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Oxidation of octyl α-D-glucopyranoside to octyl α-D-glucuronic acid, catalyzed by several ruthenium complexes, containing a 2-(phenyl)azopyridine or a 2-(nitrophenyl)azopyridine ligand

Alexandra E. M. Boelrijk, Anja M. J. Jorna, Jan Reedijk *

Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands

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Abstract

The oxidation of octyl α-D-glucopyranoside by $NaBrO_3$, catalyzed by a number of ruthenium polypyridyl complexes was investigated. Both $[Ru(azpy)_2(H_2O)_2]^{2+}$ (azpy = 2-(phenyl)azopyridine, system I) and $[Ru(naz)_2(H_2O)_2]^{2+}$ (naz = 2-(*p*-nitrophenyl)azopyridine, system II) proved to be active catalysts yielding octyl glucuronic acid (in acidic medium) and a 2,3-glycol cleavage product (in basic medium) from octyl α-D-glucopyranoside (OGP). A major side-reaction is the hydrolysis of OGP, at the C_1 position. System II appears to be more reactive than system I, which has been explained by the redox properties of the complex. Especially at pH 3 a considerable amount of 1-O-octyl α-D-glucuronic acid is formed without the formation of hydrolysis products. Mechanistic studies, using results from reactions with cyclobutanol in combination with spectroscopic data, indicate that a Ru(IV)=O species is the active catalytic species. Two new complexes were synthesized, $[Ru(terpy)(azpy)(H_2O)](ClO_4)_2$ (terpy = terpyridine, system III) and $[Ru(terpy)(naz)(H_2O)](ClO_4)_2$ (system IV). Both complexes are less active than system I and II. The origin of the reduced activity can lie in the fact that the ruthenium site is sterically less accessible, or because of oxidative instability of the complex, as indicated by electrolysis experiments.

Keywords: Oxidation; Ruthenium-polypyridyl catalysts; Carbohydrates

1. Introduction

The oxidation of alcohols to corresponding aldehydes, ketones or acids is an important synthetic process [1–3]. The reagents commonly used for selective alcohol oxidation often utilize toxic metals such as chromium, employ high temperatures, strong acids or strong bases and suffer from poor selectivity and low product yield [4]. Catalytic alternatives are therefore of interest and indeed in recent years a variety of catalytic oxidations of organic substrates by transition metal complexes have been investigated [4]. During the past decade a still emerging polypyridyl-oxo chemistry of ruthenium, based on the higher oxidation states Ru(IV), Ru(V) and Ru(VI) has been reported [5]. A key to the formation of high-oxidation state complexes is the loss of protons and stabilization by electron donation from bound hydroxo- or oxo-groups. Because of their reported high oxidation potentials and stability, these complexes have already proved their ability to act as stoichiometric and even catalytic oxidants [5]. Most investigations so far have been concentrated on the oxidation of simple alcohols to aldehydes

* Corresponding author.

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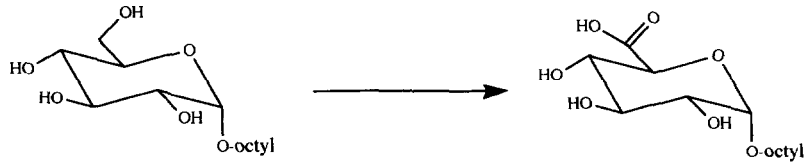

OGP OGA

Fig. 1. Oxidation of octyl glucopyranoside (OGP) to octyl glucuronic acid (OGA).

and acids (i.e. benzylic alcohol, isopropanol, ethanol and methanol) [5]. Other more sophisticated and industrially attractive alcoholic substrates would be unprotected sugar moieties.

Selective oxidation of carbohydrates and their derivatives yielding carboxylates with useful and interesting chemical and physical properties can be of great importance for future world needs [6]. Homogeneous oxidation routes are likely to show advantages over the heterogeneously catalyzed reactions in being more reactive, more selective and having the opportunity to be used for oxidation of insoluble substrates (like sugar polymers, which are impossible to oxidize by heterogeneous catalysis over Pt/Pd alloys [6,7]).

An earlier study [8] described the oxidation of unprotected model sugars, like alkyl glucopyranosides (octyl α-D- and methyl α-D-glucopyranoside, abbreviated as OGP and MGP, respectively) by $NaBrO_3$, catalyzed by three different high-valent ruthenium species, ruthenium tetraoxide, perruthenate and ruthenate. These reactions yield different products depending on the ruthenium species used (Fig. 1).

An investigation of the oxidation of alkyl glucopyranosides catalyzed by ruthenium polypyridyl complexes was undertaken for two reasons. It was desired to find a solution for the observed catalyst instability (due to irreversible product coordination [8]), which might be avoided by the presence of chelating polypyridyl ligands. Furthermore, the ligand environment of transition metal coordination complexes can exert a profound influence on the stability, redox potential, reactivity and substrate selectivity of transition metal centers [9]. In general, ligand influence can be considered in terms of electronic and steric ligand effects. Initially the *tc*-$[Ru(azpy)_2(H_2O)(X)]^{2+}$ complex (azpy = 2-(phenyl)azopyridine, X is H_2O or pyridine [10]) was chosen as a promising oxidation catalyst. The abbreviation, *tc*, stands for an isomer with the pyridine units mutually trans and the azo groups coordinating cis (see Fig. 2). The ligand azpy has the advantage of forming stable Ru(II) complexes with high oxidation potentials, originated from the strong π-accepting properties of the ligand. The Ru(II)/Ru(IV) couple of $[Ru(azpy)_2(H_2O)(py)]^{2+}$ is reported to be 1.15 V vs. SCE (SCE is saturated calomel electrode) in acidic environment [11]. The crystal structure of the *tc* isomer of $[Ru(azpy)_2(H_2O)_2]^{2+}$ [12], clearly shows that the ruthenium site can easily be approached by the sugar moiety.

A coordinating ligand which features a decrease in the σ-donor strength and an extra increase in the π-accepting properties would be expected to increase the E° of the Ru(II)/Ru(IV) couple of the complex even more. Therefore the catalytic properties of a ruthenium(II) complex with 2-((4-nitrophenyl)azo)pyridine (naz) were also studied. The ligand naz is a stronger π-acid than

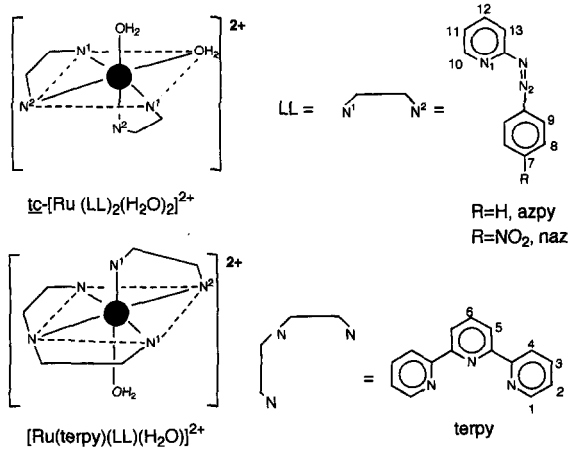

Fig. 2. Structures of ligands and complexes, relevant to this study.

azpy and therefore will show a greater stabilization of Ru(II) in the corresponding naz complexes, just as has been observed before by Krause and co-workers [13].

To investigate the effect of steric changes in the complex on the oxidation ability of the complexes towards alkyl glucopyranosides, also two novel ruthenium complexes were synthesized, namely $[Ru(terpy)(azpy)(H_2O)]^{2+}$ and $[Ru(terpy)(naz)(H_2O)]^{2+}$ (terpy = terpyridine). Molecular modelling figures [14] suggest that the Ru=O site of this type of complexes, due to the ligand structure, is less attainable for the sugar, than the site of the complexes with the general formula $[RuL_2(H_2O)_2]^{2+}$.

In this paper an extensive study is reported on the use of ruthenium–azpy and ruthenium–naz coordination complexes as oxidation catalysts for alkyl glucopyranosides. Using the chosen ruthenium complexes containing the different ligands, the effect of steric and electronic changes in the ligands on the catalytic oxidation ability of the ruthenium complexes towards octyl α-D-glucopyranoside could be studied. A communication describing preliminary results has appeared [1].

2. Experimental

2.1. Reagents and substrates

$RuCl_3 \cdot (H_2O)_x$ (x is approximately 3) was used as obtained from Johnson Matthey. Octyl α-D-glucopyranoside was prepared from octanol and D-glucose, according to a reported method [15]. Purity was checked by NMR and HPLC and proved to be satisfactory. 2-(phenyl)azopyridine (azpy) [16], 2-(4-nitrophenyl)azopyridine (naz) [17], $Ru(terpy)Cl_3$ (terpy = terpyridine) [18], *tc*-$[Ru(azpy)_2(H_2O)_2](ClO_4)_2$ [9] and *tc*-$[Ru(naz)_2Cl_2]$ [13] were synthesized according to literature procedures. All the other complexes were prepared as described below. $NaBrO_3$ and all other chemicals were purchased (analytical grade). For the analytical measurements Millipore water was used.

2.2. Syntheses

General

A general problem of all the syntheses, described below is the high aqueous solubility and hygroscopic properties of the complexes, which makes it hard to precipitate them. Co-precipitation of small amounts of LiCl or $NaClO_4$ could not always be prevented, which complicates elemental analysis. However, the molarity of the catalyst solutions, used for the reactions described in section 2.3 and 2.4 was always checked with ^1H NMR spectroscopy, to prevent errors in stoichiometry.

[Ru(terpy)(azpy)Cl]Cl

117 mg $Ru(terpy)Cl_3$, 49 mg 2-(phenylazo)pyridine and 15 mg LiCl were dissolved in 25 ml of a ethanol/water mixture (v:v 75:25). 0.075 ml triethylamine was added to the solution and the mixture was refluxed for 4 h. After cooling and filtration, the remaining solution was reduced in volume to approximately 10 ml, under reduced pressure and allowed to stand overnight at 4°C. The precipitate that was formed was isolated by filtration and was recrystallized from boiling water. Orange–brown (micro) crystals could be obtained. Yield, 61 mg (39%). ^1H NMR (CD_3OD, ppm vs. TMS): 9.90 (d, H_{13}); 8.82 (d, H_{10}); 8.46 (m, $2H_1$, H_5 and H_{11}); 8.19 (m, H_{12}, H_6); 8.08 (m, $2H_2$); 7.45 (dd, $2H_3$); 7.35 (d, $2H_4$); 7.21 (m, H_7); 7.04 (dd, H_{10}); 6.25 (d, H_9). Anal. Calcd for $RuC_{26}H_{20}N_6Cl_2 \cdot 5H_2O$: C, 46.07; H, 4.46; N, 12.39; Cl, 10.45. Found: C, 45.22; H, 4.46; N, 12.13; Cl, 11.35.

[Ru(terpy)(azpy)(H$_2$O)](ClO$_4$)$_2$

60 mg of [Ru(terpy)(azpy)Cl]Cl and 42 mg of $AgClO_4$ were dissolved in 10 ml of an acetone/water mixture (v:v 75:25) and refluxed for 1.5 h. The AgCl precipitate was filtered off and the filtrate was reduced in volume under reduced pressure. To this solution a saturated solution of $NaClO_4$ in water was added. Orange (micro) crys-

tals could be isolated. Yield 32 mg (43%). ^{1}H NMR (D_2O, ppm vs. DDS): 9.82 (d, H_{13}); 9.38 (d, H_{10}); 8.40 (m, $2H_1$, $2H_5$ and H_{11}); 8.10 (m, H_{12}, $2H_2$ and H_6); 7.45 (t, $2H_3$); 7.39 (d, $2H_4$); 7.15 (m, H_7); 6.95 (dd, H_8); 6.19 (d, H_9). Anal. Calcd. for $RuC_{26}H_{22}N_6O_9Cl_2 \cdot 3H_2O$: C, 39.60; H, 3.58; N, 10.66; Cl, 8.99. Found: C, 39.25; H, 3.32; N, 10.66; Cl, 9.00.

[Ru(terpy)(naz)Cl]Cl

This complex was synthesized according to the same procedure as [Ru(terpy)(azpy)Cl]Cl. Yield 26%. ^{1}H NMR (CD_3OD, ppm vs. TMS): 9.90 (d, H_{10}); 8.88 (d, H_{13}); 8.50 (d, $2H_1$); 8.48 (d, $2H_5$); 8.45 (t, H_{12}); 8.24 (t, H_{11}); 8.16 (d, H_6); 8.10 (t, $2H_2$); 7.95 (d, $2H_8$); 7.48 (t, $2H_3$); 7.33 (d, $2H_4$); 6.53 (d, $2H_9$). Anal. Calcd for $RuC_{26}H_{19}N_7O_2Cl_2 \cdot 5H_2O \cdot 0.3$ LiCl: C, 42.44; H, 3.97; N, 13.29; Cl, 11.21. Found: C, 42.85; H, 3.65; N, 12.96; Cl, 11.55.

[Ru(terpy)(naz)(H_2O)](ClO_4)$_2$

This complex was synthesized according to the same procedure as [Ru(terpy)(azpy)(H_2O)](ClO_4)$_2$. Yield 15%. ^{1}H NMR (D_2O, ppm vs. TMS): 9.45 (d, H_{10}); 8.96 (d, H_{13}); 8.58 (d, $2H_1$); 8.53 (d, $2H_5$); 8.52 (t, H_{12}); 8.34 (t, H_{11}); 8.27 (d, H_6); 8.23 (t, $2H_2$); 7.98 (d, $2H_8$); 7.51 (t, $2H_3$), 7.49 (d, $2H_4$), 6.52 (d, $2H_9$). Anal. Calcd. for $RuC_{26}H_{21}N_7O_{11}Cl_2 \cdot 5H_2O \cdot 0.2NaClO_4$: C, 34.93; H, 3.49; N, 10.97; Cl, 8.72. Found: C, 34.83; H, 3.64; N, 10.33; Cl, 8.47.

tc-[Ru(naz)$_2$(H_2O)$_2$](ClO_4)$_2$

30 mg *tc*-[Ru(naz)$_2$$Cl_2$] was suspended in 3 ml Millipore water. To this suspension 27 mg $AgClO_4$ was added. After 2 h of heating under reflux, the solution was filtered and the remaining solution was evaporated to dryness. Recrystallization of the residue from boiling water yielded dark crystals. Yield 12 mg (31%). ^{1}H NMR (D_2O, ppm vs. TMS, for the *tc* isomer): 8.88 (d, H_{10}); 8.76 (d, H_{13}); 8.44 (t, H_{11}); 8.14 (d2H_8); 7.95 (t, H_{12}); 7.08 (d, $2H_9$). During this reaction 10% of the *tc* isomer was converted into the *cc*-[Ru(naz)$_2$(H_2O)$_2$](ClO_4)$_2$, which co-precipitated with the *tc* isomer, as could be detected with ^{1}H NMR spectroscopy, which showed 2 times 6 signals, which is characteristic for a *cc* isomer [10]. Anal. Calcd. for $RuC_{22}H_{20}N_8O_{14}Cl_2 \cdot 3NaClO_4 \cdot H_2O$: C, 22.44; H, 1.88; N, 9.51; Cl, 15.05. Found: C, 22.38; H, 2.68; N, 8.97; Cl, 15.35.

2.3. Catalytic procedure for the oxidation of OGP

All oxidation reactions were performed at 60°C, unless stated otherwise, in a thermostated bath. In each oxidation experiment the ratio OGP:$NaBrO_3$:catalyst was 1000:4000:1. A typical reaction procedure was as follows: In 4.5 ml of 0.2 M phosphate buffer pH 7.0, 108 mg (0.375 mmol) OGP and 225 mg (1.5 mmol) $NaBrO_3$ were mixed. To this stirred thermostated solution, 0.5 ml 0.2 M phosphate buffer pH 7.0, containing 3.75×10^{-4} mmol of ruthenium catalyst was added. At different time intervals a sample of 0.5 ml was taken from the reaction solution, diluted with 0.5 ml methanol and analyzed by HPLC.

2.4. Catalytic procedure for octanol, cyclohexylmethanol, glycerol, cyclohexanol, cyclohexane and cyclobutanol

The typical procedure was as follows: 100 mg of substrate was dissolved in 5 ml water after which 4 molar equivalents of $NaBrO_3$ and 0.001 molar equivalents of ruthenium complex were added. For certain substrates tetraphenylphosphanium chloride had to be added to the reaction mixture to prevent solubility problems. The reaction was stirred at room temperature or 60°C, depending on the substrate (see Table 2), for several hours after which the aqueous solution was extracted with ether and methylene chloride (in order to extract the substrate and products which do not contain an acid group), acidified and again extracted (in order to extract the products which contain acid group(s)). The organic layers were

dried over $MgSO_4$ and analyzed by gas chromatography.

2.5. Measurements

The analysis procedure for OGP and its reaction products by reverse phase HPLC has already been described before by us and others [8,18]. In order to isolate pure product samples for mass spectrometry and NMR, preparative HPLC was performed on a ET 250/1 in./20 Nucleosil $7C_{18}$ column with a methanol/acetate buffer mixture (70:30, v:v) as eluent. Products that did not have an octyl chain and therefore did not have a retention time on the reverse phase C_{18} column, were analyzed by ^1H NMR, spectra were recorded on a Bruker WM-300 MHz spectrophotometer in DMSO-d_6. Mass spectra were recorded on a Finnigan MAT SSQ-710 mass spectrometer, equipped with a Finnigan MAT electrospray interface. The samples were dissolved in 50% methanol in water containing 1% acetic acid. UV–Vis spectra were recorded on a thermostated Hewlett Packard HP852a diode array spectrometer. Elemental analyses were performed by the microanalytical laboratory of Groningen University, Groningen, the Netherlands.

The acid dissociation constants for $[Ru(naz)_2(H_2O)_2]^{2+}$ to give $[Ru(naz)_2(H_2O)(OH)]^{+}$ and $[Ru(naz)_2(OH)_2]^{2+}$ were determined spectrophotometrically. Aliquots of complex were diluted with a variety of phosphate buffers ranging in the pH 3.0–12.0 to give final ruthenium concentrations of 0.05×10^{-3} M at 0.2 M ionic strength. UV–Vis spectra were recorded from 440 nm to 650 nm for each buffered solution and the wavelength of the maximum absorption of each spectrum was plotted against the pH of the solution. The obtained graph showed two pK_a's for the subsequent dehydronation steps: pK_{a1}, 7.6 ± 0.2 and pK_{a2}, 8.7 ± 0.1.

Cyclic voltammetric measurements were accomplished with a Bioanalytical Systems voltammetry controller (EE1011-00) unit. The resulting voltammograms were recorded using a BAS *X–Y* recorder. A single compartment cell with a three-electrode configuration was used. The reference electrode was a silver/silver chloride electrode with a 3 M NaCl paste filling (Ag/AgCl) or a saturated calomel electrode (SCE), the used counter electrode was a platinum wire and the working electrode was a platinum electrode or a glassy carbon disk (BAS). Solutions were thoroughly degassed with argon and all voltammetric measurements recorded under a positive pressure of this gas. In order to allow some comparison with the literature data, we point out that under our experimental conditions $E^r_{1/2}$ for the couple bis(cyclopentadienyl)iron(II)/iron(III) was 0.432 V vs. Ag/AgCl. The $E_{1/2}$ values reported in this work were computed from cyclic voltammetric wave forms as the half-sum of anodic and cathodic peak potentials. Controlled potential electrolysis were executed in a double-walled Pyrex cell with a Pt working electrode. The used reference electrode was SCE. The experiment was performed at a fixed potential of 1.25 V by using a Metrohm 641 VA potentiostat. The cell was purged with argon during electrolyses.

3. Results and discussion

3.1. Oxidation of OGP, catalyzed by $[Ru(azpy)_2(H_2O)_2]^{2+}$

Product analysis of the reactions of OGP with the catalytic systems, described in the experimental part, showed that two major reactions are operative, i.e. an oxidation reaction yielding alcohol oxidation products and a hydrolysis reaction yielding octanol and glucose as reaction products. Table 1 summarizes the different results obtained. For simplification and clarification, the oxidation selectivity is calculated compared to other oxidation products, containing an octyl chain. The overall selectivity for OGA is lower, when taking the hydrolysis reaction into account.

There is definitely a positive effect of the ligands on the catalyst stability in comparison with simple ruthenium–oxo species. The $[Ru(azpy)_2(H_2O)_2]^{2+}$ system is still active after

Table 1
Oxidation data of octyl α-D-glucopyranoside (OGP) to its octyl α-D-glucuronic acid (OGA) by different catalytic systems (I–IV, see text) in (mmol product)/(mmol catalyst) (±5%)

pH	System	45 min [a]		90 min [a]	
		oxidation	hydrolysis	oxidation	hydrolysis
3.0	I	9(100)	0	27(100)	0
7.0	I	300(65)	464	351(56)	424
10.0	I	–	–	57(35)	57
3.0	II	190(100)	8	283(100)	107
7.0	II	100(45)	194	126(43)	507
10.0	II	310(51)	406	261(62) [b]	485
3.0	III	–	–	–	23
7.0	III	20(95)	51	40(92)	171
10.0	III	–	–	–	38
3.0	IV	1(90)	78	26(91)	77
7.0	IV	100(53)	269	119(58)	336
10.0	IV	206(47)	310	232(47)	358

[a] The selectivity for OGA compared to the other oxidation products containing an octyl chain is given in parentheses. The complete pH dependence of the activity of system I and II was given in Fig. 3.
[b] Some overoxidation products are hydrolyzed, which causes the overall oxidation to decrease.

600 turnovers, while the previously studied RuO_4 oxidation catalyst was only active up to about 85 turnovers [8]. For system I, using *tc*-$[Ru(azpy)_2(H_2O)_2]^{2+}$ as the catalyst, the rate and selectivity are pH dependent (see Fig. 3).

At acidic pH (3–5.5) octyl glucuronic acid is the major oxidation product (selectivity up to 100%) as could be detected by HPLC, ^{13}C NMR and mass spectrometry analysis ($[M+NH_4]^+$ m/z 324 and $[M+Na]^+$ m/z 329). Apart from this oxidation reaction, hydrolysis of the octyl chain from the glucose unit also takes place as a separate reaction. Octanol and its oxidized product, octanoic acid, could be detected by HPLC. Unfortunately, the glucose part reacts further to low-molecular weight overoxidized products, which were impossible to identify separately. The oxidation product 1-O-octyl α-D-glucuronic acid appears to be remarkably hydrolysis stable. This fact has been observed before in the oxidation of OGP heterogeneously catalyzed over Pt and Pd alloys [6]. At basic pH (7–10), a second octyl-containing oxidation product, in addition to 1-O-octyl glucuronic acid, can be observed, which could be characterized by mass spectrometry and gave a $[M+NH_4]^+$ m/z 340 and $[M+Na]^+$ m/z 345 peaks. The molecular weight M is 322, which indicates that the product is a result of 2,3-glycol cleavage (see Fig. 4). A second indication for the structure of this side product is the fact that this product cannot be obtained from octyl glucuronic acid as an over-oxidation product in system I; this excludes the possibility of an alkyl sugar acid with a keto group at one of the three secondary carbon atoms.

It has already been observed before that the pH is a potentially important variable in using aqua/oxo polypyridyl ruthenium complexes as oxidants in a reaction solution. For example, while isopro-

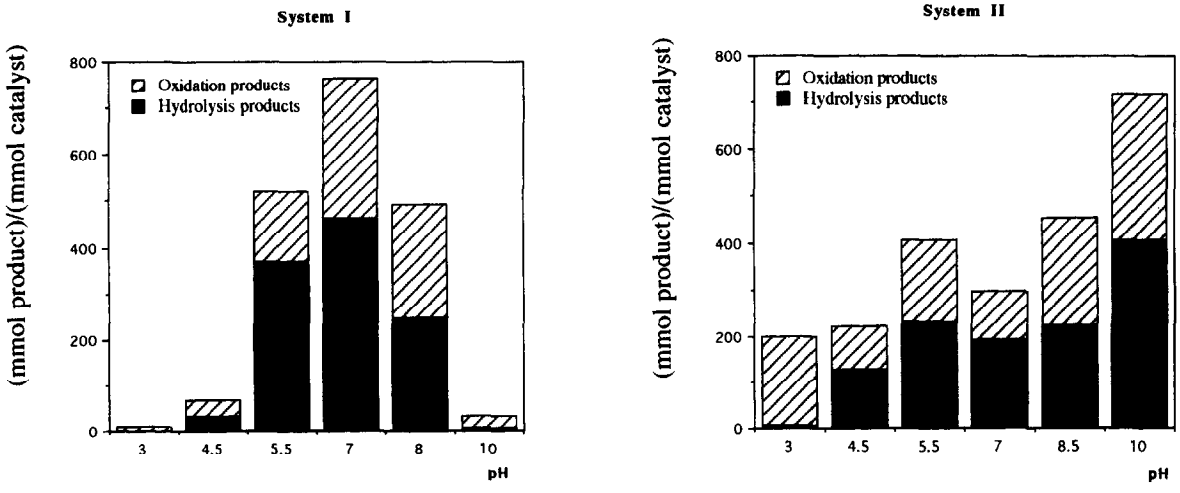

Fig. 3. pH dependence for the activity of system I and II.

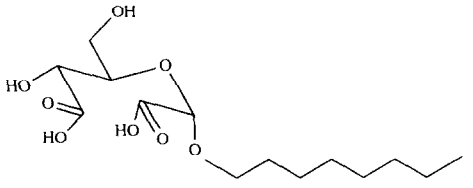

Fig. 4. Proposed side product of the reaction of system I or II with OGP at basic pH's, a 2,3-glycol cleavage product.

pylalcohol is virtually unreactive towards $[Ru(terpy)(phen)(O)]^{2+}$ (phen = phenanthroline) in acidic solution, the oxidation of isopropylalcohol is rapid in alkaline solution [20]. For the reaction with OGP, described in the present paper, the catalytic activity of $[Ru(azpy)_2(H_2O)_2]^{2+}$ has its optimum around pH 7, while its activity is quite low both at acidic as well as at basic pH. This suggests that the partially dehydronated form of the complex, $[Ru(azpy)_2(H_2O)(OH)]^{+}$, which is the predominant form of the complex at pH 7 (the pK_a's for the two possible water dehydronation steps are for this specific complex, $pK_{a1} = 6.88$, $pK_{a2} = 8.60$ [10]), is the most reactive species.

Although originally our interest was mainly devoted to the oxidation of alkyl glucopyranosides, we also found hydrolysis activity of the described ruthenium complexes. All ruthenium complexes described in this work show both hydrolysis and oxidation activity on octyl α-D-glucopyranoside. In the specific case of $[Ru(azpy)_2(H_2O)_2]^{2+}$ the maximum hydrolysis reactivity is, like its oxidation activity, around pH 7. This means that the partly dehydronated complex is also the most reactive species in the hydrolysis reaction. In fact the catalyzed hydrolysis at pH 7 could be a useful reaction in itself for the hydrolysis of compounds that cannot be hydrolyzed under acidic conditions using the classical routes. The selective hydrolysis of other sugar-containing substrates than OGP is currently under consideration.

3.2. Reaction mechanism

To gain more insight in the reaction path of the catalyst in system I, an oxidation reaction at pH 7.0 was followed by diode array UV–Vis spectroscopy. The spectra are reproduced in Fig. 5.

The absorption spectrum of *tc*-$[Ru(azpy)_2(H_2O)_2]^{2+}$ $NaBrO_3$ in aqueous solution (—) (is characterized by a visible band at 559 nm which is characteristic for metal-to-ligand charge transfer (MLTC) $d\pi \rightarrow \pi^*$ transitions. When the complex reacts with $NaBrO_3$, the MLTC band disappears yielding a characteristic spectrum for a high-valent ruthenium complex (- - -). After a certain reaction time an adduct between the high-valent ruthenium species and the alkyl glucopyranoside appears to be formed which displays a spectrum featuring an absorption maximum at 395 nm (— ··· —). When the reaction mixture is left overnight, the original Ru(II) spectrum reappears, which indicates the complete reduction of the catalyst and complete oxidation of the substrate (and probably part of the solvent).

To study the mechanistic features of this reaction in some more detail, cyclobutanol was reacted in the catalytic system described above. Over a wide pH range (3–11) cyclobutanone was found to be the sole product of the reaction, which indicates that the catalytic system operates via a two-electron transfer in the oxidation step [19]. The

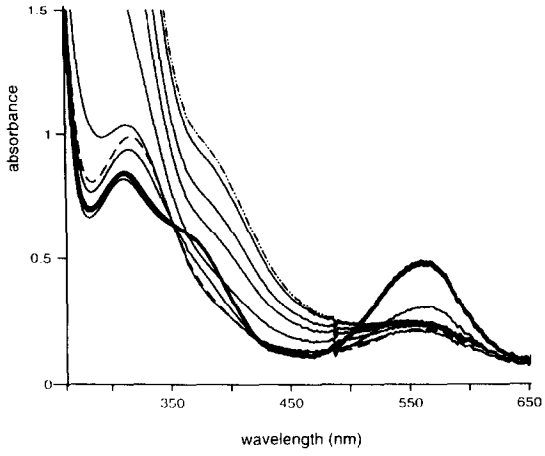

Fig. 5. UV–Vis spectra as a function of reaction mixture with the system I at pH 7.0. A spectrum was taken every minute of the thermostated sample at 60°C. Original spectrum of $[Ru(azpy)_2(H_2O)_2]^{2+}$ at $t = 0$ min (—). The (- - -) spectrum shows the partial formation of a high-valent ruthenium species by reaction of the Ru(II) complex with $NaBrO_3$. The (— ··· —) spectrum is due to the reaction of the high-valent complex with the alkyl glucopyranoside.

fact that cyclobutanone is the only observed product under both acidic and neutral or basic pH conditions, suggests that the pH dependence of the rate and selectivity for the OGP oxidation cannot be attributed to a change from a one- to a two-electron transfer mechanism. Moreover, this result indicates that the active catalytic species is either a Ru(IV), or a Ru(VI) species (2 or 4 oxidation levels above Ru(II)).

When these results are compared with the oxidation results obtained with $[Ru(azpy)_2(H_2O)(py)]^{2+}$ (py = pyridine) as the catalyst instead of $[Ru(azpy)_2(H_2O)_2]^{2+}$, pronounced similarities were observed between the two systems. Although the pH dependence of both reactions is different [The $[Ru(azpy)_2(H_2O)(py)]^{2+}$, ($pK_a = 6.88$), is hardly active at pH's greater than pH 7.0], the overall reactivity and selectivity for the already described oxidation products are the same. Also, with $[Ru(azpy)_2(H_2O)(py)]^{2+}$ as a catalyst, octyl-glucuronic acid is formed with high selectivity at acidic pH, whereas at more neutral conditions the 2,3-glycol cleavage product is formed in a considerable amount. The number of turnovers per hour for oxidation and hydrolysis are comparable for both catalysts. Electrochemical studies and studies with Ce(IV), reported by Goswami et al. [11] revealed that the complex $[Ru(azpy)_2(H_2O)(py)]^{2+}$ is oxidized by a reversible two-electron/two-proton electrode process into a Ru(IV)–oxo complex (E°_{298} 1.15 V vs. SCE). The similarities in the catalytic activity and selectivity between the $[Ru(azpy)_2(H_2O)_2]^{2+}$ and the $[Ru(azpy)_2(H_2O)(py)]^{2+}$ complex lead to the conclusion that a Ru(IV)=O indeed is the active species in the system, using $[Ru(azpy)_2(H_2O)(py)]^{2+}$ as the catalyst, and most probably is the active catalyst in the system, using $[Ru(azpy)_2(H_2O)_2]^{2+}$ as the catalyst. The hydrolysis mechanism is also believed to proceed via a high-valent ruthenium species. The low-valent Ru(II) complex is not able to hydrolyse alkyl glucopyranoside. Only after the addition of $NaBrO_3$ to the reaction mixture, hydrolysis of OGP takes place. Whether the same high-valent species is responsible for the oxidation, as well as the hydrolysis reaction is not clear yet; however, the similar dependence of both reactions on the pH of the reaction mixture suggests that this is the case.

Because of the existence of at least two reaction paths (i.e. hydrolysis and oxidation), interpretation of kinetic data is difficult. To obtain thermodynamic parameters, oxidation experiments of OGP were performed at different temperatures. When the initial rate of overall disappearance of OGP (oxidation and hydrolysis) is plotted at different temperatures as in an Eyring plot, a linear relation is obtained, yielding a $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ at 298 K of respectively 384.9 J mol^{-1} K^{-1} and -129.7 J mol^{-1} K^{-1}. The negative entropy value indicates that the rate-limiting step observed for the OGP oxidation by system I involves an increase in organisation of the transition state as compared to the ground state. However, when separate Eyring plots are made for the hydrolysis and oxidation, linear relations are not obtained, suggesting the involvement of pre-equilibria. The hydrolysis reaction was found to be more sensitive to temperature changes than the oxidation reaction. This could be explained by the amount of an extra entropy profit, gained by the increase of the number of molecules, which is caused by the hydrolysis of OGP.

3.3. Oxidation of other alcohols, catalyzed by $[Ru(azpy)_2(H_2O)_2]^{2+}$

Data for the oxidation of 1-octanol, cyclohexylmethanol (CHM), cyclobutanol, cyclohexanol, glycerol and cyclohexane with $NaBrO_3$, catalyzed by $[Ru(azpy)_2(H_2O)_2]^{2+}$ are summarized in Table 2.

As can be seen from the results, cyclohexanol, a secondary alcohol, is not very reactive in the catalytic system, while cyclobutanol, another secondary alcohol, is quite reactive. Cyclohexylmethanol is converted completely to cyclohexylcarboxylic acid and octanol is oxidized to its corresponding acid via the aldehyde form.

Table 2
Oxidation of several substrates by system I

Substrate	Conditions	Products (yields)
cyclobutanol	24 h, RT	cyclobutanone (100%)
cyclohexanol [a]	24 h, 60°C	cyclohexanone (14%)
cyclohexylmethanol [a]	24 h, 60°C	cyclohexylcarboxylic acid (100%)
octanol[a]	24 h, 60°C	octanoic acid (85%) octanal (7%)
glycerol [b]	4 h, 60°C	glyceric acid (14.8%) hydroxyacetic acid (17.8%)
cyclohexane [a]	24 h, 60°C	cyclohexanol (trace)

[a] Tetraphenylphosphanium chloride had to be added to these reactions to increase solubility.
[b] Longer reaction times will lead to more degradation into hydroxyacetic acid.

Glycerol is partly oxidized to glyceric acid, but unfortunately hydroxyacetic acid is a major side product. Detailed mechanistic studies by Meyer and co-workers [5,20] have identified two possible pathways for the oxidation of alcohols by ruthenium–oxo complexes, either a hydrogen atom pathway, or a hydride transfer. If one of these two pathways were operative for the $[Ru(azpy)_2(H_2O)(O)]^{2+}$ complex, one would expect a higher reactivity for a secondary alcohol, like cyclohexanol, than for a primary alcohol like cyclohexylmethanol. The inverted rates observed for the oxidation of cyclohexanol and cyclohexylmethanol (Table 2) by system I might well be a consequence of steric hindrance between the secondary alcohol and the ruthenium complex in the transition state, which has been postulated earlier [21,22]. When a less sterically hindered secondary alcohol like cyclobutanol is reacted, the expected high reactivity of a secondary alcohol compared to a primary alcohol like cyclohexylmethanol is found. When the data in Table 2 are compared with results in the literature [5,20,21,23] for the catalytic oxidation of this kind of alcohols, it can be concluded that, $[Ru(azpy)_2(H_2O)_2]^{2+}$ appears to be quite a stable catalyst, able to perform a large number of turnovers without being deactivated (>1000 turnovers for the oxidation of CHM). The same pH dependence of the activity of the catalyst as was observed in the oxidation of OGP, was also found in the oxidation of cyclohexylmethanol. This indicates that the pH dependence of the catalytic reactivity in the oxidation of OGP by $[Ru(azpy)_2(H_2O)_2]^{2+}$ is not caused by specific substrate–catalyst interactions, but is the same for different substrates and, therefore, characteristic for the catalyst.

3.4. Oxidation of OGP, catalyzed by $[Ru(naz)_2(H_2O)_2]^{2+}$

Synthesis and analysis of $[Ru(naz)_2(H_2O)_2]^{2+}$

Krause et al. [13] have demonstrated that naz is a stronger π acid than azpy and that this property is reflected in its complexes. The complex of *tc*-$[Ru(naz)_2Cl_2]$ was synthesized and characterized and it was reported that $[Ru(naz)_2Cl_2]$ undergoes very slow chloride substitution, due to the stronger π-acceptor properties of naz [13]. Despite this we were able to isolate and characterize the *tc*-$[Ru(naz)_2(H_2O)_2](ClO_4)_2$ complex, although a slight isomerisation to the *cc* isomer could not be prevented. Therefore the oxidation experiments, which are described below, had to be performed with a mixture of the *tc* and *cc* isomer ($tc/cc=9$). The two pK_a's of the water dehydronation equilibria of the *tc*-$[Ru(naz)_2(H_2O)_2](ClO_4)_2$ complex have been determined spectrophotometrically as pK_{a1}, 7.6 ± 0.2 and pK_{a2}, 8.7 ± 0.1.

Oxidation of OGP, catalyzed by $[Ru(naz)_2(H_2O)_2]^{2+}$

The results of the oxidation of OGP, catalyzed by $[Ru(naz)_2(H_2O)_2]^{2+}$ are reported in Table 1 and Fig. 3. Striking differences are observed between the above results with

$[Ru(azpy)_2(H_2O)_2]^{2+}$ (system I) and with $[Ru(naz)_2(H_2O)_2]^{2+}$ (system II) as a catalyst. First the pH dependence of the catalytic activity is completely different for the two systems. Whereas system I has its maximum activity around pH 7, system II has an increasing oxidation and hydrolysis reactivity with increasing pH from 3 to 10. In fact only a small difference in pH dependence was expected (i.e. a shift of the maximum reactivity towards a higher pH, due to the higher pK_a's of the complex in system II). The observed pH dependence of the $[Ru(naz)_2(H_2O)_2]^{2+}$ complex strongly suggests that the molecular interaction between the sugar and the catalyst is different in system I compared to system II. The only chemical difference between the two catalysts lies in the NO_2 group at the para position of the phenyl ring. This substituent will not induce a different three-dimensional catalyst structure; however, interactions between the NO_2 group on the catalyst and hydroxy groups on the sugar could lead to different interactions between the sugar and the catalyst (i.e. hydrogen bridging, polar interactions). An interesting observation has been made with system II, at pH 3.0. At this pH system II has a considerable higher reactivity than system I, while conserving a high selectivity for the oxidation reaction compared to the hydrolysis reaction. After 45 minutes of reaction, 20% of OGP is converted into 19.6% of octylglucuronic acid with only 0.4% of hydrolysis products. This result is a major improvement using $[Ru(azpy)_2(H_2O)_2]^{2+}$ as the catalyst, which gives only 0.9% of conversion after 45 min under the same conditions.

To investigate the influence of the different isomeric forms of the catalyst on the catalytic activity, several oxidation experiments were performed with other ratio's of *cc* and *tc* isomer. These experiments proved that the different isomeric forms did not differ much in reactivity or selectivity. Only a small increase in hydrolysis activity compared to oxidation activity for the *cc* isomer compared to the *tc* isomer could be observed. Oxidation of cyclobutanol by system II, did only yield cyclobutanone at neutral and basic pH, but at pH 3 a small amount of crotonaldehyde (16%) could be detected next to 84% of cyclobutanone. This experiment suggests that both an one-electron (leading to crotonaldehyde and a two-electron mechanism (leading to cyclobutanone) are operative in the oxidation step at acidic pH and that the oxidation mechanism therefore is likely to be more complicated than that in system I.

In conclusion, it can be stated that changing a ruthenium–azpy complex into an isostructural ruthenium complex containing a ligand that has better π-accepting properties may result in a major change in pH dependence of the catalytic reactivity and selectivity of the specific complex. For the present specific system the change in ligand results in a higher catalytic oxidation reactivity at pH 3.0 for $[Ru(naz)_2(H_2O)_2]^{2+}$ compared to $[Ru(azpy)_2(H_2O)_2]^{2+}$, with a minimum amount of hydrolysis activity.

3.5. Oxidation of OGP, catalyzed by $[Ru(terpy)(azpy)(H_2O)]^{2+}$ and $[Ru(terpy)(naz)(H_2O)]^{2+}$

Synthesis and properties of the catalysts

To investigate the influence of a terpyridine ligand on the catalytic oxidation reactivity of a ruthenium complex, two novel ruthenium complex species. $[Ru(terpy)L(H_2O)]^{2+}$, where L is azpy or naz, were synthesized via the chloride derivatives. The complexes have been analyzed and characterized by ^1H NMR spectroscopy and elemental analysis as described above. Both the chloride- and aqua-form of the complexes were subjected to cyclic voltammetric studies. The

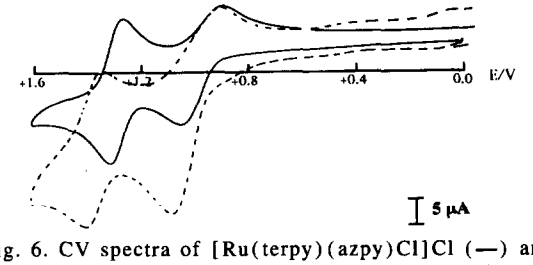

Fig. 6. CV spectra of [Ru(terpy)(azpy)Cl]Cl (—) and [Ru(terpy)(naz)Cl]Cl (- - -) in CH_3CN with $(C_4H_9)_4N^+(PF_6)$. Scan rate 100 mV/s. Reference electrode Ag/AgCl (for details, see Experimental).

[Ru(terpy)(azpy)Cl]Cl and [Ru(terpy)(naz)Cl]Cl complex gave both a response in acetonitrile/TBAP (tetrabutylammonium hexafluorophosphate) solution near +1.0 V vs. Ag/AgCl (see Fig. 6), which can be attributed to chloride oxidation [24].

A second response is found for both complexes at 1.30 V vs. Ag/AgCl for the azpy derivative and 1.40 V vs. Ag/AgCl for the naz derivative. Those couples yield a peak separation of 60–70 mV, depending on the scan rate, and show a linear relation between the current and the square root of the scan rate, indicating a (quasi) reversible one-electron transfer. This response can be attributed to the Ru(II)/Ru(III) couple. Literature examples, like [Ru(terpy)(phen)Cl](PF$_6$) (phen = phenanthroline) and [Ru(terpy)(bpy)Cl](PF$_6$) (bpy = bipyridine), show the presence of a reversible redox couple, Ru(II) to Ru(III) at 0.84 V [20] and 0.83 V vs. Ag/AgCl [25], respectively. The replacement of a bipyridine ligand by an azpy or naz ligand causes a large anodic shift of 470 mV and 560 mV, respectively. The reason for this increase of the Ru(II)/Ru(III) couple, indicating an increase of stabilization of Ru(II) relative to Ru(III), is the stronger π-acid properties of azo-containing ligands [10], compared to the bipyridine ligand.

Also the cyclic voltammetric behaviour of both [Ru(terpy)(azpy)(H$_2$O)]$^{2+}$ and [Ru(terpy)(naz)(H$_2$O)]$^{2+}$ in phosphate buffer were studied. The [Ru(terpy)(azpy)(H$_2$O)]$^{2+}$ and the [Ru(terpy)(naz)(H$_2$O)]$^{2+}$ complexes both gave a chemically irreversible response at, respectively, 0.85 V and 0.95 V vs. SCE (pH 7.0, 0.1 M phosphate buffer). To study the irreversibility of the complex, the [Ru(II)(terpy)(azpy)(H$_2$O)]$^{2+}$ complex was electrolysed (electrolysis at 1.25 V for 4 h) and analyzed by ^{1}NMR spectroscopy, which showed severe oxidative degradation of the ligand (no details of the products were studied).

Oxidation of OGP, catalyzed by [Ru(terpy)(azpy)(H$_2$O)]$^{2+}$ and [Ru(terpy)(naz)(H$_2$O)]$^{2+}$

The oxidation results with both terpyridine containing catalysts are included in Table 1. Both catalysts in general appear less reactive than the [Ru(azpy)$_2$(H$_2$O)$_2$]$^{2+}$ and [Ru(naz)$_2$(H$_2$O)$_2$]$^{2+}$ complexes. In fact [Ru(terpy)(azpy)(H$_2$O)]$^{2+}$ (system III) is not an active catalyst, yielding only low amounts of oxidized and hydrolyzed products. On the other hand [Ru(terpy)(naz)(H$_2$O)]$^{2+}$ (system IV) is more reactive than the azpy derivative. Especially at neutral to basic pH conditions the oxidation and hydrolysis activity is quite high, although it is lower than that of its [Ru(naz)$_2$(H$_2$O)$_2$]$^{2+}$ counterpart. The different pH dependencies which were observed with system I (containing [Ru(azpy)$_2$(H$_2$O)$_2$]$^{2+}$, maximum reactivity around neutral pH) and system II (containing [Ru(naz)$_2$(H$_2$O)$_2$]$^{2+}$, maximum reactivity at basic pH) are also observed with the terpyridine derivatives. System III has its optimum activity around pH7 and is virtually inactive at acidic and basic conditions, while system IV has its optimum activity at more alkaline conditions.

In summary, one could state that the terpyridine derivatives show similar catalytic selectivity characteristics as the diaqua complexes described above, but that they are (much) less active. This could be due to the fact that the ruthenium site is more sterically hindered by the terpyridine ligand, or by oxidative degradation of the complex under the reaction conditions, as in fact could be shown by electrolysis. The naz derivative is more reactive than the azpy derivative, as would be expected from its better π-accepting properties.

4. Conclusions

The oxidation of octyl α-D-glucopyranoside, catalyzed by several ruthenium polypyridyl complexes was investigated. $[Ru(azpy)_2(H_2O)_2]^{2+}$ (system I) and $[Ru(naz)_2(H_2O)_2]^{2+}$ (system II) were found to be active catalysts for oxidation and hydrolysis reactions, yielding primarily octyl glucuronic acid (at acidic pH) and a 2,3-glycol cleavage product (at basic pH) as oxidation products from octyl α-D-glucopyranoside, and octanol and glucose as hydrolysis products. Also simple aliphatic alcohols can easily be oxidized, catalyzed by system I using $NaBrO_3$ as a co-oxidant. Both complexes are stable catalysts and are able to perform a large number of turnovers. Mechanistic studies on the oxidation reaction with $[Ru(azpy)_2(H_2O)_2]^{2+}$ suggest that $[Ru(azpy)_2(H_2O)(O)]^{2+}$ is the active species in the oxidation cycle.

$[Ru(terpy)(azpy)(H_2O)]^{2+}$ and $[Ru(terpy)(naz)(H_2O)]^{2+}$, two new complexes, were synthesized, characterized and tested for their oxidative abilities. Both complexes proved to be less active than the complexes used in system I and II, although the $[Ru(terpy)(naz)(H_2O)]^{2+}$ complex was more active than the $[Ru(terpy)(azpy)(H_2O)]^{2+}$ complex. As deduced from electrolysis, this decrease in reactivity could be caused by a less accessible ruthenium site, or from instability of the complex under oxidative conditions.

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