NaOH catalyzed condensation reactions between levulinic acid and biomass derived furan-aldehydes in water

Ananda S. Amarasekara*, Timila B. Singh, Eve Larkin, Muhammad A. Hasan and Hau-Jun Fan*

Department of Chemistry, Prairie View A&M University, Prairie View, Texas 77446, USA

E-mail: asamarasekara@pvamu.edu Tel: +1 936 261 3107; fax: +1 936 261 3117

Abstract: NaOH catalyzed condensation reaction between 5-hydroxymethylfurfural and levulinic acid in water gives a 2.5 : 1 mixture of aldol products: (*E*)-6-[5-(hydroxymethyl)furan-2-yl]-hex-4-oxo-5-enoic acid and (*E*)-3-[5-(hydroxymethyl)furan-2-yl]methylene-4-oxo-pentanoic acid in 82 % combined yield. A similar reaction between furfural and levulinic acid gives the linear polymer, *poly*[1-carboxymethyl-4-(furan-2-yl)-2-oxo-butane-1,4-diyl] in 91 % yield.

Keywords: aldol reaction • furfural • 5-hydroxymethylfurfural • levulinic acid • renewable resources

1. Introduction

The increasing concern over declining petroleum reserves has promoted the current explorations for renewable resources based fuels as well as platform chemicals for chemical and polymer

industries. Triglycerides, succinic acid, lactic acid, glycerol, 5-hydroxymethylfurfural (HMF, **1**), furfural (F, **2**), and 4-oxopentanoic acid or levulinic acid (LA, **3**) produced from plant based biomass are in the forefront of this new generation of feedstocks (Gallezot, 2012) (Climent et al., 2014) (Gandini, 2008). 5-Hydroxymethylfurfural and furfural have found a special place in this category of chemicals as these furan-aldehydes are dehydration products of C-6 and C-5 sugars derived from depolymerization of the key biomass polysaccharides cellulose and hemicellulose (Amarasekara, 2011), (Hu et al., 2012), (Gandini, 2010). During the acid catalyzed dehydration of C-6 sugars to produce HMF, depending on the reaction conditions this furan can undergo rehydration as a subsequent step, resulting a fragmentation to levulinic and formic acids. The C-5 keto acid formed is a versatile building block for the synthesis of various chemicals such as levulinate esters, γ -valerolactone, 1,4-pentanediol, α -angelica lactone, 2-methyltetrahydrofuran (Lange et al., 2012), and δ -amino levulinic acid (Sheldon, 2014). A number of these LA derivatives have been used as building blocks for the preparation of polymers as well as fuel precursors (Climent et al., 2014), (Alonso et al., 2013), (Amarasekara and Hawkins, 2011), (Amarasekara and Wiredu, 2014a). Aldol condensation of furfural and 5-hydroxymethylfurfural with acetone is known to yield typical aldol products in 1:1 molar ratio reaction and excess aldehyde yields double-aldol condensation products (West et al., 2008), (O'Neill et al., 2013).

Dumesic and co-workers first investigated the aldol condensation of furan aldehydes and a series of ketones in THF-aq. NaOH as a synthetic approach to build C-6-15 range molecules that could be converted to deoxygenated liquid transportation fuels (West et al., 2008), (Chheda and Dumesic, 2007), (Barrett et al., 2006). In addition, Patel et al. reported the self-polycondensation

of the acetone-furfural adduct, 2-furfurylidene methyl ketone to give a furfural-acetone polymer when refluxed in aq. NaOH (Patel and Patel, 1983). Recently, we have shown that cellulose or dry corn stover powder can be directly converted to a mixture of HMF and furfural - acetone aldol condensation products in a single-reactor operation by heating in acetone at 120 °C in the presence of Brønsted acidic ionic liquid catalysts (Amarasekara and Wiredu, 2014b). Where ionic liquid was used as a multi-purpose catalyst for depolymerization, dehydration and aldol condensation reactions. Aldol condensation between furfural and levulinic acid is known to give δ -furfurylidenelevulinic acid in low yields when Na₂CO₃ is used as the base in water and water-ethanol mixtures (Hachihama and Hayashi, 1954), (Iwakura and Hayashi, 1960). In addition Subbiah et al. have recently reported the formation of 2,5-dihydroxymethylfurfural and 5-hydroxymethyl furanoic acid from HMF in aq. NaOH *via* Cannizzaro reaction (Subbiah et al., 2013). However, as far as we are aware there are no reports on aldol condensations between 5-hydroxymethylfurfural and levulinic acid. Our interests (Amarasekara and Hawkins, 2011), (Amarasekara et al., 2009), (Amarasekara et al., 2012) in preparation of renewable resources based building blocks as polymer and fuel precursors has led us to explore the NaOH catalyzed condensation reactions between levulinic acid and biomass derived furan-aldehydes.

2. Materials and methods

2.1. General methods

Levulinic acid, 5-hydroxymethylfurfural, furfural and sodium hydroxide (99.9%) were purchased from Aldrich Chemical Co. ¹H NMR Spectra were recorded in DMSO-*d*₆ or CDCl₃ on a Varian Mercury plus spectrometer operating at 400 MHz and chemical shifts are given in ppm

downfield from TMS ($\delta = 0.00$). ^{13}C Chemical shifts were measured relative to $\text{DMSO-}d_6$ and converted to δ (TMS) using δ (DMSO) = 39.51, and in CDCl_3 converted to δ (TMS) using δ (CDCl_3) = 77.00. FT-IR spectra were recorded on a Thermo Nicolet IR 200 spectrometer using KBr pellets. UV-Vis Spectra were recorded on a Carey 50 UV-Vis spectrophotometer using 1 cm quartz cells. Number average molecular weight M_n and polydispersity index (PDI) of the polymer samples were measured on a Waters gel permeation chromatography (GPC) system with Waters Styragel columns, UV detector and using tetrahydrofuran (THF) as the solvent. Elemental analysis was performed at QTI laboratories, New Jersey, USA. Thermogravimetric analysis was carried out in air on a Perkin Elmer Diamond TG/DTA system in 25–800 °C temperature range, 10 °C/min, and using Pt crucibles.

2.2. NaOH catalyzed condensation reactions between levulinic acid and 5-hydroxymethylfurfural

A mixture of 5-hydroxymethylfurfural (0.880 g, 6.984 mmol) and levulinic acid (2.025 g, 17.46 mmol) in 3 mL of water was cooled in an ice bath. Sodium hydroxide (0.754 g, 18.86 mmol) was dissolved in 6 mL of water, cooled to 0 °C and added into the stirred levulinic acid, HMF mixture and allowed to warm to room temperature in about an hour. The mixture was further stirred at room temperature for 48 h, and then acidified with 1.0 M aq. HCl. The resulting solution was extracted with methylene chloride (3x15 mL) and the combined methylene chloride layer was washed with water (3x10 mL), dried (anhydrous Na_2SO_4) and concentrated in the rotary evaporator to give the crude product as a yellow oil. Which was chromatographed on silica, eluting with 2-15% methanol in methylene chloride to give two products.

Major product: **4**, (*E*)-6-[5-(hydroxymethyl)furan-2-yl]-hex-4-oxo-5-enoic acid. Colorless viscous oil, 0.916 g, 58.6% yield.

Anal. Calc. for C₁₁H₁₂O₅: C, 58.93; H, 5.39. Found: C, 58.66; H, 5.60. UV (MeOH) $\lambda_{\max}$ 320 nm. IR (KBr) 706, 770, 953, 1022, 1191, 1280, 1404, 1521, 1671, 2847, 2917, 3388 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, 22 °C, TMS) δ 2.71 (2H, t, J = 6.8 Hz, CH₂), 2.93 (2H, t, J = 6.8 Hz, CH₂), 3.82 (1H, bs, OH), 4.65 (2H, s, CH₂-OH), 6.39 (1H, d, J = 3.2 Hz, Fu), 6.62 (1H, d, J = 3.2 Hz, Fu), 6.65 (1H, d, J = 15.6 Hz, =CH-CO), 7.31 (1H, d, J = 15.6 Hz, =CH-Fu), 11.10 (1H, bs, COOH). ¹³C NMR (100 MHz, CDCl₃, 22 °C, TMS) δ 29.7, 35.6, 57.6, 110.6, 117.1, 122.6, 129.1, 150.8, 156.8, 177.1, 197.6

Minor product: **5A**, (*E*)-3-[5-(hydroxymethyl)furan-2-yl]methylene-4-oxo-pentanoic acid.

Colorless viscous oil, 0.367 g, 23.4 % yield.

Anal. Calc. for C₁₁H₁₂O₅: C, 58.93; H, 5.39. Found: C, 58.61; H, 5.54. UV (MeOH) $\lambda_{\max}$ 320 nm. IR (KBr) 709, 792, 884, 1068, 1049, 1180, 1277, 1378, 1626, 1650, 2920, 2973, 3419 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, 22 °C, TMS) δ 2.42 (3H, s, CH₃), 3.74 (2H, s, CH₂), 4.20 (1H, bs, OH), 4.55 (2H, s, CH₂-OH), 6.36 (1H, d, J = 3.2 Hz, Fu), 6.67 (1H, d, J = 3.2 Hz, Fu), 7.28 (1H, s, =CH-Fu), 11.25 (1H, bs, COOH). ¹³C NMR (100 MHz, CDCl₃, 22 °C, TMS) δ 25.2, 29.7, 57.1, 110.2, 118.6, 128.7, 130.1, 150.3, 157.9, 176.6, 199.2.

2.3. NaOH catalyzed condensation reaction between levulinic acid and furfural

A mixture of furfural (0.960 g, 10.00 mmol) and levulinic acid (1.160 g, 10.00 mmol) in 20 mL water was cooled in an ice bath. Sodium hydroxide (0.680 g, 17.00 mmol) was dissolved in 30 mL water, cooled to 0 °C and added into magnetically stirred levulinic acid furfural mixture and

allowed to warm to room temperature in about an hour. The mixture turned to yellow in 1-2 minutes, to dark brown in about 5 minutes, and was further stirred at room temperature for 48 h. Then acidified with 1.0 M aq. HCl; while acidification polymeric product separated as a pale yellow solid mass, which was filtered and repeatedly washed with deionized water (200 mL) to remove acid and salts. The crude polymer was dried in air and purified by soxhlet extraction for 20 h, using cyclohexane as the solvent.

poly[1-carboxymethyl-4-(furan-2-yl)-2-oxo-butane-1,4-diyl] (**8**), 1.765 g, 91 % yield. Anal. Calc. for C₁₀H₁₀O₄: C, 61.85; H, 5.19. Found: C, 61.55; H, 5.28.

¹H and ¹³C NMR spectra of the polymer **8** are in the article (figure 3a,b); IR spectrum and TGA-DTGA plot are in the supplementary material figures 4 and 5.

3. Results and discussion

Hydroxide ion catalyzed room temperature condensation reaction between HMF and LA was studied using HMF : LA molar ratios in the range of 1:1 to 1:4, with excess aq. NaOH as the base. Earlier attempts to use ethanol, THF, ethanol-water and THF-water as solvents failed to produce any products and unreacted starting materials were recovered. The best condensation product yield of 82 % was achieved for the aqueous phase reaction using HMF : LA : NaOH molar ratio of 1: 2.5: 2.7 and allowing the reaction at room temperature. Thin layer chromatographic monitoring (silica, 10% MeOH in CH₂Cl₂) of the reaction showed complete disappearance of HMF after 48 h, and the formation of two products. At this time reaction was quenched by neutralization with 1.0 M aq. HCl and the products were isolated by solvent extraction into CH₂Cl₂. Then two products in 2.5 : 1 (w/w) ratio were separated by column chromatography on silica, eluting with 2-15% methanol in CH₂Cl₂ as the solvent. The isolated

products were characterized by elemental analysis, IR, UV, ^1H and ^{13}C NMR spectroscopy. The major product was identified as the linear adduct, (*E*)-6-[5-(hydroxymethyl)furan-2-yl]-hex-4-oxo-5-enoic acid (**4**) as shown in figure 1, by spectroscopic methods. ^1H NMR spectrum of **4** showed two olefinic protons of the enone system at 6.65 and 7.31 ppm as two doublets with 15.6 Hz coupling constant, indicating the *trans* - geometry.

The minor adduct showed only one olefinic hydrogen at 7.28 ppm as a singlet, as expected for a product from aldol condensation resulting from C-3 carbanion. The geometry of the enone system in the minor branch adduct is not evident from the NMR spectroscopic data; all attempts to produce crystals suitable for X-ray crystallography were also not successful. Therefore, we have resorted to a DFT calculation to predict the probable geometry of the minor adduct. In this study we have compared the calculated $\Delta E^\circ(\text{solv})$, ΔE° , $\Delta E^\circ_{\text{ZPE}}$, ΔH° , and ΔG° values of possible isomeric structures of **5** with the linear adduct **4**. The relative energies of linear HMF-LA adduct and selected isomeric structures of branched HMF-LA adducts (**5A-C**) calculated using 6-311++G(d') basis set are shown in table 1. The isomeric structure (*E*)-3-[5-(hydroxymethyl)furan-2-yl]methylene-4-oxo-pentanoic acid (**5A**) showed the lowest values in all the branched structures studied, and as a result **5A** is the most likely stereo-structure for the minor adduct.

The condensation between furfural (**2**) and levulinic acid (**3**) was also studied using F : LA molar ratios in the range of 1:1 to 1:4 with excess aq. NaOH as the base as shown in figure 2. This reaction was found to be more rapid than reaction between HMF and LA; solution turned to yellow within 1-2 minutes and to a dark brown color in approximately 5 minutes when the

reactions were started at 0 °C and allowed to warm to room temperature in about an hour. Thin layer chromatography monitoring (silica, 10% MeOH in CH₂Cl₂) of the reaction showed the formation of 6-8 products in samples withdrawn after 5 min. and polymerization afterwards. The neutralization of reaction mixture with 1.0 M aq. HCl resulted a separation of a yellow gummy polymer as a solid mass, which could be purified by soxhlet extraction with cyclohexane. The best condensation polymer product yield of 91 % was achieved for the aqueous phase reaction using F : LA : NaOH molar ratio of 1: 1: 1.7, with 5 mL H₂O per mmol of furfural. This reaction was started at 0 °C and allowed to warm to room temperature in about an hour and stirred at room temperature for 48 h, before neutralization. The attempts to isolate intermediates from the initial stage of the reaction at 0 °C were not successful due to rapid polymerization.

The proposed route for polymerization is shown in figure 2, where we believe that, first furfural (**2**) reacts with LA (**3**) in aq. hydroxide ion catalyzed aldol condensation as in the case of HMF-LA reaction, resulting two aldol condensation products **6** and **7** shown in figure 2. Then carbanion formed in α -position of one aldol adduct can undergo Michael addition to other aldol adduct (figure 2). Interestingly, Michael additions between two molecules of the same aldol adduct will also result similar connectivity in growing the polymer chain producing polymer **8**. The polymer was characterized by elemental analysis, GPC molecular weight determination, IR, TGA-DTGA, ¹H and ¹³C NMR spectroscopy. The proton NMR recorded in DMSO-*d*₆ showed overlapped broad peaks for aliphatic and furan protons, whereas the broad absorption at 12.1 ppm in figure 3a can be assigned to the carboxylic acid proton. All 10 carbons could be identified in the ¹³C NMR spectrum recorded after 50K scans (rd = 2.0 s) (figure 3b). The peaks at 106, 111, 142 and 155 ppm were assigned to the furan ring; carboxylic acid and ketone peaks

are at 174 and 198 ppm respectively. The four aliphatic carbons are indicated by peaks at 32, 35, 37 and 47 ppm (figure 3b). New F-LA condensation polymer, *poly*[1-carboxymethyl-4-(furan-2-yl)-2-oxo-butane-1,4-diyl] **8** showed an average DP of 56 and polydispersity index of 1.6 from polymer samples prepared in duplicate experiments. TGA-DTGA plot showed that the polymer is stable up to about 280 °C in air.

4. Conclusion

We have shown that aq. NaOH catalyzed condensation of HMF and LA gives two isomeric aldol adducts in 2.5 : 1 ratio, and these all renewable resources based C-11 furanic-enone acids can be considered as potential building blocks or precursors for polymer synthesis as well as renewable fuels. In contrast to HMF-LA aldol condensation products, F-LA products undergo self-Michael additions, as well as with other aldol-adduct, resulting a furanic-keto acid polymer. This green synthesis method provides a simple route to an all renewable resources based highly functionalized stable new polymeric material in excellent yields.

Acknowledgements

Authors would like to thank American Chemical Society-PRF grant UR1-49436, NSF grants CBET-0929970, CBET-1336469, HRD-1036593, and USDA grant CBG-2010-38821-21569 for financial support

Figure 1. **Figure 2.**

Figure 3.

Table 1.

Isomeric structure	ΔE° (solv)	ΔE°	$\Delta E^\circ_{\text{ZPE}}$	ΔH°	ΔG°
4	0.00	0.00	0.00	0.00	0.00
5A	1.90	-0.98	-1.21	-1.27	0.55
5B	6.80	3.39	3.24	3.13	4.69
5C	9.73	7.92	7.43	7.51	8.45

Figure/Table Captions

Figure 1. Aldol condensation of 5-hydroxymethylfurfural (HMF, **1**) with levulinic acid (LA, **3**) in aq. NaOH, **4** : **5A** = 2.5 : 1

Figure 2. Aldol-Michael polymerization of furfural (F, **2**) with levulinic acid (LA, **3**) in aq. NaOH producing *poly*[1-carboxymethyl-4-(furan-2-yl)-2-oxo-butane-1,4-diyl] **8**

Figure 3. ^1H (**a**) and ^{13}C (**b**) NMR spectra of *poly*[1-carboxymethyl-4-(furan-2-yl)-2-oxo-butane-1,4-diyl] **8** in DMSO- d_6 , * solvent

Table 1. The relative energies of linear HMF-LA adduct **4** and selected isomeric structures of branched HMF-LA adducts (**5A-C**) calculated using 6-311++G(d') basis set (kcal/mol)

References

- Alonso, D.M., Wettstein, S.G., Dumesic, J.A., 2013. Gamma-valerolactone, a sustainable platform molecule derived from lignocellulosic biomass. *Green Chem.* 15, 584-595.
- Amarasekara, A., Wiredu, B., 2014a. Acidic Ionic Liquid Catalyzed One-Pot Conversion of Cellulose to Ethyl Levulinate and Levulinic Acid in Ethanol-Water Solvent System. *Bioenerg. Res.*, 1-7.
- Amarasekara, A., Wiredu, B., 2014b. Single reactor conversion of corn stover biomass to C5–C20 furanic biocrude oil using sulfonic acid functionalized Brönsted acidic ionic liquid catalysts. *Biomass Conv. Bioref.* 4, 149-155.
- Amarasekara, A.S., 2011. 5-Hydroxymethylfurfural based polymers, in: Mittal, V. (Ed.), *Renewable Polymers, Synthesis, Processing and Technology*, 1 ed. Wiley-Scrivener, Salem, MA.
- Amarasekara, A.S., Green, D., Williams, L.D., 2009. Renewable resources based polymers: Synthesis and characterization of 2,5-diformylfuran-urea resin. *Europ. Polym. J.* 45, 595-598.
- Amarasekara, A.S., Hawkins, S.A., 2011. Synthesis of levulinic acid-glycerol ketal-ester oligomers and structural characterization using NMR spectroscopy. *Europ. Polym. J.* 47, 2451-2457.
- Amarasekara, A.S., Wiredu, B., Razzaq, A., 2012. Vanillin based polymers: I. An electrochemical route to polyvanillin. *Green Chem.* 14, 2395-2397.
- Barrett, C.J., Chheda, J.N., Huber, G.W., Dumesic, J.A., 2006. Single-reactor process for sequential aldol-condensation and hydrogenation of biomass-derived compounds in water. *App. Catal. B: Environ.* 66, 111-118.
- Chheda, J.N., Dumesic, J.A., 2007. An overview of dehydration, aldol-condensation and hydrogenation processes for production of liquid alkanes from biomass-derived carbohydrates. *Catal. Today* 123, 59-70.
- Climent, M.J., Corma, A., Iborra, S., 2014. Conversion of biomass platform molecules into fuel additives and liquid hydrocarbon fuels. *Green Chem.* 16, 516-547.
- Gallezot, P., 2012. Conversion of biomass to selected chemical products. *Chem. Soc. Rev.* 41, 1538-1558.

336
337 Gandini, A., 2008. Polymers from renewable resources: A challenge for the future of
338 macromolecular materials. *Macromolecules* 41, 9491-9504.
339
340 Gandini, A., 2010. Furans as offspring of sugars and polysaccharides and progenitors of a family
341 of remarkable polymers: A review of recent progress. *Polym. Chem.* 1, 245-251.
342
343 Hachihama, Y., Hayashi, I., 1954. The preparation of polyamides containing heterocyclic groups
344 from furfural and levulinic acid. *Die Makromolekulare Chemie* 13, 201-209.
345
346 Hu, L., Zhao, G., Hao, W., Tang, X., Sun, Y., Lin, L., Liu, S., 2012. Catalytic conversion of
347 biomass-derived carbohydrates into fuels and chemicals via furanic aldehydes. *RSC Advances* 2,
348 11184-11206.
349
350 Iwakura, Y., Hayashi, K., 1960. Polyamide and copolyamides derived from

351 1-methylpyrrolidine-2, 5-di- β -propionic acid. Studies of synthetic polymer derived from

352 levulinic acid. *Die Makromolekulare Chemie* 36, 178-189.
353
354 Lange, J.-P., van der Heide, E., van Buijtenen, J., Price, R., 2012. Furfural—A Promising
355 Platform for Lignocellulosic Biofuels. *ChemSusChem* 5, 150-166.
356
357 O'Neill, R.E., Vanoye, L., De Bellefon, C., Aiouache, F., 2013. Aldol-condensation of furfural
358 by activated dolomite catalyst. *App. Catal. B: Environ.* 144, 46-56.
359
360 Patel, A.A., Patel, S.R., 1983. Synthesis and characterization of furfural-acetone polymers.
361 *Europ. Polym. J.* 19, 231-234.
362
363 Sheldon, R.A., 2014. Green and sustainable manufacture of chemicals from biomass: State of the
364 art. *Green Chem.* 16, 950-963.
365
366 Subbiah, S., Simeonov, S.P., Esperanca, J.M.S.S., Rebelo, L.P.N., Afonso, C.A.M., 2013. Direct
367 transformation of 5-hydroxymethylfurfural to the building blocks 2,5-dihydroxymethylfurfural
368 (DHMF) and 5-hydroxymethyl furanoic acid (HMFA) via Cannizzaro reaction. *Green Chem.* 15,
369 2849-2853.
370

371 West, R.M., Liu, Z.Y., Peter, M., Gärtner, C.A., Dumesic, J.A., 2008. Carbon-carbon bond
372 formation for biomass-derived furfurals and ketones by aldol condensation in a biphasic system.
373 J. Molecul. Catal. A: Chem. 296, 18-27.
374
375

*Graphical Abstract***NaOH catalyzed condensation reactions between levulinic acid and biomass derived furan-aldehydes in water**

Ananda S. Amarasekara*, Timila B. Singh, Eve Larkin, Muhammad A. Hasan and Hau-Jun Fan*