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Analytical challenges in direct oxidation of L-sorbose

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ABSTRACT

A review of literature concerning direct platinum catalyzed oxidation of L-sorbose reveals great differences in selectivity obtained by different researcher groups. Thus, the question arises whether or not the results reported up to now are comparable at all. In order to clarify this issue, two heterogeneous platinum catalysts known from literature as well as one in-house platinum catalyst were applied in the oxidation of L-sorbose under equal reaction conditions. All samples were analyzed using two different HPLC methods. Selectivity towards 2-keto-L-gulonic acid was determined on the basis of these analytical data. A comparison revealed a great discrepancy between the results, which can be found in relevant publications and the results of this study.

1. Introduction

L-sorbose and 2-keto-L-gulonic acid (abbreviated to 2-KGA in the following) are the intermediate products for vitamin C production via Reichstein–Grüssner route (Fig. 1) [1]. This multi-stage industrial process using D-glucose as starting material and including different chemical and biotechnological steps was developed in the early 1930s and being constantly improved since then. At the moment, the transformation of L-sorbose into 2-keto-L-gulonic acid requires additional labour-intensive and time-consuming protection and deprotection steps. Direct selective catalytic sorbose oxidation in just one step might simplify the process significantly and reduce manufacturing costs. This issue has therefore been subject of intense research for many years [2–18]. Heterogeneous platinum based catalysts were found to be promising for sorbose oxidation with oxygen in aqueous medium. Results concerning the selectivity towards 2-KGA formation of about 60% at 90–95% sorbose conversion were published in [2]. A selectivity of 63% at 79% conversion was reported some decades later [4]. In more recent studies a selectivity of 67% at 58% sorbose conversion was reported using a commercial platinum catalyst [5] and about 80% selectivity at 50% conversion when a modified catalyst was used [8]. The problem concerning the reliability of the analysis methods used in previous works was already pointed out in [5]. Investigations concerning catalyst development for this reaction were carried out at our institute as well [10,11], in which selectivities of about 50% could be achieved using different polymer stabilized platinum catalysts. Shortly afterwards another research group reported of significantly higher selectivity (more than 95%) obtained with similar catalytic systems [15,17,18]. In general, direct comparison of catalytic results from literature is difficult because different groups used diverse catalysts, reaction conditions and analytical methods. The scope of this work was a comparison of selected platinum catalysts and reaction conditions with particular emphasis on the selectivity towards 2-keto-L-gulonic acid formation determined with two different analytical methods. For this purpose, one of the in-house platinum catalysts and in-house sorbose oxidation conditions were examined in addition to the catalysts and conditions known from literature [5,16].

2. Experimental

2.1. Catalyst preparation

The commercial catalyst 5% Pt AP RD code 286064, BASF Italy (5% Pt/Al_2O_3, formerly code 7004, or Escat 24, Engelhard), was mainly used by Baiker's group [5–7,9]. In this study, the catalyst was pre-reduced by introducing a hydrogen gas stream into the catalyst suspension in deionised water for 6 min immediately before the addition of sorbose and the beginning of oxidation.

1.72% Pt/HPS (hypercrosslinked polystyrene MN-270, Purolite) catalyst, which was used by Sulman's group, was prepared according to the procedure described in literature [16]. For the preparation of 15 g catalyst 0.645 g dihydrogen hexachloroplatinate(IV) hydrate

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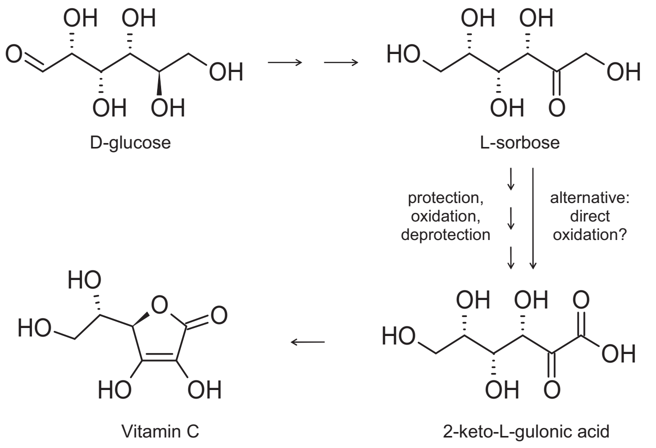

Fig. 1. Scheme of the Reichstein–Grüssner process (and direct oxidation of L-sorbose as an alternative route).

(40.0% Pt, Chempur) were dissolved in 30 ml tetrahydrofuran (≥99.5% p.a., ACS reagent, Carl Roth) and added to 14.74 g of HPS MN-270. The suspension was stirred for 10 min and dried at 70 °C for 24 h. The precursor was used for sorbose oxidation without prior reduction [16].

For the preparation of the in-house 1% Pt/Al_2O_3 (vTI) catalyst (12.5 g) 12.38 g alumina (Puralox KR-90, Sasol) were dispersed in 220 ml deionised water at ambient temperature. 31.25 ml dihydrogen hexachloroplatinate(IV) hydrate stock solution (4 g Pt l^{-1}, H_2PtCl_6 hydrate containing 40.0% Pt, Chempur) were added at once to the vigorously stirred suspension. After 45 min 0.33 g sodium borohydride (96% $NaBH_4$, Sigma–Aldrich) were dissolved in 15 ml water and added in one portion to the suspension. When gas formation was completed, the catalyst was filtered, washed with warm (50–60 °C) deionised water and dried overnight at 70 °C.

2.2. L-sorbose oxidation

L-sorbose oxidation was carried out in a thermostated glass reactor (volume 500 ml) equipped with thermometer, pH electrode SL 80–120 pH (Schott), burette, glass frit for oxygen supply, reflux condenser and mechanical stirrer (1000 rpm). The catalyst was suspended in deionised water and heated to the desired temperature. The catalyst 5% Pt/Al_2O_3 (BASF) suspended in water was pre-reduced with hydrogen. The reaction was started by addition of sorbose (L-(−)-sorbose, ≥98.0%, Sigma) solution and by introducing oxygen at atmospheric pressure into the suspension. The pH was kept constant at a desired value by addition of a titration reagent (sodium carbonate anhydrous extra pure, Merck; sodium hydrogen carbonate, ≥99.7%, p.a., ACS reagent, Riedel-de Haën; sodium hydroxide, ≥99%, Carl Roth) solution using a TitroLine alpha plus titration unit (Schott). Samples of the reaction mixture were filtered and analyzed by HPLC. Sorbose oxidation was carried out using three different sets of reaction conditions, two of them (referred to as A and B) from literature [5,16] and one additional (C) for comparison. Unlike the conditions from [5], in A the oxygen flow rate was held constant at a value of 500 ml min^{-1}. All reaction conditions applied in this work are summarized in Table 1.

2.3. Analysis

The samples were analyzed by HPLC using a Shimadzu system (pump LC-10AT, autosampler SIL-10A, UV detector SPD-6AV, RI detector RID-6A and CLASS-LC10 program). Two HPLC methods were applied to all experiments to separate sorbose and reaction products and to determine their concentrations using the external standard method. The one method is described by Baiker's group in [7] and the other was developed for comparison. None of the analytical methods Sulman's group applied in their work was used in this comparative study. They used either the iodometric method of Heyns [19] for 2-KGA determination [12,13], which is known to be obsolete and unreliable [5], or the description of the newer HPLC and GC methods did not include sufficient details [13,16] such as HPLC column dimensions [16] so that those methods could not be replicated.

Method I, referred to as "Nucleosil" [7]: The separation was carried out at 30 °C on a 250 mm × 4.6 mm HPLC column (the 250 mm × 4 mm column from [7] is not commercially available at present) filled with Nucleosil-5 NH_2 resin (Macherey–Nagel) using a solution of 4.5 g KH_2PO_4 in 330 ml water and 670 ml acetonitrile at a flow rate of 0.8 ml min^{-1} (70 bar) as eluent. Detection of sorbose was carried out with the RI detector [7]. In addition, the UV detector (210 nm) was used for exacter 2-KGA determination. Samples were diluted 10-fold with water.

Method II, developed for comparison and referred to as "Aminex": The separation was carried out at 40 °C on two 300 mm × 7.8 mm Aminex HPX-87H HPLC columns (Bio-Rad) connected in series using aqueous sulphuric acid solution (5 mmol l^{-1}) at a flow rate of 0.4 ml min^{-1} (85 bar) as eluent. UV detector (210 nm) was applied for determination of 2-KGA concentration and RI detector for sorbose determination. Samples were diluted 20-fold.

Selected samples were analyzed by HPLC using the method of the standard addition. Certain amounts of sorbose and 2-KGA were added to the original samples and the experimental concentrations after the addition were compared to the calculated concentration values.

3. Results and discussion

3.1. Analysis

The comparison of the concentrations of L-sorbose and 2-KGA and, thus, conversion and selectivity, showed a good correlation between the data obtained by the two different HPLC methods. The difference in selectivity at moderate sorbose conversion degrees was mainly below 5%. Further on, the results of the standard addition (addition of certain amounts of sorbose and 2-KGA to the original sample and comparison of the concentrations before and after the addition) showed good results for sorbose and 2-KGA for both methods as well. The deviation from the calculated concentration after the standard addition was less than 5% value for all samples. This is a sign that rather reliable sorbose and 2-KGA concentration and also conversion and selectivity results could be obtained using these two analysis methods.

In some cases, however, the differences between the results obtained by the Nucleosil and the Aminex method were more pronounced. In particular this concerned the concentration of 2-KGA and the selectivity at higher conversion degrees of sorbose.

Examples of the concentration-time diagrams for the Pt/Al_2O_3 (BASF) catalyst, which illustrate these, are shown in Fig. 2. In these diagrams it can be clearly seen that the difference between the concentrations of 2-KGA and, thus, the selectivity, determined using the different HPLC methods, is particularly high under Sulman's group reaction conditions B and that this difference increases with an increasing sorbose conversion degree. The reason for this discrepancy probably results from an incomplete separation of the various sample components by HPLC and, thus, difficulties concerning an accurate peak-area determination [20]. An example is shown in Fig. 3 for the Pt/Al_2O_3 (BASF) catalyst used under conditions A.

Table 1
Reaction conditions of L-sorbose oxidation.

Reaction conditions	pH	T [°C]	$c_{0,\text{sorbose}}$ (mmol l^{-1})	c_{Pt} (g l^{-1})	O_2 flow rate (ml min^{-1})	Titration reagent	Ref.
A	7.3	50	100	0.225	500	Na_2CO_3	[5]
B	7.7	70	106	0.390	840	$NaHCO_3$	[16]
C	8.0	50	100	0.400	500	NaOH	This study

Table 2
Selectivity achieved with the catalysts Pt/Al_2O_3 (BASF), Pt/HPS and Pt/Al_2O_3 (vTI) at different reaction conditions (A, B and C) at sorbose conversion degree of 50% and time required for reaching 50% conversion: a comparison of the results obtained using different HPLC methods and of literature data.

Catalyst	Reaction conditions	Selectivity (%)[a]		Time for $X = 50\%$ (min)	
		Nucleosil	Aminex	Nucleosil	Aminex
Pt/Al_2O_3 (BASF)	A	44	48	290	335
	B	22	35	30	40
	C	38	31	55	40
Pt/HPS	A	–[b]	–[b]	–[b]	–[b]
	B	20[c]	15[d]	>1440	>1440
	C	9[e]	27[f]	>1440	>1440
Pt/Al_2O_3 (vTI)	A	22	32	60	80
	B	25	30	50	50
	C	19	24	55	55

Literature results: Pt/Al_2O_3 (BASF), reaction conditions A: 67% selectivity at 58% sorbose conversion [5]; Pt/HPS, reaction conditions B: > 95% selectivity at 100% sorbose conversion [16].

[a] At $X = 50\%$ sorbose conversion.
[b] No reaction.
[c] $X = 35\%$.
[d] $X = 46\%$.
[e] $X = 12\%$.
[f] $X = 4\%$.

Two samples at different sorbose conversion degrees are compared to each other. Sample 3 was taken after 70 min reaction time and 30% sorbose conversion and sample 6 after about 24 h reaction time and 80% sorbose conversion, cp. Fig. 2, the diagram on the left.

Both chromatograms show signals of unidentified substances in close vicinity to the 2-KGA peaks. These signals are not baseline-separated. Thus, the determined concentration of 2-KGA is higher than the actual 2-KGA concentration, particularly if the amount of the by-products in question increases, i.e. the reaction product

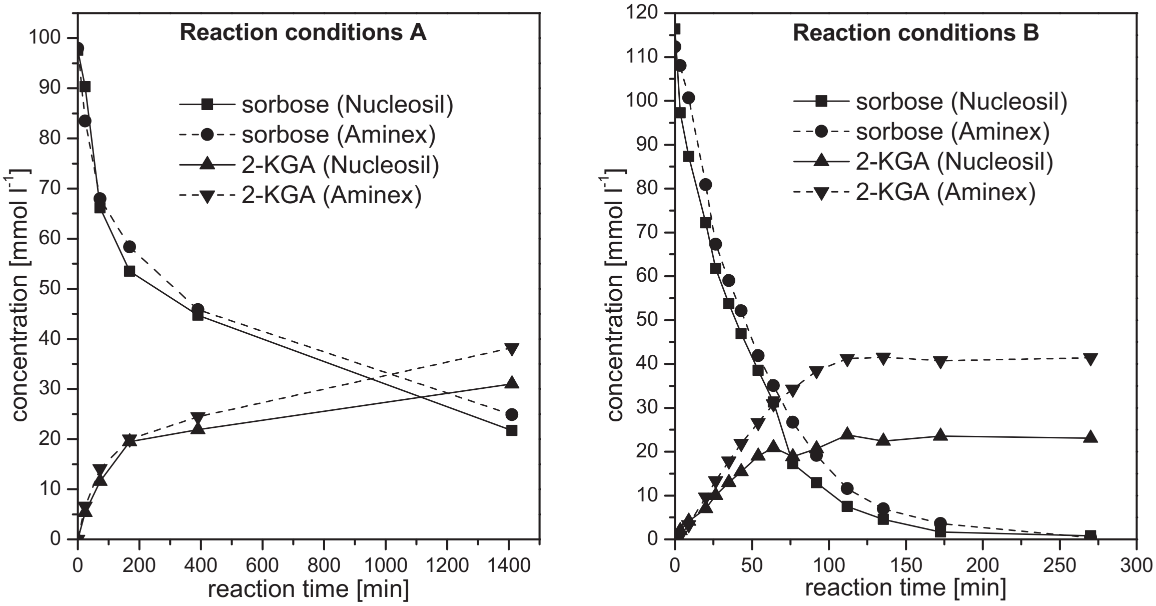

Fig. 2. Examples of concentration-time diagrams (5% Pt/Al_2O_3 (BASF), reaction conditions A and B; HPLC methods Nucleosil and Aminex applied for determination of concentrations of L-sorbose and 2-KGA).

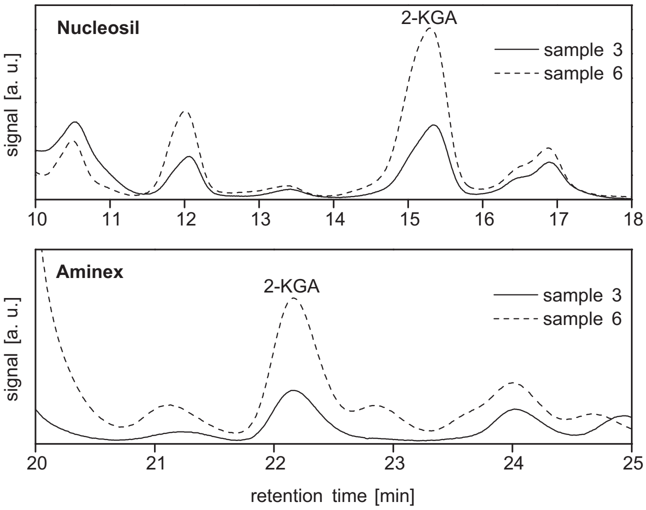

Fig. 3. Examples of chromatograms (5% Pt/Al_2O_3 (BASF), reaction conditions A, samples no. 3 and 6, HPLC methods Nucleosil and Aminex applied for determination of concentrations of L-sorbose and 2-KGA), UV detector.

which is detected at 22.9 min retention time in sample 6, the lower chromatogram.

In general, both HPLC methods have their particular advantages and disadvantages. The determination of 2-KGA is probably more precise when the Nucleosil method is used. However, the quantification of sorbose might be less accurate, because several large peaks, which can be observed by UV detection, are eluted at retention times equal or very similar to sorbose. These interfering substances cannot be well detected by the RI detector, which is used for sorbose quantification, but they can still disturb the determination of sorbose concentration. Further disadvantages of this method are high consumption of acetonitrile and unsatisfactory long-term durability of the column material because of a high phosphate salt concentration in the eluent. The Aminex method allows precise determination of sorbose, because no further peaks are eluted at similar retention times. Further on, the column material is very durable, the eluent is environmentally friendly and inexpensive, but, as mentioned before, the quantification of 2-KGA is inferior to the Nucleosil method.

In summary, both HPLC methods are suitable for the determination of sorbose and 2-KGA concentrations in direct sorbose oxidation. However, one has to keep in mind that these methods are mostly very well suited for routine analysis in catalyst screening but sometimes they can provide inaccurate results.

3.2. Catalysis

All three catalysts were active in sorbose oxidation with the exception of Pt/HPS catalyst when applied at mild reaction conditions (A). Under these conditions Pt/Al_2O_3 (BASF) and Pt/Al_2O_3 (vTI) catalysts showed relatively high initial rates of sorbose conversion but both were strongly deactivated in the course of the reaction and achieved only a conversion degree of about 80% after 24 h reaction time. Full sorbose conversion could only be achieved using both Pt/Al_2O_3 catalysts under conditions C within less than 300 min as well as the Pt/Al_2O_3 (vTI) catalyst under conditions B. More catalyst and higher pH was applied for both B and C compared to the very mild conditions A, in the case of B the temperature was increased by 20 °C. On Pt/Al_2O_3 (BASF), conditions B, 85% sorbose could be converted within 550 min reaction time. In general, the catalyst Pt/HPS showed the lowest activity compared to the other two platinum catalysts. Only a sorbose conversion degree of about 50% could be achieved after more than 24 h. The selectivity of the catalysts and reaction times at different reaction conditions are summarized in Table 2. For both the selectivity and the reaction time two different values are shown which refer to the different HPLC methods, Nucleosil and Aminex. For a better comparability of the catalysts the same conversion degree X of 50% was chosen as a reference point at which selectivity to 2-KGA and times required for reaching 50% conversion of sorbose are listed.

Both the selectivity results and the times required for reaching 50% conversion of sorbose measured by the two different HPLC methods were mostly in good agreement. However, in some cases the discrepancy between the selectivity data was significant. The difference in selectivity obtained with Nucleosil vs. Aminex was the highest for Pt/Al_2O_3 (BASF), reaction conditions B (13% difference), and Pt/Al_2O_3 (vTI) catalyst, reaction conditions A (10% difference), mainly due to the differing concentrations of 2-KGA, and in the case of Pt/HPS, conditions C (18% difference), exclusively due to the differing sorbose concentrations. Thereby the discrepancy between the selectivity results obtained with both HPLC methods was more pronounced for samples taken at higher sorbose conversion degrees. The highest selectivity (44% or 48%, depending on the analysis method) could be achieved with Pt/Al_2O_3 (BASF) when applied at the mild reaction conditions A, which is in rather good agreement with literature data [5]. The other two catalysts Pt/Al_2O_3 (vTI) and Pt/HPS exhibited significantly lower selectivities which did not exceed 20–30%. This means that the selectivity of 95% at full sorbose conversion reported in [16] is much too high compared to the data presented in this study (only 20% selectivity at moderate sorbose conversion degrees). This extreme difference of about 75% leads to the conclusion that the reliability of the selectivity results of direct sorbose oxidation presented in [12–18] is generally questionable.

4. Conclusions

Different supported platinum catalysts, including two catalysts known from literature, were applied in direct oxidation of L-sorbose. Similar concentrations and, thus, conversion and selectivity results were obtained using two independent analysis methods. None of the catalysts tested at different reaction conditions exhibited selectivities higher than 50%, so that the results from literature, especially those reported in [16], could not be confirmed in this study.

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