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# Chemical Conversion of Sugars to Lactic Acid by Alkaline Hydrothermal Processes

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The restricted availability of fossil resources urges humankind to identify possibilities for the use of renewable and environmentally friendly resources as an alternative. In this regard, biomass has long been considered an appealing feedstock for the sustainable production of fuels and chemicals. The world biomass production capabilities are extremely large. In a recent study, it was demonstrated that the European economic area alone is expected to generate 295 million tons of oil equivalents in 2030 (approximately 15 % of the overall energy demand) from environmentally-compatible primary biomass.[1] In principle, part of it can be used as the source of several commodity building blocks for the chemical and pharmaceutical industries. Recently, intense academic and industrial research has been focused on the development of technologies for the conversion and valorization of raw biomass.[2] Hydrothermal reactions have proved to be an efficient strategy to upgrade cellulosic biomass into useful materials for different types of applications.[3] However, the use of this technique for the selective generation of fine chemicals is more troublesome and is plagued in some cases by the generation of mixtures of products containing monosaccharides,[4] 5-hydroxymethylfurfural,[5] organic acids, and biocarbons.[6] Among many others, lactic acid (LA) has been identified as a possible product of the hydrothermal treatment of cellulosic biomass. This compound represents an important platform chemical for the generation of biodegradable plastics[7] and other commodity chemicals, including ethyl lactate (a green organic solvent)[8] or 1,2-propanediol.[2b] With the scope of improving the efficiency of the hydrothermal LA synthesis from biomass, several model studies on the conversion of mono- and disaccharides have recently been reported, with Lewis-acidic catalysts showing promising results.[9] Interestingly, the use of alkaline reaction conditions for the conversion of glucose to LA has been known for a long time.[10] Recently, Yan et al. reported the use of sodium and calcium hydroxide for the hydrothermal treatment of glucose or biomass with LA yields of 20–27 % for 60 s reactions at 300 °C.[11] In an improvement of the method, yields of 42 % were reported by using Zn or Ni as a co-catalyst.[12] More recently, Sánchez et al. reported similar results by using calcium hydroxide for longer reaction times.[13] Reports in the literature have focused on the use of sodium or calcium hydroxide; therefore, we decided to investigate the use of alternative bases for the alkaline hydrolysis of biomass, starting with glucose as a model substrate. Herein, we report the use of barium hydroxide as the base, which under hydrothermal conditions affords LA in yields up to 57 %.

Initially, we focused on investigating the hydrothermal treatment of glucose by using and comparing different bases. In 1996, Yang et al. demonstrated that the presence of divalent cations enhances the selective formation of LA during alkaline hydrolysis.[14] Considering this, we screened hydroxides of monovalent and divalent cations as well as nucleophilic bases such as ammonium hydroxide. We performed the reactions in dilute solutions (0.025 M with respect to glucose) to reduce the formation of cross-aldol condensation products. The solutions were heated to 220 °C in sealed autoclaves for 12 h and then analyzed by using HPLC. The results are summarized in Table 1.

**Table 1.** Effect of different bases on the conversion of glucose into LA.[a]

| Entry | Base | Conc. [M] | Yield | | |
|---|---|---|---|---|---|
| | | | LA [%][b,c] | FA [%][b,d] | AA [%][b,e] |
| 1 | NaOH | 0.05 | 17 | n.d. | n.d. |
| 2 | NaOH | 0.1 | 15 | 5 | 16 |
| 3 | $NH_4OH$ | 0.1 | traces | 2.9 | 5.3 |
| 4 | $NaOH/BaCl_2$ | 0.1 | 40 | 5 | 9.4 |
| 5 | $Ca(OH)_2$ | 0.05 | 49 | 4.7 | 6.5 |
| 6 | $Sr(OH)_2$ | 0.05 | 40 | 5.9 | 7.6 |
| 7 | $Ba(OH)_2$ | 0.05 | 53 | 4.4 | 5 |

[a] Reaction conditions: glucose (0.025 M), base, 220 °C, 12 h, autoclave. [b] Determined by HPLC analysis. [c] Lactic acid. [d] Formic acid. [e] Acetic acid.

The presence of divalent cations proved to be crucial to increase the yield of LA. As demonstrated through control experiments by using glucose, hydroxides of monovalent cations afforded LA in low yield even at higher loadings (Table 1, entries 1 and 2). Similarly, the use of nucleophilic bases such as ammonium hydroxide (entry 3) resulted in trace amounts of LA, and was accompanied by considerable browning, probably caused by Maillard reactions.[15] Finally, the use of calcium, strontium, or barium hydroxide afforded LA in good yields. Interestingly, a combination of sodium hydroxide and barium chloride (entry 4) resulted in the efficient formation of LA, confirming the key role of divalent cations. During alkaline hydrolysis, the formation of char was limited and small amounts of insoluble material were generated, which was usually composed of insoluble carbonates produced through the decarboxylation of organic acids. NMR and HPLC analyses were used to identify formic acid (FA), acetic acid (AA), and pyruvaldehyde as the major byproducts. The presence of the latter

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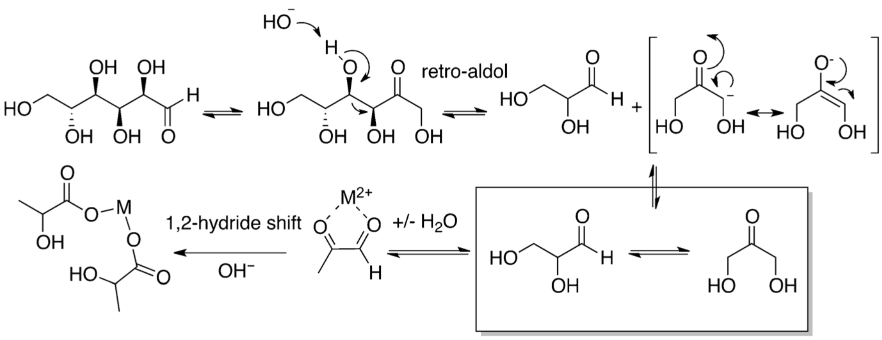
could be explained by considering the proposed reaction mechanism for the formation of LA, which is depicted in Scheme 1. Through a dynamic equilibrium, the isomerization of glucose to fructose is followed by retro-aldol splitting of the $C_6$ backbone into two $C_3$ fragments along the the retrosynthetic path of glucose biosynthesis. Dehydration of dihydroxyacetone (DHA) or glyceraldehyde (Gly) affords pyruvaldehyde, which can then be converted to LA via a 1,2-hydride shift (similar to the benzylic acid rearrangement). Notably, basic conditions are essential for this shift as neutralization removes LA from the equilibrium.



**Scheme 1.** The proposed reaction mechanism for the formation of LA.

Consistent with the proposed mechanism, we observed that pyruvaldehyde afforded LA in a 64 % yield when reacted for 8 h at 220 °C with 2 eq. of barium hydroxide. Furthermore, experiments with 1-$^{13}$C-glucose showed strong $^{13}$C incorporation at positions C1 and C3 of LA, which was in agreement with the chain splitting into two $C_3$ fragments (DHA and Gly, which are interconvertible through a dynamic equilibrium; see the Supporting Information). The generation of AA and FA during the hydrothermal hydrolysis of glucose and biomass has been extensively reported and has been described as the result of the decomposition of LA.[16]

We further optimized the reaction in a tubular microfluidic reactor. Microfluidic systems are characterized by optimal temperature programmability, which is associated with a high surface-to-volume ratio[17] that leads to a very sharp heating and cooling profile. We surmised that under this setup, LA could be generated within seconds. In these experiments we excluded calcium hydroxide as its solubility decreases at higher temperatures and is, therefore, incompatible with a microfluidic setup. We focused on bases with higher relative solubility and, for reaction times of two minutes, barium hydroxide exhibited the best results and was more efficient than sodium or strontium hydroxide (Table 2). Interestingly, the solubility of barium hydroxide shows a remarkable increase at higher temperatures,[18] making it a valuable candidate for shorter reactions at higher loadings. The superior activity of barium could be ascribed to the size of its ionic radius, which allows for optimal coordination of the two carbonyl groups in methylglyoxal, thereby catalyzing the 1,2-hydride shift.[16] The alkaline hydrolysis of glucose in the microreactor was further optimized for barium hydroxide. The reaction showed clear temperature dependence, with reaction yields proportional to the temperature increase, as demonstrated by reacting glucose with a stoichiometric amount of base at temperatures up to 275 °C for two minutes (Figure 1). However, increasing the reaction temperature did not result in a considerable improvement in the yield. Considering the experiments with longer reaction times, we regarded these yields as transient.

As the reaction proceeded, acids were generated, resulting in a progressive decrease in the pH of the reaction mixture. Indeed, at approximately 2 eq. of base per mol of glucose, neutrality was reached with an associated drop in LA formation. Therefore, the use of excess base favors the generation of LA, as shown in Table 3. In this set of experiments the best results were obtained by using 8 eq. of base for 3 min (Table 3, entry 5). Extending the reaction time did not affect the yield further. Having identified barium hydroxide as a very promising reagent for the alkaline hydrolysis of sugars, we extended the method to the conversion of bio-

**Table 2.** Effect of different bases on the conversion of glucose into LA for short reaction times.[a]

| Entry | Base | Conc. [M] | LA Yield [%][b] |
|---|---|---|---|
| 1 | NaOH | 0.025 | 9 |
| 2 | $BaCl_2$ | 0.025 | 5 |
| 3 | $Sr(OH)_2$ | 0.025 | 11 |
| 4 | $Ba(OH)_2$ | 0.025 | 27 |

[a] Reaction conditions: glucose (0.025 M), base, 250 °C, 120 s, microreactor. [b] Determined by HPLC analysis.

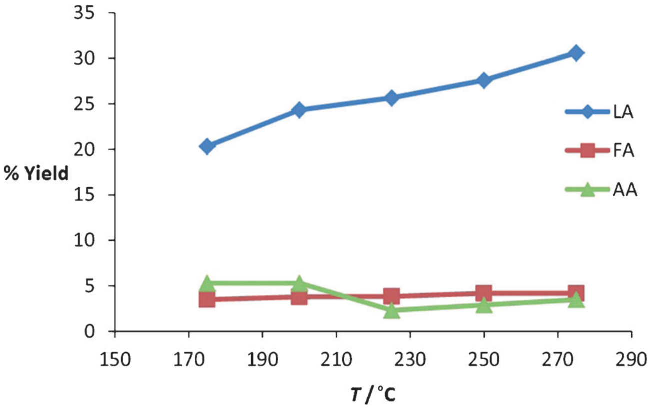


**Figure 1.** The effect of temperature on the conversion of glucose (0.025 M) to LA (120 s with equimolar barium hydroxide in microreactor).

**Table 3.** Effect of base concentration and reaction time on the conversion of glucose into LA.[a]

| Entry | Base | Conc. [M] | *t* [s] | LA Yield [%][b] |
|---|---|---|---|---|
| 1 | $Ba(OH)_2$ | 0.025 | 120 | 27 |
| 2 | $Ba(OH)_2$ | 0.05 | 120 | 38 |
| 3 | $Ba(OH)_2$ | 0.05 | 180 | 43 |
| 4 | $Ba(OH)_2$ | 0.1 | 120 | 52 |
| 5 | $Ba(OH)_2$ | 0.1 | 180 | 57 |

[a] Reaction conditions: glucose (0.025 м), base, 250 °C, microreactor. [b] Determined by HPLC analysis.

mass. Because of the low solubility of raw biomass or cellulose in water and the insoluble precipitates generated throughout the reaction, the hydrolysis was performed in autoclaves despite the suboptimal heat-transfer and temperature profiles. The autoclave setup, however, is more convenient because cellulose and other biopolymers require longer reaction times compared to monosaccharides as chain hydrolysis has to precede the retro-aldol fragmentation of monosaccarides.

Experiments performed on a 10 g scale (0.1 м) at 220 °C for 1 h with 2 eq. of base resulted in the complete consumption of the starting material and the formation of LA in a 50 % yield. Interestingly, the direct treatment of cellulose under the same unoptimized conditions provided LA in a 42 % yield. Increasing the substrate concentration but retaining the original temperature and reaction time resulted in a slight decrease in LA yield (30 % for 1 м glucose; 25 % for 1 м cellulose). Under these conditions considerable amounts of 2-hydroxybutyric acid (12 %) and glycolic acid (4 %) were detected in the product mixtures (determined by NMR analysis) in addition to FA (5 %) and AA (not determined). A C2–C3 retro-aldol mechanism can explain this, which competes with the C3–C4 fragmentation that occurs for the simple glucose reaction. We speculatively attributed this side reaction to fragmentation events that occurred because of the secondary structure of cellulose. Finally, direct treatment of rye straw (116 $g L^{-1}$, 1 h) afforded LA with a yield of 25 % (*w/w* of straw). Interestingly, under these conditions lignin precipitated out of solution as the reaction proceeded and was easily isolated at the end of the process by using simple filtration (see the Supporting Information). The method of alkaline digestion can, therefore, be considered as a very convenient alternative to the organosolv lignin preparation.[19] At the end of the reaction, barium can be precipitated by adding stoichiometric amounts of sulfuric acid. Alternatively, it can be recovered from the solution in the form of barium carbonate by precipitation with carbon dioxide.[20] Although neutralization of the reaction mixture represents a complication, technical solutions have been provided by the biotech industries that currently produce LA through fermentation schemes.[21] Alternatively, methods for the continuous recovery of carbonates have been described[20] and can be combined with the hydrothermal synthesis of LA in a flow process. Barium occurs in nature mostly in the form of sulfate (barite) or carbonate (whiterite), from which barium hydroxide is derived; therefore, the precipitation methods for barium (described above) represent the first steps towards the recycling of barium hydroxide.

In conclusion, we have demonstrated the alkaline hydrothermal treatment of glucose and biomass, such as cellulose and straw, as a simple method for the preparation of LA. Different bases were screened and the hydroxides of alkali earth metals were shown to yield the best results. The application of the method in a flow setup was also reported and proved particularly efficient when barium hydroxide was used for the reaction with glucose. Yields of up to 57 % were obtained in only 3 min, which to the best of our knowledge, are among the highest reported for the preparation of LA from biomass by using simple chemical methods. This method could be of great potential for the chemical industry, especially for its applicability to raw cellulosic biomass as it has the potential to compete with the established biotechnological fermentation processes. The simultaneous generation of different commodity chemicals including LA, FA, AA, glycolic acid, and lignin highlights the method as a valuable candidate as an entry step for new biorefinery schemes.

## Experimental Section

Experimental details are given in the Supporting Information.

## Acknowledgements

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**Keywords:** biomass · biorefinery · hydrothermal synthesis · lactic acid · microreactor

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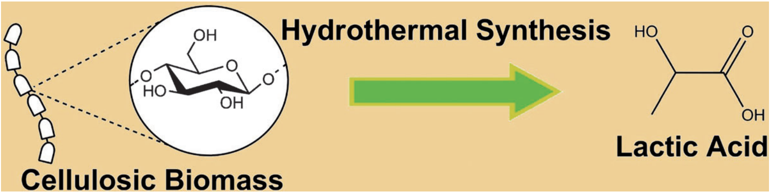

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**Chemical Conversion of Sugars to Lactic Acid by Alkaline Hydrothermal Processes**

**Some like it hot:** Lactic acid is an important commodity chemical that is mainly used in the food industry or for the manufacture of biodegradable plastics. A highly efficient strategy for the conversion of carbohydrates from biomass to lactic acid through alkaline hydrolysis in superheated water is presented.