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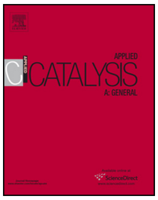

Rate-limiting steps in bromide-free TEMPO-mediated oxidation of cellulose—Quantification of the *N*-Oxoammonium cation by iodometric titration and UV–vis spectroscopy

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ABSTRACT

A iodometric titration method was introduced to study the conversion of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to the corresponding *N*-oxoammonium cation (TEMPO$^+$) by hypochlorite in the absence and presence of bromide ion. The validity of the titration was verified with UV–vis spectroscopy combined with a multivariate curve resolution (MCR) algorithm to calculate the concentrations and spectral signatures of the pure components (i.e., TEMPO, Cl(+1) and TEMPO$^+$). The formation of the oxoammonium cation was successfully followed during the activation of TEMPO by HOCl and HOBr. It was found that HOBr is a more effective activator for TEMPO than HOCl is. Moreover, the importance of a separate activation step for TEMPO with bromide-free TEMPO oxidations could be identified with this titration method. The content of TEMPO$^+$ was also monitored during the TEMPO-mediated oxidation of a cellulosic pulp by hypochlorite in the absence and presence of bromide. It was found that the oxidation of the alcoholic groups by TEMPO$^+$ was generally the rate-determining step and much slower than the regeneration of TEMPO$^+$ through oxidation of the hydroxylamine by HOCl and HOBr. However, at high pH the latter reaction became rate-limiting.

1. Introduction

The chemistry of catalytic oxidation of alcohols with oxoammonium ion in aqueous media was reported decades ago [1–4]. The fast and selective oxidation of primary alcohols to carboxylates via aldehydes by oxoammonium ion was introduced later [5]. More recently, this method was applied to the oxidation of cellulose [6] and to the preparation of nanofibrillated cellulose (NFC) [7,8]. Altogether, this oxidation has gained a vast research interest [9–21]. The TEMPO-mediated oxidation reduces drastically the energy consumption during the pulp disintegration to NFC, which is a transparent gel consisting of individual cellulose microfibrils and microfibril bundles. The energy consumption of the nanocellulose production via a TEMPO-mediated oxidation can be reduced from 700 to 1400 MJ kg^{-1} (microfibrillated cellulose (MFC) process with a high pressure homogenizer treatment) to less than 7 MJ kg^{-1} (TEMPO-oxidized NFC) [22]. NFC can be utilized, for example, as a reinforcing agent in composites [22,23]. Other applications of NCF include gas-barrier films, electronics, cosmetics, and flame-resistant materials [22].

The most widely studied TEMPO-oxidation process is based on the use of the NaBr/TEMPO/NaOCl system. The pH level during this oxidation is typically 10 or higher [10,12,13,19,22]. The amount of bromide is commonly higher than the amount of TEMPO (mass ratio 10:1) during the oxidation [7]. Moreover, some TEMPO-oxidation methods without the application of bromide have been reported in the literature [20,24]. For example, acid-neutral conditions (pH 3.5–6.8) have been applied to oxidize regenerated cellulose applying a TEMPO/NaOCl/NaClO$_2$ procedure without the use of bromide [24]. With this low pH range, high carboxylate contents for the oxidized pulps (4 mmol COOH/g) have been reported after an extended reaction time of almost 80 h. In addition, an electro-mediated oxidation has been used to oxidize the primary hydroxyl groups of cellulose to carboxylates without the addition of either NaOCl or

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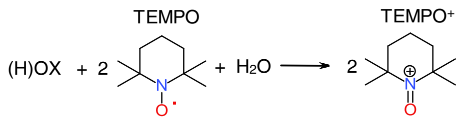


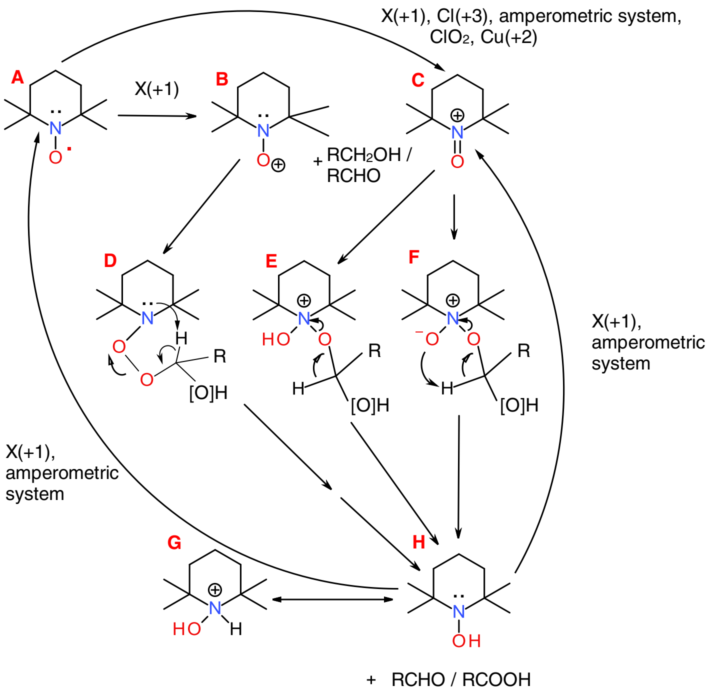
Scheme 1. Modified activation mechanism of TEMPO radical by HOX [11].

NaBr. In this oxidation, TEMPO or a TEMPO derivative is used with an amperometric system for the oxidation of the pulp. However, achieving a carboxylate content of 1 mmol g^{-1} of pulp requires a 48 h oxidation, which indicates an extremely low reaction rate [20]. As a conclusion, the TEMPO-mediated oxidations without bromide are slower compared to the ones that apply bromide. However, a process without bromide would be of interest since its presence in the waste water streams is highly undesired [11].

The role of bromide as a radical TEMPO activator has not yet been clearly elaborated. The lack of an analysis method for $TEMPO^+$ impedes the study of the catalytic cycle of the TEMPO-mediated oxidation. On one hand, it has been proposed that the primary oxidant, e.g., NaOBr when NaOCl is present (Scheme 1), oxidizes the hydroxyl amine to oxidized TEMPO via a radical intermediate [12,25]. On the other hand, NaOCl has been proposed to activate TEMPO at pH 10 prior to the NaOBr/TEMPO oxidation without a radical TEMPO intermediate [22]. Both $NaClO_2$ and NaOCl have been proposed as TEMPO activators during the TEMPO oxidation under the low pH conditions (pH 3.5–6.8) [21,24,26]. HOBr has been proposed to be the activator for TEMPO during the NaBr/TEMPO/NaOCl oxidation at pH 10.8 where the formation of HOBr in the presence of ClO^- and Br^- promotes the conversion of TEMPO to $TEMPO^+$ in a reaction which is similar to the one shown in Scheme 1 [14]. A similar reaction was proposed earlier by de Nooy et al. [9].

The pK_a values of HOCl (7.5) and HOBr (8.7) define the applicable pH level during the TEMPO activation. At pH > pK_a the hypohalous acids exist increasingly as hypohalites that are inactive in the catalytic oxidation. Accordingly, the NaBr/TEMPO/NaOCl oxidations take place under higher pH level than the NaOCl/TEMPO oxidations [11]. The complexity of the system and the number of the reactions involved are substantial when both HOCl and HOBr are present in the solution [27]. Interestingly, the NaBr/TEMPO/NaOCl (pH 10) oxidation of starch without a separate TEMPO activation step is reported to be three times faster than the NaOCl/TEMPO oxidation [11]. However, the reaction rates of the initial conversion of TEMPO to $TEMPO^+$ and its catalytic reaction with starch were not studied separately [11].

Several reaction paths have been proposed for the TEMPO-mediated oxidation of the primary and secondary hydroxyl groups. However, some of the elementary reactions, e.g., the conversion of the hydroxylamine (TEMPOH) to $TEMPO^+$ and the initial conversion of TEMPO to $TEMPO^+$, are lacking plausible reaction mechanisms. Scheme 2 summarizes the most commonly proposed reaction routes and mechanisms published so far. The conversion of TEMPO to $TEMPO^+$ (A → C) has been quite often left without explanation in the early studies [4,5]. Nevertheless, some routes for this conversion have been proposed, even though the reaction mechanisms have not been addressed. $TEMPO^+$ has been proposed to form during a reaction between $CuCl_2$ and TEMPO [3]. Similarly, the formation of $TEMPO^+$ during a reaction between Br(+1) and TEMPO [14,18,25,28] as well as between Cl(+1) and TEMPO [11,16,24,26,29] or Cl_2 and TEMPO [30] have been reported in numerous studies. In addition, the conversion of TEMPO to $TEMPO^+$ has been proposed to take place during a reaction with $NaClO_2$ under neutral and acidic conditions [26] and during a reaction between ClO_2 and TEMPO via a transition complex intermediate [31,32]. Despite the vast research interest on the TEMPO-mediated oxidation, the reaction mechanisms for the formation of $TEMPO^+$ still remain unrevealed.



Scheme 2. Proposed reaction routes for TEMPO-mediated oxidation of primary and secondary alcohols.

The TEMPO-mediated oxidation of alcoholic groups has been suggested to proceed via an A → C → F → H route under alkaline conditions and via an A → C → E → H route under acidic conditions, where the formation of a reactive complex (E and F) is generated by a nucleophilic attack of an alcoholate anion on the nitrogen atom of $TEMPO^+$ [5,10,12,22,33,34]. Additionally, an A → B → D → H route has been proposed to occur under alkaline conditions, where the formation of a reactive complex (D) is generated by a nucleophilic attack of an alcoholate anion on the oxygen atom of TEMPO [34]. Moreover, hydroxylamine has been proposed to shift to the protonated hydroxylamine H → G under low pH [12,35]. Furthermore, the conversion of TEMPOH to $TEMPO^+$ (H → C) is proposed to take place under alkaline conditions with [7,12,36] and without [11,22,26,29,37–39] the radical intermediate by a reaction with *X*(+1) or by applying an amperometric system.

For the present, only few elementary reaction rate constants for the TEMPO-mediated oxidation process have been determined. Some kinetic studies have been published with primary and secondary alcohols. The equilibrium constant (K) for the formation of a complex (F) with MeO^- and $TEMPO^+$ (1.3×10^{13} M^{-1}) is reported to be 10^6 times larger than that for the formation of the corresponding *i*-PrO^- complex (1.1×10^7 M^{-1}) [34]. In addition, the rate constants for the reactions between aldehydes/alcohols and $TEMPO^+$ under alkaline conditions have been studied [9]. Those reactions were followed by monitoring the consumption of hypochlorite [9]. However, measuring hypochlorite consumption does not allow differentiating between the reaction of $TEMPO^+$ with the alcohol and the conversion of TEMPOH to $TEMPO^+$. Thus specific quantification of $TEMPO^+$ would be useful for the determination of the rate constants for the individual reactions in the catalytic cycle. In addition, it is obvious that the mechanism of the conversion of TEMPO or TEMPOH to $TEMPO^+$ is not clearly defined due to the rival reaction routes which have been proposed in the earlier studies. Therefore, a method for the determination of $TEMPO^+$ would be a useful tool within this field of research.

In this study, we introduce a iodometric titration method to quantitatively monitor $TEMPO^+$ during TEMPO-mediated oxida-

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tion of alcohols. The validity of the iodometric titration method is verified with UV–vis absorption spectroscopy by fitting with the spectra of the pure components, i.e., TEMPO, Cl(+1) and $TEMPO^+$, as calculated by a multivariate curve resolution algorithm (MCR). Moreover, the method with UV–vis spectroscopy and MCR algorithm can be applied separately to quantify both $TEMPO^+$ and TEMPO. The iodometric titration method [1,2,30,40] is applied to study a separate activation step of TEMPO prior to the TEMPO-mediated oxidation. Moreover, the role of HOX (e.g., HOCl and HOBr) as an activator of TEMPO is studied by the titration method. Finally, the TEMPO-mediated oxidation with a separate activation step of TEMPO and the titration method to determine $TEMPO^+$ are applied during an oxidation of a cellulosic pulp, a process commonly applied for the preparation of NFC.

2. Experimental

2.1. Materials

Industrially dried fully-bleached birch kraft pulp (Finland), fully-bleached eucalyptus kraft pulp (Brazil) and eucalyptus prehydrolysis kraft pulp (Brazil) were used as the raw materials for the TEMPO-mediated oxidation of cellulose. Xylitol (Sigma–Aldrich (St Louis)) was used as the raw material for the TEMPO-mediated oxidation of alcohol. TEMPO (Sigma–Aldrich (St Louis)) was used as a catalyst. A 13% NaOCl solution (Merck (Darmstadt, Germany)) was the primary oxidant in the TEMPO-oxidations. 22 g of orthoboric acid (VWR (Leuven, Belgium)) and 1.8 g of NaOH pellets (VWR (Leuven, Belgium)) were diluted to 2000 ml of distilled water to prepare a borate buffer (pH 8.3) in situ. 1 M NaOH (Merck (Darmstadt, Germany)), 1 M HCl (Merck (Darmstadt, Germany)), Büchi reactor (volume 1.6 dm^3), and Metrohm 718 Stat Titrino titrator with pH adjustment were applied during the pulp oxidations. UV–vis absorption spectra were measured with a Shimadzu UV-2550 spectrophotometer (Shimadzu Corporation (Kyoto, Japan)). Ion-exchanged water was used in pulp washings.

2.2. Activation of TEMPO by NaOCl

NaOCl and TEMPO were mixed in a buffer solution (pH 8.3) at room temperature. The consumption of Cl(+1) and the formation of $TEMPO^+$ were monitored by iodometric titration. In parallel experiments absorption spectra of the samples withdrawn were measured in the UV–vis region with a Shimadzu UV-2550 spectrophotometer. Reference spectra of the buffer, 2 mM TEMPO in the buffer and 4 mM NaOCl were also measured. All solutions were diluted with the buffer solution in a 1:5 ratio prior to the measurements. The concentrations of Cl(+1), TEMPO and $TEMPO^+$ were obtained through mathematical analysis of the spectra.

2.3. Oxidations of the cellulose pulps and xylitol

All oxidations were carried out in a Büchi glass reactor (1.6 dm^3) at 25 °C. The chemical dosages and the consistency of the pulp suspension were varied while its volume was 1.2 dm^3 in all experiments. Radical TEMPO was mixed with a stoichiometric excess of NaOCl in water. The pH level of the solution was adjusted to 7.5 with sulfuric acid. The solution was mixed in a closed vessel until TEMPO was completely dissolved and converted to $TEMPO^+$ by HOCl. The pulp and the activated TEMPO solution were mixed and NaOCl was added to the closed reactor by a pump. After the addition of NaOCl, pH was kept constant at the target level by adding 1 M NaOH with an automatic titrator. The oxidation rate was followed by iodometric titration until all oxidant was consumed.

Xylitol was oxidized correspondingly excluding the adjustment of oxidation solution pH with borate buffer to 8.3. Automatic titrator was not used for pH adjustment after NaOCl addition due to buffered conditions.

2.4. Conversion of residual aldehydes to carboxylates with chlorous acid

TEMPO-oxidized pulp suspension was acidified to pH 3 with HCl and $NaClO_2$ Was added (10 mM initial concentration). The suspension was mixed in the Büchi reactor for 2 h at 50 °C. Finally, the pulp was washed with pure water. CED-viscosity of the pulp was analyzed according to the standard method SCAN-CM 15.99 prior to the calculation of DP [41].

2.5. Analyzing of carboxylate and aldehyde contents of pulps

The carboxylate content of the pulps were determined by conductometric titration (SCAN-CM 65:02) using Methrohm 751 GPD Titrino automatic titrator and Tiamo 1.2.1. software. The aldehyde contents of the pulps were calculated as the difference in their carboxylate contents after and before the post-oxidation with $HClO_2$.

2.6. Iodometric titration of (Cl(+1), Br(+1)) and $TEMPO^+$

The applied titration sequence is based on the method of Wartiovaara [42] excluding the analysis of $TEMPO^+$. Wartiovaara describes a three point titration of ClO_2 and hypochlorite at pH 8.3, further titration of chlorite at pH below 2, and finally, the titration of chlorate at pH below 1. Only the alkaline (pH 8.3) titrations to determine the formed $TEMPO^+$ and Cl(+1) were conducted. The liberated iodine was titrated against $Na_2S_2O_3$ using starch as an indicator. The titration of iodine with sodium thiosulfate is based on the following reaction (Eq. (1)):

$$I_2 + 2S_2O_3{}^{2-} \rightarrow S_4O_6{}^{2-} + 2I^- \quad (1)$$

First, 25 ml of a borate buffer (pH 8.3) was added to two sample containers. Then, 0.5 ml of DMSO, which can be used as a masking agent for HOCl and HOBr, was added to one of the sample containers [43–47]. A known amount of the sample solutions together with an excess amount of KI was added to both of the sample containers. When bromine was present, the solution required stabilization for a few minutes prior to the addition of KI, since HOBr is trapped by DMSO more slowly than HOCl. All samples were titrated against $Na_2S_2O_3$ using starch as an indicator. The following reactions (Eqs. (2) and (3)) occur in the mildly alkaline medium:

$$HOX + H^+ + 2I^- \rightarrow X^- + I_2 + H_2O \quad (2)$$

$$2TEMPO^+ + 2I^- \rightarrow 2TEMPO + I_2 \quad (3)$$

The DMSO containing sample includes only the reaction product (iodine) with $TEMPO^+$, since HOCl (or HOBr) is trapped with DMSO. Iodide reduces $TEMPO^+$ to TEMPO radical [1,2,30,40]. Thus the thiosulphate consumption corresponds stoichiometrically to the amount of $TEMPO^+$ in the sample (Eqs. (1) and (3)).

2.7. UV–vis absorption spectroscopy of TEMPO/NaOCl/buffer solutions

NaOCl/TEMPO mixtures in a buffer solution (pH 8.3) were prepared and measured with a Shimadzu UV-2550 spectrophotometer correspondingly to the ones which were applied in the titrations. 2 mM TEMPO and 4 mM NaOCl solutions in the buffer media and the buffer solution without any added chemicals were measured as reference samples. All solutions were diluted with a ratio of 1/5 by the buffer solution prior to the measurements.

2.8. Mathematical reconstruction of pure spectral components from UV–vis data

First, the range of linear response in the UV–vis measurements was identified by looking at the singularities in their loading factors from principal component analysis (PCA) [48]; the range 46 assumed to be TEMPO, TEMPO$^+$, HOCl/$^-$OCl mixture (which is referred to as Cl(+1)) and a constant background consisting of a baseline and absorption by the buffer. A number of varying components equal to three was also confirmed by PCA: the first three factors explain over 99% of data variance (for data at 200–400 nm). The background, derived from the spectrum of a buffer-only solution, was subtracted from all spectra. The millimolar spectra of pure TEMPO and Cl(+1) were taken from spectra of the respective substance in buffer, after subtracting the background and dividing for the concentration. The spectrum of TEMPO$^+$ was reconstructed by an algorithm, inspired by the Multivariate Curve Resolution–Alternate Least Squares method [49], which recursively alternates least-squares fitting of the bilinear model $\mathbf{D} = \mathbf{CS} + \mathbf{E}$ and the application of constraints to the obtained solution. $\mathbf{D}$ is the $n \times w$ matrix of UV–vis measurements (n = number of measurements, w = number of wavechannels), $\mathbf{C}$ is the $n \times p$ matrix of concentrations in mmol/l (p = number of independent components, here equal to 3), $\mathbf{S}$ is the $p \times w$ matrix of spectra of pure components and $\mathbf{E}$ accounts for noise. The constraints included non-negativity of absorbances and concentrations, stoichiometric balances and monotonic decrease of reactants; they were applied by substituting any absorption or concentration that violated these constraints with the closest admissible value. The initial estimate for the spectrum of 1 mM TEMPO$^+$ was taken as the spectrum from the latest point (332 min) in the reaction mixture, subtracted by the background, divided by 1.8 (i.e., 90% of the initial 1 mM TEMPO) and again subtracted by the spectrum of 1 mM Cl(+1). The algorithm was iterated until convergence and the final spectra were used to obtain the concentrations of the corresponding substances by linear least-squares fit. All calculations were performed using MATLAB® version 8.2 R2014a (The Mathworks (USA)).

3. Results and discussion

3.1. Iodometric titration of TEMPO$^+$ and Cl(+1)

The reaction of TEMPO and NaOCl was studied in a pH 8.3 buffer solution because at this pH the content of the undissociated HOCl (pK$_a$ 7.5), that is the reactive species, is still relatively high (~14%). The reaction was monitored as a function of time by iodometric titrations with and without DMSO, which is used as a masking agent for HOCl [43–46] (S1). The formation of a reaction product was detected when DMSO was applied. This compound disappeared when an aliphatic alcohol, *n*-propanol, was added in the reaction mixture of TEMPO and NaOCl. The slow formation under the low reactant concentrations and the disappearance with the added alcohol promotes an assumption that the component is the oxidized form of TEMPO, namely TEMPO$^+$ which is reported to react stoichiometrically with iodine as described by Eq. (3) [1,2,30,40]. TEMPO$^+$ is converted to its reduced form, a hydroxylamine (TEMPOH), during the reaction with alcohols (Scheme 2). Primary aliphatic alcohols can be oxidized with TEMPO to the corresponding aldehydes in few minutes [5]. The oxidation of the alcohols with TEMPO is clearly faster with added NaBr [11]. The cocatalysis by bromide could be due to the faster activation of TEMPO to its oxidized form.

The thiosulphate consumption with the added DMSO was converted to the concentration of TEMPO$^+$ according to Eqs. (1) and (3) (Fig. 3). The concentration of Cl(+1) was obtained from the difference in the thiosulphate consumption with and without the added DMSO by applying Eqs. (1) and (2). TEMPO$^+$ was clearly formed in parallel with the consumption of Cl(+1).

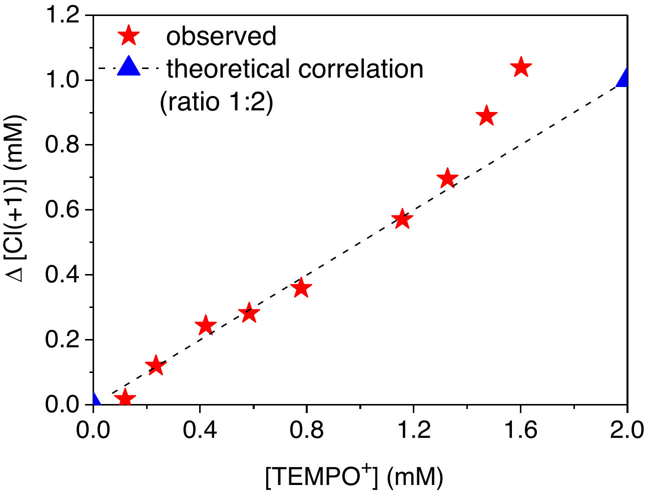

Fig. 1. The correlation between the consumed Cl(+1) and the formed TEMPO$^+$ in a reaction of 2 mM TEMPO and 4 mM NaOCl in a borate buffer (pH 8.3) at room temperature. The concentrations of TEMPO$^+$ formed and Cl(+1) consumed were obtained by iodometric titration. Corresponding correlation with reaction times added is shown in Supplementary material.

The correlation between the consumed Cl(+1) and the TEMPO$^+$ formed is further illustrated in Fig. 1. The stoichiometry of the activation reaction with HOCl and TEMPO is proposed to be 1:2 [11]. The observed results correlate with the 1:2 stoichiometry except for the longest reaction times. This deviation could be explained with the formation of ClO$_3^-$ which was detected after several hours of reaction time. The chlorate formation correlates with the self-decomposition of HOCl [27], which is more pronounced at long reaction times and especially at high Cl(+1) concentrations.

3.2. UV–vis absorption spectroscopy of TEMPO, TEMPO$^+$ and Cl(+1)

The conversion of TEMPO and Cl(+1) and the formation of TEMPO$^+$ were monitored also by UV–vis absorption spectroscopy (Fig. 3). The spectra of the reaction solutions and the corresponding spectra of Cl(+1) in the borate buffer are shown in the supplementary material. Mathematical fitting was used instead of direct observation of the absorption maxima shifting due to the overlapping of the spectra of TEMPO, TEMPO$^+$, and the Cl(+1). The mathematically reconstructed spectra of TEMPO, TEMPO$^+$, and Cl(+1), shown in Fig. 2, are based on the measurements illustrated in Supplementary material.

The formation rate of TEMPO$^+$ in 2 mM TEMPO solution, which is typically applied in the TEMPO-mediated oxidation, and the formation rate in a more concentrated TEMPO solution are compared in Fig. 4. The concentration ratio of NaOCl and TEMPO and the concentration of NaOCl clearly influence on how fast TEMPO$^+$ is formed. In the plateau point of TEMPO$^+$ formation the consumption of thiosulfate (iodometric titration in the presence of DMSO) is almost equal to the amount of TEMPO added. The results demonstrate the benefit of a separate activation step of TEMPO prior to its application as a bromide-free oxidation catalyst e.g., for the oxidation of cellulosic pulps. A separate activation of TEMPO by NaOCl at pH 7–8 can be accomplished within an half of hour when 20–40 mM TEMPO and excess of NaOCl are used (results not shown).

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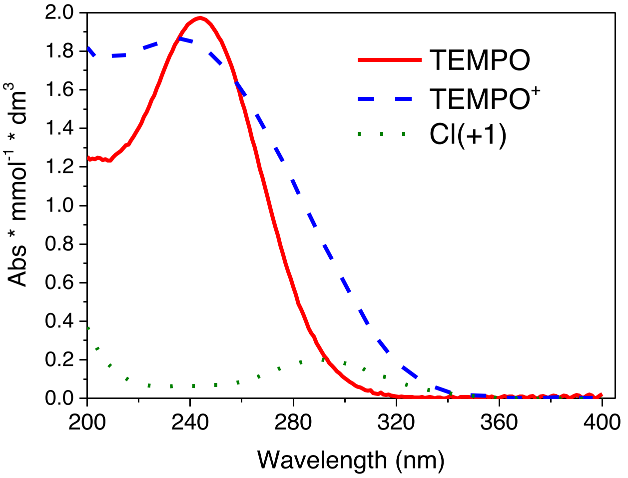

Fig. 2. Mathematically reconstructed spectra of TEMPO, TEMPO$^+$, and Cl(+1) from monitoring the reaction of 2 mM TEMPO and 4 mM NaOCl in a borate buffer (pH 8.3) by UV–vis spectroscopy at room temperature.

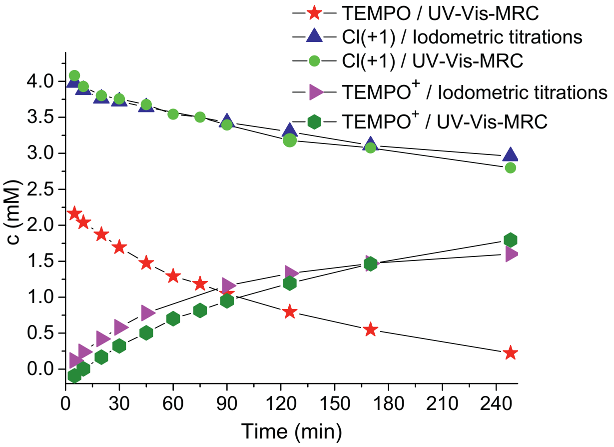

Fig. 3. Disappearance of Cl(+1) and TEMPO and formation of TEMPO$^+$ in a reaction mixture of 2 mM TEMPO and 4 mM NaOCl in a borate buffer (pH 8.3) at room temperature. The graph compares the results obtained by iodometric titration and UV–vis spectroscopy combined with MCR.

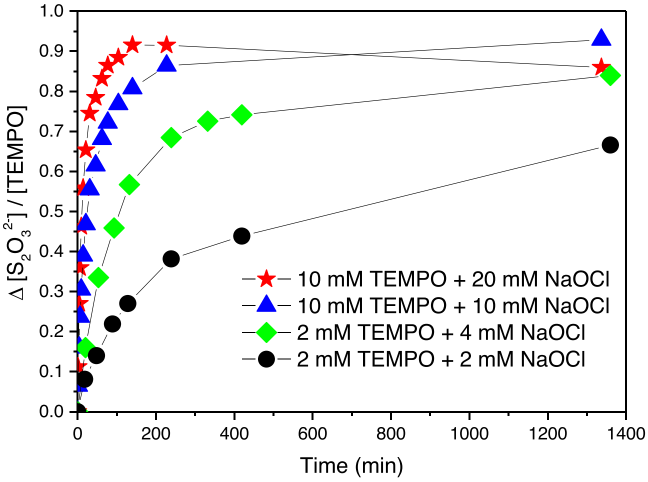

Fig. 4. Effect of the concentrations of TEMPO and NaOCl on the conversion to TEMPO$^+$ in a borate buffer (pH 8.3) as a function of time, analyzed by iodometric titration.

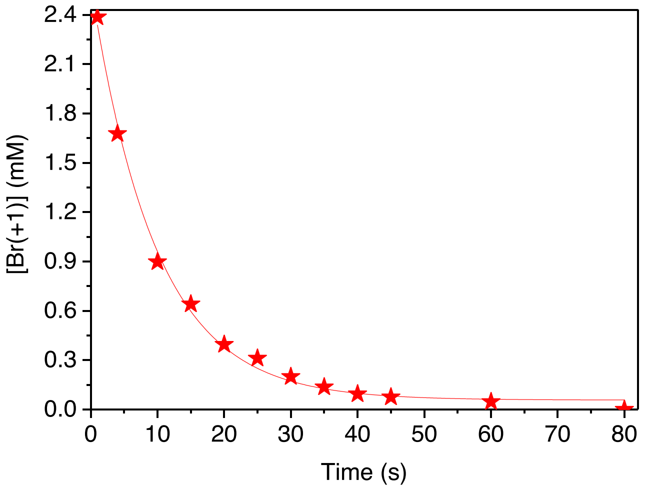

Fig. 5. The decomposition of HOBr, formed in 4 mM NaBr and 4 mM NaOCl in a borate buffer (pH 8.3) at RT, by DMSO as monitored by iodometric titration.

3.3. *Iodometric titration of TEMPO$^+$ in the presence of added NaBr*

The use of DMSO as a masking agent for HOCl has been reported widely [43–46]. DMSO can be applied as a masking agent for HOBr correspondingly [47]. However, the reaction rate between HOBr and DMSO is slower than the reaction rate between HOCl and DMSO. The required time for removing all HOBr in the mixture of NaBr and NaOCl by DMSO was determined by varying the incubation time prior to the addition of KI and starch (Fig. 5). The trapping of HOBr by DMSO appeared to follow the first order exponential decay, thus, the following equation was fitted to the titration data:

$$[\mathrm{HOBr}] = [\mathrm{HOBr}]_0 \times \exp(-kt) \tag{4}$$

where the rate constant k is 0.10 s^{-1}. Thus a delay of 2 min between the addition of DMSO and the addition of KI was considered appropriate to enable the titration of TEMPO$^+$ regardless of the amount of Br(+1) present in the sample solution.

The iodometric titration with and without added DMSO was applied for monitoring the NaBr/TEMPO/NaOCl reaction system (S2) similarly as presented in supplementary data (S1) for the TEMPO/NaOCl system. The formation rate of TEMPO$^+$ was high despite the 10 times lower concentration level compared to the bromide-free system (S1 and Fig. 3). The use of bromide as an accelerating compound of TEMPO-mediated oxidation is well known and reported [10,12]. Our experiments verify one of the important effects of bromide as a co-catalyst is the faster conversion of TEMPO to TEMPO$^+$.

The correlation between the consumption of Cl(+1)/Br(+1) and formation of TEMPO$^+$ (Fig. 6) was similar to the one detected with the TEMPO/NaOCl system (S1 and Fig. 3). In both cases the hypohalous acids were consumed and TEMPO$^+$ formed in the theoretical 1:2 ratio.

3.4. *Monitoring of the TEMPO-mediated oxidation of xylitol*

The iodometric titration of Cl(+1) and TEMPO$^+$ was applied to study the catalytic oxidation of xylitol with preactivated TEMPO (2 mM) at pH 8.3 in buffered conditions (Fig. 7). Interestingly, 30 mM NaOCl was consumed during reaction with 7.5 mM xylitol. The observed 4:1 stoichiometry corresponds to the expected conversion of xylitol into xylaric acid. The concentration of TEMPO$^+$ remained at a constant level until all hypochlorite was consumed after which also TEMPO$^+$ disappeared.

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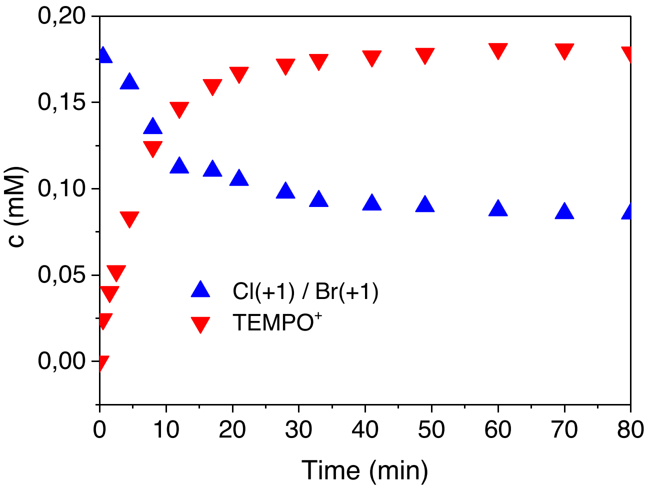

Fig. 6. Disappearance of Cl(+1)/Br(+1) and formation of TEMPO$^+$ in a reaction mixture of 0.2 mM TEMPO, 0.2 mM NaBr, and 0.2 mM NaOCl in a borate buffer (pH 8.3) at room temperature.

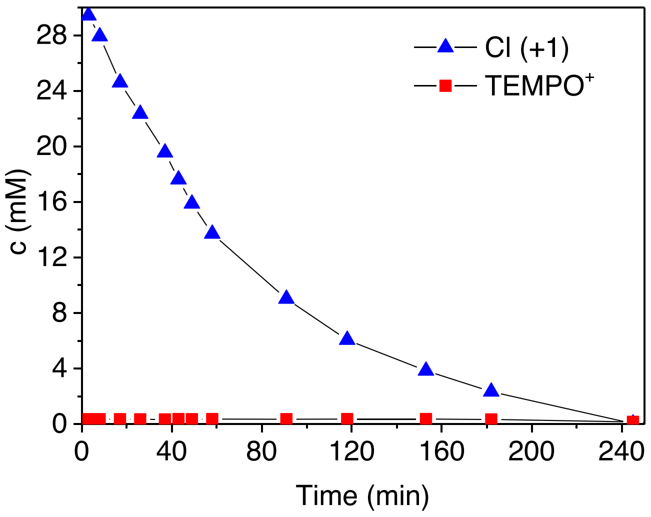

Fig. 7. Disappearance of Cl(+1) and TEMPO$^+$ during TEMPO (0.4 mM) catalyzed oxidation of a 7.5 mM xylitol with 30 mM NaOCl at room temperature. pH was buffered with borate buffer to 8.3.

3.5. *Monitoring of the TEMPO-mediated oxidation of bleached pulps by iodometric titration*

The iodometric titration of Cl(+1) and TEMPO$^+$ was applied to study the catalytic oxidation of a bleached birch kraft pulp with preactivated TEMPO (2 mM) at pH 9 that has been reported to be the optimum pH for the bromide-free oxidation [11] (Fig. 8A). During the course of the oxidation TEMPO existed mostly in the form of TEMPO$^+$, the concentration of which stayed at a constant level (1.7 mM) until all Cl(+1) was consumed (Fig. 8A). Similar observations were made with bleached eucalyptus kraft and eucalyptus prehydrolysis kraft pulps (Supplementary material). Then TEMPO$^+$ disappeared at a rate equal to the final rate of conversion of Cl(+1). These observations indicate that the oxidation of TEMPOH to TEMPO$^+$ is much faster than its oxidative reaction with the primary alcohol groups in cellulose. A similar conclusion was reported earlier by Bragd et al. [11] who found that the rate of TEMPO catalyzed oxidation of methyl α-D-glucopyranoside was unaffected by the concentration of Cl(+1). However, when pH of the reaction mixture was adjusted from 9 to 10.5 (Fig. 8B) during the reaction, TEMPO$^+$ almost disappeared (<0.2 mM TEMPO$^+$) after which the reaction

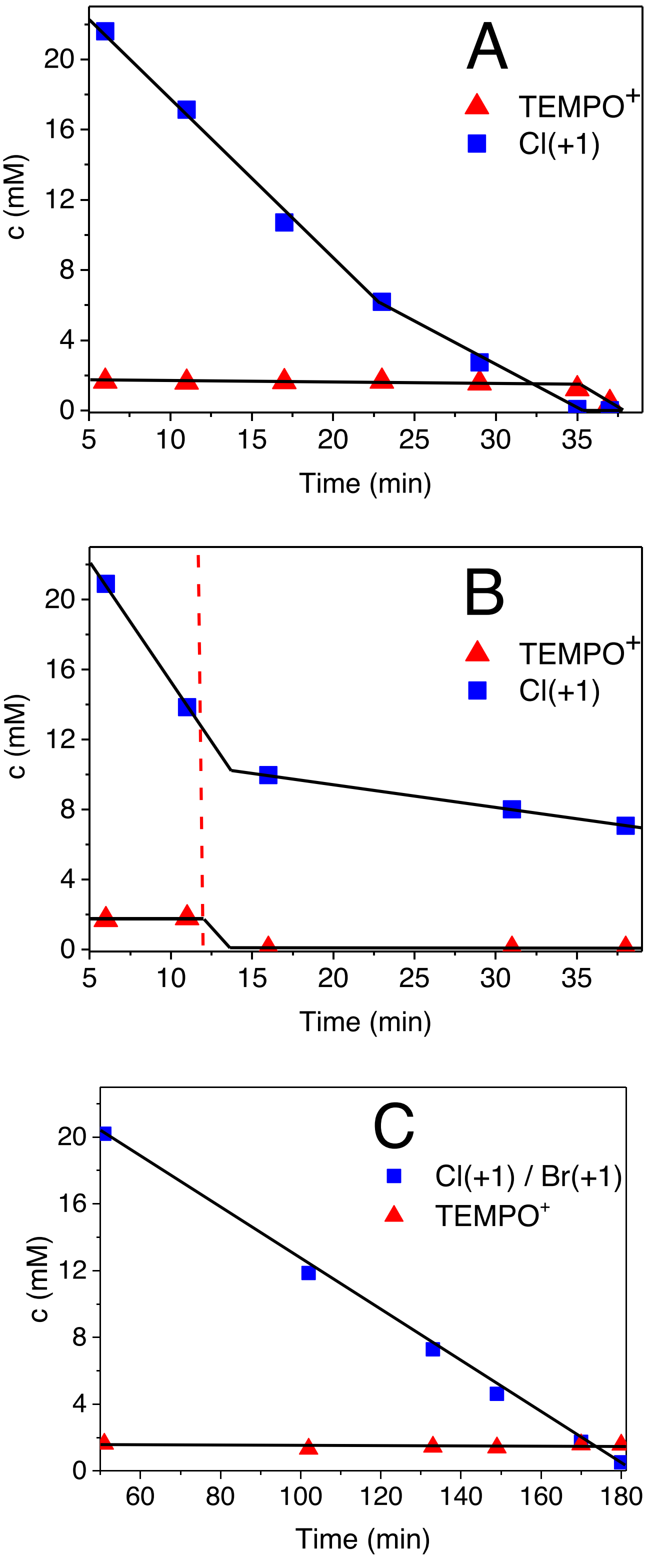

Fig. 8. Disappearance of Cl(+1) and TEMPO$^+$ during TEMPO (2 mM) catalyzed oxidation of a bleached birch kraft pulp (4% consistency) with NaOCl at room temperature. [A] Oxidation with preactivated TEMPO and 57 mM NaOCl at pH 9, [B] repetition of A oxidation except pH adjustment (9 → 10.5) with NaOH after 12 min reaction time (dash line). [C] Disappearance of Cl(+1)/Br(+1) and TEMPO$^+$ during TEMPO (2 mM) and NaBr (0.4 mM) catalyzed oxidation of a bleached birch kraft pulp (3.3% consistency) with NaOCl (97 mM) at pH 10 at room temperature. TEMPO was preactivated prior to the oxidation.

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continued with a much lower rate. Thus, at the high pH reoxidation of TEMPOH became the rate-limiting reaction, probably due to the low content of HOCl at the high alkalinity.

Under identical conditions more carboxylate and aldehyde groups (0.92 and 0.21 mmol/g, respectively) were formed in the eucalyptus prehydrolysis kraft pulp in comparison with the normal eucalyptus kraft pulp (0.75 and 0.13 mmol/g, respectively) (Supplementary material). The enhanced oxidation of the prehydrolysis kraft pulp can be explained by its lower xylan content. Similar effect of the xylan content on the oxidation of cellulosic pulps has been reported earlier [29].

When a small amount of NaBr was used as a co-catalyst, the concentration of $TEMPO^+$ stayed close to the concentration of the added TEMPO even though the oxidation was carried out at pH 10 (Fig. 8C). The bromide-assisted oxidation has been reported to be fastest at pH 10 [11]. Our results verify that the NaBr addition that leads to formation of HOBr, promotes the reoxidation of TEMPOH at least at high pH levels. In part, this can be understood by the lower degree of dissociation of HOBr (pK_a 8.7) in comparison with HOCl (pK_a 7.5). These examples demonstrate the utility of the iodometric titration in unravelling the rate-determining steps in the TEMPO catalyzed oxidation of cellulosic pulps.

4. Conclusions

The quantification of $TEMPO^+$ by iodometric titration is a useful tool for studying the chemistry of the TEMPO-mediated oxidation of primary alcohols. Similar and complementary information can be obtained by UV–vis spectroscopy combined with multivariate curve resolution, which can be applied for simultaneous quantification of Cl(+1)/Br(+1), $TEMPO^+$ and TEMPO. In general, conversion of TEMPO to $TEMPO^+$ is the slowest step in bromide-free oxidation of the alcohols by Cl(+1). The use of bromide accelerates this conversion that can also be accomplished through a separate pretreatment of TEMPO with an excess of Cl(+1) in neutral conditions. The rate of the preactivation depends on the concentrations of TEMPO and Cl(+1) and is high enough to be applied in potential industrial processes such as catalytic oxidation of cellulosic pulps. $TEMPO^+$ was the dominant form of TEMPO in the catalytic oxidation of a birch kraft pulp under optimal conditions which confirms the earlier observation on the oxidation of the hydroxymethyl groups being the rate-determining step in the catalytic process.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.apcata.2015.07.024

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