Electrochemistry Communications 12 (2010) 1149–1153

Contents lists available at ScienceDirect

Electrochemistry Communications

journal homepage: www.elsevier.com/locate/elecom

Electrogenerated acid as an efficient catalyst for the preparation of 5-hydroxymethylfurfural

Tonino Caruso, Ermanno Vasca *

Department of Chemistry, University of Salerno, Via Ponte don Melillo, 84084 Fisciano (SA), Italy

ARTICLE INFO

Article history:
Received 26 April 2010
Received in revised form 26 May 2010
Accepted 26 May 2010
Available online 9 June 2010

Keywords:
5-Hydroxymethylfurfural
Electrochemical synthesis
Electrogenerated acid

ABSTRACT

A new method for the synthesis of 5-hydroxymethylfurfural (HMF) with high yields in dimethyl sulfoxide (DMSO) is presented. By using constant-current electrolysis more than 90% of sucrose or fructose was converted to HMF at room temperature in DMSO in the presence of traces of water.

1. Introduction

Carbohydrates represent a well established alternative to fossil fuels as a renewable and economic source of energy and raw materials [1]. The development of an economically convenient method for producing 5-hydroxymethylfurfural, HMF, [1g,2] at high purity, starting from sucrose, fructose or glucose as the substrates, gained in recent years considerable attention. HMF is a versatile intermediate in the synthesis of other chemical substances [3]. Unfortunately high production cost (40–80$ per gram, depending on the manufacturer) limits its availability and uses at an industrial scale [4]. Production of sufficiently pure HMF requires high temperatures and acid catalysts to dehydrate hexoses in water [5], in DMSO [4b,6], and in biphasic water-organic solvent systems [7,8]. More recently its synthesis was reported in ionic liquids [2a,b,d,e,9], two-phase modifier [2c,10] and over solid acid and base catalyst system [2f]. Fructose showed to be the only hexose giving HMF at high yields, though usually at high temperatures, DMSO being the more suitable solvent.

Up to now using electrolysis to oxidise or to reduce carbohydrates to more versatile compounds gave unsatisfactory results. In water, solvent electrolysis leads to complex mixtures of products [11]. On the other hand, in organic solvents only the electrolysis of some monosaccharides in alcoholic-alkaline media is reported, but without the formation of any of the expected oxidation products and no other chemical of some synthetic utility [12]. Here we report a new high-yield synthesis of HMF, based on the dehydration of fructose or sucrose at room temperature by electrogenerated acid (EGA). This non conventional acidity is very effective because the EGA makes extremely acidic the solution at the anode surface [13].

2. Experimental

Electrochemical synthesis of HMF from carbohydrates was performed using constant-current coulometry. Each experiment started by transferring in the electrolysis cell a Test Solution (TS) prepared by dissolving in the chosen organic solvent a known amount of a carbohydrate and of an inorganic salt. The latter had to be present in TS in order to lower the iR drop across the electrodes, and it was selected on the basis of its solubility in the particular solvent used. Experiments were carried out in dimethyl sulfoxide, dimethylformamide and acetonitrile as the solvents. Fructose, glucose, sucrose, mannose, galactose, lactose, cellobiose and maltose were systematically investigated as the substrates.

Constant-current electrolysis was performed by using a two-compartment electrochemical cell. Compartments were separated by a porous glass frit diaphragm. Platinum foils ($1.5\ cm^2$ total surface area) were used as the electrodes.

Among the carbohydrates used as substrate, only fructose and sucrose, in DMSO, were converted into HMF with significant yields also at room temperature. In those cases the electrochemical procedure was performed by dissolving in 5.0 mL DMSO 1.0 mmol fructose or sucrose and 0.5 mmol $KClO_4$ as electrolyte (0.1 mol/L). Constant-current electrolysis at 3.0 mA was performed on the stirred solution, at room temperature.

Reaction progress was followed by drawing few microliter aliquots of Test Solution at different electrolysis stages and analyzing them by TLC and by NMR. Once the reaction was completed, reaction mixtures were extracted with 5:1 $CHCl_3$:H_2O. The organic phase was

---

* Corresponding author. Tel.: +39 89 96 9588; fax: +39 89 96 9603.
E-mail address: evasca@unisa.it (E. Vasca).

1388-2481/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.elecom.2010.05.040

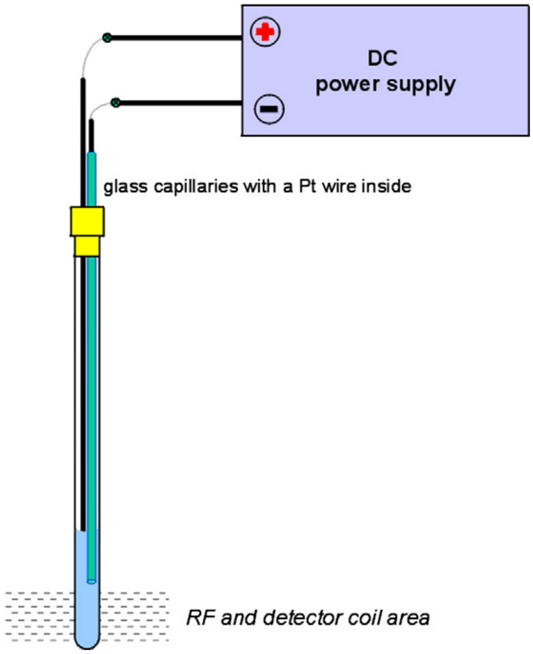


Fig. 1. Sketch of the small-scale electrolytic cell in the NMR probe.

concentrated and analyzed by HPLC on a C18 column, using a 99:1 v/v water/iso-propanol as eluent at a flow rate of 0.7 mL/min.

Further information on the reaction of these substrates were obtained by carrying out experiments in a small-scale electrolytic cell adapted to fit into an NMR tube, as in Fig. 1. Two 0.3 mm platinum wires, each one melted in a glass capillary to avoid electrical short-circuit between them, were inserted in a Teflon sheath intercalated in the NMR tube. The cathode, inserted into a Luggin capillary, was separated from the solution by a terminal porous glass frit. This way all reactions could be performed directly in deuterated DMSO and monitored by collecting ^{1}H-, ^{13}C- and DEPT-NMR spectra at selected times during the electrolysis. At the end of each electrolysis experiment, 50 μL D_2O were added to suppress the signals of the different hydroxyl groups and merge them in a single peak, in order to simplify the interpretation of protonic spectra. In this manner the number of peaks in the more informative zone of the spectrum, between 3 and 4 ppm, was reduced.

2.1. Characteristic resonance shifts of HMF

^{1}H-NMR, δ ppm (400 MHz, DMSO-d_6): 4.43 (s, 2 H), 6.53 (d, J = 3.4 Hz, 1 H), 7.42 (d, J = 3.4 Hz, 1 H), 9.45 (s, 1 H). ^{13}C-NMR, δ ppm (400 MHz, DMSO-d_6): 178.3, 163.2, 152.1, 124.8, 110.0, 56.0.

2.2. Apparatus and reagents

An Agilent E3612A power supply was used in the coulometric circuit. Current intensity was monitored with a Keithley 197 A multimeter. Spectrophotometric measurements were performed with a Perkin-Elmer Lambda EZ 201. A Thermo Surveyor Plus HPLC system, equipped with a two-wavelength UV detector (209 nm for DMSO and 284 nm for HMF) was used, and the separation was carried out on a Supelcosil™ LC-18 column (25 cm × 21.2 mm L × i.d., 5-μm particle size). ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker DRX 400 MHz spectrometer. NMR spectra in DMSO-d_6 were collected at 40 °C in order to optimize signal resolution. All reagents and solvents used were purchased from Sigma-Aldrich-Fluka.

3. Results and discussion

The ^{1}H-NMR spectra collected at different electrolysis stages in sucrose and fructose solutions are presented in Fig. 2. In parallel with electrolysis progress, a singlet relative to HMF appeared, with the doublets relative to the anomeric forms of glucose, α- and β-GP [14]. Peak integration of the spectrum in Fig. 2a shows that sucrose concentration decreases as a first-order kinetic [15].

In the same experimental conditions, fructose was the only one among the simple monosaccharides investigated which could be converted in HMF (Fig. 2b). Glucose and HMF were inert at room temperature under the electrolysis conditions used. Actually, it is reported [4b] that HMF can be oxidised to 2,5-diformylfuran, but only after prolonged electrolysis at temperatures higher than 80 °C.

HMF formed was purified and quantified by HPLC after extraction. Efficient extraction of HMF from the solvent mixture remains a quite difficult task. Separation methods suggested to remove HMF from DMSO are based on biphasic reactors in which a continuous extraction of HMF by an organic solvent is performed [1a,7,8,10].

In the present work reaction mixtures were first extracted with 5:1 $CHCl_3$:H_2O [16], monitoring by HPLC the decrease of the aldehyde signal in the aqueous phase. It was possible to keep loss below 10%. To do this, the organic solvent in which HMF was dissolved was advantageously recovered while the residual mixture was analyzed by HPLC [9c] and by UV–Vis spectroscopy, in order to determine the reaction yield and the percent conversion. HMF was isolated with 80–85% yields, which are slightly less than the ones evaluated on the basis of UV and HPLC measurements performed directly on the crude mixture (90–92%).

In order to increase the product yield, some factors affecting electrosynthesis had to be optimized. The current density, the amount of charge delivered and the electrode material were systematically varied, by setting all parameters to be constant and optimizing one at a time. The effect of applied current density on the product yield was studied in the range 0.5–6.0 mA/cm^2. The highest product yield was obtained working at 2.0 mA/cm^2.

In the course of electrolysis dimethyl sulfide, DMS, at the cathode, and dimethyl sulfone, $DMSO_2$, at the anode, were formed. Signals relative to $DMSO_2$ and DMS were revealed by NMR (Fig. 3) thus confirming that dimethyl sulfoxide is not inert toward electrolysis [17]. DMSO oxidation occurs in the presence of residual traces of water (0.1% in our solvent, by Karl Fisher), according to the anodic half-reaction (1) [17]

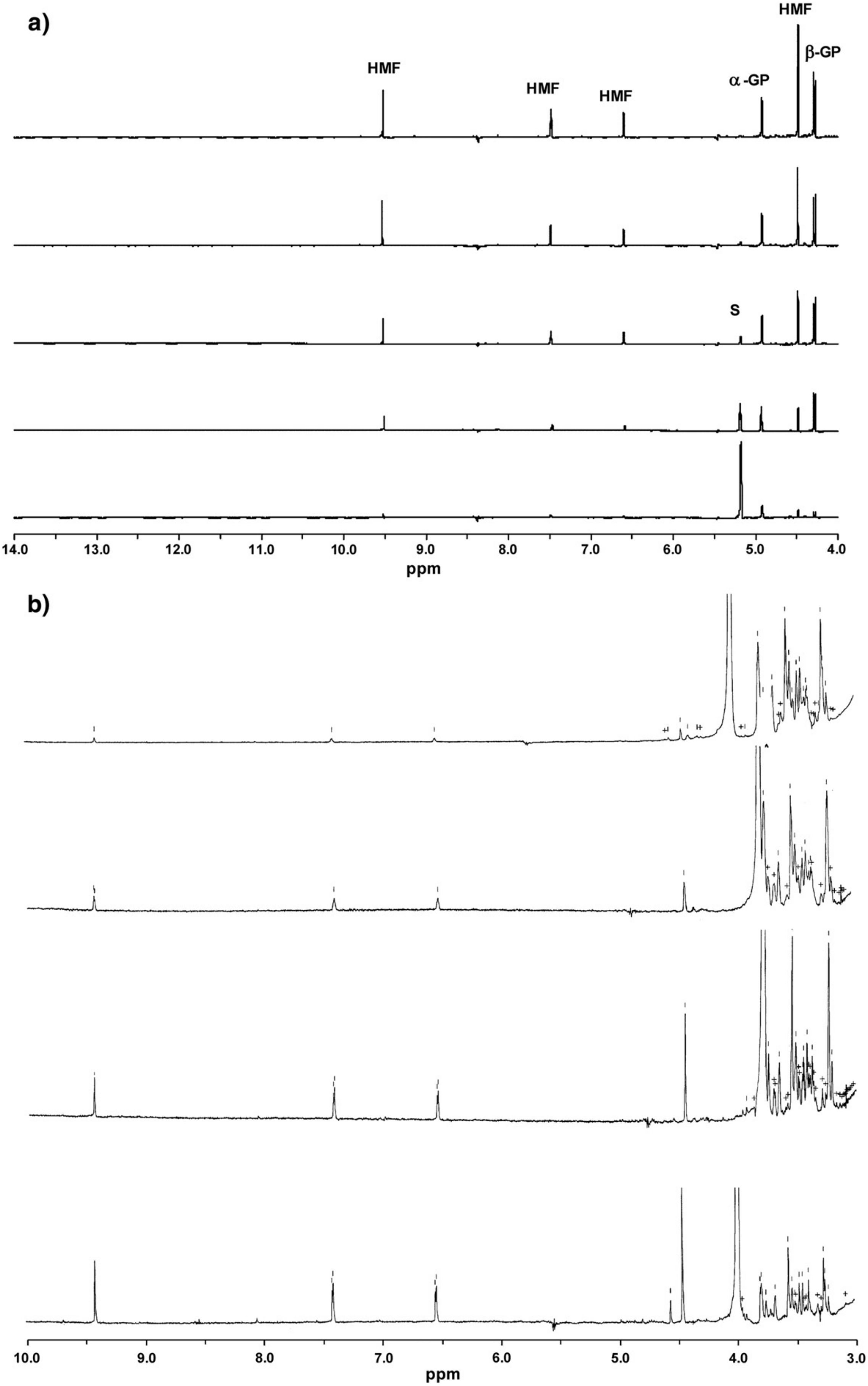
$$\mathrm{DMSO} + \mathrm{H_2O} \rightarrow \mathrm{DMSO_2} + 2\mathrm{H^+} + 2\mathrm{e^-} \tag{1}$$

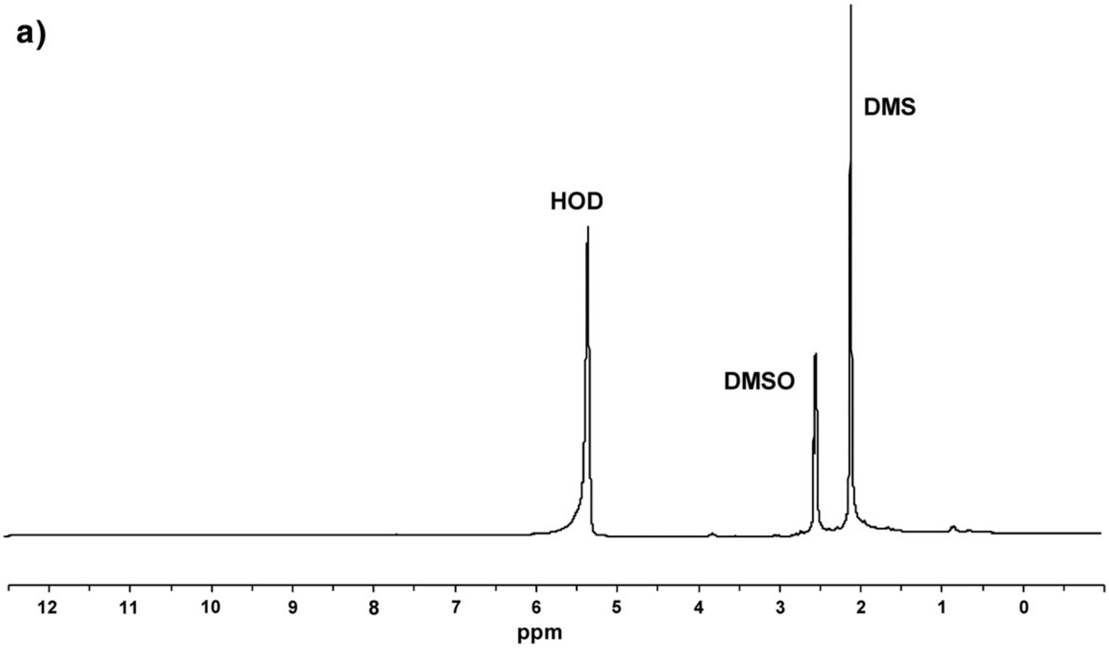
and the cathodic half-reaction (2):

$$\mathrm{DMSO} + 2\mathrm{H^+} + 2\mathrm{e^-} \rightarrow \mathrm{DMS} + \mathrm{H_2O}. \tag{2}$$

Solvent disproportion produces and consumes the same number of H^+. However it is well known that an electrogenerated acid (EGA) is a powerful acid-catalyst for several organic reactions. Oxidation of traces of water leads to a high acid concentration at the anode surface [13]. Hence H^+ electrogenerated *in situ* by water oxidation in DMSO is

Fig. 2. a) ^{1}H-NMR spectra of sucrose solutions in DMSO-d_6 recorded at increasing electrolysis times, from bottom to top: 15, 30, 45, 60, and 75 min. The three doublets at 5.18, 4.91, and 4.27 ppm correspond to the anomeric proton of sucrose (S), α-glucopyranose (α-GP) and β-glucopyranose (β-GP) respectively; b) ^{1}H-NMR spectra of fructose solutions in DMSO-d_6 recorded at increasing electrolysis times, from top to bottom: 10, 15, 30, and 45 min. ^{1}H-NMR for 5-HMF: δ ppm (400 MHz, DMSO-d_6): 4.43 (s, 2 H), 6.53 (d, J = 3.4 Hz, 1 H), 7.42 (d, J = 3.4 Hz, 1 H), and 9.45 (s, 1 H).


a)
HMF
HMF
HMF
α -GP
HMF
β-GP
S
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
ppm
b)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
ppm



b) DMSO electrolysis wiyh propylene oxide

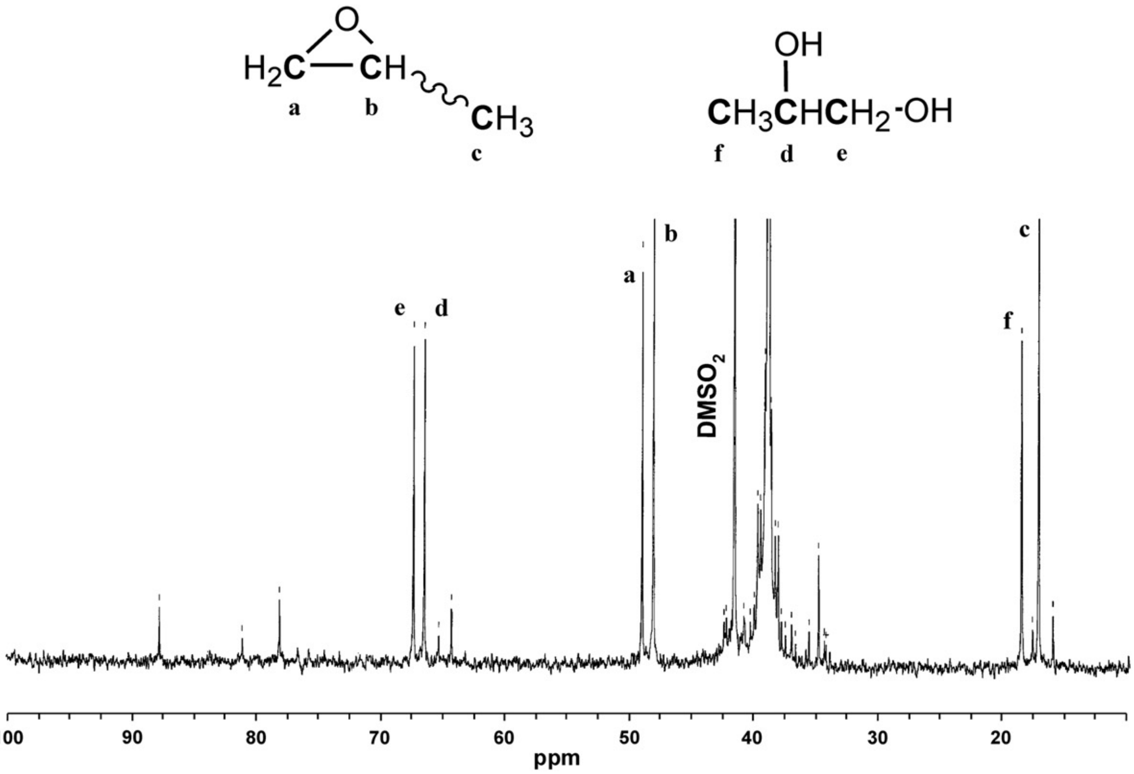


Fig. 3. a) ^{1}H-NMR spectrum of DMSO-d$_6$ electrolysed at the cathode in the presence of 0.1% water. The signal at 2.066 ppm is relative to DMS; b) ^{13}C-NMR spectrum of DMSO electrolysed at the anode in the presence of propylene oxide, showing the signals relative to DMSO$_2$, 1,2-propane diol and propylene oxide excess.

the driving force of the process and directly catalyses fructose dehydration to HMF (3)

$$C_6H_{12}O_6 \xrightarrow{H^+} C_6H_6O_3 + 3H_2O \tag{3}$$

according to the mechanism reported by Antal [18].

Water formed through reaction (3) can be directly oxidised in competition with DMSO or can sustain the electrochemical reaction (1). The net result is the production of hydrogen ions. The overall reaction (4) occurs at the anode as a result of DMSO oxidation and of the catalytic dehydration of fructose:

$$C_6H_{12}O_6 + (CH_3)_2SO \xrightarrow{H^+} C_6H_6O_3 + (CH_3)_2SO_2 + 2H_2O + 2H^+ + 2e^-. \tag{4}$$

By interrupting the current delivery HMF formation is inhibited. Constant current (2.0 mA/cm^2) must be delivered for at least 60 min

(0.08 F/mol) to convert more than 90% fructose to HMF and for 80 min (0.15 F/mol) to obtain the same result for sucrose. Sucrose dehydration according to reaction (5)

$$C_{12}H_{22}O_{11} \xrightarrow{H^+} C_6H_{12}O_6 + C_6H_6O_3 + 2H_2O \tag{5}$$

is catalysed by H^+ ions. After the glycosidic bond cleavage, with formation of glucose and of a five-member cyclic carboxonium ion [14,19]; this fructosyl intermediate loses H^+, forming an enol intermediate [18] which finally dehydrates to HMF. The electrochemically-catalysed dehydration of sucrose is expressed by reaction (6), resulting from the sum of (1) with (5):

$$C_{12}H_{22}O_{11} + (CH_3)_2SO \xrightarrow{H^+} C_6H_{12}O_6 + C_6H_6O_3 + (CH_3)_2SO_2 + H_2O + 2H^+ + 2e^-. \tag{6}$$

Formation of trace amounts of H^+ during the electrolysis was confirmed by ^{1}H-NMR on the basis of ring opening of propylene oxide to 1,2-propanediol, (Fig. 3b) [20]. Accordingly, in the presence of known amounts of pyridine (2%v/v) or imidazole (3 mM) or by saturating the solution with Na_2CO_3 no reaction was observed. Furthermore, sucrose and fructose were recovered unchanged in anhydrous conditions (DMSO distilled over CaH_2 under nitrogen and used over activated molecular sieves, 4 Å). Finally, no reaction occurred using as the substrate sucrose octaacetate, which cannot dehydrate.

4. Conclusions

It has been demonstrated that 5-hydroxymethylfurfural can be easily synthesized with 80–85% yields in DMSO as the solvent, starting from sucrose or fructose, at room temperature, by *in situ* electrogenerated acid as catalyst. The synthesis can be performed by means of constant-current electrolysis, using milder conditions than those usually reported.

References

[1] (a) Y. Román-Leshkov, C.J. Barret, Z.Y. Liu, J.A. Dumesic, Nature 447 (2007) 982;
  (b) J.N. Chheda, G.W. Huber, J.A. Dumesic, Angew. Chem. Int. Ed 46 (2007) 7164;
  (d) B. Kamm, Angew. Chem. Int. Ed. 46 (2007) 5056;
  (e) G.W. Huber, S. Iborra, A. Corma, Chem. Rev. 106 (2006) 4044;
  (f) J.N. Chheda, J.A. Dumesic, Catal. Today 123 (2007) 59;
  (g) G.W. Huber, J.N. Chheda, C.J. Barrett, J.A. Dumesic, Science 308 (2005) 1446.

[2] (a) G. Yong, Y. Zhang, J.Y. Ying, Angew. Chem. Int. Ed. 47 (2008) 9345;
  (b) S. Hu, Z. Zhang, Y. Zhou, B. Han, H. Fan, W. Li, J. Song, Y. Xie, Green Chem. 10 (2008) 1283;
  (c) J.N. Chheda, Y. Roman-Leshkov, J.A. Dumesic, Green Chem. 9 (2007) 342;
  (d) H. Zhao, J.E. Holladay, H. Brown, Z.C. Zhang, Science 316 (2007) 1597;
  (e) J.Y.G. Chan, Y. Zhang, Chem. Sus. Chem. 2 (2009) 731;
  (f) A. Takagaki, M. Ohara, S. Nishimura, K. Ebitani, Chem. Comm. (2009) 6276.

[3] (a) F.W. Lichtenthaler, Acc. Chem. Res. 35 (2002) 728;
  (b) J.O. Metzger, Angew. Chem. Int. Ed. 45 (2006) 696.

[4] (a) B.M.F. Kuster, Starch/Staerke 42 (1990) 314;
  (b) G.A. Halliday, R.J. Young, V.V. Grushin, Org. Lett. 5 (2003) 2003.

[5] (a) K. Seri, Y. Inoue, H. Ishida, Bull. Chem. Soc. Jpn 74 (2001) 1145;
  (b) M.J. Antal Jr., W.S.L. Mok, G.N. Richards, Carbohydr. Res. 199 (1990) 111;
  (c) F.S. Asghari, H. Yoshida, Ind. Eng. Chem. Res. 45 (2006) 2163;
  (d) F. Ilgen, D. Ott, D. Kralish, C. Reil, A. Palmberger, B. König, Green Chem. 11 (2009) 1948;
  (e) W. Zeng, D. Cheng, F. Chen, X. Zhan Catal. Lett. 133 (2009) 221.

[6] (a) K. Seri, Y. Inoue, H. Ishida, Chem. Lett. (2000) 22;
  (b) Y. Nakamura, S. Morikawa, Bull. Chem. Soc. Jpn 53 (1980) 3705.

[7] C. Moreau, R. Durand, S. Razigade, J. Duhamet, P. Faugeras, P. Rivalier, P. Ros, G. Avignon, Appl. Catal. A 145 (1996) 211.

[8] M. Bicker, D. Kaiser, L. Ott, H. Vogel, J. Supercrit. Fluids. 36 (2005) 118.

[9] (a) X. Qi, M. Watanabe, T.M. Aida, R.L. Smith, Jr. Green Chem. 11 (2009) 1327;
  (b) C. Moreau, A. Finiels, L. Vanoye, J. Mol. Catal. Chem. 253 (2006) 165;
  (c) S. Hu, Z. Zhang, J. Song, Y. Zhou, B. Han Green Chem. 11 (2009) 1746.

[10] (a) X. Qi, M. Watanabe, T.M. Aida, R.L. Smith, Jr Ind. Eng. Chem. Res. 47 (2008) 9234;
  (b) Y. Roman-Leshkov, J.N. Chheda, J.A. Dumesic, Science 312 (2006) 1933.

[11] (a) S.J. Yao, A.J. Appleby, A. Geisel, H. Cash, S. K. Wolfson Nature 224 (1969) 921;
  (b) P. Parpot, K.B. Kokoh, B. Beden, C. Lamy, Electr. Acta 38 (1993) 1679;
  (c) P. Parpot, K.B. Kokoh, E.M. Belgsir, J.-M. Leger, B. Beden, C. Lamy J. Appl. Electr. 27 (1997) 25.

[12] G.W. Hay, F. Smith, Canad. J. Chem. 47 (1969) 417.

[13] (a) S. Torii, Electroorganic Synthesis, Part I, Oxidation Methods, Applications Verlag Chemie, Weinheim, 1985, pp. 188–192;
  (b) S. Torii, Bull. Soc. Chem. Jpn. 58 (1985) 1859.

[14] (a) S.J. Angyal, Angew. Chem. Int. Ed. 8 (1969) 157;
  (b) S.J. Angyal, Carbohydr. Res. 263 (1994) 149;
  (c) V. Mazzoni, P. Bradesi, F. Tomi, J. Casanova, Magn. Res. Chem. 35 (1997) S81;
  (d) F.W. Lichtenthaler, S. Rönninger, J. Chem. Soc. Perkin Trans. 2 (1990) 1489.

[15] T.J. Mega, R.L. Van Etten, J. Am. Chem. Soc. 110 (1988) 6372.

[16] G. Fleche, A. Gaset, U.S. Patent No. 4,339,387, July 13, 1982.

[17] D. Vasudevan, S.S. Vaghela, G. Ramachandraiah, J. Appl. Electr. 30 (2000) 1299.

[18] M.J. Antal Jr., W.S. Mok, G.N. Richards, Carbohydr. Res. 199 (1990) 91.

[19] S.M. Oon, D.G. Kubler, J. Org. Chem. 47 (1982) 1166.

[20] (a) M. K. Dhaon, U.S. Patent No. 5,698,676, Use of propylene oxide as an acid scavenger in peptide synthesis, December 16, 1997;
  (b) A.E. Gash, T.M. Tillotson, J.H. Satcher Jr, J.F. Poco, L.W. Hrubesh, R.L. Simpson, Chem. Mater 13 (2001) 999.