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Regioselective Oxidation of Hydroxyl Groups of Sugar and Its Derivatives Using Silver Catalysts Mediated by TEMPO and Peroxodisulfate in Water

H. Kochkar,* L. Lassalle,* M. Morawietz,† and W. F. Hölderich*,[1]

*Department of Chemical Technology and Heterogeneous Catalysis, University of Technology, RWTH-Aachen, Worringerweg 1, 52074 Aachen, Germany; and †Degussa-Hüls, Rodenbacher Chaussee 4, 64304 Hanau, Germany

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Primary hydroxyl groups were oxidized regioselectively to carboxylic acid using organic nitrosonium salts generated on supported silver catalysts, which promote disproportionation of 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) in aqueous solution. The oxidation reactions were performed at pH 9.5 in a batch reactor at room temperture using heterogeneous silver catalysts and peroxides as primary co-oxidants; e.g., 99 mol% selectivity to methyl-α-D-glucopyrasiduronic acid was obtained at 90% conversion of the pyranoside using a silver carbonate–celite catalyst . The efficiency of the system was increased by adding carbonates to the silver catalyst. This result is explained by the increase of the electron charge deficiency on silver in the presence of carbonate, which accelerates the nucleophilic attack of hydroxyls and/or TEMPO. In the case of the Ag–Al_2O_3 catalyst, this result was proved by temperature-programmed desorption measurements using ammonia. With primary/secondary polyols, the selectivity for the primary hydroxyl groups is high. In addition, primary hydroxyl groups, as in the case of pyranosides, were oxidized more selectively than those of the furanosides. The observed regioselectivity is due to the sterical hindrance caused by the four methyl groups in TEMPO. © 2000 Academic Press

Key Words: **regioselective; oxidation; TEMPO; carbohydrates; silver; peroxides; carbonate.**

1. INTRODUCTION

The oxidation of alcohols is very common among organic chemical reactions and is widely used in many processes in industry. Especially, this holds true for the oxidation of primary alcohols to aldehydes or carboxylic acids.

Metal-catalyzed oxidation of alcohols to carboxylic compounds, in conjunction with co-oxidants, is an important step in the synthesis of fine chemicals (1). The oxidation of sugars and their derivatives as well as of starch and cellulose is particularly important. The oxidized carbohydrates can be used as thickening and gelling agents, in paints and resins, and as detergent co-builders and superabsorbers. That means that such oxidized compounds have an important economic impact.

The oxidation reaction should advantageously be conducted in a catalytic manner. Among the known catalytic methods, the oxidation of alcohols with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (**1**) and a co-oxidant, such as sodium hypochlorite or sodium bromide, became a very attractive tool for organic synthesis (2). The authors used the stable organic nitroxyl radical 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (**1**) as a mediator. The actual oxidant is the nitrosonium ion (**2**) (ammonium oxide), which can be obtained from (**1**) by several methods. During the oxidation, species (**2**) is reduced to hydroxylamine (**3**) (Fig. 1).

The nitroxyl radical (**1**) can be used in stoichiometric amounts by treatment with the following methods: *p*-toluenesulfonic acid or 1(*S*)-(+)-camphor-10-sulfonic acid (3) and methyl iodide (4). However, the high chemical reactivity generally hinders its isolation and purification. Fortunately, radical (**1**) can also be used in a catalytic amount as a mediator. For example, Fe(III) ions oxidize TEMPO to the nitrosonium ion (**2**), which shows good activity in the oxidation of benzyl alcohol to form benzaldehyde in a two-phase system (aqueous phase/acetonitrile or methylene chloride) (5). In this case, nitrosonium ion (**2**), which is a kind of ammonium salt, accelerates the reaction by acting as an anion transport. The disadvantage of this method is that the Fe(III) ion was used in excess (3 equiv of Fe(III) ions, 2 mol% of TEMPO, and 1 mol of substrate), which is not feasible for industrial purposes in view of environmental protection and costs.

The nitroxyl radical (**1**) can also be oxidized by cupric salts to the nitrosonium ion (**2**), which oxidizes alcohols such as benzyl alcohol and *n*-hexanol to the corresponding aldehydes, such as benzaldehyde and *n*-hexanal, the hydroxylamine (**3**), and a protonic acid. The hydroxylamine was in turn easily oxidized by cupric salts to give a nitroxyl radical (**1**) again. But it was necessary to trap the acid because it inhibits the catalytic oxidation system. Therefore, cupric hydroxide or pyridine were used

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[1] To whom correspondence should be addressed. Fax: 49 241 88 88 29. E-mail: hoelderich@rwth-aachen.de.

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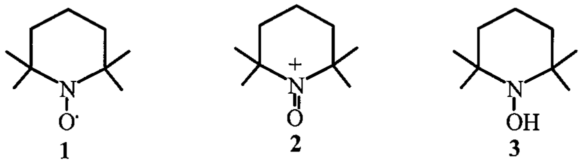


FIGURE 1

as acid-trapping agents, again in stoichiometric amounts (6, 7).

Cella *et al.* (8) performed the oxidation in the presence of *m*-chloroperbenzoic acid. Thereby, the nitrosonium ion (**2**) was generated in methylene chloride as a solvent. Using this system, a large range of alcohols could be oxidized to the corresponding aldehydes or ketones. However, alcohols having oxygen in the β-position cannot be oxidized by the nitrosonium ion and those in the δ-position react slowly. The drawback of this method is the use of an excess of *m*-chloroperbenzoic acid (1.5 mol/mol of alcohol). This fact results in many purification steps for the products.

Primary alcohols are quantitatively oxidized to aldehydes under two-phase conditions (methylene chloride–aqueous sodium hypochlorite) in the presence of catalytic amounts of 4-methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl (4-MeO–TEMPO). Co-catalysis by sodium bromide and buffering at pH 8.6 with $NaHCO_3$ are also required (9, 10).

Many authors described a method for the oxidation of primary hydroxyl groups in an aqueous phase. The reaction is mediated by TEMPO. Thereby, hypobromite is used as the regenerating oxidant, which in turn is regenerated by another hypohalite as the oxidant (see Scheme 1), preferably in the form of a salt, such as lithium hypochlorite, sodium hypochlorite, potassium hypochlorite, or calcium hypochlorite (11–13).

More recently, the oxidation of primary hydroxyl groups of polysaccharide by means of TEMPO in water has been described. These investigations are related to a process for producing completely carboxylated carbohydrates. In this process, carbohydrates having a carbonyl content of at least 75% were oxidized using the hypochlorite/bromide system (14). The amount of hypochlorite solution used was 2–2.4 mol/mol of monosaccharide unit. This clearly shows that the process produces a lot of halogenated salts, which cause some environmental pollution and corrosion problems.

The catalytic oxidation processes of primary hydroxyl groups cited above have the following disadvantages:

In two-phase systems,

(i) the oxidation of alcohol leads to the aldehyde only,

(ii) the nitroxyl radical and the co-oxidant were used in stoichiometric amounts, and

(iii) many purification steps for the products are required.

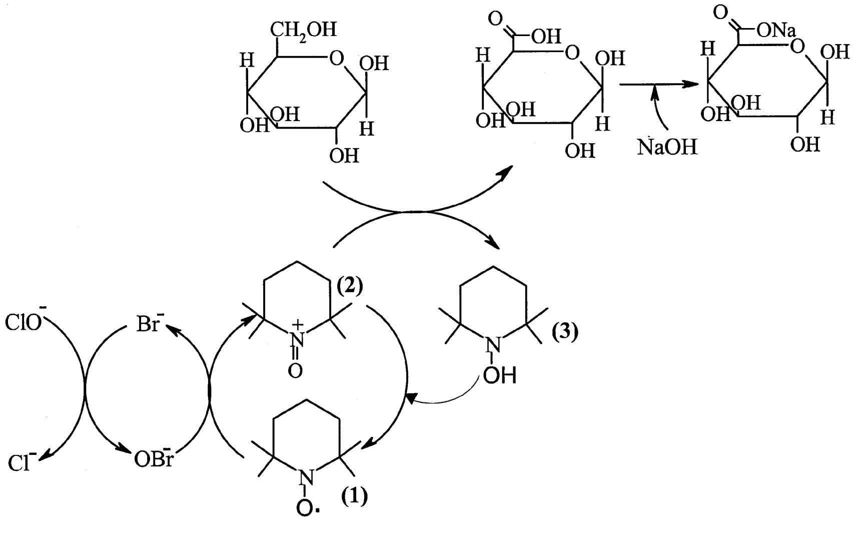
In the aqueous phase,

(i) a large excess of the co-oxidant, e.g., hypochlorite, was employed and

(ii) problems associated with this method are, sooner or later, loss of the oxidizing power of the nitroonium salts due to the concurrently generated hydrogen peroxide and molecular chlorine (15) and an accumulation of halogenated salts.

The present paper is to show another method for the catalytic oxidation of alcohols by means of nitroxyl radicals (**1**) using a heterogeneous system.

We report here a new method for the regioselective oxidation of primary hydroxyl groups over a silver catalyst/peroxodisulfate system mediated by TEMPO. The oxidation was performed first with methyl-α-D-glucopyranoside since it has been used as a model molecule.



SCHEME 1. Proposed mechanism for the oxidation of primary hydroxyl groups[11].

2. EXPERIMENTAL

2.1. *Materials*

Methyl-α-D-glucopyranoside (α-MDG), AgO, Ag_2O, $AgNO_3$, pyridine, hexamethyldisilazane, trifluoroacetic acid, perborate, percarbonate, oxone, and peroxodisulfate were bought from Aldrich. NaY was kindly provided by Zeolyst International and $AlPO_4$ and Al_2O_3 by BASF-AG (D10-10). Celite was purchased from Merck and was used after purification with hydrochloric acid (10 wt%).

Experiments were performed in a thermostated glass batch reactor of 250 ml volume, equipped with a condenser, a thermometer, and a magnetic stirrer. The pH was kept constant using a pH meter (Titroline Alpha, Schott) coupled to a pH control unit and an automatic burette (Metrohm 655, 20-ml piston) containing 1 M KOH, which consumption was recorded during the reactions.

2.2. *Preparation of the Catalysts*

2.2.1. Metal-supported on Al_2O_3, $AlPO_4$, and NaY. Ag–Na–Y, Ag–$AlPO_4$, and Ag–Al_2O_3 were prepared by incipient wetness impregnation. Silver nitrate was added to a suspension containing 10 g of the support. The mixture was stirred for 15 h and then filtrated, washed, and dried overnight at 373 K. Then the catalyst was calcined under air at 773 K for 6 h. All the surface areas, porosity, and silver content are reported in Table 1.

2.2.2. Preparation of the silver carbonate on celite. The supporting material celite was purified by washing with methanol containing 10 wt% concentrated hydrochloric acid at 25°C and afterward treated with distilled water until the mother liquor was neutral. Then the material was dried at 393 K.

To a mechanically stirred solution of silver nitrate (1.85 mmol, 0.31 g) in distilled water (50 ml), purified celite (10 g) was added. To the stirred suspension, a solution of potassium hydrogen carbonate (0.15 g) in distilled water (10 ml) was slowly added. After complete addition, stirring was continued for 10 min. The yellow-green precipitate formed was collected by filtration and dried under reduced pressure on a rotary evaporator for several hours. The catalyst contains 0.17 mmol of silver/g of celite (0.085 mmol of Ag_2CO_3/g of reagent).

TABLE 1

Characterisations of the Catalysts

Catalyst/ support	Ag (wt%)[a]	Surface area ($m^2\,g^{-1}$)	Pore diameter $\langle\phi\rangle$[b] (Å)
		Al_2O_3	
A	1.1	253	65
B	2.0	247	65
C	2.8	249	64
D	5.0	241	64
		NaY	
E	5.8	573	<12
		$AlPO_4$	
F	4.5	41	$20 < \phi < 40$

[a] Determined by ICP-AES.

[b] Determined by using the BJH method.

2.3. *Physicochemical Characterisation*

The composition of the catalysts was determined by inductively coupled plasma (ICP) after dissolution of the solids. The specific BET surface and average pore diameter were obtained from the adsorption isotherms of nitrogen at 77 K, using a Micromeritics automatic volumeter (ASAP 2000), after evacuation of the samples at 473 K for 16 h. An X-ray diffraction study was performed on a Siemens 5000 instrument equipped with a Cu lamp ($\lambda_{cu} = 1.54$ Å). The spectra were recorded from $2\theta = 5°$ to $2\theta = 100°$.

The amount of acidic sites was determined by measurements of temperature programmed desorption (TPD) of ammonia. On samples previously calcined at 673 K under helium flow (overnight), the ammonia was adsorbed for 15 min at 373 K. The temperature was increased using a ramp of 10°C/min to 1073 K. The desorbed ammonia was titrated by HCl (0.025 M) using a special titrometer coupled to a pH control unit and an automatic burette containing the acid. During the desorption, the temperature, pH, and HCl consumption were recorded.

2.4. *Oxidation Procedure*

A defined amount of substrate (5 mmol) was dissolved in 100 ml of water. Then 30 mg (0.19 mmol) of TEMPO and 10 mmol of co-oxidant were added. The system was equilibrated at 298 K and pH 9.5. The catalyst was instantaneously added to the mixture (time zero). The pH of the solution during the reaction was kept constant at 9.5 by automatic titration with 1 M KOH solution. At the end of the reaction, the mixture was neutralized by adding hydrochloric acid to a pH of 8. Then the catalyst was recovered by filtration, and water and TEMPO were removed under vacuum at 313 K. The product mixture was dried overnight under vacuum at room temperature. The oxidation degree of the substrate was determined by gas chromatography after silylation.

For silylation, e.g., 10 mg of the oxidized material was introduced into a gas chromatography tube and 600 μl of pyridine was added. The solution was stirred until the mixture was totally dissolved. Then 600 μl of hexamethyldisilazane and 150 μl of trifluoroacetic acid were added. The mixture was placed in an oven at 363 K for 30 min. After addition of *n*-decane as the internal standard, quantitative analysis was carried out. The products were analysed by a GC Siemens RGC 202 equipped with a capillary column ultra chromapack 25 m in length and a flame ionization detector (FID).

TABLE 2

Oxidation of α-MDG over Silver Catalysts Mediated by TEMPO, at pH 9.5, 298 K, Molar Ratio α-MDG/TEMPO = 26 [( ), Molar Ratio of the Substrate to Silver; Solvent, Water]

Catalyst	$(NH_4)_2S_2O_8$/ α-MDG	Conversion (%)	Selectivity (mol%)
No	2	9	86
Ag_2O (0.5)	0	49	95
AgO (0.5)	0	71	96
Ag–Al_2O_3 (108)	2	70	97

3. RESULTS AND DISCUSSIONS

3.1. Preliminary Experiments

First, a kind of model reaction, the oxidation of methyl-α-D-glucopyranoside (α-MDG), was performed (Table 2). It can be pointed out that in the presence of silver oxide catalysts the conversion depends on the oxidation state of silver: high conversion of pyranoside (α-MDG) was obtained in the case of silver in a high oxidation state. These experiments show clearly the ability of the silver oxide to activate and regenerate the TEMPO. But we noted that silver oxide was reduced to metallic silver as shown by XRD (Fig. 2), whatever the oxidation state of the silver oxide. These results support the idea that the reaction takes place in a two-step procedure (see Scheme 2).

$$2\,AgO + H_2O + 2e^- \longrightarrow Ag_2O + 2\,OH^- \quad [1]$$

$$Ag_2O + H_2O + 2e^- \longrightarrow Ag + 2\,OH^- \quad [2]$$

SCHEME 2

Using the peroxodisulfate (PDS) in combination with TEMPO but in the absence of silver oxides only a low conversion of 9% was obtained. However, when Ag–Al_2O_3 was used in the presence of a catalytic amount of nitroxyl radicals, with a molar ratio of α-MDG to silver 108, a very high selectivity to methyl-α-D-glucopyrasiduronic acid (97 mol%) was obtained at a conversion of 70%. In this procedure the silver has the function of a catalyst.

In the absence of TEMPO radicals but with Ag–Al_2O_3 and PDS the conversion was lower than 2%. This allows us to conclude that the absence of TEMPO radicals in this type of reaction makes it ineffective and nonselective, while the presence of a catalytic amount of radical increases the regioselectivity of the oxidation to a very high degree. The chosen catalysts are good for the regioselective oxidation of carbohydrates; they give high selectivities to carboxylic acid salt without cleavage of the pyranoside ring.

For the oxidation of α-MDG, Mombarg *et al.* (16) reported a conversion of about 60% after 20 h using [Ti]–MCM-41 and H_2O_2, but the selectivity to the hydroxyl group in the C6 position is low due to the decomposition of H_2O_2 and the oxidative cleavage of the vicinal diol groups. Earlier experiments (17) by our group showed that V–Y and Co–Y zeolites gave 15% and 60% conversion, respectively, with 99% selectivity to the acid.

Heyns and Paulsen (18) reviewed the platinum-catalyzed selective oxidation of monosaccharides with oxygen. They concluded that the order of reactivity of the functional

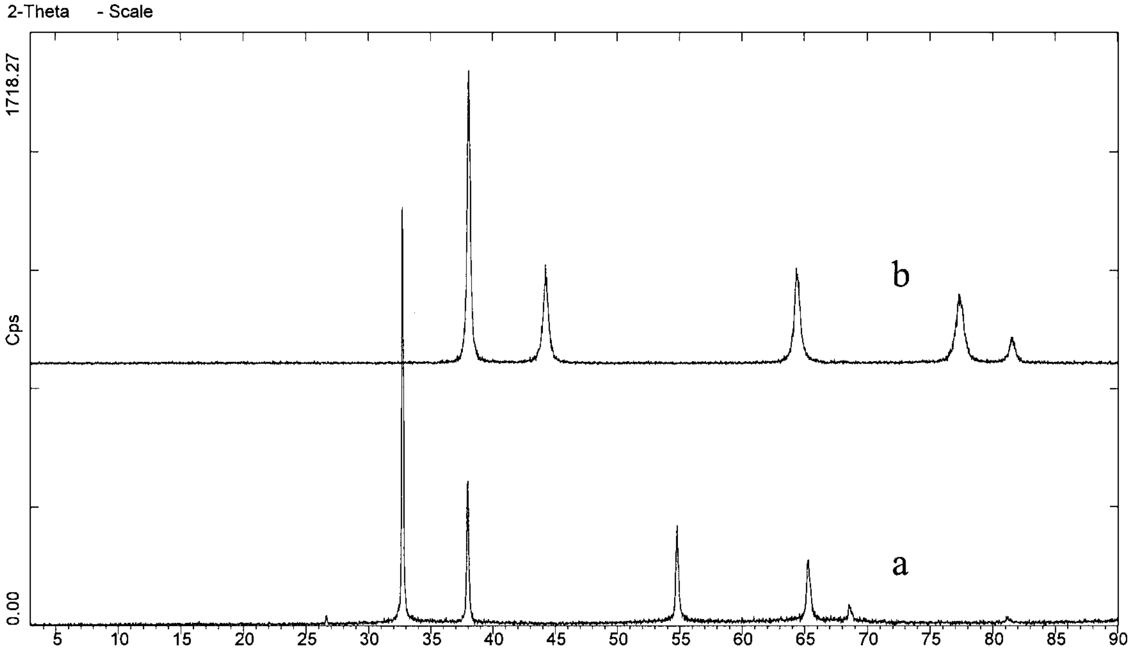


FIG. 2. X-ray spectra of (a) $Ag^{(I)}$oxide before the catalytic test and (b) after the catalytic test indicating Ag^0.

groups toward oxygen is as follows: hemiacetal > primary hydroxyl > axial hydroxyl > equatorial hydroxyl. Hence, to oxidize selectively the primary hydroxyl groups, a protection of the hemiacetal function is generally required. For the oxidation of L-sorbose, Baiker (19) proposed the use of acetone as a complexing agent. The selectivity to the ketoacid can also be improved by applying strongly adsorbing amines, so-called supported bases, instead of increasing the bulk pH of the medium. The bases used are cycloaliphatic and aromatic amines, phosphines, and aminophosphines. Nevertheless, these base modifiers have a bad effect on the activity of the catalyst (20).

On carbon-supported platinum, Schuurman *et al.* (21) showed that the activation energy for the formation of carboxylic acid from primary alcohol and oxygen at pH 10 is about 110 kJ mol^{-1}. de Nooy *et al.* (12) demonstrated, using TEMPO as a mediator, that the reaction requires only 58 kJ mol^{-1}. So this low enthalpy of activation makes the use of TEMPO very attractive. However, comparison with the present results obviously shows that a silver catalyst in combination with PDS as the co-oxidant yields better results. In addition, we do not need to protect the hemiacetal function of the monosaccharide.

3.2. *Co-oxidant Effect*

We studied the effect of the co-oxidant on the oxidation of α-MDG in the presence of TEMPO and silver supported on alumina (2 wt%). The results are reported in Table 3. Ammonium PDS achieves a very high selectivity to the acid, 99%, at 78% conversion of the α-MDG. In contrast, when the reaction was carried out in the presence of sodium percarbonate or sodium perborate as the primary oxidant, very low conversions were achieved, maintaining 99% selectivity. The reason might be that the perborate and percarbonate aqueous solutions decompose to H_2O_2, which in turn decomposes in the presence of silver to give mainly O_2 (22). To verify this hypothesis, perborate and percarbonate were replaced by H_2O_2 (35 wt%). As shown in Table 3, no activity was obtained and we noted fast decomposition of hydrogen peroxide (few minutes).

TABLE 3

Effect of the Co-oxidant

Catalyst	Oxidant	Conversion (%)	Selectivities[c] (mol%) (i)	(ii)	(iii)	(iv)
Ag–Al_2O_3	PDS	78	99	—	—	—
	Oxone	6	99	—	—	—
	Perborate	<1	99	—	—	
	H_2O_2 (35 wt%)	0	—	—	—	—
Ti–MCM-41[a]	H_2O_2 (35 wt%)	60	21	51.6	17.6	9.6
TEMPO	ClO^-/Br^-[b]	n.i.	>95	—	—	—

Note. Reaction conditions: (methyl-α-D-glucopyranoside) 5 mmol, molar ratio oxidant/α-MDG = 2; (TEMPO) 0.1 mmol, 0.50 g of catalyst, 298 K, water as the solvent, pH 9.5.

[a] See Ref. (16).

[b] See Ref. (23).

[c] (i) Methyl-α-D-glucopyrasiduronic acid; (ii) formic acid; (iii) glycolic acid; (iv) tartronic acid.

TABLE 4

Effect of the PDS/TEMPO Molar Ratio on the Catalytic Properties of Ag–Al_2O_3 Catalyst

PDS/TEMPO	Conversion (%)	Selectivity (mol%)
25	27	98
50	70	97
75	42	96
125	30	87
250	19	70

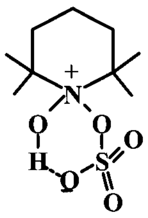
Note. α-MDG /TEMPO = 26; pH 9.5; RT; solvent, water.

However, when oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) was used, a very high selectivity of 99% is also obtained at 6% conversion of the α-MDG. In this case, oxone decomposes to give mainly O_2 and SO_4^{2-} with small amounts of PDS (22). The activity observed in this case is assumed to be related to the *in situ* formation of the PDS. Nevertheless, the conversion remained very low here due to the deposition of sulfate anions on the surface of the catalyst.

For the oxidation of α-MDG, de Nooy *et al.* (23) reported selectivity to methyl-α-D-glucopyranosiduronic acid higher than 95% using the hypochlorite/bromide system and TEMPO at pH 10, but no indication of the conversion is given. Mombarg *et al.* (16) reported 20% selectivity to methyl-α-D-glucopyranosiduronic acid at 60% conversion using [Ti]–MCM-41 and H_2O_2 as the oxidant. Using the de Nooy system, the relative rate of the reaction is about 0.02 mmol min^{-1}. In contrast, our system demonstrated an activity higher than 0.1 mmol min^{-1}. A comparison with the present results shows that the Ag–Al_2O_3 catalyst with TEMPO and PDS as the co-oxidant obviously yields better results.

3.3. *Effect of Peroxodisulfate/TEMPO Ratio*

The PDS/TEMPO molar ratio was varied between 25 and 250 (Table 4). No conversion was observed in the absence of PDS. In contrast, the conversion reaches a maximum at an approximate PDS/TEMPO ratio close to 50 and decreases at higher ratios. This result can be explained by complex formation between the cationic oxidizing agent and the sulfate anion (Scheme 3). The hydrogen bond is expected to lower the positive charge on the nitrogen, which would be the driving force in this reaction path. Miyazawa *et al.* (4) demonstrated that the nucleophilicity of the counteranion of this cationic oxidizing agent has an important effect on the catalytic properties; e.g., secondary alcohols are oxidized faster than primary alcohols in the presence of Br^-.



SCHEME 3. Supposed complex between TEMPO and sulfate anion.

The opposite results were observed in the presence of Cl^-. On the other hand, the adsorption of polar substrates or products can modify this charge (12). The selectivity to the acid decreases at high PDS ratios; this might be explained by the sulfation effect, which increases the acidity of the catalyst, resulting in the ring opening of the pyranoside.

3.4. *Effect of the Percentage of Silver*

α-MDG oxidation reactions were conducted versus the silver content supported on alumina, adjusting a molar ratio α-MDG/PDS/TEMPO = 1/2/0.1. Figure 3 illustrates conversion and selectivity to methyl-α-D-glucopyranosiduronic acid as a function of the silver percentage. α-MDG oxidation is very low in the absence of silver around 9%, whereas the conversion increases with the percentage of silver. At 2 wt% Ag, the conversion and selectivity to methyl-α-D-glucopyranoside are 78% and 98 mol% respectively. This means the silver works as a catalyst. We noted also that increasing the silver content does not affect the surface area. The BET surfaces remain around 250 m^2/g. The silver concentration was measured in the reaction medium and in the catalyst after the reaction. These measurements show that the amount of silver measured on the catalyst was the same as that introduced initially in the solution. Therefore, silver is quantitatively fixed on the catalyst.

3.5. *Stability of the Catalysts*

The $Ag–Al_2O_3$ catalyst with 5 wt% silver was used in five successive oxidation runs with a fresh charge of methyl-α-D-glucopyranoside, PDS, and TEMPO solutions. Figure 4 shows the conversion of methyl-α-D-glucopyranoside and the selectivity to methyl-α-D-glucopyrasiduronic acid as a function of the number of runs. The conversion decreases dramatically after the third run, from about 50% to 17%. These results can be explained by the formation of sulfate, which remains adsorbed on the metal surface, blocking the catalytically active centers. The effect of sulfate was verified as follows: the parent catalyst was treated by sulfate anions by wetness impregnation (SO_4^{2-} : Ag = 20 : 1) and then checked in the same conditions. The conversion obtained in this case is lower than that of the parent catalyst 40%. By means of FT-IR spectroscopy, we noted the presence of a band at 600 cm^{-1}, which is attributed to the vibration of sulfate anion (24). In conclusion, the presence of sulfate anions deactivates the silver catalyst.

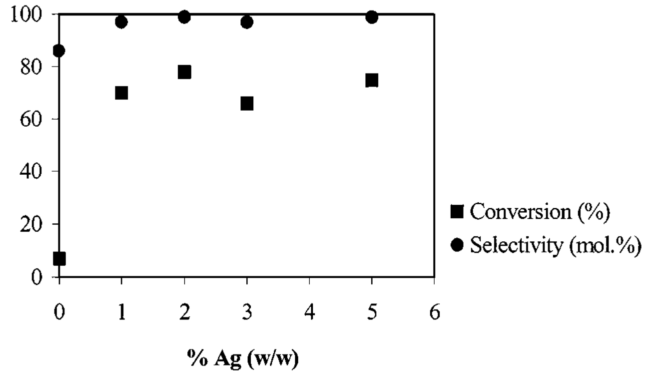


FIG. 3. Effect of the percentage of silver on the conversion of α-MDG.

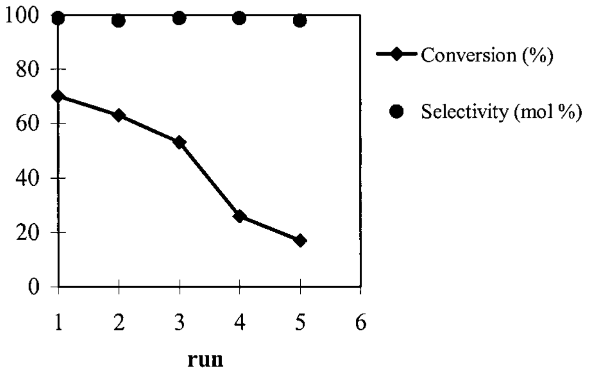


FIG. 4. Conversion of α-MDG and selectivity to methyl-α-D-glucopyuronic acid in five successive runs on Ag/Al_2O_3 catalyst: α-MDG/TEMPO = 26 (mol); oxidant/α-MDG = 2 (mol); 298 K; solvent, water; pH 9.5.

3.6. *Effect of the Support*

Four supports with different textures were checked: Al_2O_3, NaY, celite, and $AlPO_4$ (Fig. 5). The activities obtained vary in the order Ag–carbonate–celite ≫ AgY > $Ag–AlPO_4$ > $Ag–Al_2O_3$, with selectivities to methyl-α-D-

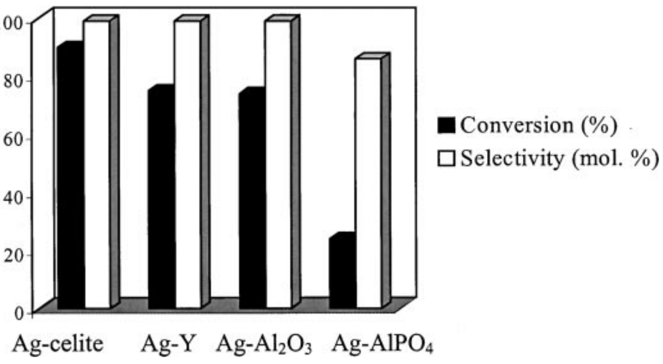


FIG. 5. Effect of the carrier.

glucopyrasiduronic acid of 99 mol%, except that the Ag–AlPO$_4$ catalyst demonstrated a 86 mol% selectivity.

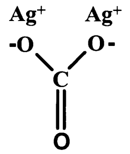
The Ag–carbonate–celite catalyst, which is commonly known as Fétizon reagent, is very active. It was reported (25) that this catalyst is a very versatile and useful oxidation agent and is one of the most important among the so-called supported reagents. Similar regiospecific oxidations of related compounds have been reported (26–28). Olefinic sugars are readily oxidized at the allylic hydroxyl groups in favour of free nonallylic groups. However, the oxidation fails completely with the corresponding acetylenic carbohydrates, which very likely undergo a cleavage leading to acetylene and aldehydes (29, 30).

The acidity of the used supports can be classified in the following order: AlPO$_4$ $\gg$ Al$_2$O$_3$ >Na–Y> celite. The low conversion of the α-MDG (20%) observed in the case of Ag–AlPO$_4$ is probably due to the low stability of the support under basic conditions (pH 9.5), whereas the final conversions obtained using Ag–Y or Ag–Al$_2$O$_3$ are nearly the same.

We suggest that the high activity observed in the case of silver carbonate on a celite catalyst, which presents a very small surface area (6 m^2 g^{-1}), is related to the carbonate ions. Carbonate ions can modify the electron density on silver to generate the activity.

3.7. *Role of Carbonate*

Methyl-α-D-glucopyranoside oxidation reactions were conducted on Ag–Al$_2$O$_3$ and Ag–Al$_2$O$_3$–(CO$_3^{2-}$) catalysts. Because the selectivity to methyl-α-D-glucopyrauronic acid is extremely high, the conversion can be conveniently measured from the amounts of potassium hydroxide added to the reaction medium to maintain a constant pH. In Fig. 6, the conversion as a function of reaction time is demonstrated over the parent Ag–Al$_2$O$_3$ catalyst and for Ag–Al$_2$O$_3$–(CO$_3^{2-}$) with CO$_3^{2-}$/Ag = 0.5 mol. The initial rate increases by a factor of 10 in the case of Ag–Al$_2$O$_3$–(CO$_3^{2-}$). This result can be interpreted by the fact that in the presence of carbonate ions, the charge density on silver decreases (Scheme 4) and then silver is more ionic. This result is supported by the following observations:



SCHEME 4. Supposed complex between silver and carbonate anion.

(i) TPD of ammonia (see Fig. 7) shows clearly that the absorbed ammonia increases after treatment of the catalyst with carbonate. This result is consistent with the idea that the silver is more ionic.

(ii) When water is replaced by a less polar solvent (cyclohexane or benzene), the conversion decreases 6% and 3%, respectively, due to less solvation of silver. This result confirms the ionicity of silver, which can be stabilized here by carbonate anions.

3.8. *Substrate Effect*

We were especially interested in the influence of the ring size because it was found that primary hydroxyl groups in pyranosides were oxidized more selectively than those in furanosides (11). The model substrates, 1,2-propanediol, α-MDG, saccharose, and potato starch, were oxidized (see Table 5). Obviously, primary alcohols are oxidized more rapidly than secondary ones. With primary/secondary polyol (1,2-propanediol), the selectivity for the primary hydroxyl groups is high and reaches 75 mol% at 90% conversion. During oxidation, the lactic acid reacts with the 1,2-propanediol to form the corresponding ester.

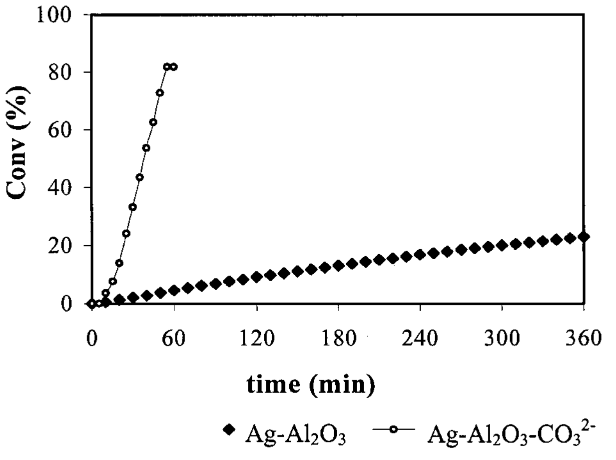


FIG. 6. Methyl-α-D-glucopyranoside conversion as a function of reaction time.

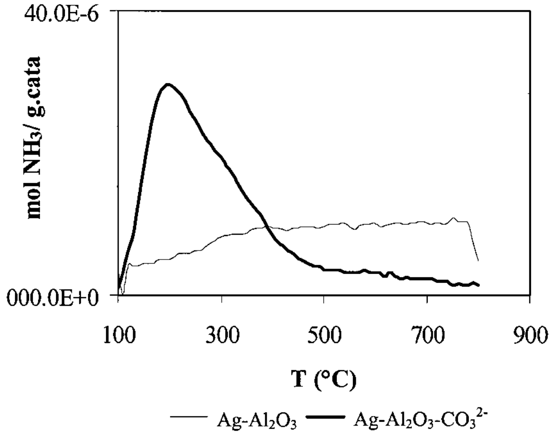


FIG. 7. Temperature-programmed desorption of ammonia from supported silver on alumina.

TABLE 5

Substrate Effect

Substrate	Conversion (%)	Selectivities (mol%)	
		acid	others
1,2-Propanediol	90	75	25[a]
α-MDG	78	99	1
Saccharose	20	100[b]	—
Starch	<1[d]	100[c]	
Starch	20[d,e]	99[c]	1

Note. 0.50 g of Ag–Al_2O_3 (2 wt%); pH 9.5; 298 K; molar ratio of substrate/TEMPO = 26; solvent, water.

[a] Products of self-esterification of lactic acid and esterification with 1,2-propanediol.

[b] Tricarboxylic acid, identified by GC-MS.

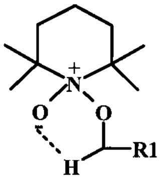
[c] Determined by ^{13}C NMR (176 ppm, carboxylic acid), FT-IR spectroscopy (1742 cm^{-1}, carbonyl function).

[d] Determined by titration.

[e] PDS is replaced by NO_2 as oxidant.

For pyranoside rings, the selectivity depends on the sterical demand of the primary hydroxyl groups. In general, the observed regioselectivity for different substrates seems to depend on the accessibility of the alcohols (Scheme 5). Primary hydroxyl groups of α-MDG were oxidized more rapidly than those of saccharose (100 mol% to the tricarboxylic acid at 20% conversion). In the oxidation of various pyranosides it appeared that the size of the ring played an important role. The oxidation of starch was not successful. This might be explained by diffusion limitations.

For comparison reasons, oxidation of starch was performed on a fluidized bed using NO_2 as an oxidant. From ^{13}C NMR, UV–visible, and FT-IR spectroscopy, we concluded that oxidation takes place regioselectively in primary hydroxyl groups (31).



SCHEME 5. Supposed complex between TEMPO and substrate.

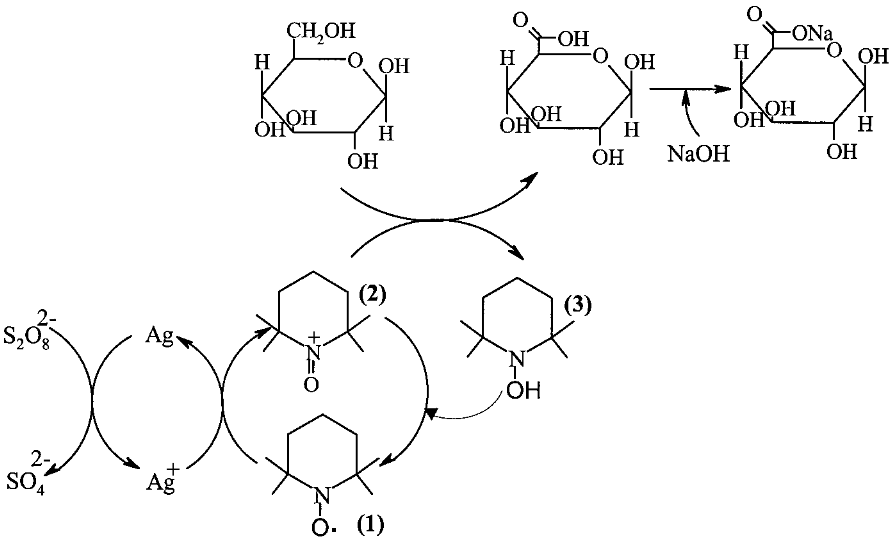
4. MECHANISM

2,2,6,6-Tetramethylpiperidinyl-1-oxy (TEMPO) can be activated under basic conditions using silver catalysts to nitrosonium salt. The latter is a strong oxidant and shows selectivity toward primary hydroxyl groups over secondary ones.

We demonstrated a modified method for the regioselective oxidation of polysaccharides. The reaction mediated by TEMPO and a silver catalyst was used as the regenerating oxidant; the reduced silver (or its equivalent) was in turn regenerated by peroxodisulfate (Scheme 6). For this reason, the TEMPO skeleton can be used as a recyclable oxidation catalyst in the presence of a secondary oxidant.

5. CONCLUSIONS

As compared with the conventional methods, the process of the present work has the following merits: Extremely high activity and selectivity are obtained in the oxidation of primary alcohols or primary hydroxyl groups, e.g., in the case of carbohydrates. More particularly, primary hydroxyl groups of methyl-α-D-glucopyranoside are oxidized regioselectively in the presence of secondary groups. Side reactions are diminished. The catalytic oxidation process presents the same advantages as the method used by



SCHEME 6. Supposed mechanism using silver catalyst, TEMPO, and peroxodisulfate as a primary oxidant.

Van Bekkum *et al.*, namely, high selectivities achieved and mild reaction conditions (oxidation at atmospheric pressure, room temperature (RT), and water as the solvent). However, the catalyst is deactivated by sulfate anions. Further investigations of the use of silver and TEMPO in carbohydrate oxidation in combination with other oxidants are in progress.

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