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Sonocatalysis of the TEMPO-mediated oxidation of glucosides

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Abstract

Ultrasound is shown to increase the rate of the TEMPO-mediated oxidation of methyl α-D-glucopyranoside or sucrose in the presence of stoichiometric amounts of sodium hypochlorite in basic aqueous medium. The reaction can then occur without the usually necessary sodium bromide, showing that ultrasound acts at the level of the formation of the nitrosonium ion, the active oxidizing species in the catalytic cycle. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

The obtention of uronic acids by selective chemical oxidation of the primary alcohols of carbohydrates has mainly been achieved with oxygen by heterogeneous catalysis over platinum [1–5]. Other attempts include electrocatalyzed oxidation [6,7] as well as bioconversions [8]. An alternative method is the TEMPO-mediated oxidation using sodium hypochlorite. This oxidation reaction is based on the reactivity of nitrosonium ions towards alcohols [9,10], further developed in a catalytic manner involving stable nitroxyl radicals such as TEMPO [11,12], and extended recently for asymmetric oxidation using a chiral analog [13]. This method was applied to carbohydrates, e.g., for the oxidation of glucosides (partially protected or unprotected) and developed by van Bekkum et al. in the case of polysaccharides [14–17]. If bleach is used, the reaction can be achieved in water, but requires bromide ions for the crucial nitrosonium formation step [10,16,18]. However, the exact role of the bromide ions is not clear. Notably, it was wondered whether other intermediate species, and in particular radicals, might be involved in the nitrosonium formation.

2. Discussion

Our group is pursuing efforts directed towards the development of new methods for the chemical utilization of sucrose as a raw material

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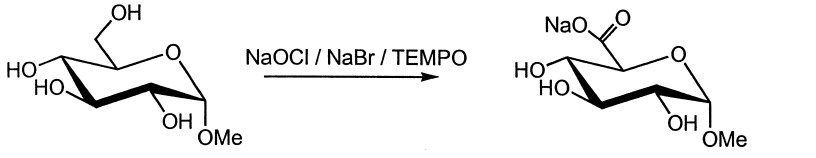
[19–21]. The potential applications of oxidized carbohydrates are mostly due to the salt complexation properties provided by the carboxylic acid functions [22–24]. This study is part of our exploration of the use of ultrasound in carbohydrate chemistry, after the work concerning the oligomerization of glucose under Fischer glycosylation conditions, in which ultrasound acted through its mechanical effects [20]. Because ultrasound is known to influence the outcome of reactions involving radical species or having single electron transfer mechanisms [25,26], and because the sonolysis of water produces oxidizing radical species, we have studied the influence of ultrasound on the oxidation of methyl α-D-glucoside and sucrose by the NaOCl/TEMPO system in basic aqueous medium.

We applied to methyl α-D-glucoside the conditions used by van Bekkum et al. Thus, reaction in water in the presence of sodium hypochlorite sodium bromide and TEMPO (respectively 2.2 equiv., 0.4 equiv. and 0.0065 equiv. per primary hydroxyl group), maintained at pH 10.5 by addition of sodium hydroxide (pH-stat) was studied under silent conditions or using ultrasound irradiation at temperatures around 5°C (Scheme 1). The reaction was followed by measuring the rate of sodium hydroxide addition which is directly connected with the oxidation reaction rate. An obvious rate enhancement was observed for the sonochemical experiment compared to the classical one. The products were identified by carbon NMR of the crude reaction medium, after quenching the excess oxidant by addition of ethanol, neutralization, and evaporation of the solvents.

To minimize the side reactions involving oxygen, the reactions were achieved under argon. The rate of sodium hydroxide addition describes a curve, in which it can be measured a maximum rate (highest slope) just after a latence delay, corresponding likely to the formation of enough nitrosonium species to start the process. In Fig. 1, a curve in the case of the reaction achieved under ultrasound and the classical reaction performed at the same temperature (5 ± 2°C) is depicted. As soon as the theoretical amount of base is added (corresponding to stoichiometric titration of the acids produced), the reaction is quenched and the residue is freeze-dried from an aqueous solution. NMR spectra were recorded and analytical ion exchange chromatography separation allowed identification of the product, as well as the conversion ratio of the starting glucoside and the analytical yield of the obtained uronic acid, after calibration with an authentic sample.

In Table 1, the results of the study of the influence of the acoustic power, the probe diameter and the frequency are reported. Glucoside conversion is nearly total, but the analytical yields are not exceeding ca. 75%. In all cases, the reaction rate increased when ultrasonic irradiation was applied. The same changes in the ultrasound characteristics was shown to promote consistent effects on the production of radicals, as it can be measured by the hydrogen peroxide formation rate, due to the sonolysis of water. This does not necessarily mean that H · or OH ·



sodium (methyl α-D-glucopyranosid)uronate

Scheme 1.

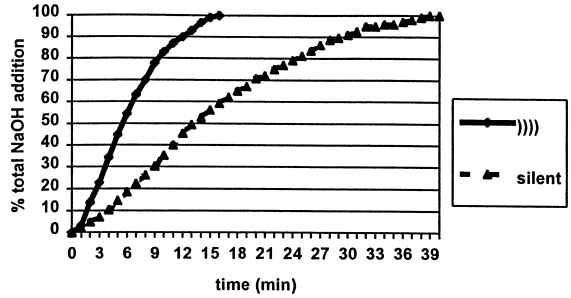


Fig. 1. Evolution of base addition as a function of time for the oxidation of methyl α-D-glucoside under classical conditions or using 500 kHz ultrasonic irradiation.

radicals are responsible for the rate enhancement, but the implication of the cavitation phenomenon is ascertained since its modulation leads to changes in the outcome of the oxidation reaction. Applying a higher frequency increases the rate acceleration, albeit to the detriment of the yield, except in an experiment performed under oxygen. This is consistent with the trapping of H · radicals by oxygen, preventing side reactions, even though more radicals are produced [27]. Under argon, the probe diameter is shown to have a crucial effect on the rate of the oxidation, and can again be connected with the generation of radical species measured by the rate of formation of hydrogen peroxide.

The same obvious rate enhancements were observed in the case of the sono-oxidation of sucrose (Table 2). The obtained tricarboxysucrose salts were quantified by analytical ion exchange chromatography. In order to calibrate the analytical system, an authentic sample was prepared from the fully protected trimethylester pentaacetate. Basic treatment (methanol/triethylamine/water) of the protected triester followed by coevaporation with water led to the triethylammonium salt of the triacid free from any other salt. The pure triester was prepared in low yield from a mixture of acids (mono-, di- and tri-) obtained by the Pt/O_2 system, by reaction with excess methyl iodide in dimethylformamide. After chromatographic purification at this stage and after acetylation (Ac_2O, Py), a small, although sufficient, amount of the protected derivative could be obtained for characterization and calibration. It was also verified that the same synthetic sequence led to the protected derivative (MPAST) from a crude TEMPO/NaOCl reaction (Scheme 2).

Table 1
Oxidation of methyl α-D-glucoside to sodium (methyl α-D-glucopyranosid)uronate: influence of ultrasound on the rate and yield of the reaction[a]

Acoustic power[b] (W/ml)	Probe diameter (mm)	Frequency (MHz)	H_2O_2 formation rate[c] (μmol/l min)	NaOH addition rate[d] (ml/min)	Yield (%)
–	–	–	–	0.7 *(0.8)*[e]	74 *(73)*[e]
0.008	35	500	0.1	0.6	76
0.03	35	500	0.3	0.7	67
0.07	35	500	1.1	1.1	68
0.12	35	500	2.3	1.4	67
0.15	35	500	3.1	1.4	73
0.22	35	500	4.0	2.0 *(1.9)*[e]	63 *(73)*[e]
0.21	35	20	3.9	2.0	67
0.21	25	20	2.1	1.1	87
0.26	13	20	0.6	0.9 *(1.3)*[e]	74 *(76)*[e]

[a]All reactions were conducted at 5 ± 2°C, using 0.65 mol% of TEMPO, 0.4 equiv. of NaBr, 2.2 equiv. of NaOCl, at pH 10.5 (pH-stat, 0.5 M NaOH), in water (0.04 M in primary alcohol), with argon degassing except otherwise noted.
[b]Determined by calorimetry.
[c]Measured by oxidation of I^- and I_3^- UV assay.
[d]Maximum slope of the curve (see text).
[e]In brackets are given the results corresponding to the reaction conducted under oxygen.

Table 2
Reaction of sucrose at 5 ± 2°C using 0.4 equiv. of NaBr[a]

Sucrose concentration (mM)	NaOCl (equiv.)[a]	TEMPO (equiv.)[a]	Conditions	Rate[b] (ml of NaOH/min)	Yield[c] (%)
40	2.2	0.0065	silent	0.8	58
40	2.2	0.0065	20 kHz	1.0	59
40	2.2	0.0065	500 kHz	1.9	80

[a]Based on primary hydroxyl groups.
[b]Maximum slope of the curve.
[c]Analytical yield (ion exchange chromatography) in sucrose tricarboxylate.

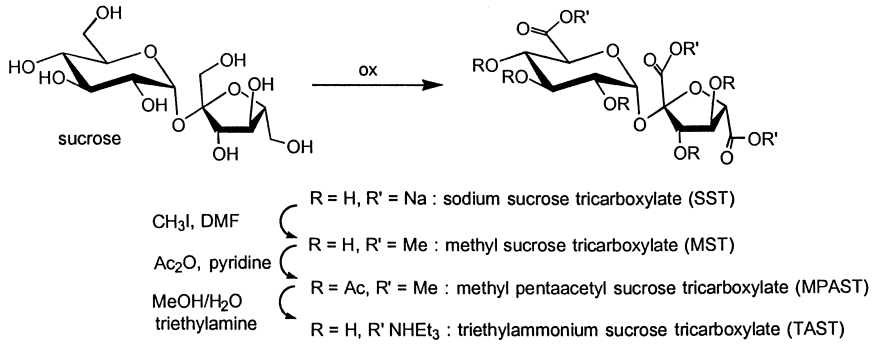
Finally, we observed that under ultrasound, *oxidation could occur in absence of sodium bromide*, whereas under silent conditions, the reaction is extremely sluggish. Furthermore, pretreatment of the oxidants by ultrasound prior addition of the carbohydrate substrate led to a significant rate increases compared to the regular conditions. Further work is currently in progress in our laboratory concerning the optimization of the sonochemical reaction and the full structural study of the sucrose oxidation products.

3. Conclusion

We confirm that the oxidation of sucrose can be achieved in good yields using the NaOCl/TEMPO/NaBr system, as it was known for other glucosides. We show that ultrasound increases the rate of the reaction. Our hypothesis is that the sonocatalysis is related with an easier formation of the nitrosonium ion from the stable radical TEMPO. These observation might suggest new clues on the role of the bromide ions in the catalytic process.

3.1. General procedure for the oxidation reactions

The reaction volume is 200 ml. A derivation to a second flask allows the permanent presence of the electrode of the pH-stat without any risk of deterioration due to ultrasound. To a solution of the carbohydrate (8 mmol of primary hydroxyl group, i.e., 1.55 g of methyl α-D-glucopyranoside or 0.91 g of sucrose) was added NaBr (0.32 g, 0.4 equiv. compared to primary hydroxyl groups) and TEMPO (8 mg, 0.65 mol% compared to primary hydroxyl groups). A ca. 12% NaOCl solution (typically 8.5 ml, 2.2 equiv. compared to primary hydroxyl groups) was adjusted at pH 10.5 first by addition of 4 M HCl, and eventually by addition of 0.5 M NaOH. The



Scheme 2.

reaction temperature was maintained at 5 ± 2°C and the pH was constant by addition of 0.5 M NaOH. The reaction was stopped by quenching excess oxidant with ethanol (10 ml) and the mixture was neutralized by addition of 4 M HCl. The resulting solution was then concentrated, freeze-dried and further analyzed by ion exchange chromatography and NMR. Analytical ion exchange chromatography was performed on a DIONEX DX-500 chromatograph using a Carbopac PA1 column (4×250 mm) with electrochemical detection (PED) in pulse amperometric mode (Au and Ag/AgCl electrodes, with a $+0.1$ V, $+0.6$ V, -0.8 V pulsation cycle) and elution with NaOH and AcONa mixtures. For the experiments at 20 kHz, the ultrasound generator was a 300-W (electric power) Vibra-Cell apparatus, coupled with titanium horns having a 13, 25 or 35 mm diameter (0.1 to 0.6 W/ml acoustic power). Acoustic power was evaluated by calorimetric measurement. For the 500 MHz experiments, the transductor was a lead titanate–zirconate ceramic pasted together with a stainless steel plate (35 mm diameter, 0.08 to 0.22 W/ml acoustic power). The structure of sodium (methyl α-D-glucopyranoside) uronate was confirmed by comparison with an authentic sample (lit. Ref. [16]). The structure of sucrose tricarboxylate was assessed after full characterization of the peracetylated trimethyl ester (MPAST, methyl (dimethyl 3,4-di-*O*-acetyl-β-D-fructofuranosylarate 2,3,4-tri-*O*-acetyl-α-D-glucopyranosid)uronate). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.04, 2.05, 2.08, 2.11, 2.21 (5 s, 15 H, 5 Ac), 3.75, 3.77, 3.81 (3 s, 9 H, 3 CO_2Me), 4.56 (d, 1H, $J_{4',5'}$ 6.5 Hz, H-5′), 4.63 (d, 1 H, $J_{4,5}$ 10.3, H-5), 4.90 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 10.4 Hz, H-2), 5.13 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-4), 5.51 (d, 1 H, $J_{3',4'}$ 6.6 Hz, H-3′), 5.54 (t, 1 H, H-3), 5.65 (t, 1 H, H-4′), 5.93 (d, 1 H, H-1); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.0, 20.4, 20.5, 20.6 (5 Ac), 52.6, 52.8, 53.2 (3 OMe), 68.4, 69.0, 69.2, 69.7, 75.4, 78.3, 78.7 (C-2,3,4,5,3′,4′,5′), 92.1 (C-1), 101.1 (C-2′), 166.1, 167.9, 168.2 (C-6,1′,6′), 169.5, 169.6, 169.7, 169.8, 170.2 (5 Ac), 174.7 (C-1′), 175.9, 176.9 (C-6,6′). Anal. Calcd for $C_{25}O_{19}H_{32}$: C: 47.18; H: 5.07. Found: C: 47.08; H: 5.09. (Table 2)

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