

This article was downloaded by: [Michigan State University]

On: 25 December 2014, At: 16:23

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcar20>

### Oxidation of Methyl $\alpha$ -D-Glucopyranoside and Some Related Compounds Catalysed by Nickel Peroxide

E. J.M. Mombarg<sup>a</sup>, A. Abbadi<sup>a</sup>, F. van Rantwijk<sup>a</sup> & H. van Bekkum<sup>a</sup>

<sup>a</sup> Laboratory of Organic Chemistry and Catalysis, Delft University of Technology, Julianalaan 136, 2628 BL, Delft, The Netherlands  
Published online: 22 Aug 2006.

To cite this article: E. J.M. Mombarg, A. Abbadi, F. van Rantwijk & H. van Bekkum (1996) Oxidation of Methyl  $\alpha$ -D-Glucopyranoside and Some Related Compounds Catalysed by Nickel Peroxide, Journal of Carbohydrate Chemistry, 15:5, 513-522, DOI: [10.1080/07328309608005671](https://doi.org/10.1080/07328309608005671)

To link to this article: <http://dx.doi.org/10.1080/07328309608005671>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

## OXIDATION OF METHYL $\alpha$ -D-GLUCOPYRANOSIDE AND SOME RELATED COMPOUNDS CATALYSED BY NICKEL PEROXIDE

E.J.M. Mombarg, A. Abbadi, F. van Rantwijk and H. van Bekkum\*

Laboratory of Organic Chemistry and Catalysis, Delft University of Technology,  
Julianalaan 136, 2628 BL Delft, The Netherlands

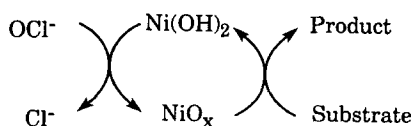
*Received November 27, 1995 - Final Form April 1, 1996*

### ABSTRACT

Nickel sulphate efficiently catalyses oxidative glycol cleavage, using sodium hypochlorite as the primary oxidant. Suspended nickel peroxide is assumed to be the active intermediate. 2,3-Butanediol was oxidised (conversion 95%) to acetate at pH <10 and 20 °C, applying a molar ratio hypochlorite: nickel:diol of 8:0.2:1. Methyl  $\alpha$ -D-glucopyranoside was initially oxidised to disodium (*R*)-2-*O*-[(*R*)-carboxylato(methoxy)methyl]erythrate. Subsequently oxidation to disodium (*R*)-2-*O*-[(*R*)-carboxylato(methoxy)methyl]glycerate took place.  $\beta$ -Cyclodextrin was preferentially oxidatively cleaved (ca. 50%) between the C(2)-C(3) carbons, although oxidation at the C(6) carbon (ca. 25%) appeared to occur as well. In contrast, maltodextrin was oxidised at the primary hydroxyl functions.

### INTRODUCTION

Chemicals and materials derived from carbohydrates are generally regarded as safe and environmentally acceptable because they are expected to be biodegradable and are derived from a renewable source. If appropriate processes for converting carbohydrates to useful products become available, it also is to be expected that the wish for a green label



**Scheme.** Reaction cycle of oxidation catalysed by nickel salts.

will accelerate the introduction of these products. In this context, selective oxidation of the commodity starch is an attractive proposition. Oxidation of the primary alcohol groups to carboxylate<sup>1</sup> would yield a product, which is structurally closely related to high-value materials such as pectinate and alginate.

Dicarboxy starch, which results from glycol cleavage of the C(2)-C(3) bond, has been reported to show good performance as a co-builder in detergent formulations.<sup>2,3</sup>

Nickel peroxide is an attractive candidate for oxidation of carbohydrates as it is easily prepared from nickel hydroxide and sodium hypochlorite, the specific surface area is high<sup>4,5</sup> and it has been reported to oxidize primary as well as secondary hydroxyl groups.<sup>4</sup> It has been observed that the reactivity of diols towards oxidation with nickel peroxide increases with enhanced hydrophilicity.<sup>6</sup> In the oxidation of benzyl alcohols nickel peroxide was a superior oxidant compared to manganese dioxide.<sup>5</sup> It is believed that oxidation processes at a nickel anode take place *via* nickel peroxide.<sup>6-10</sup> The electrochemical oxidation of the L-ascorbic acid intermediate 2,3:4,6-di-*O*-isopropylidene-L-sorbose to the corresponding L-gulonic acid derivative is an example of its application on a technical scale.<sup>11</sup> Selective oxidation of methyl  $\alpha$ -D-glucopyranoside at the (primary) C(6) hydroxyl function to the aldehyde has been reported using a nickel electrode.<sup>12</sup>

In our work we initially used nickel peroxide in stoichiometric amounts, as has generally been the case apart from electrode processes. We reasoned, however, that with hypochlorite present to drive an in-process recycle, a catalytic amount of nickel salt should suffice (Scheme).

In the present paper we report the results obtained on the oxidation of the model compound 2,3-butanediol as well as of methyl  $\alpha$ -D-glucopyranoside,  $\beta$ -cyclodextrin and maltodextrin, when applying sub-stoichiometric amounts of nickel(II) salts and the effects of pH and temperature.

**Table 1.** Nickel-peroxide-mediated oxidation of 2,3-butanediol <sup>a</sup>

pH	Temperature (°C)	Conversion (%) <sup>b</sup>	selectivity to acetate (%)
9	20	80	100
10	0	15	100
10	10	25	100
10	20	80	100
10 <sup>c</sup>	20	<2	n.d. <sup>d</sup>
10	30	<5	n.d. <sup>d</sup>
11	20	20	60
12	20	15	10

- a. Reaction conditions: 2,3-butanediol 0.5 g (5.5 mmol), NaOCl 15 wt % 19.5 g (38.5 mmol) 30.5 mL H<sub>2</sub>O and NiSO<sub>4</sub> · 6 H<sub>2</sub>O 0.262 g (1 mmol). By adding 2M NaOH the pH was kept constant. The reaction time was 25 minutes.
- b. Determined after 25 min reaction time.
- c. Blank experiment, no nickel sulphate added.
- d. Not determined.

## RESULTS AND DISCUSSION

### The Effects of pH and Temperature on Selectivity and Diol Oxidation Rate.

Schäfer and Schneider<sup>8</sup> have investigated the effect of pH on the oxidation of methyl 2,3-*O*-isopropylidene- $\beta$ -D-ribofuranoside to its uronic acid derivative at a nickel anode. Between pH 8.5 and 14 the yield increased with the pH.

Because preliminary experiments had indicated that glycol cleavage predominated in the nickel peroxide-mediated oxidation of methyl  $\alpha$ -D-glucopyranoside, we selected 2,3-butanediol as a model system. The nickel peroxide (black solid, 180 m<sup>2</sup>/g) remained essentially undissolved ( $< 10^{-6}$  M) during the oxidation. Therefore we assume that oxidation takes place at the NiO<sub>x</sub> surface. The effect of the pH and the reaction temperature are compiled in Table 1.

At pH  $\leq 10$  2,3-butanediol was selectively oxidised to acetic acid. Formic acid and carbonate, which result from over-oxidation, were not observed. The reaction proceeded slowly with low selectivity at pH  $\geq 11$ . Subsequent reactions were performed at pH 10,

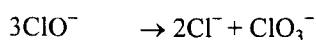
**Table 2.** Effect of the amount of hypochlorite on the conversion<sup>a</sup> of 2,3-butanediol.

molar ratio NaOCl: diol	conversion to acetate (%)
5	48
6	60
7	80
8	95

a. Conditions: 20 °C, pH 10, 25 min reaction time after which a plateau was reached in all reactions. Formulations see Table 1.

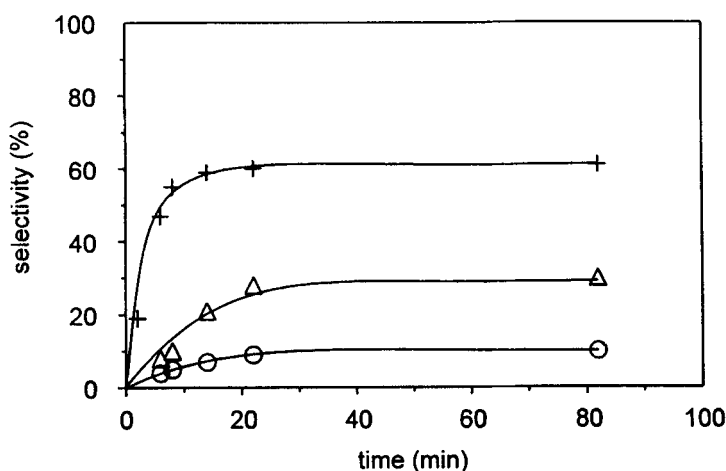
because below this value HOCl would be present which partakes in an uncatalysed background reaction. Reactions were performed at 20 °C; lower temperatures resulted in a slow reaction, whereas at 30 °C a strongly exothermic runaway reaction took place.

It became apparent (see Table 2) that 8 mol of hypochlorite per mol of reactant are required to achieve an essentially quantitative conversion whereas in theory 3 moles should be sufficient. We ascribe this effect to nickel catalysed disproportionation of hypochlorite, according to:



**Oxidation of Methyl  $\alpha$ -D-Glucopyranoside.** On the basis of the above results we performed the oxidation of methyl  $\alpha$ -D-glucopyranoside (**1**), using 8 eq. of sodium hypochlorite at pH 10 and 0 °C because **1** is a rather sensitive compound. The reaction initially proceeded rapidly, but it slowed down after 20% of **1** had reacted. By using a very large excess of hypochlorite (20 eq.) the conversion could be enhanced to 60%. In the absence of nickel sulphate no reaction was observed.

Upon HPLC analysis of the reaction product, disodium (*R*)-3-*O*-[(*R*)-carboxylato-(methoxy)methyl]erythrate (**3**) and  $\alpha$ -methyl glucuronide as well as tartronate, formate and carbonate were identified by comparison with reference compounds. A sixth reaction product, disodium (*R*)-3-*O*-[(*R*)-carboxylato(methoxy)methyl]glycerate (**4**) was

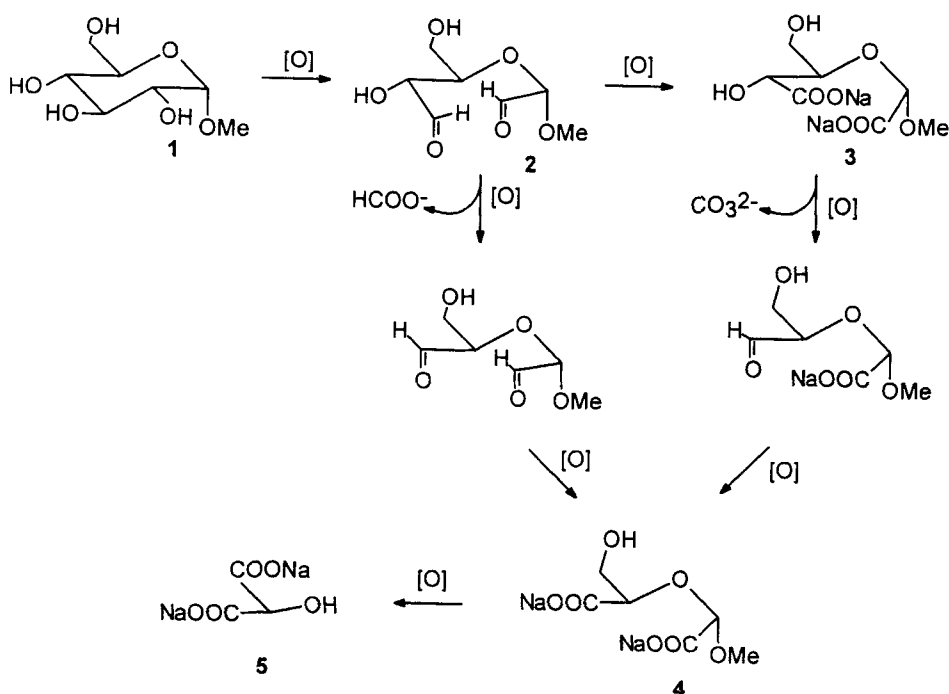


**Figure 1.** Selectivity of the nickel peroxide catalysed oxidation of methyl  $\alpha$ -D-glucopyranoside towards glycol cleavage, **3** and **4** (+),  $\alpha$ -methyl glucuronate (o) and tartronate, **5** ( $\Delta$ ) vs. time.

isolated by ion-exchange chromatography and identified using  $^{13}\text{C}$  NMR. These NMR data are in accordance with the results of Nieuwenhuizen et al.<sup>13</sup>

The course of the reaction is graphically depicted in Figure 1 from which it becomes clear that the products are formed in parallel, not consecutive, reactions. The products of glycol cleavage (**3** and **4**) accounted for 60% of converted **1** (see also Figure 2). By analogy with diol cleavage by periodate<sup>14</sup> and hypochloric acid<sup>15</sup> we assume that **3** and **4** are formed in stages *via* the dialdehyde **2**. C(3)-C(4) cleavage in the aldehyde stage (**2**) would result in the formation of formic acid whereas cleavage of the dicarboxylate (**3**) gives rise to carbonate as the side-product. Oxidation of the primary (C(6)) hydroxyl group, leading to  $\alpha$ -methyl glucuronide, played only a minor role. The formation of tartronic acid (**5**) makes it clear that oxidation of **1** is accompanied by cleavage of the glycosidic bond.

Upon reuse, the wet catalyst showed the same properties as the nickel sulphate catalyst except that the strong sodium hydroxide consumption in the first two minutes was not observed. This strong sodium hydroxide consumption (2 eq.) is probably due to formation of nickel hydroxide. When the catalyst is dried the activity is strongly

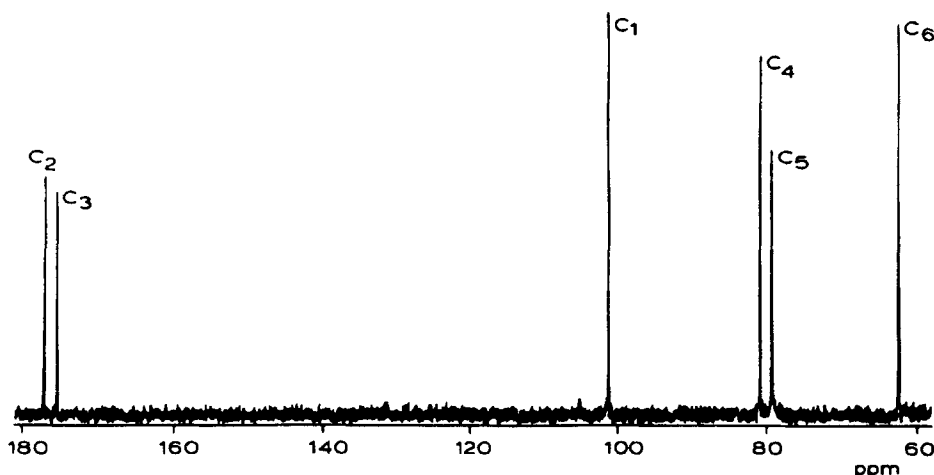


**Figure 2.** Main pathways postulated for the oxidation of methyl  $\alpha$ -D-glucopyranoside with nickel peroxide

decreased. This might be due to some sintering of the material during the drying process leading to a lower surface area of the dried catalyst.

**Oligosaccharides.** We undertook the oxidation of the oligosaccharides  $\beta$ -cyclodextrin (formulation  $\text{OCl}^-:\text{Ni}:\text{glucose units } 8:0.2:1$ ) and maltodextrin (DP 16) (formulation  $\text{OCl}^-:\text{Ni}:\text{glucose unit } 8:0.2:1$ ). Oxidations of both reactants was observed. Based upon  $^{13}\text{C}$  NMR analysis, maltodextrin reacted mainly via glycol cleavage and products of oxidation at C(6) were not observed. Carbonate was also found, probably resulting from chain degradation starting at the reducing end.

$\beta$ -Cyclodextrin partially reacted under the oxidising conditions. Consequently, the symmetry is lost which complicates the  $^{13}\text{C}$  NMR spectrum. By comparison with the  $^{13}\text{C}$  NMR spectrum of Floor et al.,<sup>16</sup> which is depicted in Figure 3, it is concluded that glycol moieties (C(2)-C(3)) are cleaved with a selectivity of 50% and oxidation at C-6 occurs to about 25% based upon the decrease in C(6) signal.



**Figure 3.**  $^{13}\text{C}$  NMR spectrum (101 Mhz) of glycol-oxidized  $\beta$ -cyclodextrin as published by Floor et al.<sup>16</sup>

We tentatively conclude that the selectivity of the heterogeneous nickel peroxide catalyst towards glycol cleavage is influenced by steric effects. The selectivity changes from 85% (methyl  $\alpha$ -D-glucopyranoside) to 60% if access to the glycol unit is sterically hindered ( $\beta$ -cyclodextrin). Nickel peroxide catalysed oxidation might be an economical and environmentally interesting process if a more efficient (co-)oxidant becomes available

## EXPERIMENTAL

**Materials.** Methyl  $\alpha$ -D-glucopyranoside and  $\beta$ -cyclodextrin were purchased from Janssen Chimia. Maltodextrin was a generous gift of V-Labs Inc.. Nickel sulphate was procured from Merck and sodium hypochlorite from Chemproha. Trifluoroacetic acid was purchased from Janssen and ammonium hydrogen carbonate from J.T. Baker Chemicals.

**General Procedures.** All oxidation experiments were performed in a magnetically stirred, thermostatted reaction vessel of 100 mL. During the oxidation the pH was kept constant using a pH meter (Metrohm 654), a pH controller (Metrohm 614) and a motor



burette (Metrohm 655) containing 2.00 M aqueous sodium hydroxide. Samples were analysed by HPLC on a system consisting of a Millipore 590 pump and a Perkin Elmer ISS-100 autosampler, a Shodex RI SE-51 RI detector, a Shimadzu SPD-6A UV detector at 215 nm, and a Spectra Physics SP4270 integrator. A Phenomenex organic acid column was used with aqueous 0.01 M trifluoroacetic acid as the mobile phase at 60 °C. A Benson BA-X8 anion exchange column was used at 85 °C to monitor the charged compound using aqueous buffer of 0.162 M ammonium sulphate and 0.038 M magnesium sulphate at pH 8.  $^{13}\text{C}$  NMR spectra were recorded on a Varian VXR-400S spectrometer using 30 %  $\text{D}_2\text{O}$  in  $\text{H}_2\text{O}$  as solvent and *tert*-butyl alcohol as internal reference.

**Preparative Anion Chromatography.** A column (Pharmacia 28x140 mm) was packed with anion exchange resin (Dowex 1X 8-200) and used at a flow of 50 mL  $\text{h}^{-1}$  using an LKB 2232 Microperpex S peristaltic pump. A Millipore R403 Differential Refractometer was used for detection. The mobile phase was filtered and degassed. The reaction product was brought onto the column, then the neutral compounds were flushed with water. The mobile was replaced by 0.5 M ammonium hydrogen carbonate to elute the anionic compounds. The different fractions were lyophilized several times to evaporate the ammonium hydrogen carbonate.

#### **Oxidation of 2,3-Butanediol.**

1. *pH and temperature dependence.* 2,3-Butanediol (0.5 g, 5.5 mmol) was dissolved in a mixture of aqueous sodium hypochlorite 15 wt % (19.5 g, 39 mmol) and 30.5 mL water. The solution was brought at the reaction temperature (See Table 1), the pH of the solution was adjusted to the desired value by adding concentrated hydrochloric acid. The pH was kept constant during the reaction by addition of 2 M sodium hydroxide solution as described above,  $\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$  (0.262 g, 1 mmol) was added and after 25 minutes the amounts of acetic acid and formic acid in the reaction mixture were measured.
2. *Conversion optimum.* 2,3-Butanediol was oxidised at pH 10 and 20 °C. using varying amounts of hypochlorite. Appropriate amounts of hypochlorite solution (15% active  $\text{Cl}_2$ ) (13.75 g (27.5 mmol), 16.5 g (33 mmol), 19.5 (39 mmol) or 22.3 g (44 mmol)) was diluted with water to a total weight was 50 g. To these solutions 2,3-butanediol (0.5

g, 5.5 mmol) and nickel sulphate (0.262 g, 1 mmol) were added. After 25 minutes the NaOH consumption came to a standstill after addition of 12 mmol sodium hydroxide. The conversion of 2,3-butanediol into acetate was determined by HPLC.

**Methyl  $\alpha$ -D-Glucopyranoside.** Methyl  $\alpha$ -D-glucopyranoside (1 g, 5.15 mmol) was dissolved in sodium hypochlorite solution (15% active  $\text{Cl}_2$ ) 20.5 g (41 mmol) and 29.5 g of water at 0 °C, the pH was adjusted at 10 by addition of concentrated hydrochloric acid, and nickel sulphate (0.262 g, 1 mmol) was added. The reaction came to a standstill after addition of 15 mmol sodium hydroxide. The amounts of substrate and reaction products were determined using HPLC. The 2,4-dicarboxylate **4** was isolated using preparative anion exchange chromatography.  $^{13}\text{C}$  NMR:  $\delta$  178.6, 175.7 [ $\text{COO}^-$  (C-2, C-4)], 102.4 [C-1], 82.2 [C-5], 64.4 [C-6], 55.0 [ $\text{OCH}_3$ ]. The use of nickel chloride leads to the same results.

**$\beta$ -Cyclodextrin.**  $\beta$ -Cyclodextrin (1 g, 0.88 mmol) was dissolved in sodium hypochlorite solution (15% active  $\text{Cl}_2$ ) (20.5 g, 40 mmol) at 0 °C, the pH was adjusted at 10 by addition of concentrated hydrochloric acid and nickel sulphate (0.262 g, 1 mmol) was added. After 16 h (15 mmol sodium hydroxide) the reaction mixture was centrifuged and the supernatant was analysed using quantitative NMR. The selectivity was determined by integrating the signals of primary and secondary carbons.

**Maltodextrin.** Maltodextrin MD-6 (1 g, 0.03 mmol) was dissolved in sodium hypochlorite solution (15% active  $\text{Cl}_2$ ) (20.5 g, 40 mmol) at 0 °C, the pH was adjusted to 10 by addition of concentrated hydrochloric acid, and nickel sulphate (0.262 g, 1 mmol) was added. After 16 h (16 mmol sodium hydroxide) the reaction mixture was centrifuged and the supernatant was analysed using quantitative NMR.

## ACKNOWLEDGEMENT

Thanks are due to Dr. A. Sinnema and Dr. J.A. Peters for recording the NMR spectra. The Financial Support by the Dutch Ministry of Agriculture, Nature Management and Fishery through its special program on carbohydrate oxidation is gratefully acknowledged.

## REFERENCES

1. A. E. J. de Nooy, A. C. Besemer and H. van Bakkum, *Recl. Trav. Chim. Pays-Bas*, **113**, 165 (1994).
2. A. C. Besemer and H. van Bakkum, *Starch/ Stärke*, **46**, 101 (1994).
3. H. Koch, R. Beck and H. Röper, *Starch/ Stärke*, **45**, 2 (1993).
- 4a. M. V. George and K. S. Balachandran, *Chem. Rev.*, **75**, 491 (1975);
- 4b. M. V. George in *Organic Synthesis by Oxidation with Metal Compounds*; W. J. Mijs and C. R. H. I. de Jonge, Eds.; Plenum Press: New York, 1983, p 373.
5. K. Nakagawa, R. Konaka and T. Nakata, *J. Org. Chem.*, **27**, 1597 (1962).
6. H. Ruholl and H. J. Schäfer, *Synthesis*, 54 (1988).
7. J. Kaulen and H. J. Schäfer, *Tetrahedron*, **22**, 3299 (1982).
8. H. J. Schäfer and R. Schneider, *Tetrahedron*, **47**, 715 (1991).
9. I. G. Casella, T. R. I. Cataldi, A. M. Salvi and E. Desimoni, *Anal. Chem.* **65**, 3143 (1993).
10. T-C. Wen, C-C. Hu and Y-J Li, *J. Electrochem. Soc.*, **140**, 2555 (1993).
11. P. Seiler and P. M. Robertson, *Chimia*, **36**, 305 (1982).
12. D. Court and D. Pletcher, *Abstr. Nr. 334*, Spring Meeting of the Electrochemistry Soc. 1984, Cincinnati, Ohio.
13. M.S. Nieuwenhuizen, A.P.G. Kieboom and H. van Bakkum, *Starch/ Stärke*, **37**, 192 (1985).
14. D. de Wit, Ph.D. Dissertation, Delft University of Technology, 1992.
15. R. L. Whistler and R. Schweiger, *J. Am. Chem. Soc.*, **79**, 6460 (1957).
16. M. Floor, Ph.D. Dissertation, Delft University of Technology, 1989.