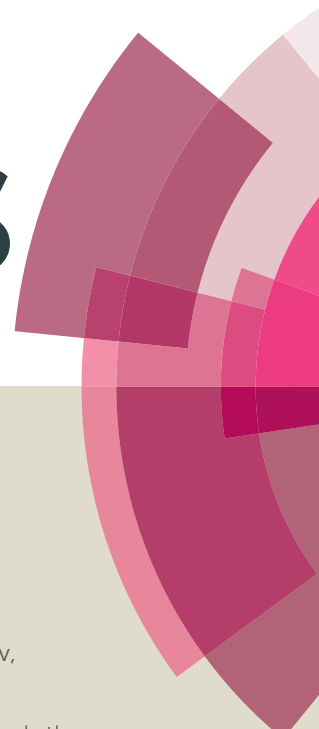


RSC Advances



This article can be cited before page numbers have been issued, to do this please use: E. Meller, A. Aviv, Z. Aizenshtat and Y. Sasson, *RSC Adv.*, 2016, DOI: 10.1039/C6RA06050A.



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This *Accepted Manuscript* will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

Preparation of halogenated furfurals as intermediates in the carbohydrates to biofuel process

Elad Meller, Avishay Aviv, Zeev Aizenshtat*, Yoel Sasson*

The Institute of Chemistry, Casali Institute for applied Chemistry, The Hebrew University of Jerusalem Edmund Safra campus in Givat Ram 91904 Israel

Emails: zeev@vms.huji.ac.il; yoel.sasson@gmail.com;

Elad.meller@mail.huji.ac.il; avishay.aviv@mail.huji.ac.il

Corresponding author: Elad Meller

The Hebrew University of Jerusalem. Institute of Chemistry, Casali Bld. room 208 B Edmund Saphra Campus. Phone 972-2-6585561 Fax 972-2-6585318

Abstract

Lignocellulose derived halogenated furfurals are important chemicals that can serve as starting materials for diverse products such as drugs, polymers and fuels, including fuel additives. In this paper a protocol for the synthesis of 5-chloromethyl furfural (CMF) and 5-bromomethyl furfural (BMF) is put forward. The proposed process is based on a two liquid phases reaction composed of an aqueous hydrochloric or hydrobromic acid phase and 1,2-dichloroethane (DCE) organic phase. We have optimized and compared the yields of CMF and BMF in an open flask and in a closed reaction vessels. Utilization of the close reaction vessel resulted in not only higher yields in a shorter reaction time but also eliminated the necessity of the customary lithium salts additives previously advocated for this process. These additives were required in the open reaction systems in order to achieve reasonable yields. While a closed reaction vessel was previously reported for the production of CMF, and in this work its production was further improved, it is the first time a close vessel protocol for the production of BMF has been reported. In addition, improvement of the substrate to organic solvent ratio has been carried while yields of halogenated furfurals were maintained almost intact. NMR and UV-vis spectroscopy were used for identification and quantification of the products.

Introduction

As a consequence of depleting petroleum resources and increasing demand for energy as well as augmented awareness to the negative environmental impact of petroleum based energy production, mankind is seeking for renewable green fuels that can replace fossil fuels.¹ Amongst the available renewable energy resources (solar, wind, geothermal etc) only biomass can supply organic carbon in liquid form that may serve as fuel for transportation.² At present there are two industrial scale processes for biofuel production: the first is the conversion of vegetable oils to fatty acid esters, known as biodiesel, *via* transesterification.^{3,4} The second is the production of bio-ethanol from glucose fermentation.^{5,6} However, these methodologies rely mainly on agricultural farmlands utilized towards fuel production instead of food production. Furthermore, calculations proved that even if all farmlands were exploited to produce oil-based fuels it would not cover even a small fraction of the annual energy consumption today.⁷ Therefore, other non-edible resources of biomass must be considered in order to supply the increasing energy demand. Lignocellulose is a very attractive source for biofuels since it is the most abundant material in plants. It is much more abundant in nature than lipid based biomass.^{8,9} In contrast to sugars and starch, using lignocellulose as a raw material for fuel production does not compete with food production since it is not edible. Lignocellulose consists of cellulose (40-50%), hemicellulose (20-40%) and lignin (20-30%).¹⁰ While the first two macromolecules comprised of chains of 6 or 5 carbon sugar molecules, lignin is composed from phenylpropane and methoxy groups.¹¹ Lignocellulosic biomass can be converted to ethanol by a two-step process; hydrolysis and a subsequent fermentation (see Fig. 1 Scheme 1). In this process the hydrolysis step is performed on cellulose and hemicelluloses, while the lignin fraction of lignocellulose is inert and must be separated from the mixture.¹² The first step of the process is the hydrolysis of the poly-sugars using dilute acid or enzymatic system, and the second step involves of the mono-sugars fermentation to ethanol using yeasts or bacteria.^{13,14}

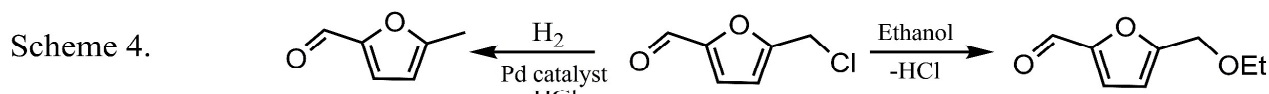
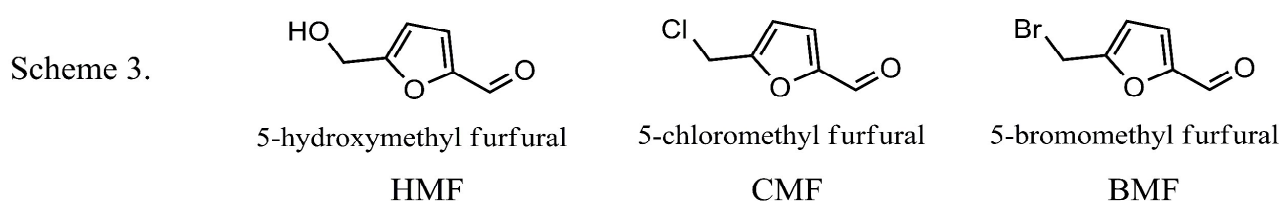
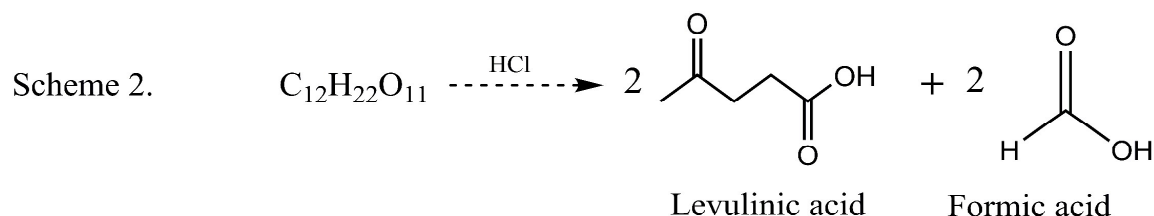
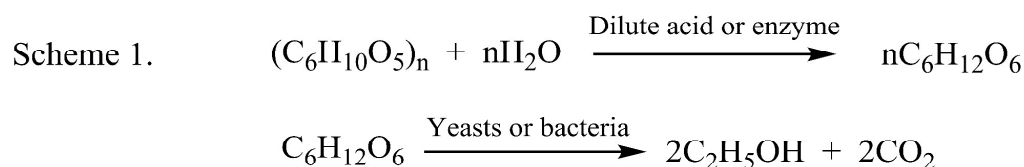


Fig. 1 Summary of several reactions and products from carbohydrates based biomass: Scheme 1- Two step bio-ethanol production from cellulose; first step includes the catalytic hydrolysis of cellulose to glucose sugar monomers with dilute acid or enzyme as catalyst following a step involves fermentation to ethanol and carbon dioxide using yeasts or bacteria. Scheme 2- Conversion of sucrose to levulinic acid and the by product formic acid using diluted hydrochloric acid (This is a multistep reaction). Scheme 3- The chemical structure of 5-hydroxymethyl furfural, 5-chloromethyl furfural and 5-bromomethyl furfural. Scheme 4- Possible fuels synthesized from CMF *via* etherification with ethanol or *via* catalytic hydrogenation.

The conversion of cellulose to ethanol is not only expensive and time consuming (in addition to several additional limitations), but it also exhibits a poor atom economy.^{6,15} From the original carbon atoms in the reactant only 2/3 are retained in the product and the other 1/3 are removed in the form of CO₂. In addition, this process requires large vessels and removal of large quantities of water that consumes energy.

In an alternative approach cellulose (or hemicellulose) is converted in a multistep reaction to levulinic acid and formic acid (see Fig. 1 Scheme 2).^{16,17} In this process 5/6 of the reactant's carbons are retained in the product, and the other 1/6 carbons are discharged in the form of formic acid. It has been reported by Cha and Hanna that the activity of mineral acids in the hydrolysis of carbohydrates to levulinic acid decrease in the following order- HBr>HCl>H₂SO₄.¹⁸ Levulinic acid can be transformed into biofuels in several routes. One route is the esterification with an alcohol thus producing levulinate ester.^{19,20} Alternatively, levulinic acid can undergo hydrogenation/deoxygenation to form γ -valerolactone that can proceed in a following step to various valuable products and fuels such as hydrocarbons, valeric esters and 2-methyltetrahydrofuran by hydrogenation or esterification.^{21,22,23} It was found that the transformation of carbohydrates to levulinic acid takes place *via* the intermediate 5-hydroxymethyl furfural (HMF, Fig. 1 Scheme 3).^{24,25} In the case of HMF all the carbon atoms originated from the reactant are retained, and the carbon atom economy is 100%. In this spirit, researchers examined methods for HMF production and utilization as a platform for biofuel synthesis such as 5-alkoxymethylfurfural and 2,5-dimethylfuran.²⁶ Ionic liquid systems were also demonstrated for this aim.^{8,27,28} However, the most promising results were reported by Mascal and Nikitin, who demonstrated the conversion of cellulose into 5-chloromethyl furfural (CMF, Fig.1 Scheme 3) in a biphasic system of aqueous hydrochloric acid phase containing LiCl and an organic 1,2-dichloroethane (DCE) phase.²⁹ An important facet in this approach is the continuous extraction of the aqueous phase with organic solvent. In this manner CMF is removed from the aqueous phase and therefore it does not continue to react and form levulinic acid and/or other products. However, the major drawbacks of this protocol are the prolong reaction time (30h) and the utilization of lithium chloride, which is expensive and call for further treatment steps.

Mascal and Nikitin improved the above protocol by reducing the reaction time and solvent amount along with eliminating of LiCl salt. These advancements were achieved by working in a closed reaction apparatus.³⁰ Kumari et al., demonstrated in another interesting study the formation of 5-bromomethyl furfural (BMF, Fig. 1 Scheme 3) from cellulose and other carbohydrates using a biphasic system of aqueous layer containing hydrobromic acid and LiBr and an organic layer of toluene.³¹ There are two potential pathways to obtain a biofuel from BMF or CMF: reacting these intermediates with alcohol to form an ester, or hydrogenating them to form methyl furfural (see Fig. 1 Scheme 4).^{30,31}

In the present study the formation of CMF and BMF was modified to be more applicable industrially than previously reported. CMF and BMF preparation in an open reaction apparatus was compared to a closed reaction apparatus. An optimization of reaction parameters in a closed reaction system has been carried for both CMF and BMF and the formation of BMF without assistance of LiBr is reported for the first time. In addition several improvements in the synthesis of halogenated furfurals were demonstrated. It should be noted here that in the results section we address only to CMF and BMF yields. However, many side reactions can occur during CMF and BMF synthesis and byproducts such as HMF, levulinic acid and humic substances can be found in the aqueous phase as reported by Mascal and Nikitin.^{29,30} Nonetheless, these compounds are found in low amounts and we will not refer to them in this work since we intended to focus on the improvements in CMF and BMF preparation.

Materials and methods

Materials

Cellulose microcrystalline powder, 1,2-dichloroethane (DCE) 99%, hydrobromic acid 48% and hydrobromic acid 62% were purchased from Sigma Aldrich. Hydrochloric acid 37% was purchased from Holland Moran LTD. Table sugar was used as a source for sucrose. In order to obtain HCl or HBr solutions in different concentrations, the appropriate acid was diluted with deionized water. For column chromatography silica gel 60 (0.04-0.063mm) purchased from Merck-LTD and sand (50-70 mesh particle size) purchased from Sigma Aldrich were used as stationary phase while dichloromethane AR

purchased from Bio-Lab LTD was used as the eluent. DMSO-d⁶ purchased from Cambridge Isotope Laboratories Inc was used for NMR spectroscopy.

CMF and BMF synthesis

For reaction in an open apparatus, 1g of the carbohydrate was placed in a round bottom flask. 15ml of an aqueous HCl or HBr solution containing 0.5-4g of LiCl or LiBr, respectively, was added. Then 35ml of organic solvent, DCE, was added. The aqueous phase acidity was adjusted by diluting the appropriate acid to the desired concentration. The round bottom flask was placed in an oil bath preheated to the desired temperature, 50-90°C, and the biphasic system was vigorously stirred. After 30min the reaction was stopped, the organic phase was separated, and another 35ml of DCE was added before the reaction vessel has been returned to the oil bath and the reaction proceeded for another 30min. This process was repeated for a total time of 4h. At the end of reaction the total organics were dried over anhydrous magnesium sulfate, and the product was further analyzed.

The procedure for a reaction in a close apparatus is quite similar. In this case 0.3-0.6g of the carbohydrate was measured and placed in a pressure tube, which was used as the reaction vessel. Then 7ml of an aqueous acid solution, adjusted to the desired acid concentration, and 10-20ml of organic solvent, DCE, were added. The pressure tube was sealed and located in an oil bath preheated to the desired temperature, 80-115°C. After 1-2h the vessel was removed from the heated oil bath and the organic phase was separated from the aqueous phase. Then, the aqueous phase was extracted with DCE for 1-3 more times, depends on the specific experiment (the acid kind, the solvent amount). The total reaction time was between 3-4h. At the end of reaction the combined organic layer was dried over anhydrous magnesium sulfate, and the product was further analyzed.

Product identification and quantification

The identification of CMF and BMF products at the end of reaction has been carried with NMR spectroscopy. Once CMF and BMF have been identified calibration curves of the UV-vis spectra for molar absorption coefficient of these materials were established and used for yields calculations by means of CMF and BMF concentrations determination.

For identification with NMR, CMF and BMF have been isolated and purified. The isolation process was carried, after the evaporation of the organic solvent, by standing

column chromatography composed of silica gel 60 (0.040-0.063mm) and sand (50-70 mesh particle size). Dichloromethane was used as the mobile phase. Then dichloromethane was evaporated and the isolated product was examined by NMR spectroscopy, Bruker DRX-400 instrument (see supporting information).

The product yield was calculated by measuring CMF and BMF concentrations using UV-vis spectroscopy. UV-vis spectra were recorded with Varian Cary 100 Bio spectrophotometer, at a wavelength range of 800-200nm. The molar absorption coefficients of CMF and BMF were calculated using calibration curves (see supporting information).

Results and discussion

CMF and BMF formation in an open reaction vessel

Sucrose, glucose and cellulose were tested as starting materials for CMF preparation. Table 1 summarizes the yields obtained with an open reaction system at 70°C, with 0.5g LiCl, for CMF preparation from the above substrates.

Table 1. CMF yields obtained under different condition from various carbohydrates.

Substrate	HCl concentration	Reaction time	Yield
Sucrose, 1g	10M	4h	35%
Glucose, 1g	10M	4h	7.4%
Cellulose, 1g	12M	4h	5.5%
Cellulose, 1g	12M	8h	9.4%

* Experiments for Table 1 have been carried out at 70°C with 0.5g LiCl, 15ml HCl solution and 35ml DCE that was replaced every 30min.

The results in Table 1 clearly show that sucrose reacts with HCl to produce CMF faster than glucose and cellulose. Solutions of 10M HCl were used for reactions with sucrose and glucose. However, when a solution of 10M HCl was applied for the conversion of cellulose to CMF, the reaction yield was so low that the maximal acid concentration, 12M, had to be used. We can see from Table 1 that CMF yield from cellulose after a

reaction time of 4h was 5.5%, and that extending the reaction time to 8h improved the yield to 9.4%.

The critical parameters for CMF production from sucrose in an open reaction system were determined. Fig. 2 demonstrates the effect of temperature and HCl concentration on CMF yield from sucrose.

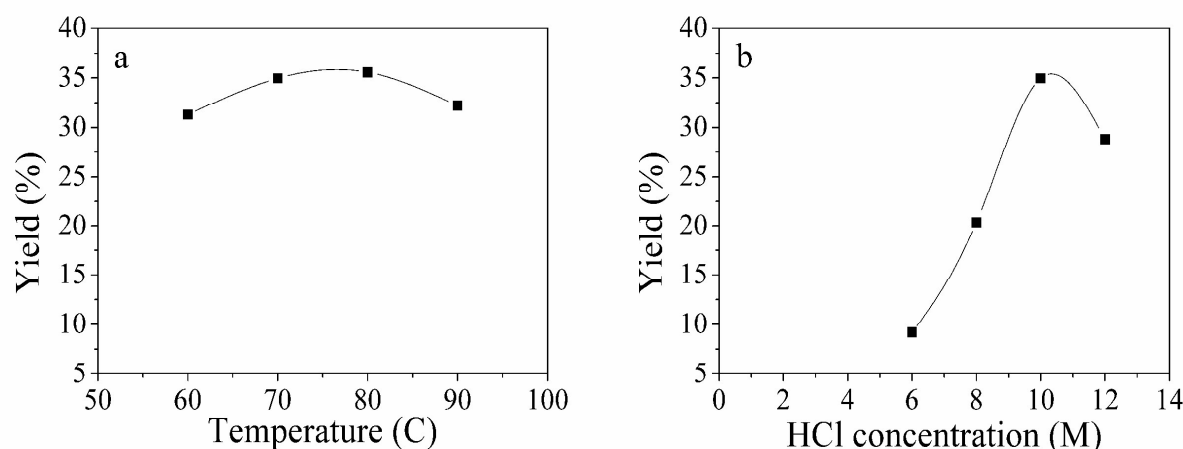


Fig. 2 CMF yield from sucrose as a function of: (a) temperature, 60-90°C, with constant HCl concentration of 10M and (b) HCl concentration, 6-12M, with constant temperature of 80°C. All reactions were carried out with 1g of sucrose, 0.5g LiCl, 15ml HCl solution, 35ml DCE that was replaced every 30min and reaction time of 4h.

The results presented in Fig. 2 are for reactions in an open reaction system. In each run 0.5g of LiCl was added and the organic solvent was replaced after every 30min. The results reveal that the biphasic reaction is much more sensitive to HCl concentration than to temperature. In Fig. 2 (a) the effect of temperature at constant acid concentration of 10M was determined, and in Fig. 2 (b) the effect of HCl concentration with constant temperature of 80°C was determined. At HCl concentration of 6M CMF yield of 9.2% is obtained, while at 10M CMF yield is about 35%. Higher acid concentrations give lower CMF yields, probably as a consequence of increased polymerization to humic materials, as reported in literature.^{29,30} When different temperatures were applied, under constant HCl concentration of 10M, the yields did not vary to a greater extent. The highest CMF yield, 35.6%, was achieved when temperature of 80°C was employed. Lower and higher temperatures lead to a small decrease in yields, utilizing reaction temperatures of 60°C and 90°C resulted in yields of 31.3% and 32.2%, respectively.

The same substrates, sucrose, glucose and cellulose, were examined also in BMF synthesis with HBr (48%, 8.89M) reagent. Table 2 summarizes the results of experiments with HBr 8.89M, at temperature of 70°C and with 0.5g LiBr, for the preparation of BMF.

Table 2. BMF yields obtained at different conditions from various carbohydrates.

Substrate	Reaction time	Yield
Sucrose, 1g	4h	37.8%
Glucose, 1g	4h	41.9%
Cellulose, 1g	4h	15.2%
Cellulose, 1g	10h	37.7%

* Experiments for Table 2 have been carried out at 70°C with 0.5g LiBr, 15ml 8.89M HBr solution and 35ml DCE that was replaced every 30min.

Table 2 shows that under the above conditions the yield of BMF from sucrose is 37.8%, almost the same as for CMF. However, as the results imply, glucose and cellulose are more receptive to halogenated furfural formation with HBr than with HCl. Under similar conditions, BMF yield from cellulose is 15.2%, while CMF yield is about 3 times lower, 5.5%. For BMF formation from cellulose, extending the reaction time from 4h to 10h resulted in a higher BMF yield of 37.7%. The difference in acid reactivity is very pronounced with glucose as a substrate. At the same reaction time and temperature, BMF yield from glucose is 41.9% while CMF yield is only 7.4%, even though the number of LiCl moles used in reaction is twice the number of LiBr moles. The most important factors in BMF preparation from cellulose are the temperature and the amount of LiBr salt (see Fig. 3).

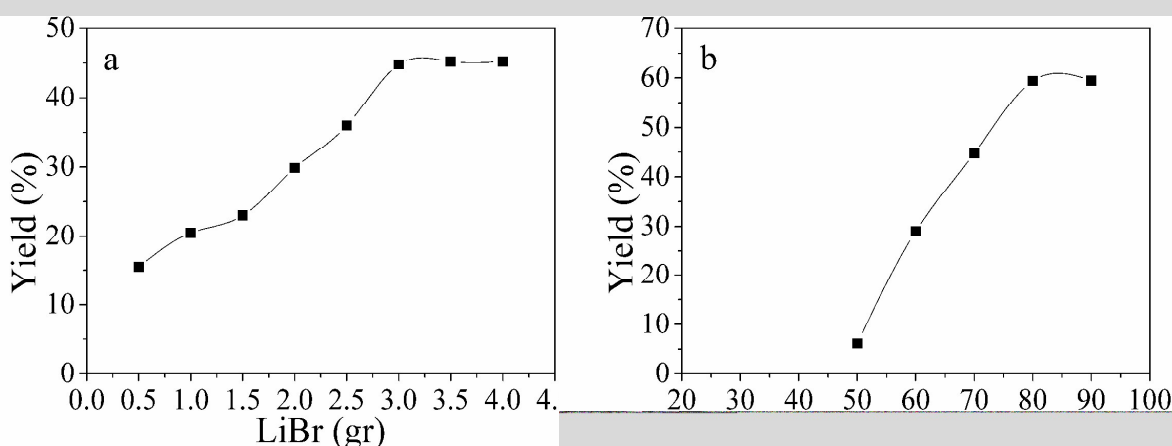


Fig. 3 BMF yields from cellulose as a function of: (a) LiBr salt amount, 0.5-4g, with constant temperature of 70°C and (b) temperature, 50-90°C, with constant LiBr amount of 3.5g. All reactions were carried out with 1g of cellulose, 15ml 8.89M HBr solution, 35ml DCE that was replaced every 30min and reaction time of 4h.

The experiments presented in Fig. 3 (a) were carried out at constant temperature of 70°C and for Fig. 3 (b) with constant amount of LiBr, 3.5g. For both, the acid concentration was 8.89M. From Fig. 3 (a) we can see that increasing the amount of LiBr has an immense impact on BMF yields from cellulose. BMF yield of 15.2% was obtained with 0.5g LiBr (0.0057 mole), while with 3.5g LiBr (0.04 mole) the yield has been ascended to 45.3%. From Fig. 3 (b) we may conclude that the temperature has much stronger impact on BMF formation than on CMF formation. Increasing the temperature from 50°C to 90° increased the yield of BMF from 6% to 59.5% (reached already at 80°C).

These results show that HBr is more reactive than HCl in the conversion of cellulose and glucose to halogenated furfural in an open reaction system. There are number of reasonable explanations for the difference between HCl and HBr reactivity: first, the acidity of HBr is higher than HCl acidity ($K_a = 1 \times 10^9$ for HBr compared to $K_a = 1 \times 10^6$ for HCl) and as a consequence it is more reactive in this reaction. A second possible explanation relates to the volatility of the above acids. HCl is more volatile than HBr (with boiling points of about 50°C and of 122°C, respectively) and it may evaporate out of the system before it reacts. The third explanation might relate to the mechanism of the reaction. It is possible that under the above conditions CMF formation has a different mechanistic path in comparison with BMF formation. It seems reasonable to conclude from the above results that the isomerization step is the slow step when HCl/LiCl system

is used. On the other hand, it does not seem to be the case when HBr/LiBr system is applied. This conclusion originates not only by the higher yields of BMF as compared to CMF yields from cellulose and glucose, but also by the fact that BMF yields from these substrates are also higher than the yields obtained from sucrose.

CMF and BMF formation in a close reaction vessel

LiCl and LiBr play an important role in the conversion of carbohydrates to furfurals, and discarding these lithium salts has a great economical and environmental advantages. In order to eliminate LiCl and LiBr salts experiments were carried in a close reaction system. This modification resulted in an enhancement of halogenated furfural yields from the various carbohydrates. CMF and BMF formation were tested in a glass pressure tube (a close reaction vessel). BMF and CMF preparation in the pressure tube from cellulose were optimized as a function of temperature and acid concentration. Results are shown in Fig. 4 and Fig. 5. CMF and BMF yields obtained in a close reaction system in the absence of Li salts were higher than the yields of the corresponding experiments performed in the presence of a Li salt in an open reaction vessel. For CMF preparation in a close reaction system, temperatures of 90-110°C and HCl concentrations of 9-12M were examined. These experiments were carried out with 0.3g of cellulose, 7ml of acid solution and 20ml of DCE. After 2h the reaction was stopped and the organic solvent was removed, the aqueous phase was extracted with 20ml of organic solvent and then another 20ml of DCE was added and the reaction vessel placed again in the heated oil bath for another 2h. The results are presented in Fig. 4.

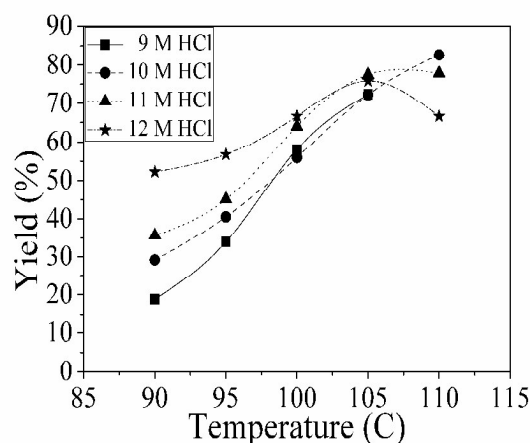


Fig. 4 The effect of temperature (90–110°C) and HCl concentration (9–12M) on CMF yields in a close reaction system. All reactions were carried out with 0.3g cellulose, reaction time of 4h, 7ml HCl solution and 20ml DCE that was removed after 2h and replaced with fresh portion of 20ml DCE. Before the addition of a new DCE portion the aqueous phase was extracted once with 20ml DCE.

It should be emphasized again that the experiments presented in Fig. 4 were carried out in the absence of LiCl. The highest CMF yield, 82.6%, was obtained with HCl concentration of 10M and at temperature of 110°C. At the same reaction time and without using LiCl we were able to achieve a significantly higher CMF yield from cellulose in a close reaction system than in an open reaction system at 70°C with LiCl. This phenomenon can be attributed to the higher acidity evolved at elevated temperatures, an acidity which could not be achieved in an open reaction system at lower temperatures. Increasing the temperature in the open reaction system was not effective as a consequence of HCl volatility at high temperatures.

Similar approach was adapted for BMF formation with HBr as the acidic reagent, without using LiBr. BMF production in a close reaction system was never reported. The total amount of organic solvent used in BMF preparation was higher than for CMF preparation since the aqueous phase was extracted twice (in contrast to one extraction for CMF preparation) with 20ml DCE when the reaction was stopped after 2h and the organic solvent was removed. The variations in HBr concentration here were subtler than for HCl, namely 8.5–9M, because BMF yield was more sensitive to variations in HBr concentration in a close reaction system. Temperatures between 80–105° were examined. The results for BMF preparation in a close reaction vessel are presented in Fig. 5.

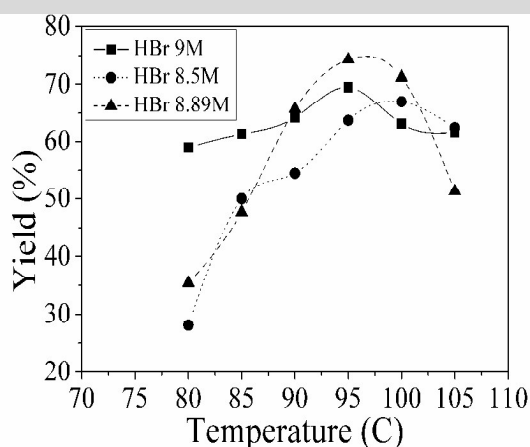


Fig. 5 The effect of temperature (80-105°C) and HBr concentration (8.5-9M) on BMF yields in a close reaction system. All reactions were carried out with 0.3g cellulose, reaction time of 4h, 7ml HBr solution and 20ml DCE that was removed after 2h and replaced with fresh portion of 20ml DCE. Before the addition of a new DCE portion the aqueous phase was extracted twice with 20ml DCE.

The results shown in Fig. 5 demonstrate that the optimal temperature and HBr concentration are 95°C and 8.89M (HBr 48%), respectively. Here, BMF yield at the optimal point was 74.3%. We may conclude that BMF yields were improved significantly when the reaction was carried out in a close reaction vessel. With the open reaction system the highest yield was 59.5%, while with a close reaction system the highest yield was 74.3%.

Substrate to solvent ratio

Closed reaction system was proven to be the most effective for high yield production of halogenated furfurals, BMF and CMF. These systems also enable the elimination of LiCl and LiBr, which were needed in the customary systems described in literature. However, improving the ratio of the organic solvent volume to the substrate loading, i.e. using minimum solvent amount and maximal substrate loading, is also highly desirable. In the systems described in section 3.2 the overall amounts of organic solvent used were 80ml DCE for CMF and 120ml DCE for BMF, or 266.7ml/1g cellulose for CMF and 400ml/1g cellulose for BMF. Improving the organic solvent volume/substrate-loading ratio is a key parameter in order to make the process industrially applicable. Experiments comparing different solvent volume/substrate-loading ratio have demonstrated the effect of this ratio on CMF and BMF yields. These experiments were performed with 0.3g of cellulose at the optimal temperature and acid concentration (10M HCl and 110°C for CMF and 8.89M HBr and 95°C for BMF). The results are summarized in Fig. 6.

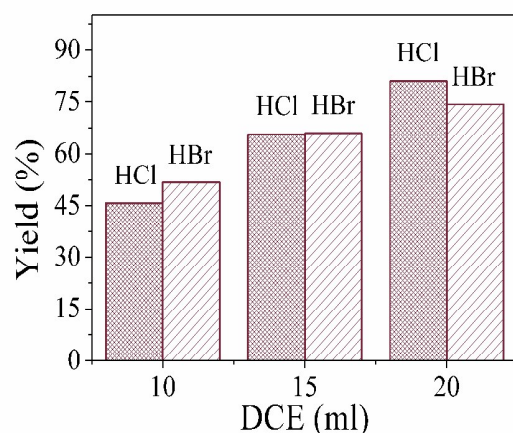


Fig. 6 The effect of the organic solvent, 1,2-dichloroethane (DCE), volume on CMF and BMF yield from cellulose. The volume described here is the initial volume of 1,2-dichloroethane, and also the volume used in each extraction.

The results in Fig. 6 show that the optimal volume of DCE is 20ml. At this volume of DCE the CMF yield is 82.6% and BMF yield is 74.3%. As the volume of the organic solvent decreased, the yield of the product was lower, probably as a result of a lower portion of product being able to dissolve in the organic solvent. In order to find improvements in organic solvent volume/substrate-loading ratio optimization of reaction parameters with lower ratio of organic solvent volume to substrate loading was necessary. To test lower proportion of organic solvent volume to the substrate loading, cellulose amount was doubled from 0.3g to 0.6g, and DCE volume in reaction and in each extraction was reduced to 15ml. Fig. 7 summarizes the results of these experiments for both CMF and BMF preparation.

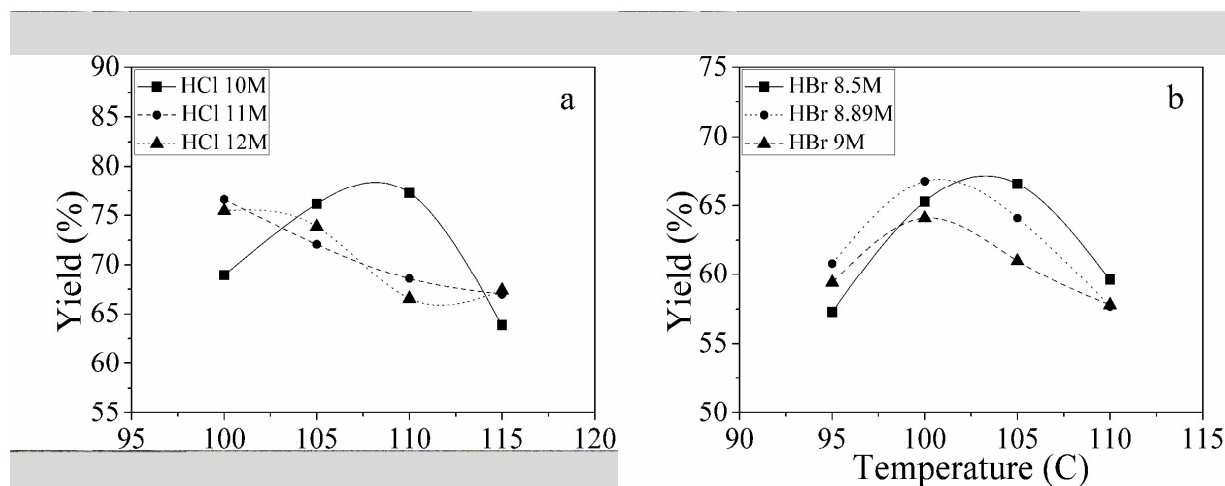


Fig. 7 The effect of temperature and acid concentration on: (a) CMF yield with HCl as an acid in a close reaction system, and (b) BMF yield with HBr as an acid in a close reaction system. All reactions were carried out with 0.6g cellulose, reaction time of 3h, 7ml HCl or HBr solution and 15ml DCE that was removed after every 1h and replaced with fresh portion of 15ml DCE. Before the addition of a new DCE portion the aqueous phase was extracted once or twice with 15ml DCE for CMF and BMF, respectively.

In experiments carried out and presented in Fig. 7 the extraction time was reduced from 2h to 1h, and the reaction time was reduced from 4h to 3h. After every hour the organic solvent was removed and extraction of the aqueous phase with another portion of DCE was performed once for CMF and twice for BMF. We can see from Fig. 7 (a) that an optimal CMF yield of 77.3% was recorded when 10M HCl solution and temperature of 110°C were applied, and from Fig. 7 (b) that an optimal BMF yield of 66.8% was recorded when 8.89M HBr solution and temperature of 100°C were applied. The decrease in yields recorded for increased cellulose loading and reduced organic solvent volume were 7.5% for BMF and 5.3% for CMF. In addition, although the reaction time was reduced the number of extractions increased since the reaction was stopped and extracted after every 1h in this case, instead of after every 2h. However, using volume of 15ml DCE instead of 20ml in reaction and in each extraction brings to a net improvement in the organic solvent volume/substrate-loading ratio. Now for 1g of cellulose we use a total of only 150ml DCE for CMF preparation and 225ml DCE for BMF preparation. These proportions are also much better in comparison with those reported in literature, namely 1120ml DCE/1g cellulose for CMF and 585ml toluene/1g cellulose for BMF.^{30,31}

Conclusions

CMF and BMF preparation from various biomass-derived carbohydrates was studied and optimized in a biphasic system of an aqueous HCl or HBr layer and an organic DCE layer. An open reaction system showed that LiCl and LiBr are needed for the reaction in order to receive reasonable yields of CMF and BMF, respectively. In addition, results indicate that in an open reaction system HBr/LiBr system is more reactive than HCl/LiCl system for the conversion of glucose and cellulose to halogenated furfural. CMF

formation and BMF formation in a close reaction apparatus were demonstrated. Experiments proved that operating in a close reaction system at higher temperatures have three important advantages over open reaction system: first, higher yields of 82.6% CMF and 74.3% BMF were achieved at lower reaction time compared to the optimized yields attained with an open reaction system. Second, LiCl and LiBr were no longer needed for the reaction to proceed. This fact has a great impact on the possible application of the process, since using lithium halides would make the process more expensive and less environmentally friendly. Third, the total volume of the organic solvent, DCE, was reduced- instead of using 1120ml and 585ml of organic solvent per 1g cellulose for CMF and BMF, respectively, as reported in literature, we needed only 266.7ml and 400ml of DCE per 1g cellulose for CMF formation and BMF formation, respectively. Nonetheless, in order to make the process more efficient the organic solvent volume/substrate-loading ratio was further improved. By performing more extractions at shorter periods of time between extractions (extractions performed after every 1h with total reaction time of 3h instead of after 2h and a total reaction time of 4h), while the amount of cellulose substrate was increased from 0.3g to 0.6g and of the organic solvent volume decreased from 20ml to 15ml. Then yields of 77.3% of CMF and 66.8% of BMF were recorded. Now the efficacy of the system was improved since only 150ml and 225ml DCE per 1g cellulose were used for CMF and BMF preparation, respectively.

Acknowledgments

We thank the Israel Strategic Alternative Energy Fund (I-SAEF) for financial support of this research. Special thanks for supporting in part the Ph.D. scholarship of E.M.

References

1. I. Dincer, *Renewable Sustainable Energy Rev.* 2000, 4, 157-175.
2. G. W. Huber, A. Corma, *Angew. Chem., Int. Ed.* 2007, 45, 7184-7201.
3. F. Ma, M. A. Hanna, *Bioresour. Technol.* 1999, 70, 1-15.
4. K. Narasimharao, A. Lee, K. Wilson, *J. Biobased Mater. Bioenergy.* 2007, 1, 19-30.
5. M. O. S. Dias, A. V. Ensinas, S. A. Nebra, R. M. Filho, C. E. V. Rossell, M. R. W. Maciel, *Chem. Eng. Res. Des.* 2009, 87, 1206-1216.
6. M. Balat, H. Balat, C. Oz, *Prog. Energy Combust. Sci.* 2008, 34, 551-573.
7. S. Lestari, I. Simakova, A. Tokarev, P. Maki-Arvela, K. Eranen, D. Y. Murzin, *Catal. Lett.* 2008, 122, 247-251.

8. O. O. James, S. Maity, L. A. Usman, K. O. Ajanaku, O. O. Ajani, T. O. Siyanbola, S. Sahu, R. Chaubey, *Energy Environ. Sci.* 2010, 3, 1833-1850.
9. J. A. Geboers, S. Van de Vyver, R. Ooms, B. Op de Beeck, P. A. Jacobs, B. F. Sels, *Catal. Sci. Technol.* 2011, 1, 714-726.
10. H. Kobayashi, H. Ohta, A. Fukuoka, *Catal. Sci. Technol.* 2012, 2, 869-883.
11. C. N. Hamelinck, G. Van Hooijdonk, A. P. C. Faaij, *Biomass Bioenergy*. 2005, 28, 384-410.
12. P. Alvira, E. Tomas-Pejo, M. Ballesteros, M. J. Negro, *Bioresour. Technol.* 2010, 101, 4851-4861.
13. Y. Sun, J. Cheng, *Bioresour. Technol.* 2002, 83, 1-11.
14. M. Galbe, G. Zacchi, *App. Microbiol. Biotechnol.* 2002, 59, 618-628.
15. F. W. Bai, W. A. Anderson, M. Moo-Young, *Biotechnol. Adv.* 2008, 26, 89-105.
16. D. W. Rackemann, W. O. S. Doherty, *Biofuels, Bioprod. Biorefin.* 2011, 5, 198-214.
17. K. Yan, C. Jarvis, J. Gu, Y. Yan, *Renewable Sustainable Energy Rev.* 2015, 51, 986-997.
18. J. Y. Cha, M. A. Hanna, *Ind. Crops Prod.* 2002, 16, 109-118.
19. K. Y. Nandiwale, S. K. Sonar, P. S. Niphadkar, P. N. Joshi, S. S. Deshpande, V. S. Patil, V. V. Bokade, *Appl. Catal., A*. 2013, 460-461, 90-98.
20. D. R. Fernandes, A. S. Rocha, E. F. Mai, C. J. A. Mota, V. T. da Silva, *Appl. Catal., A*. 2012, 425-426, 199-204.
21. J. C. Serrano-Ruiz, D. J. Braden, R. M. West, J. A. Dumesic, *Appl. Catal., B*. 2010, 100, 184-189.
22. J. M. Tukacs, D. Kiraly, A. Stradi, G. Novodarszki, Z. Eke, G. Dibo, T. Kegl, L. T. Mika, *Green Chem.* 2012, 14, 2057-2065.
23. K. Yan, Y. Yang, J. Chai, Y. Lu, *Applied Catalysis, B: Environmental* 2015, 179, 292-304.
24. J. Horvat, B. Klaic, B. Metelko, V. Sunjic, *Tetrahedron Lett.* 1985, 26, 2111-2114.
25. M. Mascal, E. B. Nikitin, *ChemSusChem*. 2010, 3, 1349-1351.
26. R. J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, J. G. de Vries, *Chem. Rev.* 2013, 113, 1499-1597.
27. X. Qi, M. Watanabe, T. M. Aida, Smith Jr R. L. Smith Jr, *Cellulose*. 2011, 18, 1327-1333.
28. Y. J. Pagan-Torres, T. Wang, J. M. R. Gallo, B. H. Shanks, J. A. Dumesic, *ACS Catal.* 2012, 2, 930-934.
29. M. Mascal, E. B. Nilitin, *Angew. Chem.* 2008, 120, 8042-8044.
30. M. Mascal, E. B. Nikitin, *ChemSusChem*. 2009, 2, 859-861.
31. N. Kumari, J. K. Olesen, C. M. Pedersen, M. Bols, *Eur. J. Org. Chem.* 2011, 1266-1270.

Graphical abstract

Efficient processes for the production of CMF and BMF are demonstrated in a biphasic system of aqueous acid and 1,2-dichloroethane.

