Available online at www.sciencedirect.com
ScienceDirect
Catalysis Today 121 (2007) 92–99
CATALYSIS TODAY
www.elsevier.com/locate/cattod

From renewable raw materials to high value-added fine chemicals—Catalytic hydrogenation and oxidation of D-lactose

Jyrki Kuusisto [a,*], Anton V. Tokarev [a], Elena V. Murzina [a], Mattias U. Roslund [b], Jyri-Pekka Mikkola [a], Dmitry Yu. Murzin [a], Tapio Salmi [a]

[a] *Laboratory of Industrial Chemistry, Process Chemistry Centre, Department of Chemical Engineering, Faculty of Technology at Åbo Akademi University, Biskopsgatan 8, FI-20500 Turku, Finland*
[b] *Laboratory of Organic Chemistry, Faculty of Mathematics and Natural Sciences at Åbo Akademi University, Biskopsgatan 8, FI-20500 Turku, Finland*

Available online 4 January 2007

Abstract

Kinetics and reaction mechanism of catalytic hydrogenation and oxidation of D-lactose were studied in three-phase laboratory reactors. Catalyst screening results and influence of temperature, pressure, catalyst loading and pH are reported as D-lactose was either catalytically hydrogenated to lactitol or oxidized to lactobionic acid. The product yield was significantly influenced by reaction conditions and catalyst choice. Additionally, during oxidation and hydrogenation processes, catalyst deactivation was severe under non-optimized conditions. Temperature dependency of lactose mutarotation was determined by NMR analysis.

Keywords: Lactose; Lactitol; Lactobionic acid; Hydrogenation; Oxidation; Mutarotation; NMR

1. Introduction

Lactose, a milk sugar, is a reducing disaccharide consisting of glucose and galactose moieties, bound together with a β 1–4 glycosidic linkage. In aqueous solution at 20 °C, lactose exists in two anomeric forms: 62.7% as β-lactose and 37.3% as α-lactose [1]. The lactose content of milks from different mammals varies between 0 and 9%. For example, cow milk contains about 4.9% and human milk about 6.7% of lactose [2]. The estimated annual worldwide availability of lactose as a by-product from cheese manufacture is several million tons [2,3]. However, only about 400,000 t/a lactose is processed further from cheese whey [4]. Non-processed whey causes an environmental problem due to its high biochemical (BOD) and chemical oxygen demand (COD) [3]. The relatively low solubility of lactose in water limits its use in many applications. Another restricting factor is the inability of lactose intolerant people, who have a low level of lactase enzyme in the body, to digest milk sugar [2]. Therefore, development of value-added products from waste generated during cheese manufacturing processes is welcomed. Lactitol (by hydrogenation), lactulose (by isomerization) and lactobionic acid (by oxidation) are the industrially most important lactose derivatives [5–9].

Lactitol is a sugar alcohol, derived by catalytic reduction of the glucose part of the disaccharide, lactose. Lactitol is suitable for development of sugar-free, reduced calorie and low glycaemic index products, showing e.g. non-cariogenic and prebiotic properties [10]. Sugar alcohols, such as lactitol, xylitol and sorbitol, are commonly prepared in industry by catalytic hydrogenation of corresponding sugar aldehydes over sponge nickel and ruthenium on carbon catalysts [11–17].

Sodium salt of lactobionic acid is synthesized by catalytic oxidation of glucose moiety of lactose. The largest commercial use of lactobionic acid is as a major constituent of organ preservation fluids during transplantation procedure [18]. Sugar aldehydes are oxidized catalytically in aqueous alkaline medium at relatively moderate temperatures (40–70 °C) with

* Corresponding author. Tel.: +358 2 2154574; fax: +358 2 2154479.
E-mail address: jkuusist@abo.fi (J. Kuusisto).

0920-5861/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.cattod.2006.11.020

air or molecular oxygen under atmospheric pressure. Earlier it has been found that platinum and palladium supported on carbon catalysts are good carbohydrate oxidation catalysts, especially when promoted with bismuth [19–22]. Previously it has been shown that supported gold catalysts have an excellent activity and long term stability for sugar oxidations [23–25]. The combined lactose oxidation and hydrogenation scheme is displayed in Fig. 1.

2. Experimental

2.1. Dynamic NMR measurements of lactose mutarotation in D_2O

All proton NMR spectra were recorded on a Bruker Avance 600 NMR spectrometer. A Bruker variable temperature unit (B-VT3000) controlled the sample temperature. Proton spectra were recorded at 600.13 MHz using a 5 mm direct broadband probe equipped with z-axis pulsed field gradient capability. ^{1}H measurements were performed in D_2O, referenced to DSS (2,2-dimethyl-2-silapentane-5-sulfonate sodium salt, 0.00 ppm). All experiments were repeated three times at each temperature, and the reported values are the average from these measurements. To study the mutarotation of lactose 30 mg lactose monohydrate (Leprino Foods) was mixed with 500 μl D_2O. The prepared solution was stored over night at room temperature under mixing and DSS was added just prior the NMR analysis. The temperature dependence was determined after solution was held at each measurement temperature at least for 2 h. In an another experiment, 15 mg of lactose monohydrate was mixed with 500 μl D_2O and the mutarotation kinetics was determined as a function of time, at 20 °C, after D_2O addition.

2.2. Lactose hydrogenation experiments

The lactose hydrogenation experiments were carried out batchwise in a three-phase laboratory scale reactor (Parr Co.) operating at 20–70 bar and between 110 and 130 °C. The catalyst loadings of supported noble metal catalysts varied between 4 and 11.2 g/l and in case of nickel catalysts, between 11.2 and 44.8 g/l. The D-lactose concentration was 1.31 mol/l in the majority of experiments. The reactor was equipped with a heating jacket, a cooling coil, a filter (0.5 μm metal sinter) in a sampling line and a bubbling chamber (for removing dissolved air from the liquid phase prior the hydrogenation experiments). The effective liquid volume of the reactor was about 125 ml (total volume 300 ml) and it was equipped with a hollow shaft concave blade impeller to ensure efficient mixing and gas dispersion into the liquid phase. The impeller rate was fixed at 1800 rpm in all of the kinetic experiments to ensure operation at the kinetically controlled regime [28]. The median particle size of sponge nickel catalyst was below 35 μm and for Ru/C catalyst less than 20 μm, thus the mass transfer resistance inside the catalyst particles was negligible.

2.3. Lactose oxidation experiments

A special shaker reactor (Parr Co.) for in situ catalyst potential measurements was constructed. It is an attractive alternative to stirred systems, since, first, it is convenient for catalyst potential measurements and, second, avoids appearance of stagnant zones of solution, thus improving gas to liquid mass transfer. The developed reactor consists of dry and wet compartments giving possibilities to operate at elevated pressures, since not only part of the electrode should be immersed into reaction media, but also

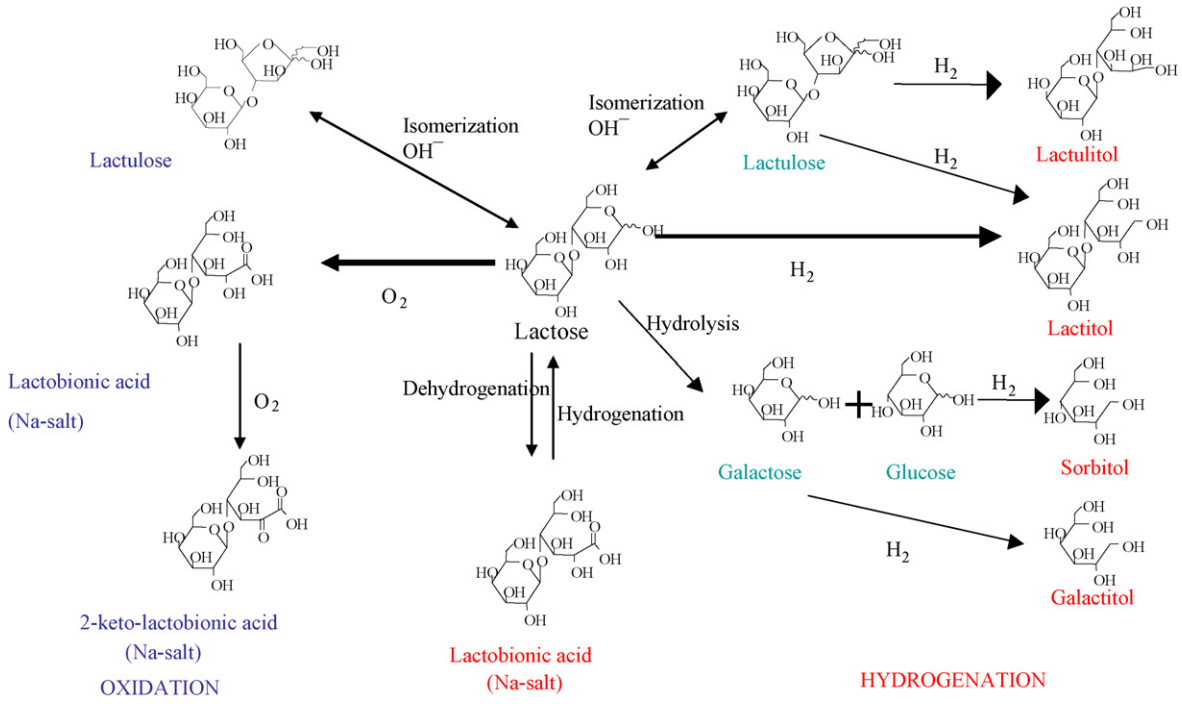

Fig. 1. The combined lactose oxidation (to the left) and hydrogenation (to the right) scheme.

electrodes for pH and potential measurements should be kept under the same pressure as a whole. To ensure constant composition of a gas mixture over reaction media, it is necessary to use a continuous gas flow through the reactor. To this end a special stainless steel cooler was constructed to separate gas from the liquid. A constant ratio between nitrogen and oxygen in the gas mixture is maintained by mass flow controllers (Brooks 5850E). The overall flow was 20 ml/min, oxygen flow being 2.5 ml/min in the majority of experiments. The stainless steel cup of the reactor is used as an electrode collector for measurements of the catalyst potential. For this purpose all parts of the reactor are electrically isolated from the shaking device (mechanical part of "3916 Hydrogenating Apparatus" Parr® with shaking frequency four double movements per second). The lactose oxidation experiments were carried out operating at 50–70 °C, at pH from 6 to 8 and oxygen concentration between 12.5 and 37.5% at atmospheric pressure. The catalyst amount was 0.5 g, the effective liquid volume of the reactor was 100 ml (total volume 250 ml) and D-lactose concentration 0.0996 mol/l in majority of the experiments. Potential measurements were performed versus Ag/AgCl electrode. Constant pH of reaction media was maintained by automatic titration device (Metrohm Titrino 751) at pH-stat mode, since a constant pH level is important for kinetic studies and to avoid undesired side reactions. Electrochemical potential measurement of the catalyst reflects the situation about adsorbed species on the catalyst surface in situ. The steady-state catalyst potential provides real on time information on the balance between oxidation and reduction processes and thus offers an instrument for controlling the rate of oxygen supply, selectivity and catalyst deactivation.

Table 1
Temperature dependency of lactose equilibrium and mutarotation kinetics at 20 °C in deuterium oxide

Temperature (°C)	Time (min)	α-Lactose (%)	β-Lactose (%)
20	Equilibrium	37.7	62.3
40	Equilibrium	38.4	61.6
80	Equilibrium	39.5	60.5
95	Equilibrium	40.3	59.7
20	6	97	3
20	18	93	7
20	60	87	13
20	77	85	15

2.4. HPLC analysis

The reactor contents were analysed off-line with a High Performance Liquid Chromatography (HPLC, HP 1100), equipped with a Biorad Aminex HPX-87C carbohydrate column. $CaSO_4$ (1.2 mM) in deionized water was used as a mobile phase, since calcium ions improved the resolution of lactobionic acid [26].

3. Results and discussion

3.1. Dynamic NMR measurements of lactose mutarotation in D_2O

In crystalline form, before dissolution, lactose is exclusively in α-form. Lactose monohydrate did not contain any detectable amount of impurities according to the proton NMR analysis. At

Table 2
Lactose hydrogenation, some catalyst screening and parameter evaluation results (56 g lactose in 84 g deionized water)

Catalyst	m_{CAT} (g)	Metal (%)	T (°C)	p (bar)	$CMA_{30\%}$ (mmol/min g)	$Conv._{30\ min}$ (%)	$Yield/con_{max}$ (%)
5% Ru/C	0.84	5	120	50	46.6	35.1	96.0/99.5
5% Ru/C	1.12	5	120	50	58.8	55.2	97.3/100
5% Ru/C	1.40	5	120	50	65.5	71.6	98.1/100
5% Ru/C	1.12	5	110	40	29.8	30.6	97.6/99.7
5% Ru/C	1.12	5	110	60	46.6	42.7	98.2/99.7
5% Ru/C	1.12	5	130	40	106.9	82.6	95.5/100
5% Ru/C	1.12	5	130	60	128.9	88.1	95.9/100
5% Ru/MgO	1.12	5	120	50	80.4	47.8	17.4/63.9
3% Ru/HPS	1.12	3	120	50	19.4	13.8	60.1/68.0
5% Ru/SiO_2	1.12	5	120	50	9.9	15.0	34.0/42.6
5% Ru/Al_2O_3	1.12	5	120	50	9.5	18.9	18.4/39.9
5% Ru/TiO_2	1.12	5	120	50	–	2.0	1.8/10.0
5% Pd/C	1.12	5	120	50	–	0.4	3.5/10.2
5% Pt/C	1.12	5	120	50	–	1.2	4.9/8.4
2% Au/CeO_2	0.50	2	120	50	–	5.6	2.3/19.3
74% Ni/SiO_2	2.8	74	120	50	1.5	47.9	77.0/98.0
30% Ni/Al_2O_3	2.8	30	120	50	1.0	17.7	80.6/86.6
Sponge Ni A	1.4	94	120	50	2.2	44.5	95.7/99.1
Sponge Ni A	2.8	94	120	50	2.2	65.1	97.1/100
Sponge Ni A	5.6	94	120	50	3.0	90.2	97.9/100
Sponge Ni B	2.8	94	110	20	0.5	26.1	89.2/91.8
Sponge Ni B	2.8	94	110	70	1.2	48.2	98.6/99.9
Sponge Ni B	2.8	94	130	20	1.7	56.8	89.4/99.0
Sponge Ni B	2.8	94	130	70	2.6	84.6	96.6/100

m_{CAT} = catalyst loading, metal (%) = active metal loading, $conv._{30\ min}$ = conversion after 30 min, $yield/con_{max}$ = lactitol yield at maximum conversion. Sponge Ni A (Activated Metals), sponge Ni B (Acticat), $CMA_{30\%} = 0.3C_{0,lactose} \times 1000/\tau_{30\%} m_{cat} \omega_{metal}$, $CMA_{30\%}$ = characteristic metal activity, $\tau_{30\%}$ = reaction time required for 30% lactose conversion (min), ω_{metal} = active metal loading.

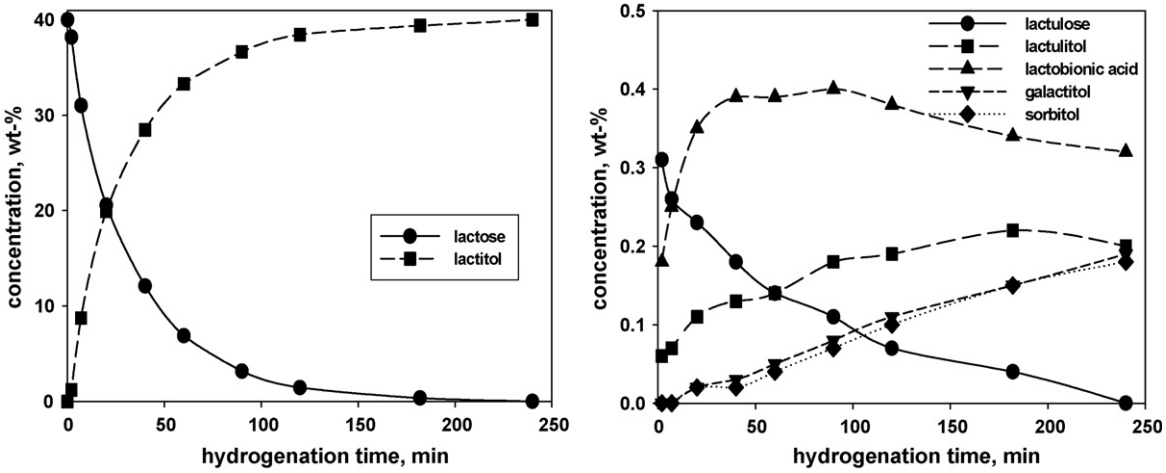

Fig. 2. Evolution of concentrations of lactose and lactitol (on left) and by-products (on right) as lactose was hydrogenated over 22.4 g/l (5% of lactose weight) sponge nickel catalyst at 120 °C and 55 bar H_2.

room temperature, lactose exists in D_2O as α-lactose (37.7%) and β-lactose (62.3%). Furanose or acyclic aldehyde forms of lactose were not detected. According to NMR analysis, the α/β-ratio of lactose at room temperature resembles what has been measured by polarimetric methods for lactose [1] and by NMR for glucose [27]. The relative amount of α-lactose increased only slightly with increasing temperature as shown in Table 1. Lactose mutarotation kinetics at room temperature is relatively slow as indicated in Table 1, but according to Holsinger [1], the rate of lactose mutarotation increases 2.8 times with a 10 °C rise in temperature.

3.2. Lactose hydrogenation results

The performances of several ruthenium (Ru/C, Ru/TiO_2, Ru/SiO_2, Ru/Al_2O_3, Ru/MgO, Ru on crosslinked polystyrene), nickel (various sponge nickel catalysts, Ni/Al_2O_3, Ni/SiO_2, $NiCr/SiO_2$), platinum (Pt/C), palladium (Pd/C, PdPt/C) and gold (Au/C, Au/Al_2O_3, Au/CeO_2, Au/TiO_2) catalysts, in the hydrogenation of lactose to lactitol in aqueous solutions, were studied in the batch reactor. Some of the catalyst screening and parameter evaluation results are summarized in Table 2. The main hydrogenation product was lactitol, while small amounts of

Table 3
Catalyst screening and parameter evaluation results for lactose (99.6 mmol/l) oxidation

Catalyst	Parameters values[a]	$CMA_{30\%}$	Lactose conversion (30 min)	Max LBA yield[b] and respective lactose conversion
5% Pd/C (Degussa)	50 °C	5.84	79	–
	60 °C	6.30	91.7	80.5/91.0
	70 °C	7.73	93.2	83.6/87.3
5% Pd/C (Aldrich)	pH 6	3.99	46.9	–
	pH 7	5.78	76.2	–
	pH 8	5.70	92.9	83.9/92.8
5% Pd/C (Degussa)	O_2-content 12.50%	6.30	91.7	80.5/91.0
	O_2-content 17.50%	8.74	92.5	79.8/89.6
	O_2-content 25.00%	9.40	89.8	82.2/92.9
	O_2-content 37.50%	13.76	60.5	–
1% Pd/C (Alfa)	Pd dispersion 27%	4.85	30.6	–
5% Pd/C (Aldrich)	Pd dispersion 18%	4.60	92.9	83.9/92.8
10% Pd/C (Aldrich)	Pd dispersion 14%	2.55	91.7	78.3/86.5
2% Au/Al_2O_3[c]	m = 100 mg	45.93	29.4	96.8/97.7
2% Au/CeO_2[c]	m = 500 mg	11.10	36.3	99.1/100
5% Pt/Sibunit (IOC, Moscow)	$Pt(NH_3)_4(HCO_3)_2$	1.23	35.6	–
	H_2PtCl_6	3.22	63.1	–

[a] Here stated values if they were different from conditions chosen as a standard (60 °C, pH 8, oxygen content 12.5 %, catalyst loading 500 mg).
[b] Absence of values means that reaction was too slow to reach maximum point where LBA concentration starts to decrease due to consecutive reaction (duration of all experiments was 200 min).
[c] Self-synthesized catalyst.

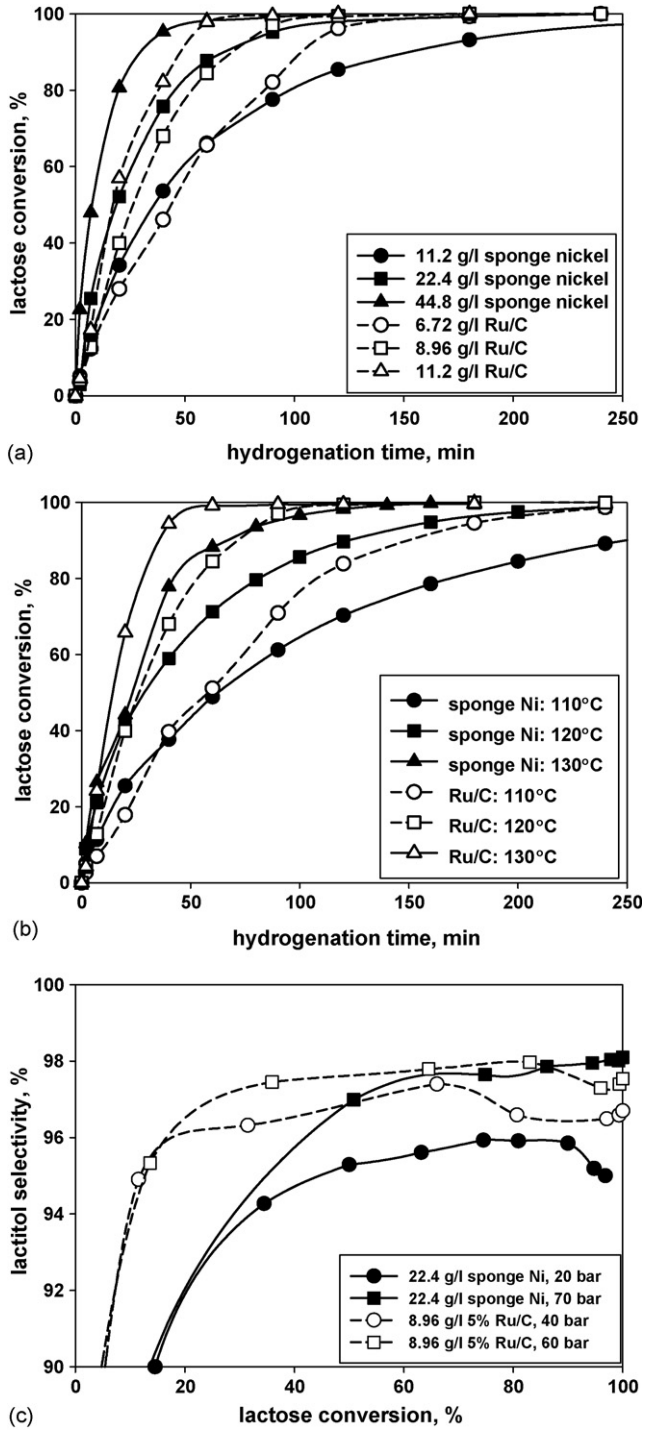

Fig. 3. Lactose (1.31 mol/l) hydrogenation over sponge nickel and 5% Ru/C catalysts: (a) influence of catalyst amount on lactose conversion at 120 °C and 50 bar H_2; (b) influence of temperature on conversion over 22.4 g/l sponge nickel and 8.96 g/l Ru/C at 50 bar; and (c) influence of hydrogen pressure on lactitol selectivity at 120 °C.

lactulose, lactulitol, sorbitol, galactitol and lactobionic acid were detected as by-products (Fig. 1). The Ru/C and sponge nickel catalysts showed the best performance of the studied catalysts. Especially, lactitol selectivities were high both over sponge nickel and Ru/C catalysts. Reaction mechanism and kinetics of lactose hydrogenation over sponge nickel catalyst in aqueous solutions are reported in Ref. [28]. Typical kinetic curves with product distributions on sponge nickel are shown in Fig. 2.

As expected, higher conversion rates were obtained at increased catalyst amounts (Fig. 3a). Lactitol selectivities at 100% lactose conversion level were to some extent higher when high catalyst loadings were used, with selectivity varying between 96.5 and 98.1% at 120 °C and 50 bar H_2. Moreover, there was a clear difference in the by-product distribution at altered catalyst amounts, due to pH and mass transfer (g/l and l/s) effects. For instance, low catalyst loadings led to increased lactose hydrolysis and thus, to higher galactitol and sorbitol formation. An increased hydrogenation temperature clearly improved the reaction rate as revealed by the experiments between 110 and 130 °C (Fig. 3b). From the Arrhenius plots at the temperature range carried out at 383–403 K and pressure ranges of 20–70 bar, it was found that the apparent activation energy for lactose hydrogenation over sponge nickel was 44–52 kJ/mol, while the value was 72–84 kJ/mol for Ru/C. An increased hydrogen pressure had a positive effect on the reaction rate, but the influence was clearly more pronounced at a low pressure range.

The lactitol selectivity decreased as hydrogen pressure was decreased (Fig. 3c) or reaction temperature increased, varying from 90 to 99% within the studied experimental range. Hydrogen mass-transfer limited conditions (inefficient mixing, low hydrogen pressure or high hydrogen consumption due to high catalyst loading, pH and reaction temperature) promote the formation of lactobionic acid. Acidity and low reaction rate favours lactose (and lactitol) hydrolysis and thus, galactitol and sorbitol formation. An increased pH of the reaction solution, favours lactose isomerisation leading to an increased lactulose and lactulitol formation. An optimum pH range for lactose hydrogenation is anticipated being between 5.5 and 6.5. Since the lactose hydrogenation rate increases at higher pH values, elevated pH favour either adsorption of lactose on the catalyst surface or the surface reaction or suppresses catalyst deactivation caused by lactobionic acid formation. Both increased alkali content and increased temperature promote

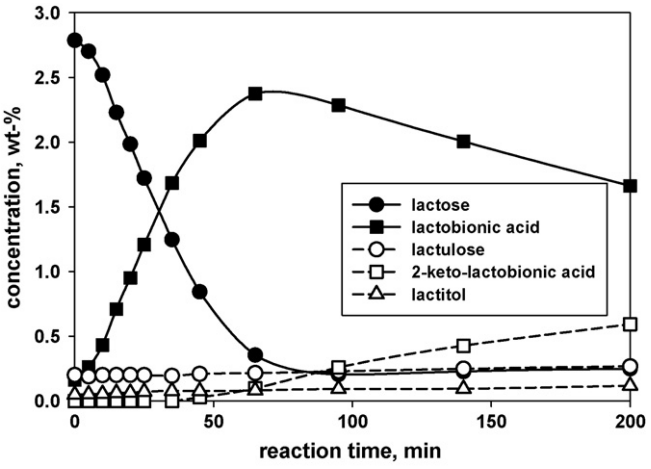

Fig. 4. Evolution of concentrations of lactose, lactobionic acid, 2-keto-lactobionic acid, lactulose and lactitol as lactose was oxidized (oxygen content 12.5 vol.%) over 5% Pd/C catalyst at 70 °C and pH 8.

the formation of ionized sugar species. After ionization, the hydroxyl groups of the glucose unit are re-oriented and the hydration mantle around the sugar anion will be disrupted, which favour interaction between sugar anion and the catalyst [30]. However, lactitol selectivity decreases drastically at alkaline pH range, due to increased lactose isomerization reaction. Adsorption of one of the by-products, lactobionic acid, on the catalyst surface has been proved to be one of main reasons causing catalyst deactivation [28].

3.3. Lactose oxidation results

Lactose oxidation was studied over various supported noble metal catalysts in the shaker reactor under in situ catalyst potential measurement. Some catalyst screening and parameter evaluation results are summarized in Table 3. During the first stage, lactose is oxidized to lactobionic acid, which is in a consecutive reaction oxidized to 2-keto-lactobionic acid. Moreover, small amounts of lactulose (isomerization product of lactose) and lactitol (formed during the reaction start up) were detected as by-products. The lactitol formation, which is the main hydrogenation product of lactose, could even be considered as an evidence of the oxidative dehydrogenation mechanism. A typical kinetic curve with product distributions is displayed in Fig. 4.

The lactose oxidation rate clearly accelerates with increasing pH value (Fig. 5a). In an alkaline solution the catalyst deactivation by product adsorption is suppressed, since lactobionic acid deprotonation and desorption in alkaline media increases, thus no longer occupying the active sites of the catalyst surface. If the initial rate of oxidation is fast enough, oxygen dissolved in the solutions is totally consumed by reacting with the organic molecule on the metal surface. The reaction rate is then limited by gas–liquid oxygen mass transfer, or simply not enough oxygen is fed into reactor as seen at early stage of reactions (Fig. 5a and b) and the risk for over-oxidation of the catalyst is suppressed [29]. Table 3 demonstrates that lactose oxidation with 37.5% oxygen had the highest initial reaction rate, but the catalyst deactivated rapidly due to over-oxidation of metal. Moreover, one can conclude that decrease of the catalyst activity is delayed at elevated temperatures (Fig. 5b), since then the adsorption of lactobionic acid on the active sites of catalyst is weaker.

It is interesting to note that over 2% Au/CeO_2 catalyst consecutive oxidation step of lactobionic acid to 2-keto-lactobionic acid did not take place at all. On the 5% Pd/C catalyst, the lactose oxidation rate started to decrease at 70–90% lactose conversion as consecutive oxidation of lactobionic acid to 2-keto-lactobionic acid is becoming more significant and lactobionic acid selectivity starts to drop drastically (Fig. 5c). High lactobionic acid selectivities and lactose conversion levels were achieved over various supported gold catalysts. These results will be a subject of a separate paper.

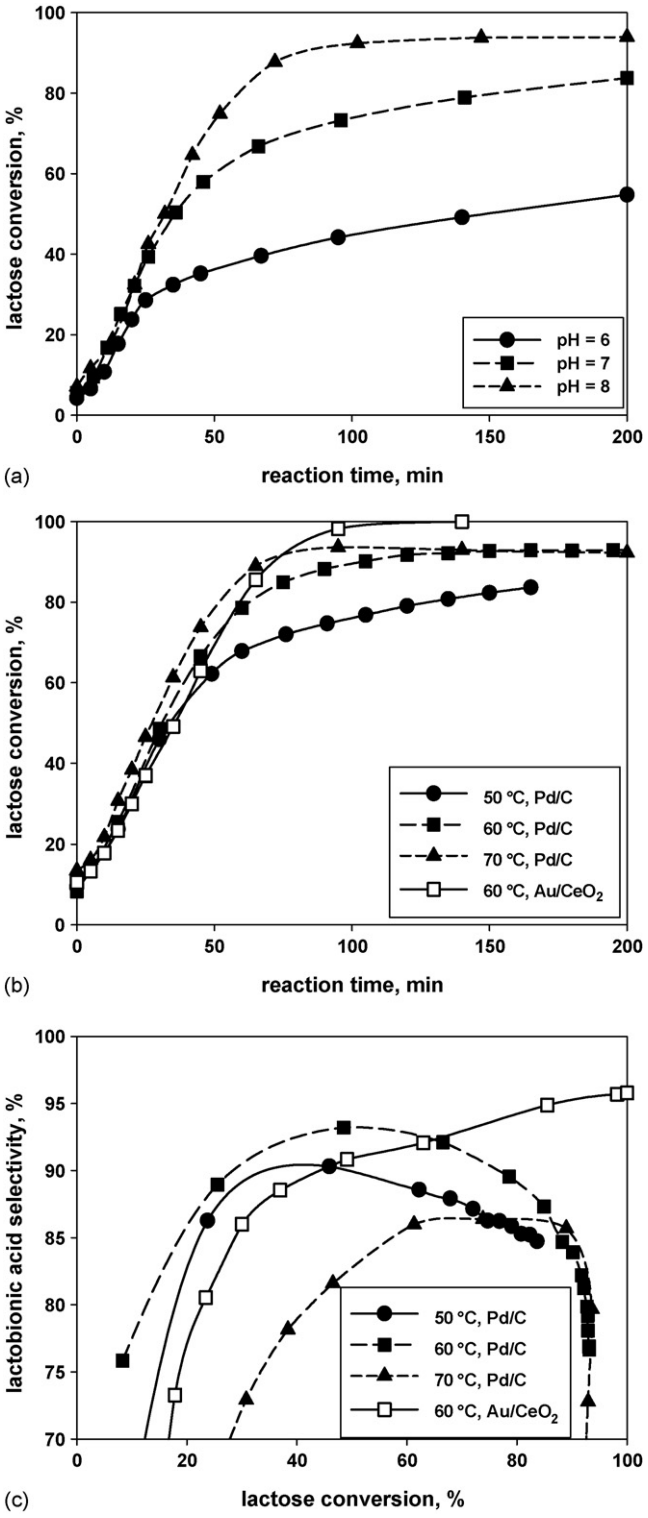

Fig. 5. Lactose oxidation (12.5% O_2) over 0.5 g 5% Pd/C and 2% Au/CeO_2 catalysts: (a) influence of solution pH on conversion over Pd/C catalyst at 60 °C; (b) effect of temperature and catalyst on lactose conversion at pH 8; and (c) influence of reaction temperature and catalyst on product selectivity at pH 8.

3.4. Catalyst stability

Catalyst deactivation was severe during consecutive lactose hydrogenation batches (Fig. 6a). Deactivation over sponge nickel took place faster than over Ru/C. The recycled sponge nickel catalyst was not able to adsorb the same amount of hydrogen as the fresh one [28]. This indicates that active sites of the sponge nickel catalyst were blocked during repeated lactose

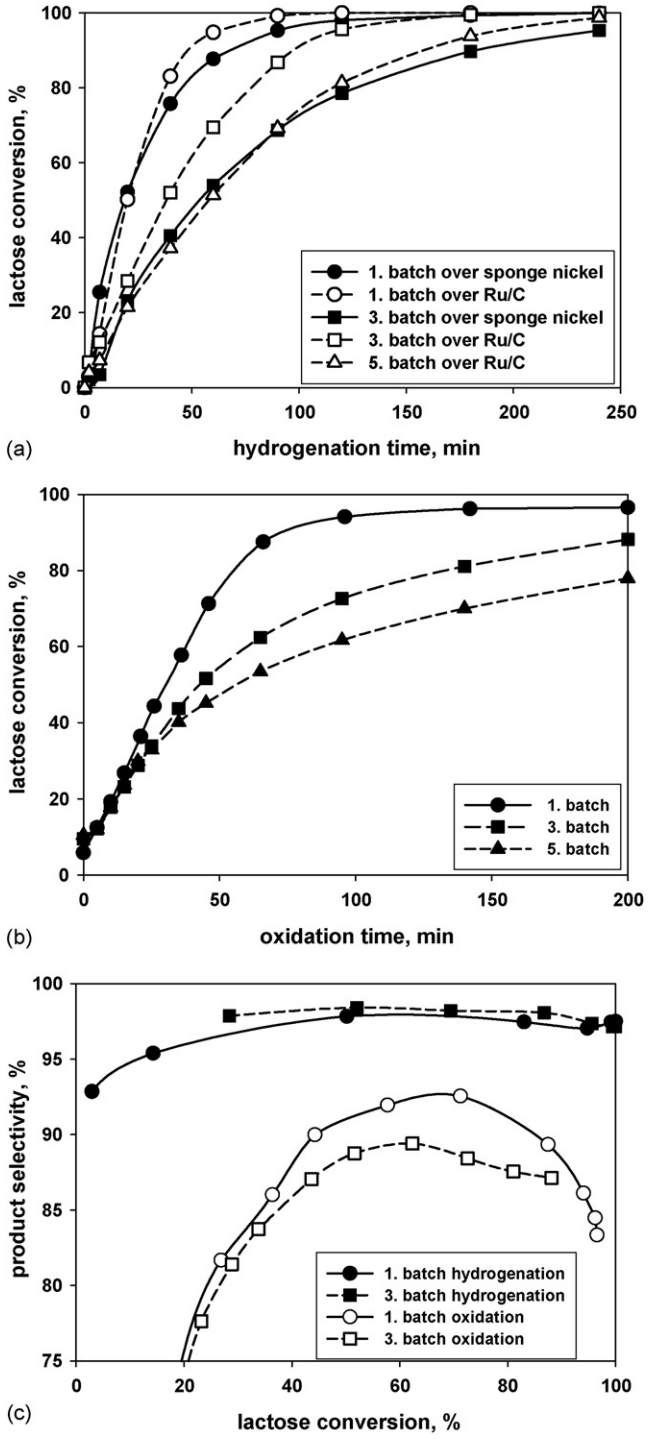

Fig. 6. Catalyst deactivation during consecutive lactose hydrogenation and oxidation batches: (a) lactose hydrogenation over sponge nickel and 5% Ru/C catalysts at 120 °C and 50 bar; (b) lactose oxidation over 5% Pd/C catalyst at 60 °C and pH 8; and (c) product selectivities over lactose hydrogenation (over Ru/C) and oxidation (over Pd/C) batches.

hydrogenations. After five batches, recycled Ru/C catalyst had a substantially lower specific surface area (622 m^2/g) compared to the fresh one, reduced at 200 °C (807 m^2/g). Of all by-products, only lactobionic acid had an inhibiting effect on lactose conversion and deactivated the catalyst. Low hydrogen pressure enhanced catalyst leaching [28], due to increased lactobionic acid formation.

Catalyst deactivation during consecutive lactose oxidation over Pd/C catalyst was severe (Fig. 6b). Only 6% of the catalyst amount was lost during these five batches, clearly indicating substantial deactivation. Lactobionic acid adsorption and surface oxidation slowly diminish the amount of active sites on the catalyst. Selectivities of both lactose hydrogenation and oxidation products decreased to some extent as the catalysts were recycled (Fig. 6c). Generally, catalytic hydrogenation of lactose led to a higher selectivity than oxidation. However, higher lactobionic acid yields can be achieved also in lactose oxidation (e.g. over supported gold catalysts).

4. Conclusions

Both, catalytic lactose oxidation and hydrogenation reactions can be carried out with high product yields, requiring optimum reaction conditions and catalysts. During lactose hydrogenation, high temperature, high acidity and slow main reaction rate favour lactose hydrolysis, leading to increased galactitol and sorbitol formation. On the other hand, too high pH increases lactose isomerization and thus, lactulose and lactulitol formation. Additionally, lack of hydrogen on the catalyst surface leads to increased lactobionic acid formation. Of all by-products, only lactobionic acid had an inhibiting effect on lactose conversion by catalyst deactivation. The highest lactitol yields were obtained over Ru/C and sponge nickel catalysts at temperatures 110–120 °C and hydrogen pressures over 50 bar.

The optimum pH for lactose oxidation is between 8 and 9. Lactose oxidation catalysts deactivate rapidly at low pH and at high oxygen concentrations in the lactose–lactobionic acid solutions. pH values exceeding 9 and high oxidation temperatures result in a decrease of the lactobionic acid selectivity. The highest lactobionic acid yields were obtained on supported gold catalysts. A detailed discussion of the kinetic behaviour of electrochemical potential is the subject of a separate paper [31].

Acknowledgements

This work is part of the activities at the Åbo Akademi Process Chemistry Centre within the Finnish Centre of Excellence Programmes (2000–2011) by the Academy of Finland. Financial support from the National Technology Agency (TEKES), Danisco Sweeteners and Graduate School of Chemical Engineering is gratefully acknowledged.

References

[1] V.H. Holsinger, in: N.B. Wong (Ed.), Fundamentals of Dairy Chemistry, 3rd ed., Van Nostrand Reinhold Company, New York, 1988, p. 297.
[2] P. Linko, Lactose and lactitol, in: G. Birch, K. Parker (Eds.), Nutritive Sweeteners, Applied Science, NJ, 1982, p. 109.
[3] M. Hu, M.J. Kurth, Y.-L. Hsieh, J.M. Krochta, J. Agric. Food Chem. 44 (1996) 3757.

[4] K.-G. Gerling, International Dairy Federation, Whey Proceedings of the Second International Whey Conference, 1998, p. 251.
[5] M. Harju, Bull. Int. Dairy Fed. 289 (1993) 27.
[6] R.A. Visser, M.J. van den Bos, W.P. Ferguson, Bull. Int. Dairy Fed. 233 (1988) 33.
[7] W.A. Roelfsema, B.F.M. Kuster, M.C. Heslinga, H. Pluim, M. Verhage, 6th ed., Ullmann's Encyclopedia of Industrial Chemistry, Vol. 19, VCH Weinheim, 2003,, p. 21.
[8] H.E.J. Hendriks, Doctoral Thesis: selective catalytic oxidations of lactose and related carbohydrates, Technische Univ. Eindhoven, The Netherlands, 1991.
[9] A. Montilla, M.D. del Castillo, M.L. Sanz, A. Olano, Food Chem. 90 (2005) 883.
[10] http://www.danisco.com (13.3.2006).
[11] T. Saijonmaa, M. Heikonen, M. Kreula, P. Linko, Milchwissenschaft 33 (1978) 733.
[12] P. Gallezot, P.J. Cerino, B. Blanc, G. Flèche, P. Fuertes, J. Catal. 146 (1994) 93.
[13] P. Gallezot, N. Nicolaus, G. Flèche, P. Fuertes, A. Perrard, J. Catal. 180 (1998) 51.
[14] B. Kusserow, S. Schimpf, P. Claus, Adv. Synth. Catal. 345 (2003) 289.
[15] K. van Gorp, E. Boerman, C.V. Cavenaghi, P.H. Berben, Catal. Today 52 (1999) 349.
[16] B.W. Hoffer, E. Crezee, P.R.M. Mooijman, A.D. van Langeveld, F. Kapteijn, J.A. Moulijn, Catal. Today 79–80 (2003) 35.
[17] J.-P. Mikkola, R. Sjöholm, T. Salmi, P. Mäki-Arvela, Catal. Today 48 (1999) 73.
[18] J.H. Southard, F.O. Belzer, Annu. Rev. Med. 46 (1995) 235.
[19] H.E.J. Hendriks, B.F.M. Kuster, G.B. Marin, Carbohydr. Res. 204 (1990) 121.
[20] M. Wenkin, P. Ruiz, B. Delmon, M. Devillers, J. Mol. Catal. A 180 (2002) 141.
[21] A. Abbadi, H. van Bekkum, J. Mol. Catal. A 97 (1995) 111.
[22] A. Abbadi, K.F. Gotlieb, J.B.M. Meiberg, H. van Bekkum, Appl. Catal. A 156 (1997) 105.
[23] Y. Önal, S. Schimpf, P. Claus, J. Catal. 223 (2004) 122.
[24] S. Biella, G.L. Castiglioni, C. Fumagalli, L. Prati, M. Rossi, Catal. Today 72 (2002) 43.
[25] J. Kowalczyk, B.A. Haji, U. Prüße, H. Berndt, I. Pitsch, DE 2003-10319917, 2003.
[26] P.J. Simms, K.B. Hicks, R.M. Haines, A.T. Hotchkiss, S.F. Osman, J. Chromatogr. A 667 (1994) 67.
[27] Y. Zhu, J. Zajicek, A.S. Serianni, J. Org. Chem. 66 (2001) 6244.
[28] J. Kuusisto, J.-P. Mikkola, M. Sparv, J. Wärnå, H. Heikkilä, R. Perälä, J. Väyrynen, T. Salmi, Ind. Eng. Chem. Res. 45 (2006) 5900.
[29] M. Besson, P. Gallezot, Catal. Today 57 (2000) 127.
[30] E. Crezee, B.W. Hoffer, R.J. Berger, M. Makkee, F. Kapteijn, J.A. Moulijn, Appl. Catal. A 251 (2003) 1.
[31] A.V. Tokarev, E.V. Murzina, J. Kuusisto, J.-P. Mikkola, K. Eränen, D.Yu. Murzin, J. Mol. Catal. A 255 (2006) 199.