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1 Activation of TEMPO by ClO₂ for Oxidation 2 of Cellulose by Hypochlorite - Fundamental 3 and Practical Aspects of the Catalytic 4 System

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21 *ABSTRACT*

22 Bromine-free TEMPO-catalyzed oxidation of the primary alcohols by sodium hypochlorite (NaOCl) does
23 not proceed without a prior activation of the catalyst. Here we demonstrate an immediate *in situ*
24 activation of the catalyst with an equimolar addition of chlorine dioxide (ClO₂) relative to TEMPO.
25 Sodium bromide (NaBr) had a similar role in activating the catalyst although NaBr was needed in excess
26 and the activation took several minutes depending on the dosage of NaBr. The activation method, or
27 the concentration of NaBr, did not affect the bulk oxidation rate. The selectivity of the ClO₂ initiated
28 oxidation remained high up to NaOCl addition of 3 mol/kg bleached birch kraft pulp after which
29 additional loss in yield and depolymerization of cellulose were emphasized with negligible increase in
30 carboxylate content. A carboxylate content of 0.8-1 mol/kg, sufficient for easy mechanical fibrillation
31 of the pulp, was achieved under mild conditions with NaOCl addition of 2-2.5 mol/kg pulp.

32 **Keywords:** birch pulp, cellulose, carboxylates, bromide-free, ClO₂ activated TEMPO-mediated
33 oxidation, UV-Vis spectrometry

34 **Chemical compounds studied in this article:**

35	2,2,6,6-tetramethyl-1-piperidinyloxy	(PubChem CID: 2724126)
36	Chlorine dioxide	(PubChem CID: 24870)
37	Sodium hypochlorite	(PubChem CID: 23665760)
38	Sodium chlorite	(PubChem CID: 23668197)
39	Sodium hydroxide	(PubChem CID: 14798)
40	Hydrochloric acid	(PubChem CID: 313)

42 **1. Introduction**

43 The highly selective nitroxyl radical mediated oxidation of hydroxymethyl groups of
44 polysaccharides was introduced already two decades ago (Davis & Flitsch, 1993; de Nooy, Besemer, &
45 van Bekkum, 1994; de Nooy, Besemer, & van Bekkum, 1995a; de Nooy & Besemer, 1995b; Kitaoka,
46 Isogai, & Onabe, 1999; Rozantsev & Sholle, 1971). A catalytic amount of 2,2,6,6-tetramethyl-1-
47 piperidinyloxy (TEMPO) radical, some sodium bromide (NaBr) and an excess of sodium hypochlorite
48 (NaOCl) are required to selectively convert the primary alcohols to aldehydes and further to
49 carboxylates. More recently fibrillation of TEMPO/NaBr/NaOCl oxidized pulps was described to yield
50 nanofibrillated cellulose (NFC) gels, a discovery that has been widely applied in science and cellulose-
51 based materials development since then (Isogai, A, Saito, & Fukuzumi, 2011; Iwamoto, et al., 2010;
52 Saito, Okita, Nge, Sugiyama, & Isogai, 2006; Saito & Isogai; 2004, Saito, Shibata, Isogai, Suguri, &
53 Sumikawa, 2005). The extensively oxidized, negatively charged pulps are easy to disintegrate which
54 radically reduces energy use compared to fibrillation of unmodified pulps (Isogai, A, et al., 2011).

55 Hypobromite, which is formed in a reaction between NaBr and NaOCl, has been claimed to
56 convert the reduced form of TEMPO, the hydroxylamine (TEMPOH), to its oxidized form, the
57 nitrosonium ion (TEMPO⁺), that is the actual oxidant of the primary alcohol groups (Isogai, et al., 2011).
58 To oxidize most of the available hydroxymethyl groups, a large excess of NaOCl is needed, typically
59 more than twice the amount calculated from the reaction stoichiometry (Iwamoto, et al., 2010).
60 Alkaline mixtures of hypochlorite and hypobromite are somewhat unstable (Lewin & Avrahami, 1955),

and part of the added bromide is inactivated during the catalytic oxidation. Thus, rather significant amounts of NaBr are required, which is a challenge for industrial application of the process (Bragd, et.al., 2000).

To overcome the use of bromide several modifications of the original reaction system have been presented. TEMPO can be activated for oxidation without bromide by cyclic voltammetry. However, the electro-mediated oxidation is slow which reduces its applicability (Isogai, T, Saito, & Isogai, A, 2010; Isogai, T, Saito, & Isogai, A, 2011). Low reactivity is also a drawback in the proposed bromide-free catalytic oxidation by sodium chlorite (TEMPO/NaOCl/NaClO₂) under slightly acidic or neutral conditions (pH 3.5-6.8) (Hirota, Tamura, Saito, & Isogai, 2009; Saito, et al., 2009; Saito, Hirota, Tamura, & Isogai, 2010; Tanaka, Saito, & Isogai, 2012). In this system chlorous acid (HClO₂) oxidizes stoichiometrically the initially formed aldehydes to carboxylates which releases an equimolar amount of hypochlorous acid (HOCl) (Lehtimaa, et al., 2010; Chinake, Olojo, & Simoyi, 1998; Isbell & Sniegowski, 1964; Isogai & Saito, 2010; Jeanes & Isbell, 1941; Launer & Tomimatsu, 1959; Launer & Tomimatsu, 1954; Stitt, Friedlander, Lewis, & Young 1954). The oxidation of aldehydes is fastest at low pH (<2) where the equilibrium concentration of the less reactive chlorite ion is low (Lehtimaa, Kuitunen, Tarvo, & Vuorinen, 2010).

Another possibility to eliminate the use of bromide is to apply a separate pretreatment to convert TEMPO to TEMPO⁺ with hypochlorous acid prior to mixing the catalyst with the pulp and NaOCl (Pääkkönen et al., 2015). The efficiency of the catalysis could potentially decrease with time since TEMPO⁺ and TEMPOH can react with each other to form TEMPO (Israeli, et al., 2005; Sen and Golubev, 2009). The rate of this comproportionation reaction increases as a function of pH (Israeli, et al., 2005). However, it was recently shown that the catalyst exists almost exclusively as TEMPO⁺ during the

catalytic oxidation of cellulose, both in the presence and absence of bromide, and therefore the initial activation of TEMPO should be sufficient to maintain the high reactivity throughout the oxidation (Pääkkönen, et al., 2015).

The use of TEMPO with chlorine dioxide (ClO_2) as the bulk reagent to oxidize softwood kraft pulp has also been reported (Komen, Weerawarna, & Jewell, 2006). Because ClO_2 reacts very fast with TEMPO (Ganiev, et al., 1999; Ganiev, et al., 2001), we decided to study this reaction as a means to initiate the TEMPO-mediated oxidation of cellulose with NaOCl . First we studied the stoichiometry of the initiation and then applied it in the oxidation of both simple alcohols (1-propanol, 2-propanol) and a kraft pulp. These experiments enabled us to draw general conclusions on the initiation and selectivity of TEMPO-catalyzed oxidation of cellulose.

2. Experimental

2.1. Materials

Bleached birch kraft pulp (kappa number < 1, xylan content 21.5 %) was obtained from a Finnish pulp mill, TEMPO (Aldrich), ClO_2 water solution (prepared in lab), 3.5 % NaOCl solution (pH over 12, VWR), NaClO_2 (Sigma-Aldrich), n-Propanol (Riedel-deHaen), 1 M NaOH , 1 M HCl , Büchi reactor (volume 1.6 dm^3), Metrohm 718 Stat Titrino titrator (pH adjustment), Metrohm 751 GPD Titrino titrator (conductometric titration), Tiamo 1.2.1. software (conductometric titration), Shimadzu 2550 UV-Vis spectrophotometer and UVProbe 2.32 software. All washings were done with Milli-Q purified water (Millipore Corporation, resistivity 18.2 $\text{M}\Omega\text{cm}$)

102 2.2. Oxidation of bleached birch pulp

103 TEMPO was mixed with ClO_2 water solution in a closed vessel. Despite its low water solubility, TEMPO
104 was dissolved (observed as a color change from red to black) while the radical TEMPO was converted
105 to the nitrosonium ion. The pulp was mixed with water (pulp consistency 1-4 %) and transferred to the
106 Büchi reactor (continuous mixing, temperature 25-50 °C, volume of pulp suspension 1-1.2 dm³). Then,
107 the activated TEMPO solution and NaOCl were added to the reactor. The pH level was adjusted to 8 by
108 1 M NaOH with an automatic titrator after a rapid pH decrease during the beginning of the oxidation.
109 The oxidation rate was followed by iodometric titration until all HOCl had been consumed. The pulp
110 was washed through a wire cloth. The carboxylate content (SCAN-CM 65:02) and the CED-viscosity
111 (SCAN-CM 15:99) were analyzed from the washed pulp samples.

112 2.3. Conversion of residual aldehydes to carboxylates by HClO_2

113 The suspension of the oxidized pulp (1-4 % pulp consistency) was acidified with 1 M HCl to pH 2.
114 NaClO_2 (10 mM initial concentration) was added to the solution and the conversion was executed in a
115 Büchi reactor (2-3 hours, 25-50 °C). The washing and the analysis of the pulp was done by the same
116 procedure described in the previous chapter.

117 2.4. Oxidation tests with model compounds

118 n-Propanol and NaClO were mixed with water in the Büchi reactor at 25 °C. When NaBr was
119 applied, it was added to the reactor right in the beginning. When ClO_2 was applied, it was added after
120 a delay to the mixture. The pH level ascended to 11 after the NaOCl addition and decreased rapidly
121 when the oxidation reaction started. The pH level was adjusted to 10 with 1 M NaOH and an automatic

122 titrator after the rapid decrease of pH. The oxidation rate was followed by iodometric titration until all
123 HOCl was consumed.

124 2.5. Active chlorine titration

125 10 ml of KI solution (80 g/l) and 20 ml of 1 M sulphuric acid were added to an Erlenmeyer flask. A
126 known amount of the sample (unfiltered sample solution from reactor) was added to Erlenmeyer
127 bottle. NaOCl was titrated with iodometric titration.

128 The stoichiometry between chlorine (Cl_2) and the measured hypochlorite (NaOCl) is 1:1. The
129 stoichiometry between chlorine (Cl_2) and the measured chlorite (NaClO_2) is 1:2. The stoichiometry
130 between chlorine (Cl_2) and the measured chlorite (ClO_2) is 1:2.5.

131 2.6. Oxidation of TEMPO with ClO_2

132 Solutions of 1 mM TEMPO and 1 mM ClO_2 were prepared with pure water. The solutions were mixed
133 in 1:1 ratio and monitored for their absorption spectra with a Shimadzu 2550 UV-Vis
134 spectrophotometer.

135 3. Results

136 3.1. The relationship between the dynamics of TEMPO activation and NaBr addition

137 The role of NaBr in converting TEMPO radical to nitrosonium ion was explored in oxidation of n-
138 propanol with hypochlorite (Figure 1). When the concentration of the added NaBr was low enough, the
139 oxidation of the alcohol did not start immediately but an induction period was observed. The length of

140 the induction period was inversely related with the amount of added NaBr. The oxidation of the alcohol
141 proceeded fast after the induction period and the oxidation rate depended little on the concentration
142 of NaBr. Clearly, the bromide accelerated the initial formation of the nitrosonium ion, probably through
143 the formation of HOBr. The insignificance of bromide after the activation could be explained by a fast
144 reoxidation of the hydroxylamine by HOCl (Bragd, et al., 2000; Pääkkönen, et al., 2015). Thus, the key
145 for a bromine-free oxidation by hypochlorite is to apply another activator for the initial conversion of
146 the TEMPO radical

147

148 **Fig. 1.** Consumption of hypochlorite (57 mM) in TEMPO (0.09 mM) mediated oxidation of n-propanol
149 (100 mM) at pH 10 at 25 °C. Three different concentrations of NaBr were applied: 2, 6 and 16 mM.

150

151 3.2. Activation of TEMPO by ClO₂ studied by UV-Vis absorption spectroscopy

152 The TEMPO radical reacted rapidly with ClO₂ at RT (Figure 2A). The yellow color of the ClO₂
153 disappeared immediately when ClO₂ and TEMPO solutions are mixed. The pseudo-first-order rate

154 constant for the reaction between ClO_2 and 0.01 M TEMPO is $3.7 \times 10^5 \text{ s}^{-1}$ according to Ganiev (Ganiev,
155 et al., 2001).

156

157 **Fig. 2.** (a) Absorption spectra of 1 mM TEMPO, 1 mM ClO_2 and an equimolar mixture of these (1 mM
158 each). (b) The difference spectrum of 1 mM 1:1 mixture of TEMPO and ClO_2 and 1 mM TEMPO solution.

159

160 The complete reaction of ClO_2 was verified by the lack of its absorption maximum at 360 nm right
161 after the mixing of ClO_2 and TEMPO. The spectrum of the 1:1 mixture is similar to the spectrum of the
162 nitrosonium ion (Pääkkönen, et al., 2015). The difference spectrum of the reaction mixture and the
163 TEMPO solution had a maximum at 290 nm and a minimum at 245 nm (Figure 2B). According to Israeli
164 (Goldstein, Merenyi, Russo, & Samuni, 2003, Israeli, et al., 2005) the change in the absorption at 290
165 nm can be applied to detect the formation of the oxidized TEMPO while the change in the absorption
166 at 245 nm is related with the decay of the TEMPO radical.

167 3.3. ClO_2 as an activator in TEMPO-catalyzed oxidation of 1-propanol

168 Without using any added NaBr or ClO_2 the catalytic oxidation of 1-propanol was not initiated (Figure
169 3). After adding an equimolar or higher amount of ClO_2 relative to TEMPO the system was activated
170 immediately without any induction phenomenon, and the oxidation proceeded at a high rate and
171 consumed 1.8 equivalents of hypochlorite and 0.84 equivalents of sodium hydroxide at pH 10,
172 corresponding to conversion of 1-propanol mostly to propionic acid. 2-Propanol reacted only slowly
173 under similar conditions.

174

175 **Fig. 3.** Consumption of hypochlorite (60 mM) in TEMPO (0.8 mM) mediated oxidation of 2-propanol (25
176 mM) and mixture of 2-propanol and 1-propanol (25 mM + 25 mM) at pH 10 at 25 °C. No NaBr was used
177 but ClO_2 (1.3 mM) was added at reaction time of 16 min.

178

179 The consumption of NaOCl by 1-propanol depended on pH of the reaction medium (Figure 4). When
180 the ClO_2 activated TEMPO was added in the beginning of the reaction without any delay, one equivalent
181 of NaOCl was consumed in a very short time. At pH 10 the second equivalent of the oxidant was also

182 consumed rapidly while the further oxidation was slow at pH 7 and non-existent at pH 5. Thus, the
 183 oxidation rate of the aldehyde intermediate (propanal) to the acid (propionic acid) depended strongly
 184 on pH of the reaction medium.

185

186 **Fig. 4.** Effect of pH on the consumption of hypochlorite (60 mM) in TEMPO (0.8 mM) mediated oxidation
 187 of 1-propanol (30 mM) at 25 °C. No NaBr was used but TEMPO was activated by final addition of ClO₂
 188 (1.3 mM) that initiated the reaction.

189

190 3.4. ClO₂ activated TEMPO-mediated oxidation of bleached birch pulp

191 When TEMPO was first activated with equimolar amount of ClO₂ and then mixed with the pulp
 192 suspension and hypochlorite, the oxidation started immediately (Figure 5). The initial rate of the
 193 reaction was equal to that of the bromide ion assisted catalytic oxidation. After NaOCl consumption of
 194 ~2 mmol/g pulp the reaction slowed down and continued at ~1/40 of the initial rate (pH 10, 25 °C, 4 %
 195 pulp consistency, NaOCl 5 mmol/g, TEMPO 0.05 mmol/g). At the same conversion, the rate of the
 196 bromide ion (0.3 mmol/g) assisted oxidation decreased to 1/3 of the initial rate. Obviously the

197 accessible hydroxymethyl groups were initially oxidized by the nitrosonium ion while an additional
 198 oxidation of secondary alcohols with HOBr took place afterwards. In the end of the ClO_2 activated and
 199 NaBr assisted oxidations the carboxylate contents of the washed pulps were 1.03 (1.14) and 1.10 (1.34)
 200 mmol/g, respectively (values in parentheses were measured after conversion of residual aldehydes to
 201 carboxylates by HClO_2). The higher carboxylate content after the NaBr assisted oxidation probably
 202 resulted from the formation of cellulose dialdehydes (oxidation at C-2 and C-3) and their further
 203 oxidation into the corresponding carboxylates (Kuramae, Saito, & Isogai, 2014).

204

205 To further illustrate the role of HOBr in the secondary oxidation a small amount of NaBr (2 mM) was
 206 added in ClO_2 activated TEMPO catalyzed oxidation (pH 10, 25 °C, 1 % pulp consistency, NaOCl 4.5
 207 mmol/g, TEMPO 0.08 mmol/g) after NaOCl consumption of 2 mmol/g (Figure 6). The addition
 208 immediately increased the secondary oxidation rate significantly thus verifying the role of HOBr. In the
 209 end of the reaction the carboxylate content of the washed pulp was 1.02 mmol/g.

210

211 **Fig. 5.** Consumption of hypochlorite in TEMPO (2 mM) mediated oxidation of a birch kraft pulp (40 g
 212 pulp/dm³) at pH 10 at 25 °C. TEMPO was activated by ClO_2 prior to mixing with NaOCl or the catalysis
 213 was assisted by NaBr.

Fig. 6. Consumption of hypochlorite in TEMPO (0.8 mM) mediated oxidation of a birch kraft pulp (10 g pulp/dm³) at pH 10 or pH 7 at 25 °C. TEMPO was activated by ClO₂ prior to addition of NaOCl. In one experiment (pH 10, 45 mM NaOCl) NaBr (2 mM) was added at reaction time of 95 min.

The selectivity of the fast initial reaction was studied at low NaOCl charge (pH 10, 25 °C, 1 % pulp consistency, NaOCl 2.0 mmol/g, TEMPO 0.08 mmol/g). In this case the fast NaOCl consumption equaled to 1.0 mmol/g (Figure 6). The aldehyde content of the pulp suspension equaled to 0.20 mmol/g while the carboxylate content of the washed pulp was 0.57 mmol/g (value measured after conversion of residual aldehydes to carboxylates by HClO₂). The untreated pulp had a carboxylate content of 0.06 mmol/g and thus the calculated selectivity of the initial oxidation was estimated to be ~80 % (Δ CHO 0.20 mmol/g, Δ COOH 0.31 mmol/g, Δ NaOCl -1.0 mmol/g). At pH 7 the proportion of the rapidly reacting fraction of NaOCl was somewhat smaller (0.6 mmol/g).

The effect of the dosage of NaOCl on the carboxylate and aldehyde contents were studied at pH 8 at 25 °C (2-4 % pulp consistency, 2-2.5 mM TEMPO) (Figure 7A) (details of these and additional

230 experiments at higher temperatures are summarized in Table S1). The carboxylate content of the
231 oxidized pulp increased as a function NaOCl dosage until reaching a maximum level of ~1.0 mmol/g.
232 The aldehyde content of the pulps was in average ~0.15 mmol/g and was little affected by the amount
233 of NaOCl used. At NaOCl dosages < 3 mmol/g ~65 % of the spent oxidant was consumed in production
234 of aldehyde and carboxylate groups in the pulp (Figure 7B). The effect of NaOCl dosage on the
235 carboxylate formation was also demonstrated by FTIR spectroscopy (Figure S1). The lowest carboxylate
236 content to convert the oxidized pulp into NFC gel by a single pass through a fluidizer was 0.7 mmol/g
237 (without post-oxidation with HClO_2) corresponding to NaOCl charge of 2.2 mmol/g (25 °C, pH 9, 4 %
238 pulp consistency, TEMPO 0.05 mmol/g, reaction time of 80 min). Excessive use of NaOCl (5 mmol /g)
239 led to oxidation of secondary alcohol groups of xylan, C2-C3 bond cleavage of anhydroxylopyranosyl
240 units and formation of the corresponding 'dicarboxylate xylan' as shown by ^{13}C NMR spectroscopy of
241 the solubilized material (Fig. S2).

Fig. 7. (a) Effect of the dosage of NaOCl on the carboxylate and aldehyde contents of pulps oxidized using ClO_2 activated TEMPO as a catalyst. Conditions: pH 8, 25 °C, pulp consistency 2-4 %, 2-2.5 mM TEMPO. (b) Effect of the dosage of NaOCl on its consumption in formation of carboxylate (ΔCOOH) and aldehyde (ΔCHO) groups in pulp during its ClO_2 activated TEMPO-mediated oxidation. Conditions: pH 8, 25 °C, pulp consistency 3-4 %, 2 mM TEMPO. The dotted line denotes the theoretical 100 % selectivity. (c) Effect of the dosage of NaOCl on depolymerization of cellulose, quantified by the increase in $1/\text{DP}$, in pulps oxidized using ClO_2 activated TEMPO as a catalyst. Conditions: pH 8, 25 °C, pulp consistency 2-4 %, 2-2.5 mM TEMPO. (d) Effect of the dosage of NaOCl on yield of cellulose. Conditions: pH 8, 25 °C, pulp consistency 4 %, 2.5 mM TEMPO.

253 The extent of depolymerization of cellulose, characterized by change in $1/DP$, was nearly linearly
254 related with the dosage of NaOCl when it was < 3 mmol/g (Figure 7C). Overdosing of NaOCl led to a
255 rapid decrease in the selectivity and the yield of the oxidation (Figure 7D). The measured yields with
256 the dosage of NaOCl < 3 mmol/g are comparable with the yields (yield > 90 %) at corresponding NaOCl
257 dosages reported with NaBr/TEMPO/NaOCl oxidations of pulp (Isogai, A, Saito, & Fukuzumi, 2011). The
258 rate of depolymerization depended also on pH. Increasing pH from 8 to 9-10 doubled the
259 depolymerization rate, probably due to the alkali-catalyzed β -elimination reaction of the aldehyde (or
260 keto) structures. Due to the sensitivity of the oxidized pulp for β -elimination, the DP of cellulose was
261 always calculated from CED viscosity values measured from pulps stabilized by a post-oxidation by
262 $HClO_2$ that converts aldehydes to carboxylates. Thus the combination of low temperature and pH 8
263 were considered optimal conditions for production of NFC for applications, such as reinforcement, that
264 require a combination of a high viscosity and a high carboxylate content.

265 4. Discussion

266 TEMPO itself is unreactive towards alcohols and therefore its conversion to the nitrosonium ion is
267 needed to initiate the catalytic oxidation. In conventional TEMPO catalyzed oxidation this activation is
268 brought about by HOBr (NaBr + NaOCl). Relatively high NaBr addition is needed to accomplish the
269 activation in a short time. ClO_2 oxidizes TEMPO immediately and a stoichiometric amount of the oxidant
270 is enough to complete the reaction.

271 The TEMPO-mediated oxidation of cellulosic pulps occurs in two phases of different kinetics. In
272 the first stage up to ~ 2 mmol/g of NaOCl is consumed and < 1 mmol/g of the hydroxymethyl groups of

273 cellulose are oxidized to aldehyde and carboxylate groups. This fraction is < 20 % of all hydroxymethyl
274 groups of cellulose (~5 mmol/g) in a typical kraft pulp. The magnitude of the fraction is characteristic
275 for the pulp and does not depend on the activation method of the catalyst.

276 The slower secondary stage may consume lots of NaOCl without significantly increasing the
277 content of oxidized groups in the pulp. Obviously these slower reactions occur mainly in the dissolved
278 material or lead to additional dissolution of hemicelluloses or cellulose. It was recently reported than
279 in the NaBr assisted TEMPO catalyzed oxidation of hardwood pulps the dissolved xylan is almost
280 completely oxidized through cleavage of the C2-C3 bond leading to 2 equivalents of carboxylates per
281 monomer (Kuramae, Saito, & Isogai, 2014). In our bromide-free oxidations the same phenomenon was
282 observed, even though to a smaller extent (Scheme 1).

283 Our results indicate that HOBr is the main oxidant of the secondary alcohols in the conventional
284 oxidation method. When NaBr is not applied, secondary oxidation by HOCl becomes important at pH
285 7-8. This is the pH range where the pH inside the cell wall is optimal for the reaction of polysaccharides
286 with HOCl.

287 The aldehyde content of cellulose stays at a relatively high, constant level throughout the catalytic
288 oxidation. Alkali-catalyzed β -elimination is possibly a reason for why cellulose is depolymerized more
289 extensively when the oxidation is carried out at pH > 8. The stability of the oxidized pulp could be
290 increased with a post-oxidation by HClO₂ that selectively converts the residual aldehydes to the
291 corresponding carboxylates. The oxidation kinetics of 1-propanol led us to expect that a higher pH in
292 the catalytic oxidation should lead to a lower residual aldehyde content. Such an effect was, however,
293 not observed and thus the aldehyde formation still remains partly unresolved.

294

295

296 **Scheme 1.** The proposed and known reaction routes in TEMPO-mediated oxidation of cellulose (R =
 297 CH₂OH) and xylan (R = H) by HOCl and HOBr. a) Oxidation of hydroxymethyl group by TEMPO⁺ to
 298 aldehyde and further to carboxylate groups (Isogai, A, Saito, & Fukuzumi, 2011). b) Oxidation of 2,3-
 299 diols to dicarboxylates by hypohalides (Whistler & Schweiger, 1957; Kuramae, Saito, & Isogai, 2014). c)
 300 Conversion of TEMPO to TEMPO⁺ by ClO₂ or HOBr (Pääkkönen, et al., 2015) and reoxidation of TEMPOH
 301 to TEMPO⁺ by HOCl or HOBr.

302 5. Conclusions

303 Activation of the catalyst is a key step in TEMPO-catalyzed oxidation of cellulose, or primary
304 alcohols in general, by hypochlorite. In the conventional oxidation method, the activation is realized
305 through the addition of NaBr. Alternatively, a stoichiometric amount of ClO_2 can be applied for
306 immediate, *in situ* activation of TEMPO. This approach could be attractive for oxidative modification of
307 cellulosic pulps in mills that use ClO_2 in their bleaching processes. The selectivity of the oxidation
308 remains high up to carboxylate content of 0.8-1.0 mol/kg which enables easy mechanical disintegration
309 of the oxidized pulps to produce gels of fibrillated cellulose.

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313 References

314 Bragd, P. L., Besemer, A.C., & van Bekkum, H. (2000). Bromide-free TEMPO-mediated oxidation
315 of primary alcohol groups in starch and methyl α -D-glucopyranoside. *Carbohydrate Research*, 328,
316 355-363.

317 Chinake, C. R., Olojo, O., & Simoyi, R. H. (1998). Oxidation of formaldehyde by chlorite in basic
318 and slightly acidic media. The *Journal of Physical Chemistry A*, 102, 606-611.

319 Davis, N. J. & Flitsch, S. L. (1993). Selective oxidation of monosaccharide derivatives to uronic
320 acids. *Tetrahedron Letters*, 34, 1181-1184.

321 de Nooy, A. E. J., Besemer, A. C., & van Bakkum, H. (1994). Highly selective tempo mediated
 322 oxidation of primary alcohol groups in polysaccharides. *Recueil des Travaux Chimiques des Pays-Bas*,
 323 113, 165-166.

324 de Nooy, A. E. J., Besemer, A. C., & van Bakkum, H. (1995a). Highly selective nitroxyl radical-
 325 mediated oxidation of primary alcohol groups in water-soluble glucans. *Carbohydrate Research*, 269,
 326 89-98.

327 de Nooy, A. E. J., & Besemer, A. C., (1995b). Selective oxidation of primary alcohols mediated
 328 by nitroxyl radical in aqueous solution. Kinetics and mechanism. *Tetrahedron*, 51, 8023-8032.

329 Ganiev, I. M., Timerghazin, Q. K., Khalizov, A. F., Andriyashina, N. M., Shereshovets, V. V.,
 330 Volodarsky, L.B., & Tolstikov, G.A. (1999). Complexes of chlorine dioxide with nitroxyl radicals.
 331 *Tetrahedron Letters*, 40, 4737-4740.

332 Ganiev, I. M., Timerghazin, Q. K., Khalizov, A. F., Shereshovets, V. V., Grigor'ev, A. I., &
 333 Tolstikov, G. A. (2001). Complex of chlorine dioxide with TEMPO and its conversion into
 334 oxoammonium salt. *Journal of Physical Organic Chemistry*, 14, 38-42.

335 Goldstein, S., Merenyi, G., Russo, A., & Samuni, A. (2003). The role of oxoammonium cation in
 336 the SOD-mimic activity of cyclic nitroxides. *Journal of the American Chemical Society*, 125, 789-795.

337 Isbell, H. S., & Sniegowski, L. T. (1964). Tritium-labeled compounds. XI. Mechanism for the
 338 oxidation of aldehydes and aldoses-1-t with sodium chlorite. *Journal of Research of the National*
 339 *Bureau of Standards (United States)*, 68A, 301--304.

340 Isogai, A., & Saito, T. (2010). Cellulose nanofiber and process for production thereof, and
 341 cellulose nanofiber dispersion. *US 2010/0233481 A1*.

342 Isogai, A., Saito, T., & Fukuzumi, H. (2011). TEMPO-oxidized cellulose nanofibers. *Nanoscale*, 3,
 343 71-85.

344 Isogai, T., Saito, T., & Isogai, A. (2011). Wood cellulose nanofibrils prepared by TEMPO electro-
 345 mediated oxidation. *Cellulose*, *18*, 421-431.

346 Isogai, T., Saito, T., & Isogai, A. (2010). TEMPO Electromediated Oxidation of Some
 347 Polysaccharides Including Regenerated Cellulose Fiber. *Biomacromolecules*, *11*, 1593-1599.

348 Israeli, A., Patt, M., Oron, M., Samuni, A., Kohen R., & Goldstein S. (2005). Kinetics and
 349 mechanism of the comproportionation reaction between oxoammonium cation and hydroxylamine
 350 derived from cyclic nitroxides. *Free Radical Biology & Medicine*, *38*, 317-324.

351 Iwamoto, S., Kai, W., Isogai, T., Saito, T., Isogai A., & Iwata T. (2010). Comparison study of
 352 TEMPO-analogous compounds on oxidation efficiency of wood cellulose for preparation of cellulose
 353 nanofibrils. *Polymer Degradation and Stability*, *95*, 1394-1398.

354 Jeanes, A. & Isbell, H. S. (1941). Chemical reactions of the chlorites with carbohydrates. *Journal*
 355 *of Research of the National Bureau of Standards (United States)*, *27*, 125-142.

356 Kitaoka, T., Isogai, A., & Onabe, F. (1999). Chemical modification of pulp fibers by TEMPO-
 357 mediated oxidation. *Nordic Pulp & Paper Research Journal*, *14*, 279-284.

358 Komen, J. L., Weerawarna, A. S., & Jewell, R. A. (2006). Hypochlorite-free method for
 359 preparation of stable carboxylated carbohydrate products. *US 2006/7109325 B2*.

360 Kuramae, R., Saito T., & Isogai, A. (2014). TEMPO-oxidized cellulose nanofibrils prepared from
 361 various plant holocelluloses. *Reactive and Functional Polymers*, *85*, 126-133.

362 Launer, H. F. & Tomimatsu, Y. (1954). Kinetics of the chlorite-glucose reaction. *Journal of the*
 363 *American Chemical Society*, *76*, 2591-2593.

364 Launer, H. F. & Tomimatsu, Y. (1959). Stoichiometry of chlorite-aldehyde reactions. Analytical
 365 procedures. *Analytical Chemistry*, *31*, 1385-1390.

366 Lehtimaa, T., Kuitunen, S., Tarvo V., & Vuorinen, T. (2010). Kinetics of aldehyde oxidation by
 367 chlorous acid. *Industrial and Engineering Chemistry Research*, 49, 2688-2693.

368 Lewin, M., & Avrahami, M. (1955). The decomposition of hypochlorite-hypobromite mixtures
 369 in the pH range 7-10. *Journal of the American Chemical Society*, 77, 4491-4498.

370 Pääkkönen, T., Bertinetto, C., Pönni, R., Tummala, G., Nuopponen, M., & Vuorinen, M. (2015).
 371 Rate-limiting Steps in Bromide-free TEMPO-mediated Oxidation of Cellulose - Quantification of the N-
 372 Oxoammonium Cation by Iodometric Titration and UV-Vis Spectroscopy. *Applied Catalysis A*, 55, 532-
 373 538.

374 Rozantsev, E. G., & Sholle, V. D. (1971). Synthesis and Reactions of Stable Nitroxyl Radicals II.
 375 Reactions. *Synthesis*, 1971, 401-414.

376 Saito, T., Okita, Y., Nge, T., Sugiyama, J., & Isogai, A. (2006). TEMPO-mediated oxidation of
 377 native cellulose: Microscopic analysis of fibrous fractions in the oxidized products. *Carbohydrate*
 378 *Polymers*, 65, 435-440.

379 Saito, T., & Isogai, A. (2004). TEMPO-Mediated Oxidation of Native Cellulose. The Effect of
 380 Oxidation Conditions on Chemical and Crystal Structures of the Water-Insoluble Fractions.
 381 *Biomacromolecules*, 5, 1983-1989.

382 Saito, T., Shibata, I., Isogai, A., Suguri, N., & Sumikawa, N. (2005). Distribution of carboxylate
 383 groups introduced into cotton linters by the TEMPO-mediated oxidation. *Carbohydrate Polymers*, 61,
 384 414-419.

385 Saito, T., Hirota, M., Tamura, N., & Isogai, A. (2010). Oxidation of bleached wood pulp by
 386 TEMPO/NaClO/NaClO₂ system: Effect of the oxidation conditions on carboxylate content and degree
 387 of polymerization. *Journal of Wood Science*, 56, 227-232.

388 Sen, V. D., & Golubev, V. A. (2009). Kinetics and mechanism for acid-catalyzed
389 disproportionation of 2,2,6,6-tetramethylpiperidine-1-oxyl. *Journal of Physical Organic Chemistry* 22,
390 138-143.

391 Stitt, F., Friedlander, S., Lewis, H. J., & Young, F. E. (1954). Photometric Determination of
392 Glucose in Presence of Fructose. *Analytical Chemistry*, 26, 1478-1484.

393 Tanaka, R., Saito, T., & Isogai, A. (2012). Cellulose nanofibrils prepared from softwood cellulose
394 by TEMPO/NaClO/NaClO₂ systems in water at pH 4.8 or 6.8. *International Journal of Biological*
395 *Macromolecules*, 51, 228-234.

396 Whistler, R., & Schweiger, R. (1957) Oxidation of amylopectin with hypochlorite at different
397 hydrogen ion concentrations. *Journal of the American Chemical Society*, 79, 6460-6464

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Supplementary data

Activation of TEMPO by ClO₂ for Oxidation of Cellulose by Hypochlorite - Fundamental and Practical Aspects of the Catalytic System

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Materials and methods

1. Oxidation on bleached birch pulps

TEMPO was activated with >equimolar amount of ClO₂. The pulp was mixed with water (pulp consistency 1-4 %) and transferred to a Büchi glass reactor (continuous mixing, temperature 25-50 °C, volume of pulp suspension 1-1.2 dm³). Then, the activated TEMPO solution and NaOCl were added to the reactor. The pH level was adjusted to 8 by 1 M NaOH with an automatic titrator after a rapid pH decrease during the beginning of the oxidation. The oxidation rate was followed by iodometric titration until all NaOCl had been consumed. The pulp was washed on a wire cloth. The carboxylate content (SCAN-CM 65:02) and CED viscosity (SCAN-CM 15:99) were analyzed from the washed pulp samples.

2. FTIR spectroscopy analysis

All pulp samples were washed with pure water and dried prior to FTIR analysis. FTIR spectra were collected in the mid-infrared region by using a Bio-Rad FTS 6000 spectrometer (Digilab, Randolph, MA, USA) equipped with a MTEC PAC300 photoacoustic detector. Win-IR Pro V3.4 software (Digilab, Randolph, MA, USA) was used to baseline correct the FTIR spectra. The spectra were normalized relative to the cellulose peak at 1161 cm⁻¹ (Kaitao, et al., 2016) .

3. ^{13}C NMR analysis

Solution state ^{13}C NMR measurements were performed in D_2O at 27°C on a Bruker Avance III spectrometer operating at 100.61 MHz for ^{13}C . 1,3,5 -Trioxane was used as an internal standard for chemical shift (93.1 ppm). The spectra were acquired with a spectral width of 240 ppm, a relaxation delay of 1.5 s, 64K data points, and 30K number of scans. The spectral data was processed using TopSpin 3.0 software.

Results

Figure S1. FTIR spectra of birch kraft pulps oxidized with ClO_2 activated TEMPO and NaOCl (0.68, 1.37 and 3.2 mmol/g) under conditions similar to those presented in Figure 5. The spectrum of the unoxidized pulp is shown as a reference. The absorption band at 1604 cm^{-1} represents the carboxylate functionality (Abidi, Cabrales & Haigler 2014).

Figure S2. ^{13}C NMR spectra of freeze-dried filtrates from oxidation of birch kraft pulp under conditions similar to those presented in Figure 5. ClO_2 activated TEMPO was used as the catalyst with NaOCl dosages of a) 5.0 mmol/g, b) 2.3 mmol/g, and c) 0 mmol/g. ^{13}C shifts of xylan and dicarboxylate xylan were assigned according to (Kovacs & Hirsch, 1980) and (Kuramae, Saito, & Isogai, 2014), respectively.

Table S1. Summary of oxidations of birch kraft pulp by (A) ClO_2 activated TEMPO and NaOCl at pH 8 and (B) post-oxidation of these pulps by HClO_2 to convert the residual aldehydes to carboxylates.

Oxidation	T ($^{\circ}\text{C}$)	Pulp consistency (%)	TEMPO (mM)	ClO_2 (mM)	NaOCl (mmol g^{-1})	Carboxylates (mmol g^{-1})	CED-viscosity (ml/g)
A	50	1	1.3	2.3	3		
B	50	1				0.92	430
A	35	1	0.8	1.2	3		
B	35	1				0.97	321
A	50	1	0.8	1.65	3		
B	50	1				0.95	308
A	50	2	2	4.4	3	0.82	223
B	50	1				0.93	433
A	50	2.4	2	4.4	3.75	0.93	179
B	50	0.8				1.06	329
A	25	2	2	4.3	3	0.93	215
B	50	1				1.07	463
A	25	3	2	4.3	1.5	0.51	236
B	50	1				0.64	402

A	25	4	2	4.4	2.2	0.67	215
B	50	2.8				0.8	408
A	25	4	2.5	5.6	2.7	0.86	223
B	25	4				1.02	486
A	25	4	4.2	9.9	2.7	0.78	220
B	25	4				0.97	533
A	25	4	2.5	5.6	2.7	0.9	156
B	25	4				0.97	391
A	35	4	2	7.6	2.7	0.75	152
B	35	4				0.95	343
A	35	4	2	7.1	3.2	0.91	142
B	35	4				1.1	286
A	40	4	2	9.2	3.6	0.92	135
B	40	4				1.07	235
A	35	4	2	7.8	4.5	0.94	124
B	35	4				1.19	216
A	30	4	2	7.7	5	0.97	124
B	50	4				1.12	201

References

- Abidi, N., Cabrales, L., & Haigler, C. (2014) Changes in the cell wall and cellulose content of developing cotton fibers investigated by FTIR spectroscopy. *Carbohydrate Polymers*, 100, 9-16.
- Kovacs, P. & Hirsch, J. (1980) ¹³C-N.M.R. spectra of xylo-oligosaccharides and their application to the elucidation of xylan structures. *Carbohydrate Research*, 85, 177-185.
- Kuramae, R., Saito T., & Isogai, A. (2014). TEMPO-oxidized cellulose nanofibrils prepared from various plant holocelluloses. *Reactive and Functional Polymers*, 85, 126-133.
- Zhang, K., Sun, P., Liu, H., Shang, S., Song, J., & Wang, D. (2016). Extraction and comparison of carboxylated cellulose nanocrystals from bleached sugarcane pulp using two different methods. *Carbohydrate Polymers*, 138, 237-243.