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Global kinetics of the alkaline oxidative degradations of lactose

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Abstract

The kinetics of the “classical” and the anthraquinone-2-sulfonate (AMS) catalyzed alkaline oxidative degradation of lactose and related carbohydrates have been investigated. Batch experiments were carried out at initial sugar concentrations from 100 to 375 mol m⁻³, AMS concentrations from 0 to 5 mol m⁻³, di-oxygen concentrations from 0.28 to 1.38 mol m⁻³, a pH from 11.5 to 13.5 and temperatures at 293 and 303 K. A reaction network is presented that accounts for the main products formed. Regression analysis of the experimental data, using a multi-response Marquardt algorithm, allowed the experimental data to be described adequately by a reaction sequence consisting of different oxidation pathways starting from the sugar enediolates and having the formation of the latter as the common, most important, rate-determining step.

Keywords: Alkaline oxidation, Kinetics, Lactose, Oxidative degeneration

1. Introduction

The oxidative degradation of reducing carbohydrates in alkaline media has been studied extensively in the past. For lactose (LAC) this so called Spengler–Pfannenstiel oxidation has been recently compared with the AMS–H₂O₂ catalyzed alkaline oxidative degradation [1]. Addition of catalytic amounts of AMS resulted in a significantly improved selectivity of the oxidation of lactose with oxygen into β -D-galactopyranosyl-(1→3)-D-arabinonate (GARA) and formate (FA). Moreover, in contrast to the “classical” Spengler–Pfannenstiel oxidation, this increased selectivity was maintained at temperatures up to 323 K, allowing a decrease of batch time necessary for complete conversion.

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Earlier kinetic data on the “classical” alkaline oxidative degradation of reducing carbohydrates have been given by Bamford and Collins [2], Dubourgh and Naffa [3], Roper et al [4] and de Wilt et al [5–7]. To obtain high selectivities for the cleavage products, oxidative degradations had to be carried out at low temperatures, at high pH, and at high di-oxygen concentration. For D-glucose the ratio of oxidation reactions to isomerization reactions in strongly alkaline solutions has been accounted for recently [8]. An investigation of the kinetics of both the “classical” and the AMS catalyzed alkaline oxidative degradation of lactose and related carbohydrates is reported in the present paper. The objectives of the kinetic studies were the development of the rate equations to predict the reaction mixture composition and selectivities for various process conditions, and to obtain insight in the catalytic role of AMS in the reaction sequence. The rate equations also can be used to optimize the process of sugar oxidation and to evaluate the economic feasibility.

2. Experimental

2.1 Oxidation procedure and conditions

Solutions containing α -lactose monohydrate (LAC), lactulose (LU), or D-galactose (GAL) were oxidized semi-batchwise with or without catalytic amounts of AMS as described before [1]. The pH of the reaction mixture was controlled by using a pH-electrode (Applicon GG9), a pH-meter (Radiometer PHM 82), a titrator (Radiometer TTT 80), and an autoburette (Radiometer ABU 80). The pH was set by the addition of 9 M KOH to the reaction mixture, in contrast to the experiments described before [1], which were performed in an excess of alkali at an initial $C_{\text{sugar}}/C_{\text{KOH}}$ ratio of 1 to 3. At 293 K 12 experiments were carried out and at 308 K 22 experiments, the results of which were used for regression. Some additional experiments at 298 K were only used for qualitative conclusions. Standard starting concentration was 250 mol m^{-3} . At 308 K two lactose experiments started with 125 and 375 mol m^{-3} respectively. Conditions were varied in the range $0 < C_{\text{AMS}} < 5 \text{ mol m}^{-3}$, $0.28 < C_{\text{O}_2} < 1.38 \text{ mol m}^{-3}$ and $11.5 < \text{pH} < 13.5$. Standard conditions were $C_{\text{AMS}} = 0 \text{ mol m}^{-3}$, $C_{\text{O}_2} = 1.38 \text{ mol m}^{-3}$, $\text{pH} = 13.1$ at 293 K (“classical” route) and $C_{\text{AMS}} = 2.5 \text{ mol m}^{-3}$, $C_{\text{O}_2} = 1.09 \text{ mol m}^{-3}$, $\text{pH} = 12.5$ at 308 K (“AMS” route).

2.2 Sampling and analysis

For each experimental run 6 to 12 samples were withdrawn at suitable intervals. The samples were quickly pipetted, acidified with 2 M HCl to pH 8.5–9.5, diluted and stored in the refrigerator at ca. 277 K. The samples were analyzed by HPLC as reported before and corrected for the effects of sampling and diluting [9].

2.3 Conversion and selectivity

The conversion, X , and the selectivity towards GARA, S , were calculated as

$$X = \frac{C_{\text{LAC},0} + C_{\text{LU},0} - C_{\text{LAC}} - C_{\text{LU}}}{C_{\text{LAC},0} + C_{\text{LU},0}} \quad (1)$$

$$S = \frac{C_{\text{GARA}}}{C_{\text{LAC},0} + C_{\text{LU},0} - C_{\text{LAC}} - C_{\text{LU}}} \quad (2)$$

2.4 Parameter estimation

The regression of the experimental data was based on the maximum-likelihood criterion, as outlined by Froment and Hosten [10]. Parameter estimates were obtained by applying the least square criterion to the observed product concentrations, $[P]$, and the calculated product concentrations, $[\hat{P}]$, i.e. by minimizing the residual sum of squares

$$S(\beta) = \sum_{k=1}^n \sum_{l=1}^n \sigma^{kl} \sum_{i=1}^m ([P_k]_i - [\hat{P}_k]_i)([P_l]_i - [\hat{P}_l]_i) \rightarrow \text{MIN} \quad (3)$$

n being the number of responses, m being the number of experimental time sampling points and σ^{kl} being the (k,l) elements of the inverse of the covariance matrix of the experimental errors on the responses $[P]$. The latter was estimated from a preliminary parameter estimation based upon a minimization of Eq. 3 with σ^{kl} being the elements of the unity matrix, i.e., assuming equal variances for the errors of the different responses and neglecting any correlation. Minimization was achieved with a multi-response Marquardt algorithm [11]. The calculated product concentrations, $[\hat{P}]$, were obtained by integration of the corresponding continuity equations

$$\frac{d[\hat{P}_k]}{dt} = R_{v,P_k} \quad k = 1, \dots, n \quad (4)$$

with R_{v,P_k} the net rate of production of the corresponding component.

The parameter estimates were tested for statistical significance by means of their approximate individual t values. The significance of the global regression was expressed by means of the ratio of the mean regression sum of squares to the mean residual sum of squares, which is distributed according to F [12]. A high value of the F ratio corresponds to a high significance of the global regression over the whole range of investigated conditions. The adequacy of the mathematical models used for the regression was tested by analysis of the residuals. Model discrimination was based on statistical testing of the significance of the kinetic parameters and of the global regression.

3. Experimental results

3.1 “Classical” alkaline oxidative degradation of lactose

Figs 1 and 2 show typical concentration profiles versus time for the sugar components and the oxidation products for a “classical” alkaline oxidative degradation of lactose at 293 K

3.1.1 Influence of oxygen concentration

Variation of the oxygen concentration from 0.28 to 1.38 mol m⁻³ resulted in an increase of the selectivity for GARA from ca. 25 to 66 mol% and a doubling of the pseudo first-order rate coefficient of lactose

3.1.2 Influence of pH

The influence of pH, in the range from 11.7 to 13.4, was reflected by an increase in pseudo first-order rate coefficient of lactose by a factor of 4. The selectivity for GARA increased from 18 to 81 mol%

3.1.3 Influence of temperature

The pseudo first-order rate coefficient of lactose increased by a factor of 5 when increasing the temperature from 293 K to 308 K. Many unidentified side products were formed at 308 K and the selectivity for GARA decreased from 66 to 28 mol%

Fig. 1 Concentrations of (□) LAC, (△) LU and (▽) GAL versus batch time for the “classical” oxidative degradation of lactose at 293 K. Symbols represent analyzed concentrations, full lines represent calculated concentrations, obtained by integration of continuity equations (Eq. 4) using parameter estimates from Table 2 (second column) at standard conditions.

Fig 2 Concentrations of ($\square$) GARA, (+) FA, (∇) 2-deTA, ($\triangle$) GA and LYXA ($\circ$) versus batch time for the "classical" oxidative degradation of lactose at 293 K. Symbols represent analyzed concentrations, full lines represent calculated concentrations, obtained by integration of continuity equations (Eq 4) using parameter estimates from Table 2, (second column) at standard conditions

3.1.4 Influence of feedstock

GAL, GARA, FA, GA, and 2-deTA were found to be primary reaction products for both the lactose and lactulose feedstocks. The pseudo first-order rate constant of lactulose was about 2 times greater than the pseudo first order rate constant of lactose. However, the corresponding selectivity towards GARA amounted to 24 mol% only, instead of 66 mol% for lactose at standard conditions (293 K).

3.2 AMS-catalyzed alkaline oxidative degradation of lactose

Figs 3 and 4 show typical concentration profiles versus time for the sugar components and the oxidation products for the AMS-catalyzed alkaline oxidative degradation of lactose at 308 K.

3.2.1 Influence of AMS concentration

Variation of the concentration of AMS, C_{AMS} , from 0 to 5 mol m⁻³ resulted in an increased selectivity for GARA from 25 to 88 mol%, and a doubling of the pseudo first order rate coefficient of lactose. The increase of the pseudo first order rate coefficient of lactose and the increase of the selectivity towards GARA were observed in the range $0 < C_{\text{AMS}} < 1$ mol m⁻³. Above this concentration no significant amounts of lactulose could be detected anymore.

In contrast to what has been published before [1] on experiments performed with an excess of alkali the addition of an amount of H₂O₂ up to 5 mol m⁻³ at the

Fig 3 Concentrations of ($\square$) LAC, (Δ) LU and (∇) GAL versus batch time for the AMS-catalyzed oxidative degradation of lactose at 308 K. Symbols represent analyzed concentrations, full lines represent calculated concentrations, obtained by integration of continuity equations (Eq 4) using parameter estimates from Table 3 at standard conditions

Fig 4 Concentrations of ($\square$) GARA, (+) FA, (∇) 2-deTA, (Δ) GA and ($\circ$) LYXA versus batch time for the AMS-catalyzed oxidative degradation of lactose at 308 K. Symbols represent analyzed concentrations, full lines represent calculated concentrations, obtained by integration of continuity equations (Eq 4) using parameter estimates from Table 3 at standard conditions

start of an experiment appeared to have no significant influence. It therefore must be concluded that the addition of AMS alone is sufficient for the improvement of reaction rate and selectivity. This will be further clarified when discussing the reaction sequence.

3.2.2 Influence of oxygen concentration

The influence of the oxygen concentration on the reaction was investigated at 298 K. No significant influence was observed, neither on the pseudo first order rate constant of lactose nor on the selectivity to GARA. In contrast to the “classical” alkaline oxidation the AMS-catalyzed reaction is not sensitive towards the oxygen concentration from 0.63 to 1.26 mol m⁻³.

3.2.3 Influence of pH

The influence of pH, in the range from 11.5 to 13.0, was reflected by an increase in the pseudo first order rate coefficient for lactose by a factor of 4. No significant influence on the selectivity to GARA was observed, this being again in contrast with the “classical” reaction.

3.2.4 Influence of temperature

The pseudo first order rate coefficient of lactose increased by a factor of 5 when increasing the temperature from 293 K to 308 K. Again in contrast with the “classical” reaction no significant influence was observed for the selectivity towards GARA.

3.2.5 Influence of feedstock and starting concentration

GAL, GARA, FA, GA, and 2-deTA were found to be the primary reaction products for both lactose and lactulose as feedstock. Where addition of AMS results in significant improvements for the lactose oxidation only marginal differences in the pseudo first order reaction rate coefficient and the selectivity towards GARA were observed between the “classical” and the AMS-catalyzed oxidative degradation. Lactulose performed at 298 K. In the range 125 to 375 mol m⁻³ the lactose starting concentration appeared to have no influence on rate coefficients and selectivity, indicating a reasonable ideality of the solutions.

4. Reaction network and global production rate constants

Based on the experimental results and the proposed mechanisms for both the “classical” and AMS-catalyzed alkaline oxidative degradation of lactose, as described before [1], a reaction network is presented in Fig. 5 that accounts for the main reaction products formed.

The network indicates that the following quantities can determine the kinetics: the sugar ionization constants K_L , K_U and K_G , the sugar anion enolization rate and

Fig 5 Reaction network for the "classical" and AMS-catalyzed oxidative degradation of lactose

reverse rate constants k_{e1} , k_{-e1} , k_{e2} , k_{-e2} , k_{e3} , k_{-e3} , the enediolate oxidation and reverse rate constants k_0 and k_{-0} , the peroxy anion ionization constant K_p , the peroxide cleavage rate constant k_a , the $E_{2,3}$ enediolate β -elimination rate constant k_{sp} and the enediolate shift rate constants k_s and k_{-s} . Last but not least the contribution of the AMS-catalyzed oxidation is reflected in the rate constant k_{oa} . Oxidation of enediolate $E_{2,3}^-$ by oxygen and/or AMS to β -D-galactopyranosyl-(1 $\rightarrow$ 2)-D-tetronate could be neglected as was apparent from the analytical results. Neither

the concentration of hydrogen peroxide, nor the oxygen concentration revealed an influence on the pseudo first-order rate constant of lactose and on the selectivity to GARA for the AMS-catalyzed reaction. Hence, the oxidation of $E_{1,2}^-$ via the AMS-route is considered as an irreversible process. Since reduction of AMS results in a red color and no colorization was observed during our reactions the reoxidation of reduced AMS by di-oxygen resulting in OOH^- can be considered fast and therefore, during the reaction, the concentration of AMS will be constant. Hence, in the additional, parallel route from $E_{1,2}^-$ to $GARA^-$ and FA^- the oxidation of $E_{1,2}^-$ by AMS to the ulose derivative [1] will be rate determining. The ulose derivative is rapidly oxidized by the OOH^- generated to $GARA^-$ and FA^- and could never be detected during the analytical procedures.

The β -elimination reaction of $E_{2,3}^-$ results in D-galactose and a deoxyhexodiulose derivative [1]. As the latter never appeared in the analysis it is assumed that this component is rapidly further oxidized to GA^- and $2deTA^-$. Although, in principle, D-galactose will probably react similarly as lactose it appeared that the oxidation of this sugar could be simplified taking the enolisation as the only rate limiting step and all further reactions of the enediolate as fast and irreversible. The generally low concentrations of D-galactose during lactose oxidations did not allow for a more detailed regression.

Taking into account that the enediolate and peroxide species could not be analysed and that the other products made up over 98% of the mass-balance it is clear that the rate constants presented in Fig. 5 cannot all be evaluated independently. Therefore, a simplified reaction network is given in Fig. 6, covering all the products that make up 98% of the reaction mixture and presenting the three global reactions: isomerisation, oxidation and degradation by β -elimination.

According to Fig. 6 the net rates of production of the components, $R_{v,p}$, can be given generally by

$$R_{v,p} = aC_{LAC} + bC_{LU} + cC_{GAL} \quad (5)$$

a being a combination of $\alpha k_{L,ox}$, $\alpha k_{L,iso}$ and $\alpha k_{L,\beta}$, i.e. of the global rate constants corresponding to the three reactions of lactose; b being a combination of $\alpha k_{U,ox}$, $\alpha k_{U,iso}$ and $\alpha k_{U,\beta}$, i.e. of the global rate constants corresponding to the three global reactions of lactulose; c being $\alpha k_{G,ox}$ and α being an element of $\{-1, 0, 1\}$.

For each set of process conditions i.e. at constant temperature, pH, oxygen- and AMS-concentration, an analytical integration of the set of continuity equations (eq. 4 and 5) was feasible.

Of course, the global rate constants given in Fig. 6 are functions of the above mentioned process parameters. This dependency can be understood from the reaction sequence given in Fig. 5. Using the equality of production rates following from Fig. 5 and 6, taking the ionisation of sugars and peroxides essentially at equilibrium and applying the pseudo-steady state approximation to the enediolates and peroxide, it is possible to formulate the global rate constants of Fig. 6 as explicit functions of

Table 1

Global rate constants (Fig 6) as function of the process conditions, C_{O_2} , C_{AMS} and C_{OH-} , and of the rate and equilibrium constants of the individual reactions (Fig 5)

$$\begin{aligned}
 k_{L,ox} &= f_L k_{e1} (\kappa_p C_{O_2} + \kappa_{oa} C_{AMS}) / D_L & (s^{-1}) \\
 k_{U,ox} &= f_U k_{e2} (\kappa_p C_{O_2} + \kappa_{oa} C_{AMS}) / D_L & (s^{-1}) \\
 k_{L,iso} &= f_L k_{e1} \kappa_{e2} / D_L & (s^{-1}) \\
 k_{U,iso} &= f_U k_{e2} \kappa_{e1} / D_L & (s^{-1}) \\
 k_{L,\beta} &= f_L k_{e1} \kappa_s / D_L & (s^{-1}) \\
 k_{U,\beta} &= f_U (\kappa_{e3} + \kappa_{e2} \kappa_s / D_L) & (s^{-1}) \\
 k_{g,ox} &= f_g k_{eg} & (s^{-1})
 \end{aligned}$$

with

$$\begin{aligned}
 f_L &= K_L C_{OH-} / (1 + K_L C_{OH-}) & (-) & \quad \kappa_p = C_{OH-} / (\kappa_o + C_{OH-}) & (-) \\
 f_U &= K_U C_{OH-} / (1 + K_U C_{OH-}) & (-) & \quad \kappa_{oa} = k_{oa} / k_o & (-) \\
 f_g &= K_g C_{OH-} / (1 + K_g C_{OH-}) & (-) & &
 \end{aligned}$$

$$\begin{aligned}
 \kappa_{e2} &= k_{e2} + k_{e3} k_s / k_t & (s^{-1}) \\
 \kappa_{e3} &= k_{e3} k_{sp} / k_t & (s^{-1}) \\
 k_t &= k_s + k_{e3} + k_{sp} & (s^{-1})
 \end{aligned}$$

$$\begin{aligned}
 \kappa_{e1} &= k_{e1} / k_o & (mol\ m^{-3}) & \quad \kappa_s = k_s k_{sp} / (k_t k_o) & (mol\ m^{-3}) \\
 \kappa_{e2} &= (k_{e2} + k_s k_{e3} / k_t) / k_o & (mol\ m^{-3}) & \quad \kappa_o = k_o / (k_a K_p) & (mol\ m^{-3}) \\
 D_L &= \kappa_{e1} + \kappa_{e2} + \kappa_s + \kappa_p C_{O_2} + \kappa_{oa} C_{AMS} & (mol\ m^{-3}) & &
 \end{aligned}$$

$$\begin{aligned}
 k_{L,ox}' &= f_L k_{e1} (\kappa_p C_{O_2} + \kappa_{oa} C_{AMS}) / D_L' & (s^{-1}) \\
 k_{L,\beta}' &= f_L k_{e1} \kappa_{sp} / D_L' & (s^{-1})
 \end{aligned}$$

with

$$\begin{aligned}
 D_L' &= \kappa_{e1} + \kappa_{sp} + \kappa_p C_{O_2} + \kappa_{oa} C_{AMS} & (mol\ m^{-3}) \\
 \kappa_{sp} &= \kappa_s + \kappa_{e2} \kappa_{e3} / (\kappa_{e2} + \kappa_{e3}) & (mol\ m^{-3})
 \end{aligned}$$

the process conditions and the rate constants given in Fig 5. The results are presented in Table 1.

The parameters f_L , f_U and f_G , represent the ionized fractions of LAC, LU and GAL respectively.

Altogether 12 model parameters have been used for the regression of the experimental data obtained for the "classical" alkaline oxidative degradation of lactose

at 293 K the three sugar ionization constants K_L , K_U , and K_G , the enolization rate constants k_{e1} and k_{eg} and the lumped constant κ 's κ_{e2} , κ_{e3} , κ_{-e1} , κ_{-e2} , κ_s , κ_{-0} , κ_{oa} . The physical meaning of the latter will be discussed in the next section.

At concentrations of AMS higher than 1 mol m^{-3} and with lactose as feedstock the analysed concentrations of lactulose were well below the detection limit and, therefore, the global rate coefficients $k_{U \text{ ox}}$, $k_{U \text{ iso}}$, $k_{U \beta}$ and $k_{L \text{ iso}}$ are no longer relevant, and the pseudo first-order rate coefficients $k_{L \text{ ox}}$, $k_{L \beta}$, and $k_{G \text{ ox}}$ are the only ones remaining. Applying also the pseudo-steady state approximation for lactulose, the relations given in the lower section of Table 1 for $k_{L \text{ ox}}$ and $k_{L \beta}$ can be derived. The relation for $k_{g \text{ ox}}$ stays unaffected. This results in a total of 8 model parameters to be used for the regression of the experimental data obtained for the AMS-catalyzed alkaline oxidative degradation of lactose at 308 K: the sugar ionization constants K_L and K_G , the enolization rate constants k_{e1} , and k_{eg} and the lumped constant κ 's κ_{-e1} , κ_{-0} , κ_{oa} , κ_{sp} . Of course, the AMS catalyzed oxidative degradation of lactulose cannot be described by this set of model equations.

5. Regression analysis and discussion

5.1 Parameter estimation at 293 K

For the “classical” alkaline oxidative degradation reactions α -lactose monohydrate was used as feedstock for 6 runs, lactulose for 2 runs, and D-galactose for 2 runs. For the AMS-catalyzed oxidative degradations α -lactose monohydrate was used as feedstock for a duplicate run. A total of 696 experimental data, representing the concentrations of the 9 compounds given in Fig. 6 at different reaction times, were regressed. The parameter estimation was obtained by simultaneous regression of all lactose, lactulose and D-galactose experimental data. The results of the regression analysis of the experimental data are presented in Table 2.

As can be seen from Table 2 the parameter estimates based on the “classical” oxidative degradation experiments alone (left column, 10 experiments) are in good agreement with the parameter estimates based on the total set of data, i.e. including the AMS-catalyzed oxidative degradation experiments (right column, 12 experiments).

Keeping in mind that the ionization constants depend on temperature, sugar concentration, and mode of hydration, the estimated ionization constants K_L and K_G , are in reasonable agreement with the experimental data reported by de Wit [13] and Beenackers [14]. $K_L = 0.068 \text{ m}^3 \text{ mol}^{-1}$ at 291 K, and $K_G = 0.022\text{--}0.030 \text{ m}^3 \text{ mol}^{-1}$ at 298 K.

5.2 Parameter estimation at 308 K

Simultaneous regression of all experimental results for the oxidative degradations at 308 K was not successful, since the analyses of the “classical” oxidative deg-

Fig 6 Simplified reaction network for the "classical" and the AMS-catalyzed oxidative degradation of lactose

Table 2

Comparison of parameter estimates with their individual 95% confidence intervals for both "classical" and AMS-catalyzed alkaline oxidative degradation reactions at 293 K

Parameter	Regression analysis of 10 "classical" runs (F value 5544) Estimate	Regression analysis of all 12 runs (F value 5761) Estimate
K_L ($\text{m}^3 \text{mol}^{-1}$)	0.0663 ± 0.0100	0.0539 ± 0.0080
K_U ($\text{m}^3 \text{mol}^{-1}$)	0.0629 ± 0.0193	0.0686 ± 0.0200
K_G ($\text{m}^3 \text{mol}^{-1}$)	0.0202 ± 0.0035	0.0234 ± 0.0030
k_{e1} (10^{-5}s^{-1})	1.882 ± 0.243	1.944 ± 0.239
k_{eg} (10^{-5}s^{-1})	0.823 ± 0.076	0.764 ± 0.050
κ_{e2} (10^{-5}s^{-1})	1.011 ± 0.088	1.165 ± 0.090
κ_{e3} (10^{-5}s^{-1})	1.071 ± 0.045	1.043 ± 0.041
κ_{-e1} (mol m^{-3})	0.658 ± 0.216	0.443 ± 0.163
κ_{-e2} (mol m^{-3})	0.451 ± 0.095	0.339 ± 0.117
κ_s (mol m^{-3})	0.0473 ± 0.0184	0.0375 ± 0.0160
κ_{-o} (mol m^{-3})	165 ± 49	285 ± 67
κ_{oa} (-)	$(1.621 \pm 0.077)^a$	1.569 ± 0.735

^a Estimated from the two runs with AMS separately, other constants fixed at the values from the 10 "classical" runs

Table 3

Parameter estimates with their individual 95% confidence intervals for the AMS-catalyzed oxidative degradations of lactose at 308 K

Values	Regression analysis of 2 runs (<i>F</i> value 27480)
	Estimate
k_L ($\text{m}^3 \text{mol}^{-1}$)	0.0460 ± 0.0050
K_G ($\text{m}^3 \text{mol}^{-1}$)	0.0204 ± 0.0026
k_{e1} (10^{-5}s^{-1})	15.72 ± 0.62
k_{eg} (10^{-5}s^{-1})	8.13 ± 0.46
κ_{-e1} (mol m^{-3})	1.124 ± 0.220
κ_{-o} (mol m^{-3})	39.6 ± 25.4
κ_{oa} (–)	4.89 ± 0.92
κ_{sp} ($\text{m}^3 \text{mol}^{-3}$)	0.365 ± 0.061

radations of lactose performed at this temperature showed many unidentified compounds in significant amounts. Altogether 1664 experimental data were regressed at 308 K, with α -lactose monohydrate as feedstock for 16 runs, and D-galactose for 6 runs. The results of the regression analysis of the simplified model are presented in Table 3.

5.3 Activation energies and standard reaction enthalpies

Activation energies and standard reaction enthalpies were calculated according to the Arrhenius equation and the van 't Hoff law, using the model parameters estimated by regression analysis of the experimental data at 293 K and at 308 K, see Table 4. The parameter κ_{sp} (293 K) has been calculated from the values of κ_s , κ_{e2} , κ_{-e2} and κ_{e3} using the parameter estimates reported in Table 4 (second column), leading to κ_{sp} (293 K) = 0.198 ± 0.029 , mol m^{-3} .

Since the activation energies or standard reaction enthalpies are calculated from sets of experimental data obtained at only two different temperatures, their individual 95% confidence intervals, as follows from the errors in the original data, are

Table 4

Activation energies or standard reaction enthalpies and their individual 95% confidence intervals, calculated from the parameter estimates obtained by regression analysis at 293 K (Table 2) and 308 K (Table 3)

Parameter	E_{act} or ΔH_{act} (kJ mol^{-1})
K_L ($\text{m}^3 \text{mol}^{-1}$)	-7.9 ± 9.2
K_G ($\text{m}^3 \text{mol}^{-1}$)	-6.9 ± 9.0
k_{e1} (10^{-5}s^{-1})	104.5 ± 6.5
k_{eg} (10^{-5}s^{-1})	118.3 ± 4.3
κ_{-e1} (mol m^{-3})	46.6 ± 20.8
κ_{-o} ($\text{m}^3 \text{mol}^{-3}$)	-98.7 ± 34.2
κ_{oa} (–)	56.9 ± 25.3
κ_{sp} (mol m^{-3})	26.2 ± 9.2

relatively large. No standard reaction enthalpies for the ionization of lactose and D-galactose have been reported in the literature. However, their calculated values are of the same order of magnitude as reported for D-glucose, $\Delta H_{\text{ion}} = -16.7$ kJ mol⁻¹, and D-fructose, $\Delta H_{\text{ion}} = -22.2$ kJ mol⁻¹ [15,16]. The calculated activation energies for the enolization of lactose and D-galactose are in reasonable agreement with the values reported before: $E_{\text{act}}(\text{LAC}) = 114$ kJ mol⁻¹, and $E_{\text{act}}(\text{GAL}) = 104$ kJ mol⁻¹, [1].

5.4 Reaction path analysis, evaluation of κ 's

Apart from being useful for the quantitative description of the process of lactose oxidation and isomerisation, further evaluation of the regression results obtained for the κ 's as presented in Tables 2, 3 and 4 provides further insight in the reaction sequence given in Fig. 5, keeping in mind the definitions of the κ 's in Table 1.

5.5 Rate determining step from $E_{1,2}^-$ to $\text{GARA}^- + \text{FA}^-$, κ_{-0}

The ratio of the forward to the backward reaction of the peroxides (P^- and P^{2-}) is given by $C_{\text{OH}}^- / \kappa_{-0}$ and changes from 0.3 at 293 K to 1.7 at 308 K at a pH of 13.1 and 12.5 respectively. This means that in the reaction of $E_{1,2}^-$ to $\text{GARA}^- + \text{FA}^-$ at lower temperatures the splitting of the peroxide is rate determining while at higher temperatures this is the formation of the peroxide.

5.6 Rate determining step from lactose to peroxide, κ_{-e1} , κ_{-e2}

The ratio of the rate of oxidation of $E_{1,2}^-$ to peroxides to the rate of back-formation of lactose and lactulose is given by $C_{\text{O}_2} / \kappa_{-e1}$ and $C_{\text{O}_2} / \kappa_{-e2}$ respectively. The numbers are 3.1 and 4.1 at 293 K, $C_{\text{O}_2} = 1.38$ mol m⁻³. At 308 K, $C_{\text{O}_2} = 1.09$ mol m⁻³ only κ_{-e1} could be obtained resulting in a forward to backward ratio of 1.0.

Apparently in the sequence lactose to peroxide the enolisation is especially rate determining at low temperature, while at higher temperature oxidation will also have a significant effect on the rate.

5.7 The importance of side reactions from $E_{1,2}^-$, κ_s , κ_{sp}

The rate of formation of degradation products from $E_{1,2}^-$ via $E_{2,3}^-$ relative to the rate of peroxide formation is given by $\kappa_s / C_{\text{O}_2}$. At 293 K and $C_{\text{O}_2} = 1.38$ mol m⁻³ this ratio amounts to 0.03, reflecting the relative unimportance of the shift reaction. The two terms making up κ_{sp} , κ_s and $\kappa_{-e2}\kappa_{e3} / (\kappa_{e2} + \kappa_{e3})$ give the relative importance of the side-reaction of lactose through the shift or through the isomerisation reaction. At 293 K the ratio of the two terms amounts to 0.2 which means that most

of the side-products are formed via lactulose. More experiments with lactulose are needed to substantiate if this situation still holds at higher temperatures.

5.8 Enolisation of lactulose, κ_{e2} , κ_{e3}

If it is assumed that the value of k_{-s}/k_t is small, it follows from the value of κ_{e2} at 293 K that $k_{e2} = 1.2 \times 10^{-5} \text{ s}^{-1}$ or slightly less and, depending on the ratio k_{sp}/k_t , k_{e3} will be substantially larger than $1.0 \times 10^{-5} \text{ s}^{-1}$. These values together with a somewhat smaller influence of the backward reaction for lactulose ($k_{-e2} < k_{-e1}$), results in the total enolisation rate of lactulose being higher than of lactose.

5.9 Importance of the AMS-catalyzed route, κ_{oa}

Multiplying κ_{oa} with C_{AMS}/C_{O_2} gives the rate of the oxidation of $E_{1,2}^-$ by AMS relative to the one by oxygen. With C_{AMS} being 2.5 mol m^{-3} these relative rates amount to 2.9 at 293 K, $C_{O_2} = 1.38 \text{ mol m}^{-3}$ and to 11 at 308 K, $C_{O_2} = 1.09 \text{ mol m}^{-3}$. To estimate the relative amount of GARA which is obtained through both routes these numbers have to be corrected with the ratio of forward to backward reaction of the peroxides given above. The final result is that 92% of the GARA is formed through the AMS-route at 293 K and 95% at 308 K.

6. Process simulation

6.1 “Classical” alkaline oxidative degradation of lactose

As shown by Figs. 1 and 2, the model adequately describes the experimental data of the “classical” alkaline oxidative degradation of lactose at 293 K. The Figs.

Fig. 7 Simulated global rate coefficients $k_{L,ox}$, $k_{L,iso}$ and $k_{L,b}$ and final selectivity versus C_{O_2} at 293 K and standard conditions.

Fig. 8 Simulated global rate coefficients $k_{L,ox}$, $k_{L,iso}$ and $k_{L,b}$ and final selectivity versus pH at 293 K and standard conditions

7 and 8 present the influence of the oxygen concentration and the pH on the global rate coefficients $k_{L,ox}$, $k_{L,iso}$ and $k_{L,b}$ and the selectivity for GARA at 293 K. Especially $k_{L,ox}$, and hence the selectivity for GARA, increases with increasing C_{O_2} and pH. This is in agreement with the experimental results and also with the results obtained for D-glucose and D-fructose oxidative degradation by de Wilt [7], and for isomaltulose by Roper [4]. It is clear that the “classical” alkaline oxidative degradation of reducing carbohydrates in general must be carried out at low temperatures, at high partial oxygen pressures and at high pH to obtain high selectivity.

6.2 Alkali-AMS-catalyzed oxidative degradation of lactose

As shown by Figs. 3 and 4, the simplified model adequately describes the experimental data of the AMS-catalyzed alkaline oxidative degradation of lactose at

Fig. 9 Simulated global rate coefficients $k_{L,ox}$ and $k_{L,b}$ versus C_{AMS} at 308 K and standard conditions

Fig. 10 Simulated global rate coefficients $k_{L,ox}$ and $k_{L,b}$ versus pH at 308 K and standard conditions

308 K Figs 9 and 10 present the influence of C_{AMS} and pH on the rate coefficients $k_{L,ox}$ and $k_{L,b}$ at 308 K

As can be seen from Fig 9, the rate constant $k_{L,ox}$ only depends on the concentration of AMS in the range 0–1 mol m⁻³. Above this concentration of AMS, $k_{L,ox}$, and, hence, the selectivity for GARA, does not increase significantly anymore. Fig 10 shows that $k_{L,ox}$ also significantly depends on the pH. As will be clear also from the foregoing paragraph, the influence of temperature, C_{O_2} and pH on the selectivity is largely suppressed by the addition of AMS by the opening of a new parallel oxidation route which does not depend on these parameters.

7. Conclusions

The AMS-catalyzed alkaline oxidative degradation of lactose has been compared with the “classical” alkaline oxidative degradation of lactose in a quantitative way. Based on the experimental results, a reaction network is presented that accounts for the main products formed. Regression of the experimental data, using a multi-response Marquardt algorithm, allowed the experimental data to be described adequately over a wide range of reaction conditions. Using the parameter estimates obtained at 293 K and 308 K, activation energies and standard reaction enthalpies were calculated, which are in reasonable agreement with reported experimental values. Simulations, using the obtained parameter estimates showed the quantitative effects of the process variables. The enolization step of the lactose anion was found to be the most important rate-determining step. Oxidation of the intermediate enediolate $E_{1,2}^-$ by both AMS and molecular oxygen, was found to proceed in parallel by different mechanisms. The oxidation of the enediolate $E_{1,2}^-$ by AMS can be considered as an irreversible step. Addition of H_2O_2 does not influence reaction rate and selectivity because sufficient H_2O_2 is formed, in the reoxidation of $AMSH^-$.

by di-oxygen to oxidize the intermediate ulose derivative to GARA and FA. In contrast to the “classical” oxidative degradation of lactose, the AMS catalyzed oxidative degradation of lactose does not show a dependence on C_{O_2} . Where for the oxidative degradation of lactose an increase of the temperature from 293 K to 308 K did result in a sharp decrease of selectivity to GARA, with the addition of AMS high selectivities could be maintained.

List of symbols

C_P	concentration of P, (mol m^{-3})
$C_{P,0}$	initial concentration of P, (mol m^{-3})
f_P	ionized fraction of P (–)
K	ionization constants, ($\text{m}^3 \text{mol}^{-1}$)
k	reaction rate constants (s^{-1}) or ($\text{m}^3 \text{mol}^{-1} \text{s}^{-1}$)
κ	complex reaction rate constants or rate ratios (s^{-1}), (mol m^{-3}) or (–)
$R_{v,P}$	net rate of production of P, ($\text{mol m}^{-3} \text{s}^{-1}$)
S	selectivity to GARA, (Eq. 2) (–)
t	time (s)
X	conversion, (Eq. 1) (–)

Abbreviations

AMS	anthraquinone-2-sulfonate
2deTA [–]	2-deoxy-D-tetronate
$E_{1,2}^-$	lactose 1,2-enediol anion
$E_{2,3}^-$	lactose 2,3-enediol anion
FA [–]	formate
GA [–]	glycolate
GAL	D-galactose
GARA [–]	β -O-D-galactopyranosyl-(1 → 3)-D-arabinonate
LAC	lactose
LU	lactulose
LYXA [–]	D-lyxonate
P_L^-	lactose peroxide anion
P_L^{2-}	lactose peroxide dianion

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