ELSEVIER

Journal of Molecular Catalysis A: Chemical 123 (1997) 123–130

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

Effect of ultrasound on KSF/O mediated glycosylations

Sandrine Brochette [a], Gérard Descotes [a], Alain Bouchu [a], Yves Queneau [a,*], Nathalie Monnier [b], Christian Pétrier [b]

[a] *Unité Mixte de Sucrochimie CNRS, Béghin-Say (UMR 143), c/o Eridania Béghin-Say, 27 Bd du 11 novembre 1918, B.P. 2132, 69603 Villeurbanne Cedex, France*

[b] *Laboratoire de Chimie Moléculaire et Environnement, Université de Savoie, ESIGEC, 73376 Le Bourget-du-Lac, France*

Received 19 September 1996; accepted 17 January 1997

Abstract

The catalysis of the glycosylation reaction (Fischer) by acidic clays, and in particular the montmorillonite KSF/O, was studied in the case of the glucosylation of butanol and dodecanol. The catalysis was shown to be mostly homogeneous, involving an acidity transfer from the solid to the alcoholic phase. Ultrasound promoted an intensification of this phenomenon leading to an increase of the conversion rate of glucose, which, in the case of dodecanol, gave rise to high yields of oligomeric species (mostly 1,6-polyglucose).

Keywords: Glycosylation; Montmorillonite; Ultrasound; Glucoside; Polyglucose

1. Introduction

The Fischer glycosylation reaction of alcohols [1], i.e. the acetalation of unprotected reducing carbohydrates with an alcohol under acidic conditions, is probably the most direct way for the obtention of glycosides. This straightforward process is nevertheless still the purpose of investigations [2–6] because of the three major limitations which are the lack of anomeric selectivity, the need of excess alcohol (which often serves as the solvent) and the medium heterogeneity due to the low solubility of carbohydrates in most alcohols.

In the context of our studies directed towards the understanding of the reactivity of carbohydrates in heterogeneous conditions, we have investigated the influence of using solid acid catalysts, and in particular KSF/O, together with ultrasound activation. Indeed, ultrasound was shown to increase the reactivity in highly heterogeneous systems, notably by decreasing particle size of solids and therefore increasing the interphase surface. It is also thought that this surface activation is able to create highly reactive species, notably in the field of metal catalysis. Finally, ultrasound is also known to facilitate reactions involving radical intermediates

* Corresponding author. Tel.: +33-4-72442989; fax: +33-4-72442991.

PII S1381-1169(97)00038-1

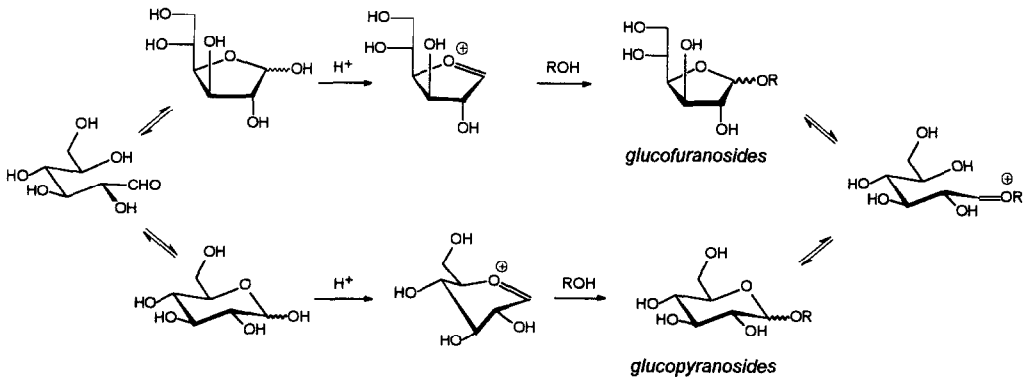


Fig. 1. Mechanism of the Fischer glycosylation reaction.

[7–10]. In the present work, it is more the mechanical aspects of ultrasound which are supposed to influence the outcome of the glycosylation reaction, which proceeds via an ionic pathway.

The glycosylation reaction mechanism, depicted in Fig. 1 for the case of glucose, lies on the kinetically controlled formation of furanosides, arising from the attack of the alcohol on the glucosyl oxonium intermediate. The furanosides are converted to the more stable pyranosides via a ring opening process [11]. If another carbohydrate molecule serves as the alcohol, then oligomeric species are produced.

The critical issues in this reaction are: the conversion rate of glucose, the furanoside/pyranoside ratio, glycoside/oligomer ratio and the anomeric selectivity. They can be influenced by several parameters, notably the nature and the quantity of the alcohol and of the acidic promoter [2–4,12,13]. Recently, montmorillonites were used as acid catalysts in various reactions [14–23] including some examples in carbohydrate chemistry [12,24,25]. Some of these solids are mesoporous sheet aluminosilicates activated through an ion exchange process during acidic treatment and having therefore acidic sites inside their multilamellar structure [26–29].

We report herein the study of the glucosylation of butanol and dodecanol as models for moderately and strongly lipophilic alcohols, providing amphiphilic glucosides which have potential industrial interest in surfactancy [30].

2. Experimental

2.1. General

Anhydrous D-glucose was purchased from Fluka Company, butanol from SDS, dodecanol and *p*-toluene sulfonic acid from Aldrich Co. and used without further purification. Tonsil and KSF/O montmorillonites were provided generously by Süd-Chemie. KSF and K10 were purchased from Aldrich Co. Reactions were monitored by TLC using aluminium silica gel plates ($60F_{254}$). Flash-chromatography separations were performed using silica gel 60H (40–63 μ) under a 1 bar pressure. Chromatography solvents were purchased from Carlo-Erba Company. Carbon nuclear magnetic resonance spectra were recorded on a Brüker AC 200 spectrometer at 50.32 MHz. High performance liquid chromatography analyses were performed using NH_2 bound columns (Nucleosil or Spherisorb) with refraction index detection (RI). Enzymatic glucose assay was done using the glucose [HK]10 kit purchased from Sigma Diagnostics, with UV absorption analysis at 340 nm. Mass spectrometry analysis was performed at the Centre d'Etudes et de Recherches sur les Macromolécules Végétales (CERMAV) at

Grenoble for FAB experiments and at the Laboratoire de Chimie Biologique CNRS UMR 111 at the University of Sciences and Technology of Lille for matrix assisted laser desorption (MALD-MS) experiments. Size exclusion chromatography was performed on Biogel P2 and P4 (Bio-Rad) with RI detection.

2.2. Ultrasound equipment

For most experiments at 20 kHz, the ultrasound generator was a 300 W (electric power) Vibra-Cell apparatus, coupled with a titanium horn having a 13 mm diameter. Acoustic power was evaluated by calorimetric measurement and was 54 W (0.6 W/ml). For checking the influence of other parameters, a Sonoreactor® from Undatim Company was used. The maximal electric power of the Sonoreactor depends on the frequency: 100 W for 20 kHz, 40W for 40 kHz and 30 W for 60 kHz. The effective total power of the apparatus is 500 W. The horns (titanium) have a diameter range from 5 to 20 mm. Acoustic power, measured by calorimetry, is a function of the frequency (from 0.1 to 0.4 W/ml). The sonicated volume was ca. 100 ml.

2.3. Experimental procedure for butyl glycoside synthesis

Glucose (17.7 g, 0.098 mol) and butanol (90 ml, 0.983 mol, 10 equiv.) were stirred and heated at 113°C either with an oil bath or using ultrasound without any other heat source. *p*-Toluene sulfonic acid monohydrate (0.177 g, 0.93 mmol) or 0.885 g of bentonite (5% w/w) were added and ca. 1 ml samples were taken out of the mixture. Each aliquot was neutralized with a small amount of triethylamine and diluted with water (1 ml) and filtered on 0.45 μm nylon Gelman Sciences microfilter. The solvent was removed under reduced pressure and the residue was analyzed by HPLC (spherisorb-NH_2, 25°C, 250 × 4.6 mm, 3:1 MeCN/water, 0.7 ml/min). TLC or preparative flash-chromatography were performed using 7:2:1 chloroform/acetone/methanol mixture. Butyl glucosides were identified by comparison with literature data [31].

2.4. Experimental procedure for dodecyl glycoside synthesis

Glucose (14.3 g, 0.079 mol) and dodecanol (90 ml, 0.396 mol, 5 equiv.) were stirred and heated at 115°C either with an oil bath or using ultrasound while regulating with external cooling. *p*-Toluene sulfonic acid monohydrate (0.143 g, 0.75 mmol) or 0.715 g of bentonite (5% w/w) were added and ca. 1 ml samples were taken out of the mixture. Each aliquot was neutralized with a small amount of triethylamine and the solids were filtered, carefully powdered then washed with hexane (5 × 50 ml). The filtrate was concentrated under reduced pressure and the residue was analyzed by HPLC (nucleosil-NH_2, 45°C, 250 × 4.6 mm, 9:1 MeCN/water, 0.8 ml/min). The solid was dried for 10 min at 60°C and 20 mm Hg and analyzed by enzymatic assay. Preparative flash-chromatography was performed using 7:2:1 chloroform/acetone/methanol mixture (same as for TLC) after elution with pure dichloromethane for excess dodecanol removal. Dodecyl glucosides were identified by comparison with literature data [31].

3. Results

The rate of the glucosylation of butanol using various solids (montmorillonites) was studied by measuring the conversion rate and the yield

Table 1
Product distribution for reactions of glucose with butanol (10 equiv.) after 1 h at 113°C using various acidic catalysts

Catalyst *	Glucose conversion (%)	Butyl glucosides (%)
5% K10	37	35
5% KSF	58	54
5% KSF/O	88	78
1% *p*-TsOH	98	90

* w/w.

Table 2
pH of 10% aqueous suspensions of some acidic solids after various treatments in butanol

Solid	No treatment [a]	2 h at RT	2 h at 113°C silent	2 h at 113°C)))) [b]
Tonsil 30/60	3.3 (6.1)	3.4	3.3	3.8
Tonsil 15/30	3.1 (3.9)	3.2	3.3	3.5
K10	3.0 (4.6)	3.2	3.3	3.6
KSF	2.1 (2.1)	2.2	2.5	2.8
KSF/O	1.9 (1.9)	2.2	2.9	3.2
KSF/O [c]	id.	2.9	3.3	3.5

[a] In brackets is given the pH of the aqueous phase after filtration of solids.
[b] 20 kHz, 0.6 W/ml.
[c] In dodecanol.

of butylglucosides after 1 h at 113°C (Table 1) and comparing with that of the reaction catalyzed by *p*-toluene sulfonic acid. Reactions throughout this study were performed between 113 and 115°C allowing at the same time reasonably fast reactions and easy temperature control, notably when using ultrasound. The rates are consistent with the relative acidity of the catalysts which can be evaluated by measuring the pH of a 10% (w/w) suspension in water (cf. Table 2). Relevant work on the characterization of clay-based K catalysts was recently reported by Figueras and collaborators [26]. It has to be noted that this acidity is still present in the water after filtration of the solid, revealing a different behaviour of the montmorillonites compared to ion exchange resins or other heterogeneous catalysts.

Since the reaction is taking place in butanol and not in water, it was tested whether this acidity transfer from the solid to the liquid phase would also occur in the conditions of the reaction, or was a consequence of the considerable pertubation of their lamellar structure due to their high affinity for water. To answer this question, the various solids were suspended in butanol and treated under different conditions (stirring at room temperature, stirring at 113°C, ultrasound at 113°C). To measure their remaining acidity, the solids were filtered and then resuspended in water allowing the estimation of the pH of the resulting mixture. Results are given in Table 2, showing that indeed, some of the acidity is transferred to butanol, as lower acidity remains in the solid after treatment. This acidity in butanol could also be detected by measuring approximately the pH of the alcoholic phase after addition of water and methanol in order to obtain an aqueous homogeneous liquid. Nevertheless, the acidity transfer phenomenon was also shown to occur in the butanol case.

The loss of acidity observed in the case of KSF/O is the largest of all tested solids and this is consistent with the fastest reaction promoted by this support and that the rate was always slightly accelerated under ultrasonic irradiation (Table 3). In contrast, no significant rate

Table 3
Product distribution for reactions of glucose with butanol (10 equiv.) after 1 h at 113°C under silent or ultrasonic [a] conditions

Conditions (w/w)	Glucose conversion (%)	Glucoside/oligomer ratio	Furanosides/pyranosides ratio
1% pTsOH silent	95	8.5	0.2
1% pTsOH))))	94	7.5	0.2
5% KSF/O silent	75	8.4	1.2
5% KSF/O))))	82	10.7	1.2

[a] 20 kHz, 0.6 W/ml.

Table 4
Influence of butanol excess quantity method for reactions of glucose after 2 h at 113°C using *p*-TsOH (1% w/w)

Butanol quantity (equivalents)	Glucose conversion (%)		Glucoside/oligomer ratio	
	silent	)))) [a]	silent	)))) [a]
10	98	97	7	8
5	96	95	5	5

[a] 20 kHz, 0.6 W/ml.

modification due to ultrasound could be detected when using an homogeneous catalysis (*p*-TsOH). It is supposed that, during the manufacturing process of these montmorillonites involving an acidic treatment which promotes cation exchange, only partial exchange could occur for some polyvalent cations (Fig. 2). As a result, this allows the reverse process when the solid is perturbed by strong structural modification due to the high affinity of KSF/O for water, or due to ultrasound via the mechanical effects of cavitation. The driving force of this phenomenon is to regain the original complexation organization of the polyvalent cations. Another explanation for the observed acid transfer could be a fast ion-exchange type process promoting rapid acidification of the medium, together with a subsequent slow dissolution, then hydrolysis of salts remaining on the surface of the clay.

Although the exact cause remains hypothetical, we show here that the catalysis of the glucosylation reaction promoted by these solids, and in particular KSF/O, which is the most efficient one, should be more considered as an homogeneous catalysis, even if they can act as heterogeneous catalysts when used after several washings with water until the filtrate is neutral. In this case, the glycosylation reaction can still be promoted, albeit at a much smaller rate.

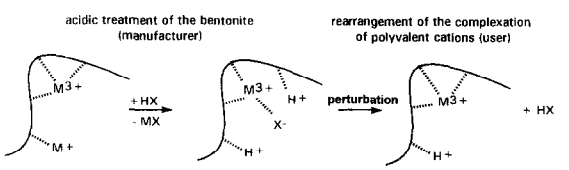


Fig. 2. Model for acid transfer from the solid to the solvent by reverse ion exchange.

The ultrasound mediated slight rate acceleration observed for the reaction catalyzed by KSF/O is the sole 'ultrasound effect' which we observed in the case of butanol and it has to be considered as a chemical proof for understanding the nature of the catalysis promoted by KSF/O in the case of the glucosylation reaction and not as a useful improvement of the reaction setup. Indeed it was verified that ultrasound physical characteristics did not influence other reaction trends such as effect of temperature, pressure, excess quantity of alcohol, together with power, frequency and probe diameter, on the rate, yields and selectivities. For example, Table 4 shows that either under classical heating conditions or using ultrasound, decreasing the excess of alcohol promotes the same change in the glucoside/oligomer ratio. Also, the furanoside/pyranoside ratio, which is depending on the catalyst, is not sensitive to the activation conditions (Table 5).

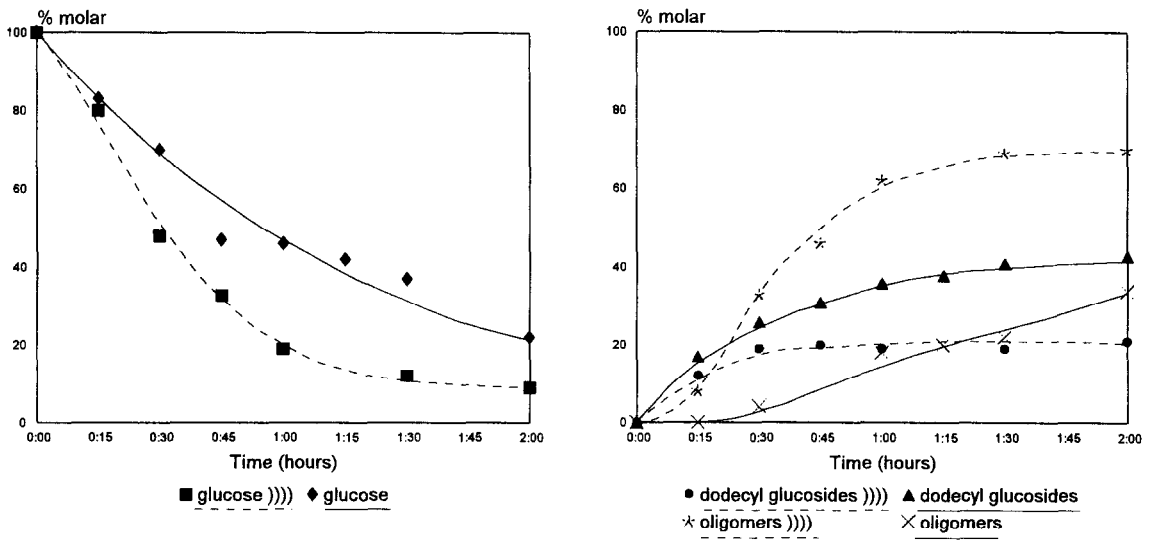
In the case of dodecanol, for which the medium is much more heterogeneous, even

Table 5
Influence of acid nature on glucoside distribution at 40% conversion of glucose (113°C, 10 equiv. of butanol)

Catalyst (w/w)	Furanoside/pyranoside ratio	
	silent	)))) [a]
5% Tonsil 15/30	3.5	–
5% Tonsil 30/60	2.8	–
5% K10	2.8	2.7
washed 5% KSF/O [b]	2.7	2.7
5% KSF	2.5	2.3
5% KSF/O	2.3	2.3
1% *p*-TsOH	1.7	2.1

[a] 20 kHz, 0.6 W/ml.
[b] Re-suspended in water and filtered until the aqueous phase was neutral.

when a soluble catalyst such as *p*-TsOH is used, we observed that ultrasound promoted dramatic changes in the reaction outcome. These differences are illustrated in Fig. 3, in which yields of glucosides as well as of oligomers are given as a function of time, for the reaction conducted under ultrasound or in 'silent' conditions with classical heating. Indeed, while the silent reaction, shown to be very sensitive to stirring efficiency, could lead to dodecyl gluco-



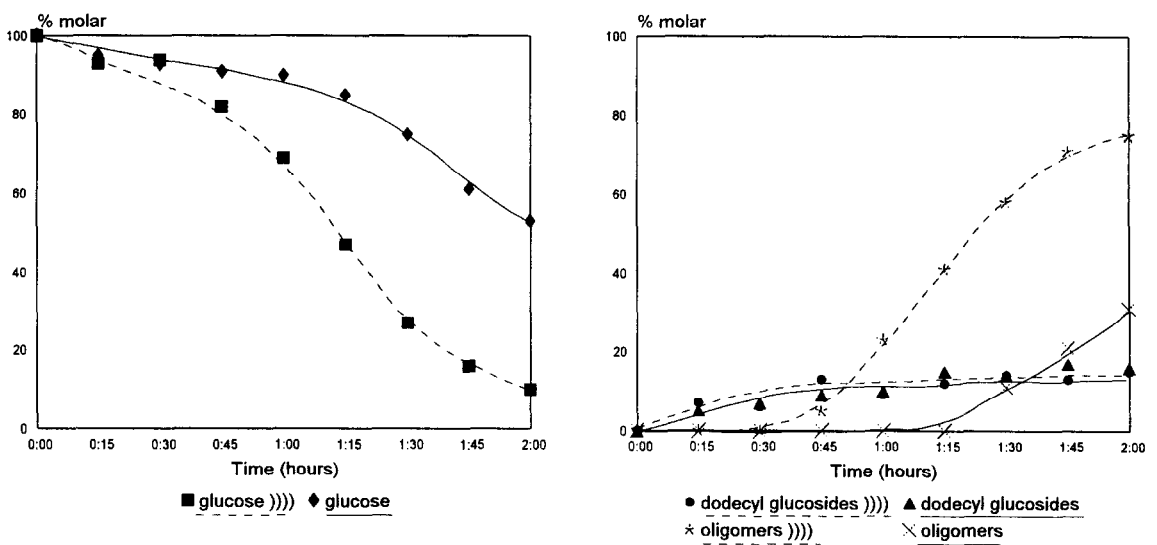
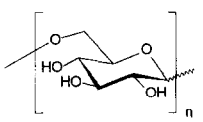


Fig. 3. Conversion rate and yields for the reaction of glucose with dodecanol at 115°C under silent conditions or with ultrasound (20 kHz, 0.6 W/ml).

sides as the major products, ultrasound directed always the reaction towards the formation of oligomers in good yield, for both acid catalyses.

The structure of the oligomers, in terms of degree of polymerisation (DP) and of glycosidic junctions, was investigated by several analytical methods, including ^{13}C NMR spectroscopy, HPLC, analytical and semi-preparative size exclusion chromatography, mass spectrometry and classical GC-MS analysis of monomers after chemical degradation. The oligomers were shown to be essentially polyglucose having a polymerisation degree from 2 to ca. 24, as seen by MALD-MS analysis. The amount of oligomers having a higher DP (over 8) decreased consistently with the DP. The same spectra allowed the identification of some side products as anhydro derivatives in little amounts for small DP and somewhat larger amounts for higher oligomers. Junctions were shown to be mostly 1,6 bonds between glucose monomers, with a low branching ratio, as seen by GC-MS after methylation, methanolysis and acetylation. All other types (1,2; 1,3; 1,4) could also be detected, in smaller quantities and in average equivalent proportions. Details for this structural analysis will be further reported.



In these experiments conducted at 115°C, the suspension of glucose, finely powdered, suddenly agglomerated. This agglomeration provided a semi-solid, highly viscous, gummy glucose phase which finally precipitated on prolonging the reaction time. After 2 h, both the liquid phase and the solids were analyzed, confirming that under ultrasonic activation, the quantity of oligomers was much higher compared to the classical reaction which was poorly reproducible. The difference was even larger when using KSF/O as catalyst (see Fig. 3). It has again to be noted that, in a similar way as for the glucosylation of butanol, the reaction rate in dodecanol measured by the conversion ratio of glucose was much more sensitive to ultrasound in the case of the reaction catalyzed by KSF/O (5% w/w) than in the *p*-TsOH (1% w/w) catalyzed reaction. Same acidity transfer to the dodecanol phase was observed (vide supra, Table 2).

The presence of water was shown to be responsible for the reaction outcome, as the addition of water to the reaction mixture prior to the experiment led to an increase of the oligomer ratio, under both silent and ultrasonic conditions (Table 6). It was controlled that the dodecyl glucoside hydrolysis was not the cause for the oligomer accumulation. The same oligomers were obtained from a suspension of glucose in diglyme containing a catalytic amount of *p*-TsOH, in absence of any alcohol, after addition of one equivalent of water. Both the silent or ultrasonic reactions led to the oligomers after the same agglomeration process (Table 6). When no water is added, ultrasound acts as a very efficient stirring method, leading to the trapping

Table 6
Yields in dodecyl glucosides and oligomers for the reaction of glucose at 115°C in dodecanol (5 equiv.) or diglyme

Conditions (w/w)	Dodecyl glucosides (%)		Oligomers (%)	
	silent	)))) [a]	silent	)))) [a]
1% *p*-TsOH 2 h, dodecanol	43	21	34	70
5% KSF/O 2 h, dodecanol	16	15	31	75
1% *p*-TsOH, 1 equiv. H_2O, 0.5 h, dodecanol	5	5	79	72
1% *p*-TsOH, 1 equiv. H_2O, 0.5 h, diglyme	–	–	59	22

[a] 20 kHz, 0.6 W/ml.

of water by the glucose suspension much faster, or at least in a more reproducible manner, than under classical conditions. Thus, the autoglycosylation process which takes place in the agglomerated glucose phase is promoted, to the detriment of the glycosylation of the alcohol which has to occur inside the liquid phase.

4. Conclusion

In this study, it has been shown that the glucosylation of butanol can be promoted by the bentonite KSF/O as acidic catalyst. High yields of butyl glucosides were obtained. Evidences for the homogeneous nature of the catalysis were given. Acidity transfer from the solid to the liquid phase was shown to occur, possibly via a reorganization of the complexation of polyvalent cations. Ultrasound was shown to enhance this acidity transfer, leading to a slight increase of the glucose conversion rate. In the case of dodecanol, the use of KSF/O under silent or ultrasonic conditions could not allow to obtain acceptable yields of glucosides. Ultrasound was shown to direct the reaction towards the formation of large amounts of oligomers, involving an autocondensation process within a semi-solid hydrated glucose phase, while classical heating and stirring led to not reproducible results.

Acknowledgements

Financial support from Béghin-Say, CNRS and Ministère de l'Agriculture et de la Pêche (Programme Aliment Demain, convention R94/10) is greatly acknowledged. We thank Professor A. Domard (University Lyon 1) for supportive and helpful discussions and for assisting us in the size exclusion chomatography study. We also thank Dr. J. Lemoine at UMR No. 111 of the CNRS (Lille) for his kind help in mass spectra analysis.

References

[1] E. Fischer, Ber. 47 (1914) 1980.
[2] A.T.J.W. de Goede, F. van Rantwijk, H. van Bekkum, Starch 47 (1995) 233.
[3] A. Lubineau, J.-C. Fischer, Synth. Commun. 21 (1991) 815.
[4] V. Ferrières, J.-N. Bertho, D. Plusquellec, Tetrahedron Lett. 36 (1995) 2749.
[5] K. Toshima, K. Tatsuta, Chem. Rev. 93 (1993) 1503.
[6] H. Kondo, S. Aoki, Y. Ichikawa, R.L. Halcomb, H. Ritzen, C.-H. Wong, J. Org. Chem. 59 (1994) 864, and references therein.
[7] J.P. Lorimer, T.J. Mason, Chem. Soc. Rev. 16 (1987) 239.
[8] J. Lindley, T.J. Mason, Chem. Soc. Rev. 16 (1987) 275.
[9] C. Einhorn, J. Einhorn, J.-L. Luche, Synthesis (1989) 787.
[10] J.M. Pestman, J.B.F.N. Engberts, F. de Jong, Recl. Trav. Chim. Pays-Bas 113 (1994) 533.
[11] R.W. Binkley, Modern Carbohydrate Chemistry, Marcel Dekker, New York, 1988, p. 87.
[12] A.T.J.W. de Goede, M.P.J. van Deurzen, I.G. van der Leij, A.M. van der Heijden, J.M.A. Baas, F. van Rantwijk, H. van Bekkum, J. Carbohydr. Chem. 15 (1996) 331.
[13] A.J.J. Straathof, H. Van Bekkum, A.P.G. Kieboom, Starch 40 (1988) 229.
[14] V.M. Thouy, P. Maitte, Bull. Soc. Chim. Fr. II 116 (1979) 264.
[15] J.M. Adams, S.E. Davies, S.H. Graham, J.M. Thomas, J. Catal. 78 (1982) 197.
[16] J.A. Ballantines, J.H. Purnell, J.M. Thomas, J. Mol. Catal. 27 (1984) 157.
[17] S. Hoyer, P. Laszlo, M. Horlovic, E. Polla, Synthesis, (1986) 655.
[18] B. Labiad, D. Villemin, Synth. Commun. 19 (1989) 31.
[19] B. Labiad, D. Villemin, Synthesis (1989) 143.
[20] R. Miranda, H. Cervantes, P. Joseph-Nathan, Synth. Commun. 20 (1990) 153.
[21] D. Villemin, B. Labiad, M. Hammadi, J. Chem. Soc., Chem. Commun. (1992) 1192.
[22] C. Cativiela, J.I. Garcia, M. Garcia-Matres, J.A. Mayoral, F. Figueras, J.M. Fraile, T. Cseri, B. Chiche, Appl. Catal. A 123 (1995) 273.
[23] S. Narayanan, K. Deshpande, Appl. Catal. A 135 (1996) 125.
[24] J.-C. Florent, C. Monneret, J. Chem. Soc., Chem. Commun. (1987) 1171.
[25] M. Csiba, J. Cleophax, A. Loupy, J. Malthête, S.D. Gero, Tetrahedron Lett. 34 (1993) 1787.
[26] T. Cseri, S. Békássy, F. Figueras, E. Cseke, L.-C. de Menorval, R. Dutartre, Appl. Catal. A 132 (1995) 141, and references therein.
[27] K. Tanabe, M. Misono, Y. Ono, H. Hattori, Stud. Surf. Sci. Catal. 51 (1989) 128.
[28] D. Kotkar, P.K. Ghosh, J. Chem. Soc., Chem. Commun. (1986) 650.
[29] D. Atkinson, G. Curthoys, Chem. Soc. Rev. 8 (1979) 475.
[30] M. Biermann, K. Schmid, P. Schulz, Starch 45 (1993) 281.
[31] A.J.J. Straathof, J. Romein, F. van Rantwijk, A.P.G. Kieboom, H. van Bekkum, Starch 39 (1987) 362.