-state approximation to a consecutive three-stage reaction having three rate constants k1, k2, and k3.[94] In Figure 32 the straight portion in the curves of dimethylmalonic acid at the beginning of the oxidations of **2a** is an indication of the consecutive reaction scheme.[95]

The proportion of the mass transfer and the kinetic regimes in the oxidation of **2a** was quantitatively estimated in Figure 34 by plotting the reciprocal of the rate of the consumption of **2a** in the function of the reciprocal of the weight of the catalyst according to the equation

$$1/r = 1/k_{mt} + 1/(k_k w), \qquad \text{Equation 3}$$

in which r is the rate of the consumption of **2a**, k_{mt} is a mass transfer factor, k_k is a kinetic factor, and w is the weight of the catalyst.[96,97]

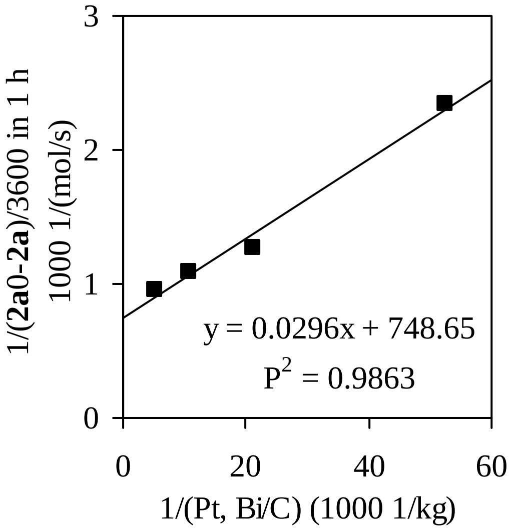


Figure 34. The molar ratios of Pt/**2a** were from left to right: 0.0100, 0.0050, 0.0025, and 0.0010.

In Figure 34 the slope of the straight line is the reciprocal of the kinetic factor k_k, while the intersection of the straight line and the y-axis is the reciprocal of the mass transfer factor k_{mt}. It is assumed that when the reciprocal of the weight of the catalyst is approaching zero at very high amounts of the catalyst the mass transfer regime is completely dominant. Thus according to Equation 3 the percentages of the mass transfer and the kinetic regimes are summarized in Table 11.

Table 11. The percentages of the mass transfer and the kinetic regimes in the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed by Pt, Bi/C.

Molar ratio of Pt/**2a**	mass transfer, %	kinetic, %
0.0100	78	22
0.0050	69	31
0.0025	59	41
0.0010	32	68

Table 11 shows that at the low amounts of the catalyst the yield of dimethylmalonic acid was probably decreased due to the deactivation of the catalyst by the over-oxidation. At the high amounts of the catalyst the density of oxygen was lower per a unit area of the catalyst surface compared to the unit area at the low amounts of the catalyst. Thus at the high amounts of the catalyst the limiting mass transfer of oxygen decreased the over-oxidation of the catalyst and favored the oxidation of 3-hydroxy-2,2-dimethylpropanoic acid to dimethylmalonic acid.

The effect of pH of the reaction mixture on the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed by Pt, Bi/C is presented in Figures 35 and 36.

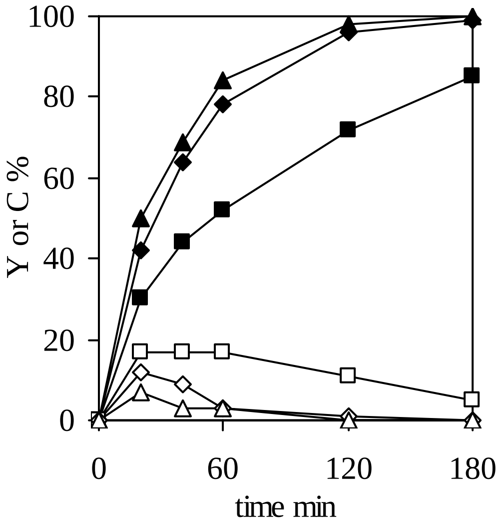


Figure 35. Self-made Pt, Bi/C catalyst. **2a** C: ■ = pH 8, ♦ = pH 10, ▲ = pH 12. **3a** Y: □ = pH 8, ◊ = pH 10, Δ = pH 12.

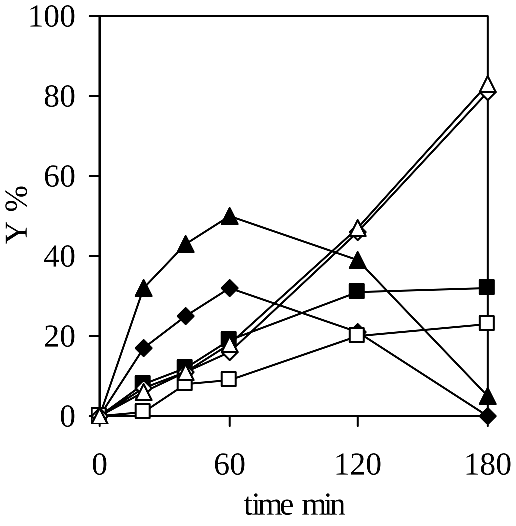


Figure 36. Self-made Pt, Bi/C catalyst. **4a** Y: ■ = pH 8, ♦ = pH 10, ▲ = pH 12. **21** Y: □ = pH 8, ◊ = pH 10, Δ = pH 12.

Figures 35 and 36 show that the conversion of **2a** and the yield of dimethylmalonic acid (**21**) increased, when pH of the reaction mixture was raised, while the difference of the conversion of **2a** and the yield of dimethylmalonic acid between pH 10 and 12 was yet small. In the literature the yield of the carboxylic acid products increased in the oxidation of glycerol[35] and L-sorbose[57], when pH was raised. The yield of dimethylmalonic acid increased also considerably, from about 20% to 80%, when pH was raised from 8 to 10 in the oxidation of **2a**.

The effect of the temperature on the air oxidation of 2,2-dimethylpropane-1,3-diol catalyzed by Pt, Bi/C is presented in Figures 37 and 38.

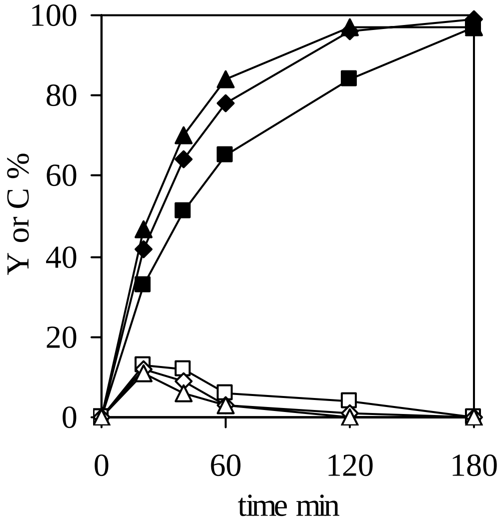


Figure 37. Self-made Pt, Bi/C catalyst. **2a** C: ■ = 20°C, ♦ = 40°C, ▲ = 60°C. **3a** Y: □ = 20°C, ◊ = 40°C, Δ = 60°C.

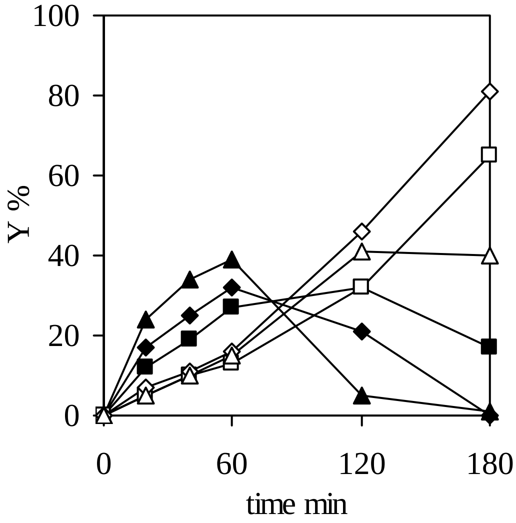


Figure 38. Self-made Pt, Bi/C catalyst. **4a** Y: ■ = 20°C, ♦ = 40°C, ▲ = 60°C. **21** Y: □ = 20°C, ◊ = 40°C, Δ = 60°C.

Figures 37 and 38 show that the conversion of **2a** increased, when the temperature of the reaction mixture was raised, while the difference of the conversion of **2a** between 40°C and 60°C was small. The yield of dimethylmalonic acid (**21**) increased, when the temperature was raised from 20°C to 40°C, while at 60°C the yield of **21** was only about 40% probably due to the decarboxylation of the diacid.[24]

The dependence of the rate constant k1 for the consumption of 2,2-dimethylpropane-1,3-diol (**2a**) on the temperature was studied by plotting ln([**2a**]/[**2a**]0) as a function of the time according to Equation 2 (Figure 39). In Figure 39 the slope of the straight lines is the opposite number of the rate constants k1 for the consumption of **2a** namely 0.000302 s^{-1}, 0.000432 s^{-1}, and 0.000493 s^{-1} at 20°C, 40°C, and 60°C, respectively. In Figure 40 ln(k1) is plotted as a function of the reciprocal of the temperature according to the Arrhenius equation

$$\ln(k1) = -E_a/RT + \ln A \qquad \text{Equation 4}$$

in which E_a is the apparent activation energy, R is the gas constant, and A is the pre-exponential factor.

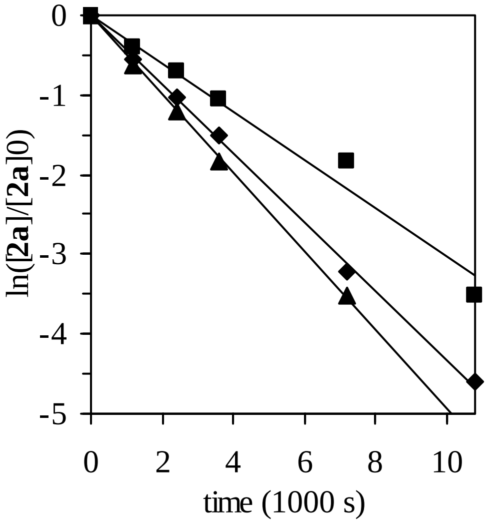


Figure 39. ■ = 20°C, ♦ = 40°C, ▲ = 60°C.

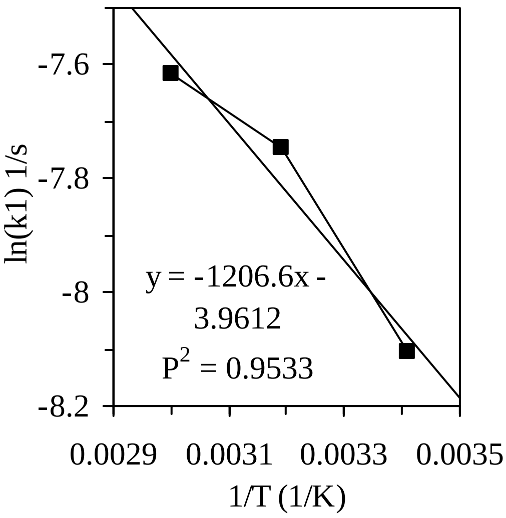


Figure 40. ■ = ln(k1) versus 1/T (Figure 39).

When e is raised to a power of -3.9612, a value of 0.019 s^{-1} is obtained for the pre-exponential factor A, and by substituting the value of the slope of the straight line in Figure 40 to Equation 4 a value of 10032 J mol^{-1} is obtained for the apparent activation energy E_a. The low value for E_a indicates that the oxidation of 2,2-dimethylpropane-1,3-diol with the used reaction conditions was operating in the regime of mass transfer.[98] The slight curving of the line connecting the squares in Figure 40 is probably caused of a decrease of the coverage of the active sites of the catalyst at high temperatures.[99]

The deactivation of the recycled catalyst in the air oxidation of 2,2-dimethylpropane-1,3-diol (**2a**) catalyzed by Pt, Bi/C is presented in Figure 41 (Entry 5 in Table 8 in Chapter 3.4). In Figure 42 the excess of the consumption of sodium hydroxide over the consumption of sodium hydroxide to 3-hydroxy-2,2-dimethylpropanoic acid (**4a**) and to dimethylmalonic acid (**21**) in the air oxidation of **2a** catalyzed by Pt, Bi/C is presented.

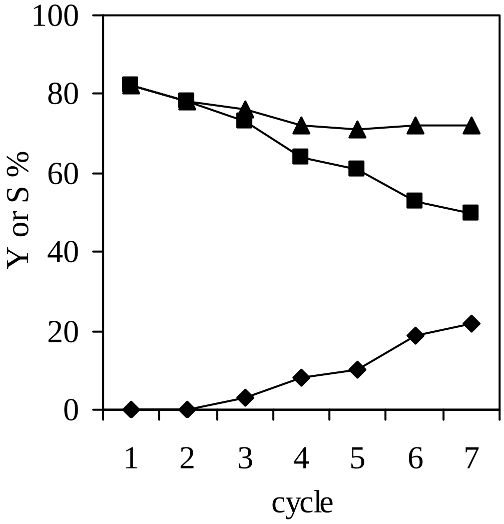


Figure 41. Self-made Pt, Bi/C catalyst, reaction time 3 h. ■ = **21** Y, ♦ = **4a** Y, ▲ = (**21** + **4a**) S.

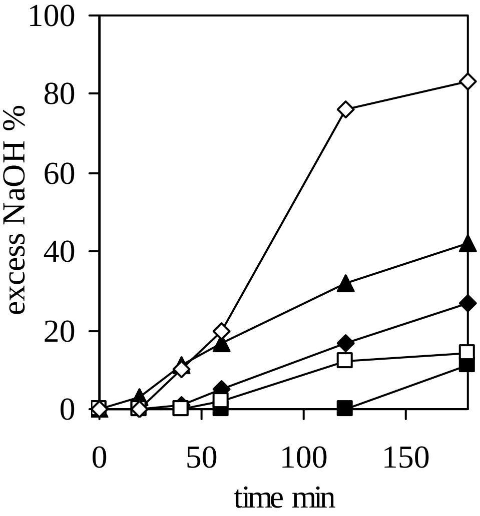


Figure 42. Self-made Pt, Bi/C catalyst. 40°C: ■ = pH 8, ♦ = pH 10, ▲ = pH 12. pH 10: □ = 20°C, ♦ = 40°C, ◊ = 60°C.

In Figure 41 the increasing yield of **4a** and the decreasing yield of **21** indicate probably of the dissolving of bismuth from the catalyst.[86] Because the combined selectivity of **4a** and **21** was still at a high level after the seven oxidations by the same catalyst, it is obvious that platinum remained quite active on the catalyst. If the catalyst was deactivated by the over-oxidation of the active sites of platinum, the activity of the catalyst can be recovered by interrupting the air flow or by bubbling argon through the reaction mixture (Table 11).[100,101] Some of the deactivating substances formed from the reactants or the reaction products can be removed by bubbling hydrogen through the reaction mixture (Chapter 3.4.1).[49,102]

In Figure 42 the excess of the consumption of sodium hydroxide indicates of the retrograde aldol reaction of the intermediate 2,2-dimethyl-3-hydroxypropanal (**3a**) (Chapter 3.3 and Scheme 2 in Chapter 1). 2-Methylpropanal and formaldehyde, which are the reaction products of the side reaction, can further be oxidized to 2-methylpropanoic acid and formic acid, which increase the consumption of sodium hydroxide. In the oxidation of **2a** at 60°C the very high excess of the consumption of the base was probably caused of the degradation of dimethylmalonic acid and the oxidation of the degradation products.

The kinetic studies of the air oxidation of 2,2-disubstituted propane-1,3-diols show that in their Pt/C and Pd/C catalyzed oxidation to 2,2-disubstituted 3-hydroxypropanoic acids the small size of the 2-substituents will enhance the rate of the oxidation. In addition, the air flow through the reaction mixture should be controlled to avoid the deactivation of the active sites of catalyst by the over-oxidation. The kinetic studies of the air oxidation of 2,2-dialkylpropane-1,3-diols to 2,2-dialkylmalonic acids by the Pt, Bi/C catalyzed oxidation of 2,2-dimethylpropane-1,3-diol with the air flow rate of 200 mL min^{-1} show that the highest yield of dimethylmalonic acid was obtained by the molar ratio Pt/reactant of 0.01, when the reaction was operating in the regime of mass transfer. The most favorable pH of the reaction mixture of this oxidation was 10. The reaction temperature of 40°C prevented the decarboxylation of the diacid.

3.7.1 Experimental

Materials. The chemicals used are described in Chapters 3.1.1, 3.3.1, and 3.4.2. All the chemicals were used as obtained from the supplier.

Preparation of Pt, Bi/C. 5% Pt, 5% Bi/C was prepared by the method B described in Chapter 3.4.2.

Characteristics of the catalysts. The characteristics of activated carbon are described in Chapter 3.3.1. The determination of the exact metal composition of Pt, Bi/C is described in Chapter 3.4.2 and the morphological investigations of Pt, Bi/C and Pt/C are described in Chapter 3.1.1.

Analyses of the reaction mixtures.

The reaction mixtures of the Pt, Bi/C catalyzed oxidations of 2,2-dimethylpropane-1,3-diol were analyzed by HPLC and GC as described in Chapter 3.3.1.

The reaction mixtures of the Pt/C catalyzed oxidations of 2,2-dimethylpropane-1,3-diol, 2-hydroxymethyl-2-methylpropane-1,3-diol, 2-ethyl-2-hydroxymethylpropane-1,3-diol, and 2,2-bis-(hydroxymethyl)propane-1,3-diol were analyzed by HPLC using a Hewlett-Packard 1090 system. 2-Hydroxymethyl-2-methylpropane-1,3-diol and 2-ethyl-2-hydroxymethylpropane-1,3-diol were detected by a refractive index detector and the carboxylic acid products by a diode array detector with a detection wavelength of 210 nm. The exact amounts of the compounds present in the reaction mixtures were determined using an external standard method.[81] The conversion of 2,2-dimethylpropane-1,3-diol was determined by GC. 3-hydroxy-2,2-bis-(hydroxymethyl)propanal and 3-hydroxy-2,2-bis-(hydroxymethyl)propanoic acid could not be analyzed.

The reaction mixtures of the Pd/C catalyzed oxidations of 2-hydroxymethyl-2-methylpropane-1,3-diol were analyzed by ^{1}H NMR as described in Chapter 3.3.1.

Oxidation procedure. The general oxidation procedure is described in Chapter 3.3.1. In the Pt/C catalyzed oxidations the reactants were dissolved in 25 mL of water, and the catalyst (0.02 equiv. of Pt) was suspended in the mixtures. The reactions were started by bubbling air 800 mL min^{-1} through the mixtures. The reaction temperatures were 20ºC, and pH of the reaction mixtures were kept at 8 by adding 1% NaOH via a pump. In the Pd/C catalyzed oxidations the reaction mixtures were stirred under H_2 for 10 min to activate the catalyst before the reactions were started by bubbling air 800 mL min^{-1} through the reaction mixtures.

4 CONCLUSIONS

The aims of this study were well reached by the experimental work presented. An environmentally benign and an economical methods for the preparation of 2,2-disubstituted 3-hydroxypropanoic acids, linear hydroxy acids, 2,2-dialkylmalonic acids, and linear dicarboxylic acids were developed. 2,2-Disubstituted propane-1,3-diols and linear primary diols were oxidized with hydrogen peroxide or air, using water as a solvent, and sodium tungstate or supported noble metals as catalysts. In these oxidations the diols are useful reactants in addition to the conventional reactants, such as hydroxyaldehydes and cycloalkanes.

The experimental work was carried out in a laboratory scale. For a further evaluation of the results of this work for the industry scaling up of the developed methods should be done. Compared to the air oxidations an advantage of the hydrogen peroxide oxidations is that they can be performed in a more concentrated reaction mixture. In addition, the sodium tungstate catalyst could be more useful when converted into a heterogeneous form. Hydrogen peroxide as an oxidant in the supported noble metal catalyzed oxidations would decrease the over-oxidation of the catalysts. In the air oxidations it could be possible to oxidize 2-substituted 2-hydroxymethylpropane-1,3-diols to 2-substituted hydroxymethylmalonic acids, if the supported noble metal catalysts were promoted with a less effective promoter than bismuth. When using a recycled Pt, Bi/C catalyst its deactivation could be avoided by bubbling hydrogen through the reaction mixture at the end of the oxidation. This could also reduce the dissolved bismuth on the surface of the catalyst.

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