Carbohydrate Research 344 (2009) 2568–2572

Contents lists available at ScienceDirect

Carbohydrate Research

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

Note

Efficient microwave-assisted synthesis of 5-hydroxymethylfurfural from concentrated aqueous fructose

Thomas S. Hansen[a], John M. Woodley[b], Anders Riisager[a,*]

[a] Centre for Catalysis and Sustainable Chemistry and Department of Chemistry, Technical University of Denmark, Building 207, DK-2800 Kgs. Lyngby, Denmark
[b] Department of Chemical and Biochemical Engineering, Technical University of Denmark, Building 229, DK-2800 Kgs. Lyngby, Denmark

ARTICLE INFO

Article history:
Received 19 August 2009
Received in revised form 23 September 2009
Accepted 30 September 2009
Available online 2 October 2009

Keywords:
Fructose
5-Hydroxymethylfurfural
Homogeneous catalysis
Microwave synthesis
Green chemistry
Renewable resources

ABSTRACT

Studies on the HCl-catalysed microwave-assisted dehydration of highly concentrated aqueous fructose (27 wt %) to 5-hydroxymethylfurfural (HMF) revealed a significant increase in the fructose conversion rate over the conventional heated systems. Water, being the most benign solvent and therefore ideal for green and sustainable chemistry, normally is a poor solvent for the dehydration process resulting in low HMF selectivities and yields. However, reaction at 200 °C with microwave irradiation with a short reaction time of only 1 s resulted in good HMF selectivity of 63% and fructose conversion of 52%, while prolonged irradiation for 60 s (or more) resulted in nearly full fructose conversion (95%) but lower HMF yield (53%). Decreasing the fructose concentration significantly improved the HMF selectivity, but possibly made the production route less attractive from an industrial point of view due to the resultant low throughput.

1. Introduction

In recent years, considerable effort has been put into the development of alternatives to the fossil-based industry of today.[1–5] Decreasing fossil fuel reserves call for the development of a new, long term, environmentally friendly and sustainable chemical source. One possibility could be provided by biomass,[6] which is abundant in most parts of the world as a product of the light-induced fixation of CO_2 in plants and algae via photosynthesis. A high number of functional groups, often hydroxyl groups, render carbohydrate biomass particularly suitable for the production of fine chemicals used in, for example, pharmaceuticals, plastics, rubbers and other polymeric materials, which typically contains functional groups of –OH or derivatives thereof. However, the number of hydroxyl groups often also results in non-selective conversions of carbohydrates, as many side reactions are possible.[7,8]

One interesting compound that is obtainable directly from the acid-catalysed dehydration of hexoses is 5-hydroxymethylfurfural (HMF).[9,10] This furan-based compound could potentially be utilised as a platform compound[11] for further processing into commercially valuable chemicals and thereby replacing a range of chemicals that are presently obtained from fossil-based sources. HMF has been known for more than a century and is produced by use of catalysts such as mineral acids,[10,12] acidic ion-exchange resins,[13] H-zeolites,[14] and with the solvent acting as catalyst, for example, in ionic liquids.[15] Environmental concerns favour water as a solvent for the reaction, but water is unfortunately not very selective for the production of HMF and many by-products comprising insoluble polymeric compounds (i.e., humins) and soluble polymers are often formed.[16] Additionally, levulinic acid (LA) and formic acid (FA) are typically also obtained from rehydration of HMF (Scheme 1) by a still poorly understood reaction mechanism, though Horvat et al.[17] have proposed a mechanism involving intermediates based on ^{13}C NMR measurements.

In order to minimise by-product formation, two-liquid phase systems enabling extraction of HMF as it is produced have also been developed.[12,18] However, from a practical point of view these reaction systems require large volumes of extracting solvent, thus making them less attractive—and possibly uneconomical—on an industrial scale. Additionally, high-boiling solvents such as dimethylsulfoxide (DMSO) have also been utilised and shown to be very effective in promoting the HMF formation. However, here removal of the solvent from the product mixture has proved quite difficult.[19]

Microwave-induced organic synthesis, traditionally employed for organometallic synthesis in particular, has proven to be very efficient in promoting the dehydration of fructose to HMF by greatly reducing the reaction time and resulting in high selectivity and yield.[20,21] A high input of energy via the microwave irradiation allows the reaction to overcome the energy barrier for product formation much faster than by conventional heating and therefore

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* Corresponding author. Tel.: +45 45252233.
E-mail address: ar@kemi.dtu.dk (A. Riisager).

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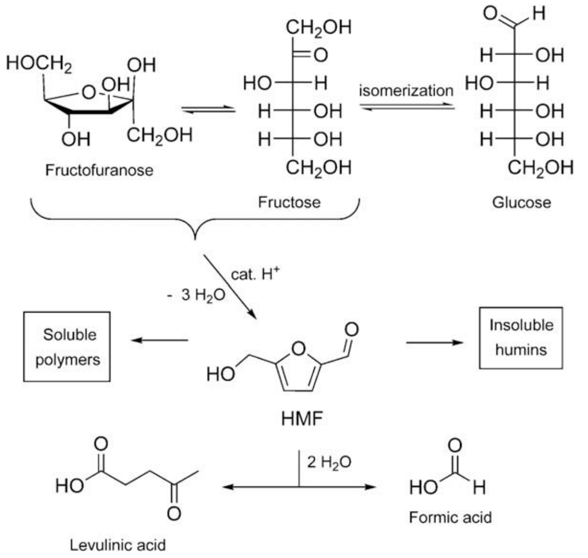
doi:10.1016/j.carres.2009.09.036



Scheme 1. Acid-catalysed synthesis of HMF from fructose and possible by-products.

speeds up the reaction significantly.[22] The aqueous, acid-catalysed dehydration of fructose to HMF is a fairly slow process that can take hours to reach full fructose conversion. Employing microwaves, however, increases the reaction rate significantly such that full conversion is reached in a matter of minutes.[20]

In this work, we report a thorough investigation of the reaction parameters in the HCl-catalysed, microwave-assisted, aqueous dehydration of fructose to HMF. To facilitate process intensification, reaction parameters were optimised with three main goals in mind: (1) the solvent has to be water, (2) the utilisation of HCl catalyst should be minimised and (3) an initial high fructose concentration should be employed. These conditions differ significantly from those employed in recent work by Qi et al.[20] who used an acetone–water system with a heterogeneous acidic ion-exchange resin catalyst. Despite very good results with this system its industrial utilisation could be hampered by generation of a highly elevated pressure from the acetone component (bp 56 °C[23]). In addition, optimisation of the system was conducted on a diluted 2 wt % fructose solution, resulting in a corresponding low space-time-yield.

2. Experimental

2.1. Materials

Fructose (99%), 5-hydroxymethylfurfural (99%), levulinic acid (98%), formic acid (99.8%) and HCl ($\geqslant$37%, p.a.) were purchased from Sigma–Aldrich and were used without further purification. Deionized water was used for the preparation of aqueous solutions.

2.2. Dehydration of fructose to HMF

The microwave-assisted fructose dehydration was performed using a microwave reactor vessel (pressure limit: 20 bar) charged with an aqueous fructose solution (30 wt %, 2.7 mL, 5.3 mmol), an aqueous HCl solution (0.10 M 0.3 mL, 0.03 mmol) and a magnetic stirrer. After being sealed with a cap, the vessel containing the mixture was mounted in a microwave apparatus (Biotage Emrys Creator, Personal Chemistry, effect range 90–300 W) and heated for a specified reaction time (reaction times refers to the time the reaction was held at a fixed terminal temperature) with preset power supply under magnetic stirring. After the reaction, the vessel was purged externally with nitrogen to allow rapid cooling to 50 °C before being removed from the chamber. Finally, the vessel was further cooled to room temperature, decapped and a sample was taken for analysis. For comparison, dehydration of fructose was also performed by conventional heating of a sealed pressure-stable glass tube (Ace, pressure limit: 20 bar) charged with an aqueous fructose solution (30 wt %, 2.7 mL, 5.3 mmol), an aqueous HCl solution (0.10 M 0.3 mL, 0.03 mmol) and a magnetic stirrer. Here the tube with the reaction mixture was placed in a preheated oil bath employed with a temperature controller (VWR, VT-5) for a specified time under stirring at a fixed temperature (reaction times were measured after a stable oil bath temperature had been reached). After the reaction, the tube was removed from the oil bath and cooled to room temperature before a sample was taken for analysis.

2.3. Product analysis

Samples of reaction products were filtered through a syringe filter (VWR, 0.45 μm PTFE) prior to analysis by high pressure liquid chromatography (HPLC, Agilent 1200 series, Bio-Rad Aminex HPX-87H, 300 mm × 7.8 mm pre-packed column). A 0.005 M H_2SO_4 mobile phase was employed as eluent at 60 °C with a flow-rate of 0.6 mL/min. Concentrations of products were determined from calibration curves obtained with reference samples, while product yields (%), product selectivities (%) and fructose conversions (%) were based on the initial concentration of fructose and calculated as:

$$\text{Product yield} = \frac{\text{Product conc}}{\text{Initial fructose conc}} \times 100\%$$

$$\text{Fructose conversion} = \left(1 - \frac{\text{Fructose conc}}{\text{Initial fructose conc}}\right) \times 100\%$$

$$\text{Product selectivity} = \frac{\text{Product yield}}{\text{Fructose conversion}} \times 100\%$$

3. Results and discussion

3.1. Dehydration without catalyst

Dehydration of fructose to HMF is, in principle, possible without a catalyst both by conventional heating and by microwave-assisted heating, though a catalyst is, of course, expected to increase the dehydration rate significantly. Initial experiments performed here with microwave heating, at 160 °C without catalyst, yielded only 5% fructose conversion and only 1% HMF, as shown in Figure 1. At lower temperatures, no significant fructose conversion occurred whereas a considerable quantity of humins were detected in all reactions above 160 °C, clearly suggesting catalyst promotion to be a prerequisite to make the dehydration selective for HMF production.

At prolonged reaction times or sufficiently high temperatures however, a build-up in LA and FA concentrations results in an acidification of the reaction mixture leading to autocatalysis of the dehydration process. The catalytic properties of the reaction by-products can thereby render control experiments without a catalyst misleading. This is clearly seen in Figure 1, where an increasing amount of formed LA and FA from 170 °C to 190 °C induced a dramatic increase in the fructose conversion rate.

3.2. pH dependence

To optimise the fructose dehydration towards HMF formation with respect to the required amount of catalyst, experiments were

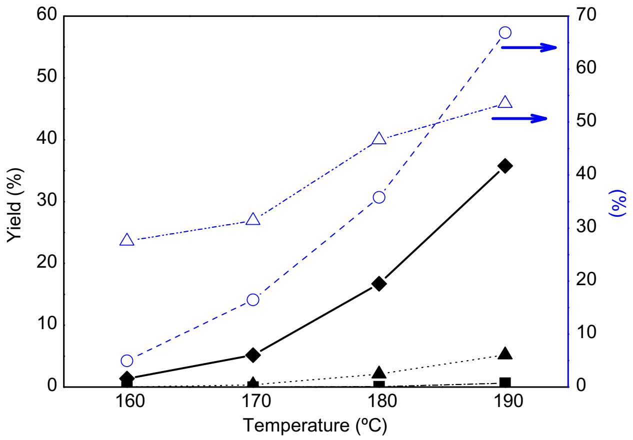


Figure 1. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of temperature in microwave-assisted dehydration of fructose (5 min reaction time, 300 W, initial fructose concentration 27 wt %).

performed with various amounts of hydrochloric acid, that is, at different initial pH values (Fig. 2).

When using a large excess of acid at a corresponding low pH value (1 M HCl, pH 0), at moderate temperature of 130 °C with 5 min microwave irradiation, 99% fructose conversion was reached. Nevertheless, rehydrated FA and LA by-products (as well as humins) were formed in relatively high yields of 39% and 30%, respectively, compared to only 28% HMF. A maximum HMF yield of 40% was obtained at a higher pH value of 0.3 (0.5 M HCl) with 70% fructose conversion, while a maximum reaction selectivity of 56% towards HMF was reached at a pH of 0.6 (0.25 M HCl), though with a lower fructose conversion of 63%. This clearly demonstrates that less acidic conditions are necessary to suppress the acid-promoted by-product formation. Hence, more benign acidic conditions (pH 2) were employed for the remaining experiments, corresponding to 0.01 M HCl and 27 wt % fructose solution, with the presence of only catalytic amounts of acid (0.5 mol % H^+).

3.3. The effect of microwaves

The use of microwaves for the dehydration revealed, as anticipated, a dramatic effect on the reaction rate in accordance with previously published results.[20] However, within the temperature ranges that we were able to test (max. 180 °C for closed pressure tube experiments), no conclusive change was found in the product distribution compared to analogous reactions carried out in a closed pressure tube using conventional oil bath heating (see Supplementary data). The product distribution is more likely dependent on other factors (such as solvent, temperature, etc.) that were investigated in this study rather than the method of heating. The primary advantage in the microwave heated system is the increase of reaction rate leading to an increased space-time-yield in potential industrial applications. In addition, very precise control of reaction temperature is maintained in the microwave apparatus whereas the conventional heated system has a rather slow response. Employing this fast temperature control, the microwave apparatus was able to quickly heat the reaction contents to 200 °C and cool the vessel down, resulting in the best yield reported in a strictly aqueous media (vide infra) primarily thought to be due to the fast and accurate temperature adjustments. In contrast, the conventional heated system is rather slow with poor control at elevated temperatures. Indeed, 180 °C was the maximum temperature achievable in this setup. Thus, in this way, both conversion rates and yields were increased significantly by employing microwaves.

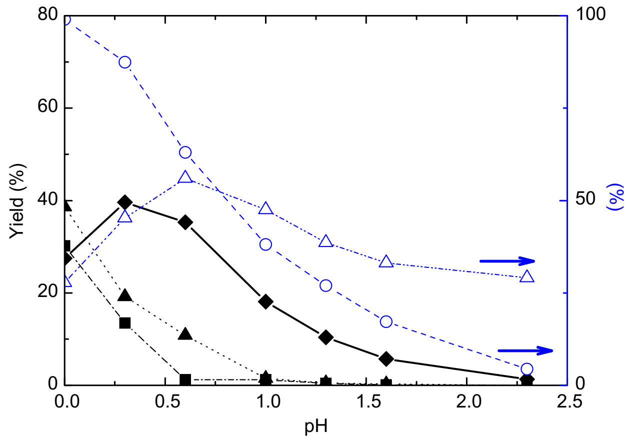


Figure 2. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of pH in microwave-assisted dehydration of fructose (5 min reaction time, 90 W, 130 °C, initial fructose concentration 27 wt %). The pH values were calculated based on the HCl concentration and does not account for the acidity of the by-products formed during the reaction.

The influence of the initially applied microwave irradiation effect on reaction performance, that is, conversion, yield and selectivity, was further studied by using varying initial microwave powers of 90 W, 150 W and 300 W. Under the tested reaction conditions, for example, reaction time of 5 min and temperature of 140 °C or 160 °C, no significant difference in either conversion or product distribution was found, thus confirming the 90 W to be sufficient to facilitate effective reaction progression (Figs. 3 and 4). Hence, conducting the reaction at higher power is more energy intensive but does not increase conversion, yield or selectivity. As shown in Figures 3 and 4, the microwave-assisted reaction was found to give 48% fructose conversion, 28% HMF yield and 59% HMF selectivity when performed at 160 °C for 5 min. with an initial fructose concentration of 27 wt % (0.01 M HCl). The corresponding reaction with conventional heating for 10 min only gave 29% fructose conversion, 12% HMF yield and 40% HMF selectivity (see Supplementary data).

3.4. Temperature dependence

As already indicated above, the microwave-assisted acid-catalysed dehydration of fructose to HMF was highly temperature

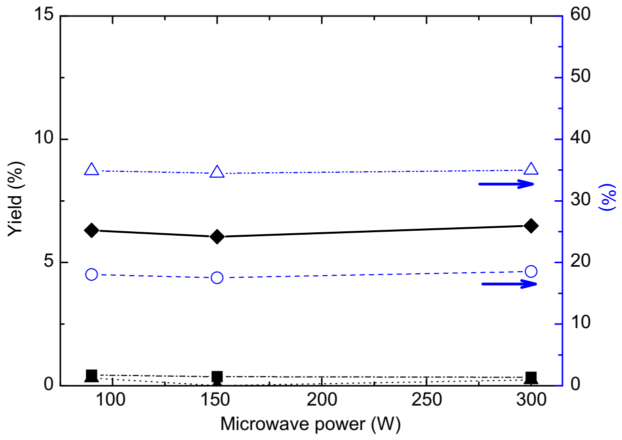


Figure 3. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of initial microwave power in dehydration of fructose (5 min reaction time, 140 °C, 0.01 M HCl, initial fructose concentration 27 wt %).

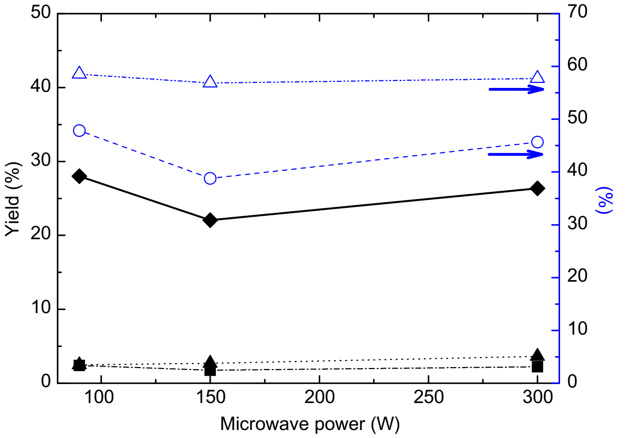


Figure 4. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of initial microwave power in dehydration of fructose (5 min reaction time, 160 °C, 0.01 M HCl, initial fructose concentration 27 wt %).

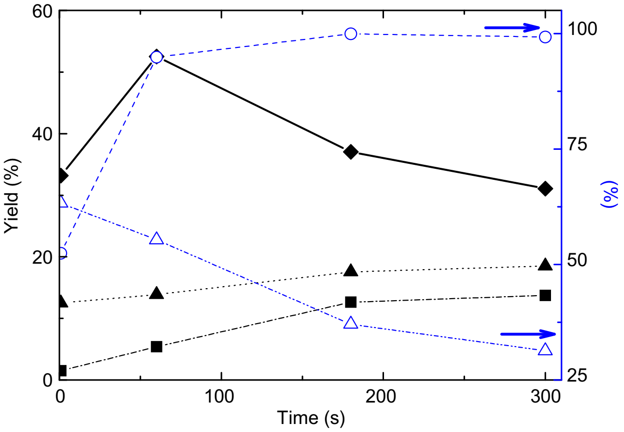


Figure 6. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of reaction time in microwave-assisted dehydration of fructose (300 W, 200 °C, 0.01 M HCl, initial fructose concentration 27 wt %).

dependent (Fig. 5). Generally, high temperatures promoted the dehydration reaction as also reported previously.[24] However, at temperatures above 160–180 °C, shorter reaction times proved necessary to diminish by-product formation by rehydration and successive polymerization which otherwise resulted in a significant decrease in HMF selectivity and yield. Hence, reactions conducted at 200 °C with microwave irradiation for 1 s resulted in 52% fructose conversion and HMF selectivity and yield of 63% and 33%, respectively. By prolonging the reaction time to 60 s the fructose conversion further increased to 95% and the HMF yield reached an optimum of 53%, whereas irradiation for 180 s provided nearly full fructose conversion (>99%) but only gave an HMF yield of 37% due to the accompanying decrease in HMF selectivity (Fig. 6).

3.5. The effect of the initial fructose concentration

By-product formation by polymerization of reaction components is one of the main challenges in the dehydration of highly concentrated aqueous fructose to yield HMF, and clearly the concentrations of this component are very important for the process. The use of low fructose concentrations reduces polymer formation, while high initial fructose concentrations are economically desirable from an industrial viewpoint due to small reactor volumes and improved product work-up.

We have investigated the dehydration reaction at 170 °C with 5 min of microwave irradiation using initial fructose concentrations from 2.25 to 45 wt % (Fig. 7).

In accordance with previously published results,[20] the highest HMF selectivity (75%) was found using the lowest fructose concentration of 2.25 wt % and the highest conversion was obtained (80%) with 45 wt % fructose. In contrast, the yields of HMF, FA and LA remained almost constant, independent of the initial fructose concentration, suggesting that the amount of by-products not detected by HPLC analysis (i.e., humins and soluble polymers) prevail at higher fructose concentrations, as anticipated.

3.6. The effect of the reaction time

When the microwave-assisted dehydration was performed at a relatively low temperature of 140 °C where by-product formation was negligible, both fructose conversion and HMF yield increased almost linearly with reaction time reaching 33% and 17%, respectively, after 20 min of reaction (Fig. 8). Similarly, the HMF selectivity concurrently increased to 52% most likely due to reversible dimerisation of fructose, which allowed monomeric fructose to be continuously reformed as HMF production progressed. Analo-

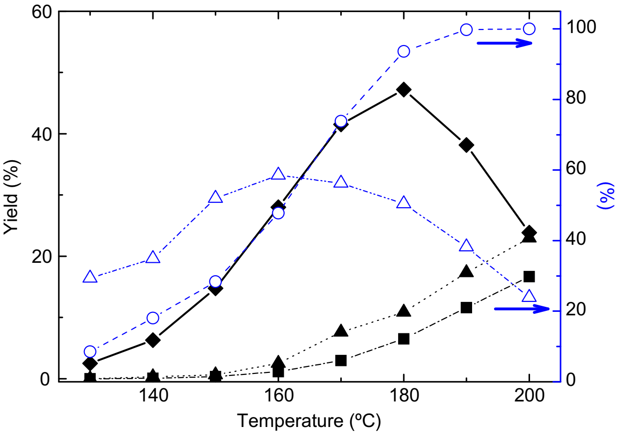


Figure 5. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of temperature in microwave-assisted dehydration of fructose (5 min. reaction time, 90 W, 0.01 M HCl, initial fructose concentration 27 wt %).

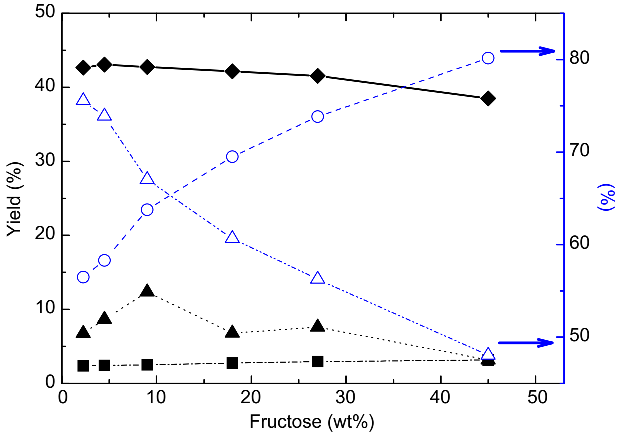


Figure 7. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of fructose concentration in microwave-assisted dehydration of fructose (5 min. reaction time, 300 W, 170 °C, 0.01 M HCl).

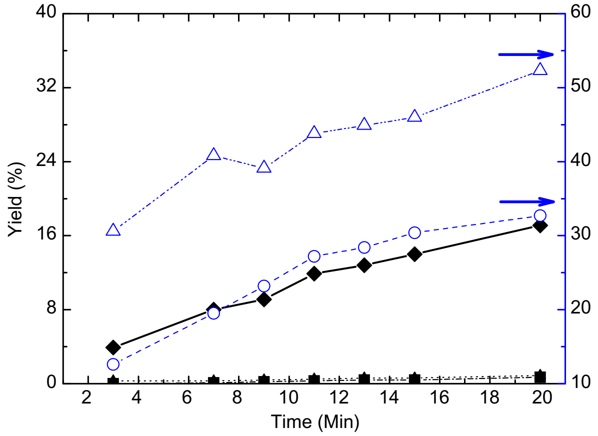


Figure 8. Yield of HMF (♦), FA (▲) and LA (■), HMF selectivity (△) and fructose conversion (○) as a function of reaction time in microwave-assisted dehydration of fructose (90 W, 140 °C, 0.01 M HCl, initial fructose concentration 27 wt %).

gous findings have also previously been described by, for example, Van Dam et al.[24] and Kuster.[25]

4. Conclusion

We have investigated the individual influence of several reaction parameters on the HCl-catalysed microwave-assisted dehydration of aqueous fructose to HMF. Combined, the results proved the dehydration process to be highly dependent on all examined parameters, except the initial power of the applied microwave irradiation (between 90 and 300 W). Importantly, however, application of microwaves significantly improved the rate of fructose conversion, and to some extent the selectivity and yield of HMF due to improved control of the temperature, compared to conventional heating.[12,16,21,24,26] The most significant single parameter in the dehydration process was found to be the initial fructose concentration which was, however, deliberately kept high in most of this study as this is attractive from an industrial perspective. Thus, only in experiments with initial fructose concentrations below 5% could HMF selectivities higher than 70% be realized. Besides fructose concentration, the temperature, pH and reaction times were also found to be important parameters for intensification of the dehydration reaction. Hence, the optimal conditions for HMF production using 27 wt % aqueous fructose solution containing 0.01 M HCl was either reaction at 200 °C with 1 s irradiation whereby a fructose conversion of 52% (HMF yield of 33%; HMF selectivity of 63%) was achieved or reaction at 200 °C for 60 s whereby a fructose conversion of 95% (HMF yield of 53%; HMF selectivity of 55%) was achieved.

The reported results are, to our knowledge, the best fructose to HMF dehydration results achieved in a purely aqueous media.[12,16,21,24,26] In particular, this has been achieved with a high initial fructose concentration and a low HCl catalyst concentration. These concentrations are somewhat different from conditions used in previously reported work, but are practically relevant when pursuing a commercially viable process with low environmental impact for HMF production. At the cutting edge of technology development it seems likely that it is only a matter of time before microwave-enhanced chemical production is routinely possible. Already the equipment for batch and continuous operation is available from several companies.[27] Clearly the use of microwaves opens new opportunities in temperature control and adjustment that are not possible by conventional heating.

Acknowledgements

We thank Professor Jan O. Jeppesen and Professor Poul Nielsen, Department of Physics and Chemistry, University of Southern Denmark for use of their microwave equipment in this study. The work was supported by The Danish National Advanced Technology Foundation and Novozymes A/S.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.09.036.

References

1. Christensen, C. H.; Rass-Hansen, J.; Marsden, C. C.; Taarning, E.; Egeblad, K. *ChemSusChem* **2008**, *1*, 283–289.
2. Ragauskas, A. J.; Williams, C. K.; Davison, B. H.; Britovsek, G.; Cairney, J.; Eckert, C. A.; Frederick, W. J., Jr.; Hallett, J. P.; Leak, D. J.; Liotta, C. L.; Mielenz, J. R.; Murphy, R.; Templer, R.; Tschaplinski, T. *Science* **2006**, *311*, 484–489.
3. Román-Leshkov, Y.; Barrett, C. J.; Liu, Z. Y.; Dumesic, J. A. *Nature* **2007**, *447*, 982–985.
4. Mascal, M.; Nikitin, E. B. *Angew. Chem., Int. Ed.* **2008**, *47*, 7924–7926.
5. Yong, G.; Zhang, Y.; Ying, J. Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 9345–9348.
6. Werpy, T.; Petersen, G. *Top Value Added Chemicals from Biomass*, Vol. 1, **2004**, 1–67; available at: http://www.osti.gov/bridge.
7. Bicker, M.; Hirth, J.; Vogle, H. *Green Chem.* **2003**, *5*, 280–284.
8. Schlaf, M. *Dalton Trans.* **2006**, 4645–4653.
9. Newth, F. H. *Adv. Carbohydr. Chem.* **1951**, *6*, 83–106.
10. Mednick, M. L. *J. Org. Chem.* **1962**, *27*, 398–403.
11. Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* **2007**, *107*, 2411–2502.
12. Román-Leshkov, Y.; Chheda, J. N.; Dumesic, J. A. *Science* **2006**, *312*, 1933–1937.
13. Rigal, L.; Gaset, A.; Gorrichon, J.-P. *Ind. Eng. Chem. Prod. Res. Dev.* **1981**, *20*, 719–721.
14. Moreau, C.; Durand, R.; Razigade, S.; Duhamet, J.; Faugeras, P.; Rivalier, P.; Ros, P.; Avignon, G. *Appl. Catal., A* **1996**, *145*, 211–224.
15. Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. *Science* **2007**, *316*, 1597–1600.
16. Cottier, L.; Descotes, G. *Trends Heterocycl. Chem.* **1991**, *2*, 233–248.
17. Horvat, J.; Klaić, B.; Metelko, B.; Šunjić, V. *Tetrahedron Lett.* **1985**, *26*, 2111–2114.
18. Chheda, J. N.; Román-Leshkov, Y.; Dumesic, J. A. *Green Chem.* **2007**, *9*, 342–350.
19. Musau, R. M.; Munavu, R. M. *Biomass* **1987**, *13*, 67–74.
20. Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L., Jr. *Green Chem.* **2008**, *10*, 799–805.
21. Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L., Jr. *Catal. Commun.* **2008**, *9*, 2244–2249.
22. Hayes, B. L. *Microwave Synthesis: Chemistry at the speed of light*; CEM Publishing, 2002.
23. *Handbook of Chemistry*, *CRC*, 89th ed.; 2008–2009.
24. Van Dam, H. E.; Kieboom, A. P. G.; Van Bekkum, H. *Starch/stärke* **1986**, *38*, 95–101.
25. Kuster, B. F. M. *Starch/Stärke* **1990**, *42*, 314–321.
26. Bicker, M.; Kaiser, D.; Ott, L.; Vogle, H. *J. Supercrit. Fluids* **2005**, *36*, 118–126.
27. http://cem.com/; http://www.biotage.com/; http://www.milestonesci.com/.