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DOI: 10.1002/cssc.201000136 C—C Bond Formation Reactions for Biomass-Derived Molecules

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There has been a tremendous interest in the utilization of biomass as feedstock to produce renewable fuels and chemicals.^[1] The major monomer building blocks of biomass are carbohydrates which are typically 5 or 6 carbons in length. Petroleumderived jet and diesel fuels are between 8 to 15 carbons in length. Therefore, to produce jet and diesel fuel from biomass, there must be a C–C bond formation from the biomass-derived molecules.^[2] However, direct C–C bond formation from carbohydrates (C₅ and C₆) is difficult due to the polyhydroxy functionalities on the carbohydrates. These polyhydroxy functionalities make the carbonyl group of the carbohydrates less reactive toward C–C bond formation because of its hemiacetal form. To overcome this problem, several research groups have converted C₅ and C₆ carbohydrates to aromatic aldehydes (Figure 1) such as furfural 1 and hydroxymethylfurfural (HMF) 2



Figure 1. Structures of furfural 1 and hydroxymethylfurfural 2.

by dehydration reaction.^[3] These aromatic aldehydes can then undergo aldol condensation reactions with acetone (C_3) to produce molecules with 8 to 15 carbons, which can then be converted into jet and diesel fuel by hydrodeoxygenations processes.

One of the challenges with the aldol condensation route is that it requires a selective dehydration process. Acetone, biobased product from acetone-bu-

tanol fermentation allows this process to be biomass based.^[4] The purpose of this study is to explore potential routes for C–C bond formation of biomass-derived compounds. We first

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Scheme 1. Proposed reaction pathway for aldol adduct.

study the aldol condensation of aromatic aldehydes (C_5) with hydroxy carbonyl compounds (C_3). We then report other C–C bond forming reactions including Baylis–Hillman and acid-catalyzed reactions of biomass-derived molecules that are used as precursors for fuel range compounds. Herein, we provide a basis for chemical routes that can be employed to create C–C bonds from biomass-derived feedstocks.

The aldol condensation with hydroxycarbonyl compounds (hydroxyacetone and dihydroxyacetone) is an important reaction in nature (typically catalyzed by enzymes).^[5] Hydroxycarbonyl compounds do not undergo aldol condensation in the presence of mineral bases due to the formation of alkoxide ion. However, amine-based catalysts [e.g., L-proline, 1,8-diazabicycloundec-7-ene (DBU), *i*Pr₂NEt] can be used to catalyze these reactions.^[6,7] These organocatalysts are low-molecularweight, nontoxic, insensitive toward moisture, reusable, and commercially available, making them a valuable tool for industrial-scale processes. In addition, these organocatalysts can potentially be heterogenized by anchoring them onto solid supports.^[8]

Scheme 1 shows a proposed reaction mechanism for furfural condensation with hydroxyacetone in the presence of an organocatalyst (i.e., DBU). This involves the formation of Z-enolate

6 stabilized by hydrogen bonding after the nitrogen atom of the catalyst induces the deprotonation of hydroxyacetone. Forming hydrogen-bonding network **5** with protonated nitrogen atom of the catalyst can also activate furfural **1**. However, the combination of steric hindrance and inductive effects make route a more favorable than route b which leads to the formation of **7**.

Table 1 summarizes our results for aldol condensation products of furfural 1 with acetone 9, hydroxy acetone 3, and dihydroxyacetone 10 in the presence of either aqueous NaOH or tertiary amine (i.e., DBU). Sodium hydroxide was unable to catalyze the condensation of furfural with both hydroxyacetone and dihydroxyacetone but it catalyzed the condensation of furfural with acetone to result in both monomeric and dimeric





products **11** and **12**. On the other hand, DBU catalyzed the condensation of furfural with hydroxyacetone and dihydroxyacetone, but not with acetone. The condensation of hydroxyacetone and dihydroxyacetone separately with furfural in the presence of DBU resulted in monomeric and dimeric products **7** and **13**, respectively. Moreover, the aldol adducts contained a mixture of diastereomers, detected by analysis of the corresponding ¹H and ¹³C NMR spectra. All the reactions were carried out at room temperature in THF (tetrahydrofuran) as the solvent. In the case of dihydroxy acetone, the reaction was performed without solvent to obtain a better yield. The conversion of furfural was more than 95% and 100% in case of the hydroxyketones and acetone, respectively.

The Morita-Baylis–Hillman reaction demonstrated in Scheme 2 is another important process for atom-economical C–C bond formation. This involves the reaction at the α -position of an activated alkene 14 (Baylis-Hillman donor, BHD) with an activated carbonyl compound (Baylis-Hillman acceptor, BHA) in the presence of tertiary amine-based catalysts [e.g., Me₃N, Et₃N, 1,4-diazabicyclo[2.2.2]octane (DABCO), DBU, imidazole, 4-dimethylamino pyridine (DMAP).^[9] Lewis acids (e.g., TiCl₄, SnCl₄) and phosphine compounds (e.g., Ph₃P, Et₃P, Bu₃P) also catalyze these reactions to form Baylis-Hillman adducts.^[10] The intermediates formed in these reactions have a great potential for further transformations to form C_7 to C_{15} carbon units. The mechanism of this reaction is well reported in the literature.^[9] Furfural 1 and hydroxymethylfurfural 2 would be Baylis-Hillman acceptors in this reaction.



Scheme 2. Mechanism of Baylis–Hillman reaction with tertiary amine as a catalyst.

The present challenge is to develop a process to produce Baylis–Hillman donors from biomass. One option would be to produce acrolein **18** or methyl vinyl ketone **19** from biomass (Figure 2). Paine et al. described a pathway to get **18** and **19**



Figure 2. Biomass-derived Baylis–Hillman donors (18, 19) and methylacrylate (20; model compound for BHD.

(BHDs; Figure 2 < xfigr2 from sugars via pyrolytic routes.^[11] Corma and co-workers showed how acrolein can be produced from glycerol.^[12] Due to the high reactivity of vinyl carbonyl species, they are difficult to work with. Herein, we report this reaction with the reasonably stable methylacrylate **20**, which is a derivative of acrolein as a BHD for model studies.

Table 2 shows the formation of Baylis–Hillman products, **21** and **22** (C_8 and C_9). This reaction can be performed with several amine catalysts; the literature shows aqueous NMe₃ and DABCO can catalyze in good yields.^[13] The reaction of the activated alkenes such as methyl vinyl ketone **19** and acrolein **18** as a BHD suffers from poor conversions, due to Michael-type dimerization of these regents under the influence of amines. These experiments prove that Baylis–Hillman reactions can be used to form C–C bonds from biomass-derived feedstocks. A remaining challenge however would be to make Baylis Hillman number of the set.

Acid-catalyzed reactions can also be used for C–C bond formation from biomass-derived compounds. Acid catalysts are commonly used for dehydration of biomass-derived products to produce furfural and HMF.^[3] However, the reactions of C–C bond formation between biomass-derived compounds under acidic conditions have not been studied so far. Scheme 3 demonstrates the process of C–C bond formation by acid catalysts. The mechanism of these reactions involve the protonation of the alcohol or the carbonyl group (furfural, HMF, and Baylis–

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Scheme 3. Acid-catalyzed condensation of furfural with furan.

Hillman adducts) followed by the addition of nucleophile **23** (furan). Using this method, structurally different substrates can produce the precursors for branched C_9 to C_{18} alkanes.

Table 3 shows the results for the acid-catalyzed reaction of furan. Scheme 3 explains the mechanism of the formation of trifuryl methane from furfural. Protonation of alcohol or aldehyde followed by the addition of furan via oxonium ion intermediate led to product formation. Similarly HMF afforded a C_{18} carbon unit. The reaction of furfural and HMF with furan required 2 h to complete. Higher concentrations of acid and longer reaction times decreased the product formation. This is due to the polymerization of furan under the influence of acid. We also observed similar condensation reactions with Baylis–Hillman adducts **21** and **22** to produce C_{12} and C_{17} carbon units, respectively. According to the reports available in literature,^[14] methyl furan also undergoes nucleophilic addition under acidic conditions and is an interesting way to make different sets of precursors for branched-chain alkanes.

A variety of C–C bond forming reactions can be carried out to convert biomass-derived molecules into larger species including: base-catalyzed aldol condensation, base-catalyzed Baylis–Hillmann reactions, and acid-catalyzed condensation reactions. These larger species can then be used to produce jet and diesel fuels from biomass. Mineral bases can efficiently



condense furfural with acetone, but cannot be used for the condensation of furfural with dihydroxyacetone and hydroxyacetone. Tertiary amine bases such as DBU can effectively condense furfural with hydroxyketones, but not with acetone. Furfural and HMF (BHA) also react with methacrylate (BHD) in the presence of tertiary amine bases to produce Baylis–Hillman adducts. Finally, catalytic amounts of sulfuric acid efficiently condense furan with furfural, HMF, and Baylis–Hillman adducts, respectively. This report thus explores potential options for C–C bond formation, which is a key step in the conversion of biomass into jet and diesel fuel.

Experimental Section

Reagents: TLC analysis was performed using Merck 5554 aluminum-backed silica plates, and the compounds were visualized using UV light (254 nm). A solution of cerium sulfate tetrahydrate and phosphomolybdic acid in 10% aqueous sulfuric acid was prepared fort this purpose. Column chromatography as performed on Silica gel 250–400 μ m was purchased from Merck. NMR spectra were recorded on a Bruker (400 MHz) spectrometer. The starting compounds furfural, hydroxymethyl furfural, methacrylate, methyl vinyl ketone, furan, H₂SO₄, hydroxyacetone, dihydroxyacetone, NaOH, acetone, aqueous NMe₃, MeOH, tetrahydrofuran, dichloromethane, and triethylamine were of analytical grade. DBU and DABCO were purchased from Aldrich and used as received.

General procedure for aldol condensation with hydroxy carbonyl compounds: Aldehyde (1 mmol) and DBU (10 mol%) was treated with hydroxy acetone (1 mmol) in THF (10 mL) or with dihydroxy acetone (0.5 mmol) at room temperature. After 12 h, the reaction mixture was concentrated (if necessary) and diluted with ethyl acetate. The organic layer was washed with saturated NH₄Cl (1× 25 mL), water (2×20 mL), and brine (1×20 mL). The ethyl acetate later was dried over anhydrous Na₂SO₄ and concentrated under vacuum for further purification.

General procedure for acid-catalyzed condensation reaction: To a solution of alcohol or aldehyde (1 mmol) in furan (5 mL), catalytic amount of sulphuric acid was added. The reaction mixture was re-

fluxed for 1–2 h (see Table 3 for details). The reaction mixture was concentrated to remove the excess furan and residue was diluted with ethyl acetate and washed with aqueous NaHCO₃ (2×10 mL). The organic layer was separated, dried (Na₂SO₄), and concentrated under reduced pressure.

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