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Formation Pathways toward 2- and 4-Methylbenzaldehyde via Sequential Reactions from Acetaldehyde over Hydroxyapatite Catalyst

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Condensation reactions of biomass derived C_2 and C_4 aldehydes form both *ortho*- and *para*-tolualdehydes (2-MB and 4-MB, respectively). The complete reaction network and the detailed mechanisms, however, have not been fully described. Here, analysis of the products formed by sequential condensation reactions of acetaldehyde and 2-butenal suggests that 2- and 4-MB products form via aromatization of 2,4,6-octatrienal and of highly reactive acyclic intermediate(s) formed via self-addition of 2-butenal, respectively. The exact positions at which C–C bonds form between C_4 co-reactants to create 4-MB products were investigated by using reactant mixtures containing combinations of 2-butenal, 2-butenol, and 3-methyl-2-butenal as model reactants. The last two reactants can form products that may be assigned to specific reaction pathways (not distinguishable during self-addition of 2-butenal) and also have decreased reactivity at specific carbon atoms. The analysis of the products suggests that 4-MB species form via 2-butenal self-addition by nucleophilic attack of the α-C to the carbonyl-C. Additionally, Diels–Alder reactions (between C_6 and C_2 intermediates) do not contribute in any significant manner to the formation of 4-MB. These findings complete the description of the reaction network that forms 2- and 4-MB from acetaldehyde on hydroxyapatite.

Introduction

Upgrading bio-derived base chemicals (e.g., ethanol, acetone) into value-added commodity chemicals or fuels will be an important component of a sustainable society. Currently, biomass fermentation produces substantial amounts of ethanol.[1–3] The amount of ethanol produced, however, exceeds its demand as a transportation fuel additive.[3] Catalytic upgrading of ethanol and its derivatives is therefore a desirable method to utilize the large amounts of ethanol while developing pathways for the renewable production of platform chemicals (e.g. 1-butanol, 1,3-butadiene, and diethylether).[1,2,4] Acetaldehyde, which is readily formed from ethanol via dehydrogenation, participates in multiple types of coupling reactions (e.g., aldol reaction, Guerbet reaction) that give larger chemical products, and the mechanisms and active surface species of these reactions have been investigated in detail[5,6] over catalysts such as hydroxyapatite (HAP),[7–11] metal oxides,[8–21] and mixed metal oxides.[22–25]

Such coupling reactions continue in a series of steps that consume primary products and form larger species.[5–7,21,26–28] While the cascades of ethanol coupling (Guerbet reaction) processes produce broad distributions of linear and branched alcohols by numerous self- and cross-condensation reactions,[7,26] narrower product distributions that provide selectivity to specific species emerge if unsaturated aldehydes (and enals) mainly participate in condensation reactions. These pathways terminate with the dehydrocyclization of C_6 and C_8 enals (e.g., 2,4-hexadienal,[29] 2,4,6-octatrienal) to form aromatic products[21,30] (e.g., benzene,[21,29] trimethylbenzene,[30] tolualdehydes[26–28]), because these products either lack the functional groups needed for further condensation reactions or possess greatly reduced reactivity as a result of combination of steric and electronic effects.[26] Among the aromatics that can form in these reaction networks, *ortho*- and *para*-tolualdehydes (specifically, 4-methylbenzaldehyde (4-MB=O) and 2-methylbenzaldehyde (2-MB=O)) have the potential to replace xylenes in the production of the large volume monomers terephthalic acid and phthalic anhydride, respectively. The formation of these C_8 aromatics (2-/4-MB=O) from acetaldehyde is difficult and provide only moderate yields (30%), because the multistep addition of acetaldehyde to growing enal chains competes with H-transfer pathways that produce mixed alcohol products.[26] Tolualdehydes do form, however, in greater yields (and with more desirable ratios of *para*- to *ortho*-isomers) by self-condensation of 2-butenal over different homogeneous and heterogeneous catalysts (NaOH,[31] proline based

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organocatalysts,[32] alkaline metal oxides,[27,33] metal oxides,[33] and modified zeolites[27,28]) and at different reaction temperatures.

A number of different reaction mechanisms have been proposed to explain the distinct selectivities towards those *ortho*- and *para*-products.[27,31–33] Notably, the reaction intermediates that are implicated in several of the proposed mechanisms are rarely observed, and to the best of our knowledge, only a single investigation of 2-butenal condensation isolated an acyclic intermediate (2-ethylidene-3-methyl-glutaraldehyde), which strongly suggested a Michael addition reaction involving the α-carbon atom on the trimethylbenzylammonium fluoride (TMBAF) catalyst.[31] Other reaction mechanisms were, however, not disproven and the mechanism by which 2-butenal couples to form differently structured acyclic and cyclic C_8 species (e.g., 2-MB=O and 4-MB=O) is still open to debate, particularly on heterogeneous oxide catalysts such as HAP. A detailed understanding of the mechanism responsible for the formation of each product isomer would provide useful guidance for the design of catalysts that may help to produce important, high volume platform chemicals (e.g., terephthalic acid) from renewable feedstocks.

Here, we describe the reaction mechanisms that produce 2- and 4-MB products from acetaldehyde and 2-butenal over HAP catalyst. Comparisons of product selectivity measured as functions of acetaldehyde (2–60%) and 2-butenal conversion (2–60%) show that sequential condensation reactions of acetaldehyde and self-addition reactions of 2-butenal account for the majority of 2-MB and 4-MB products formed, respectively (0.35–0.87 kPa reactant, 1 kPa C_2H_5OH, balance H_2, 548 K, 1.67 Ca/P). The predominant product of 2-butenal self-condensation is 2,4,6-octatrienal (>95%), which demonstrates that the nucleophilic attack of the deprotonated γ-C to the carbonyl-C of 2-butenal is the preferred reaction pathway under these conditions. Once formed, 2,4,6-octatrienal undergoes intramolecular dehydrocyclization to form 2-MB products. The viability of two previously proposed pathways to 4-MB products by 2-butenal self-condensation (nucleophilic attack of γ-C toward β-C,[27] or attack of the α-C to the carbonyl-C[33]) were tested using reactant mixtures that included different combinations of 2-butenal, 2-butenol, and 3-methyl-2-butenal. Comparisons of the product selectivities and formation rates between reactions of pure 2-butenal streams (0.05 kPa C_4H_6O, balance H_2, 548 K, 1.67 Ca/P) and those measured for mixtures with 2-butenol (0.025 kPa C_4H_6O, 0.025 kPa C_4H_7OH, balance H_2, 548 K, 1.67 Ca/P) suggest that nucleophilic attack of γ-C toward β-C occurs infrequently. Analysis of the products formed by self-condensation of 3-methyl-2-butenal, which gave only two major products, demonstrates that all products form by either nucleophilic attack of the α-C or γ-C toward the carbonyl-C. Moreover, 4-MB products do not form by the Diels–Alder (DA) reaction between ethylene and 2,4-hexadienal, because the rates for DA (measured in independent experiments: 0.1 kPa C_6H_8O, 2 kPa C_2H_4, 548 K) are approximately four orders of magnitude lower than either those for acetaldehyde and 2,4-hexadienal cross-addition or 2-butenal self-addition. Collectively, these results indicate that self-condensation reactions of 2-butenal by nucleophilic attack from the α-C position toward the carbonyl-C are the most plausible route to form 4-MB products. Overall, these findings provide a complete description of the reaction network that produces 2- and 4-MB species from acetaldehyde over HAP and show that the isomeric distribution among C_8 products depends, in part, on the relative rates of nucleophilic attack of α- or γ-carbon of 2-butenal derived carbanions to the carbonyl of 2-butenal.

Results and Discussion

Formation of 2- and 4-MB Products from Acetaldehyde

Figure 1 shows that 2-butenal is the primary product of the aldol condensation of acetaldehyde and that 2-butenal remains the most abundant product until the conversion of acetaldehyde reaches ≈40% (0.35 kPa C_2H_4O, 1 kPa C_2H_5OH, 99 kPa H_2, 548 K), which agrees with prior investigations.[26–28]

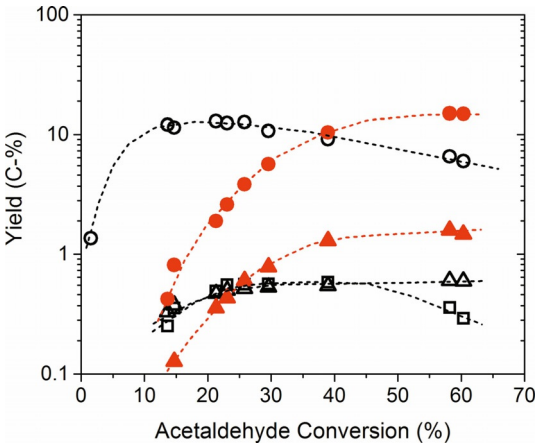


Figure 1. Product yields of sequential acetaldehyde condensation reactions (○: 2-butenal, △: 2,4-hexadienal, □: 2,4,6-octatrienal, red ●: sum of 2-MB=O and 2-MB-OH, red ▲: sum of 4-MB=O and 4-MB-OH) as a function of acetaldehyde conversion (0.35 kPa C_2H_4O, 1 kPa C_2H_5OH, 99 kPa H_2, 548 K) over HAP. Dashed lines in the figures are meant to guide the eye.

The yield of 2-butenal decreases with increasing conversion of acetaldehyde (for conversions greater than 15%), because secondary condensation reactions, which form C_6 and C_8 enal products, consume 2-butenal. First, aldol condensation of acetaldehyde to 2-butenal gives 2,4-hexadienal and subsequent condensation of acetaldehyde to 2,4-hexadienal produces 2,4,6-octatrienal.[26–28] Once formed, 2,4,6-octratrienal rapidly undergoes electrocyclization and dehydrogenation to produce 2-MB=O.[26] The combined yield for 2-MB=O and the analogous alcohol (2-methylbenzalcohol, 2-MB-OH) increases monotonically throughout the entire acetaldehyde conversion range (Figure 1), which suggests that the 2-MB products effectively terminate the sequence of condensation reactions.[26,27] The combined yields of 4-MB=O and the accompanying alcohol (4-methylbenzalcohol, 4-MB-OH) increase simultaneously, however, the 4-MB products cannot form by cyclization reactions of 2,4,6-octatrienal. Thus, other reaction pathways must

be responsible for 4-MB production. Besides the 2-MB and 4-MB products and their intermediates, other C_4–C_6 alcohols and aldehydes (e.g., 1-butanol, 1-hexanol, butyraldehyde) form as side products via direct (e.g., the Meerwein-Ponndorf-Verley (MPV) reaction) or indirect, surface-mediated H-transfer from ethanol.[26] Notably, the Ca-HAP catalyst and reaction conditions used here do not dehydrogenate C–C bonds of small oxygenates,[7,26] and therefore, saturated aldehydes and alcohols do not reform the enes or enals needed to create aromatic products.[29,30]

Figure 2 shows that the ratio of the concentrations of the 2-MB products to that of the 4-MB products (β) increases with acetaldehyde conversion with little dependence on the

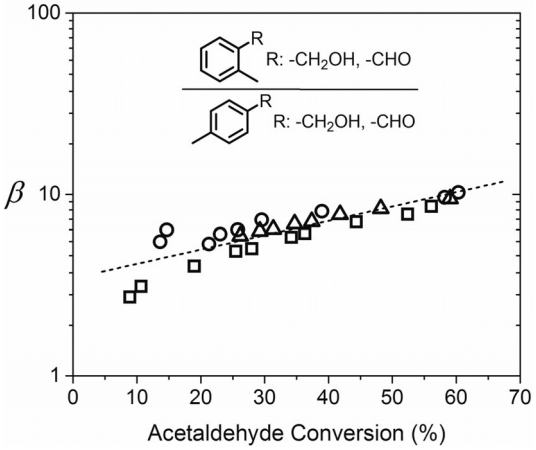


Figure 2. Ratio of 2- and 4-MB products (β) as a function of acetaldehyde conversion formed with different acetaldehyde pressure (○:0.35 kPa C_2H_4O, △:0.56 kPa C_2H_4O, □:0.87 kPa C_2H_4O) over HAP catalyst (1 kPa C_2H_5OH, 99 kPa H_2, 548 K). The dashed line is included to guide the eye.

pressure of acetaldehyde (0.35, 0.56, or 0.87 kPa C_2H_4O, 1 kPa C_2H_5OH, 99 kPa H_2, 548 K) and does not depend on the initial acetaldehyde pressure. The changes in β values suggest that pathways that form 2- and 4-MB products involve different combinations of reactive intermediates formed in situ, because the β value would not otherwise appear as a single value function of the acetaldehyde conversion. The increasing of β value shows that the ratio of the formation rates of 4-MB to 2-MB are greatest at the lowest acetaldehyde conversions, which suggests that the formation of 4-MB products involves the self-condensation reaction of 2-butenal rather than the cross-condensation of acetaldehyde and 2,4-hexadienal.[26–28,31–33]

Scheme 1 depicts the potential reaction pathways to form 2- and 4-MB products over HAP catalyst. The pathway to form 2-MB=O involves sequential aldol condensations (*AC*) of acetaldehyde with enals to form 2,4,6-octatrienal and subsequent aromatization over HAP catalyst (Scheme 1, black arrows), as described previously.[26] Changes in product selectivities with acetaldehyde conversion (Figures 1 and 2) and previous mechanistic proposals[26–28,31–33] are consistent with the formation of 2- and 4-MB=O by self-condensation of 2-butenal (red arrows in Scheme 1), but other pathways may also contribute. For example, 4-MB products may also form by cross-reaction of C_2 and C_6 intermediates, such as by the Diels–Alder reaction (Scheme 1, blue arrows). The relative rates and details of these potential C_4 self-condensation and C_2–C_6 cross-addition pathways are described in the following sections.

Formation of 2-MB and 4-MB products from 2-Butenal

Figure 3 shows the selectivity to each product as a function of 2-butenal conversion (2–60%), and the initial selectivities (extrapolated to zero conversion) and their changes reveal the sequence of steps that form each product. 2,4,6-Octatrienal has

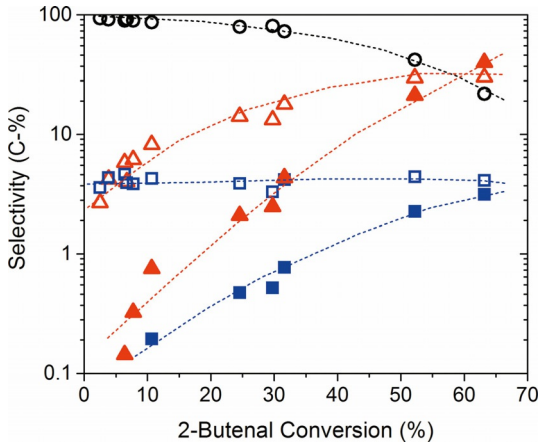
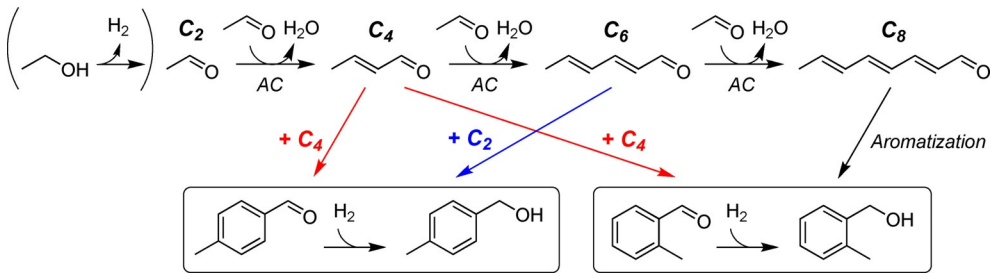


Figure 3. Product selectivity of self-condensation reaction of 2-butenal (○: 2,4,6-octatrienal, red △: 2-MB=O, red ▲: 2-MB-OH, blue □: 4-MB=O, blue ■: 4-MB-OH) as a function of 2-butenal conversion (0.35 kPa C_4H_6O, 1 kPa C_2H_5OH, 99 kPa H_2, 548 K) over HAP catalyst. The dashed lines are included to guide the eye.



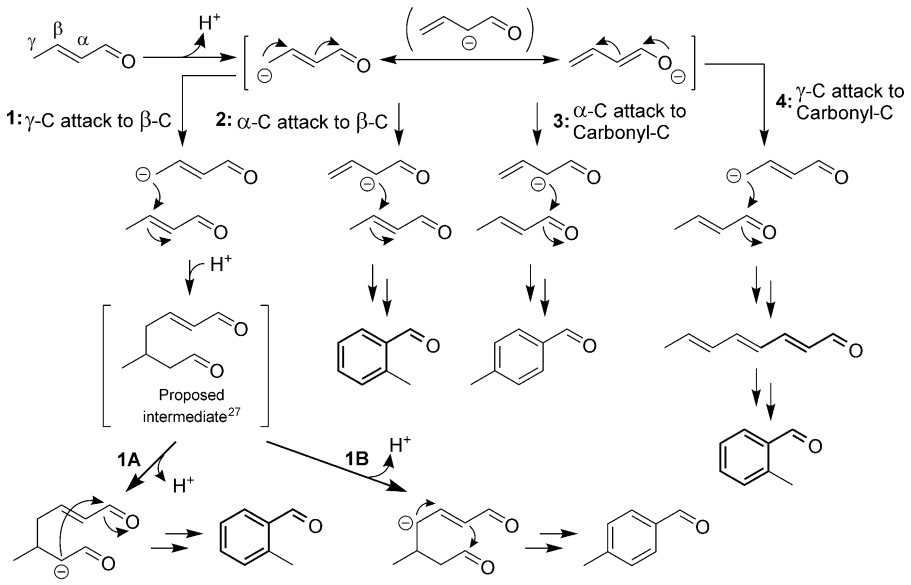
Scheme 1. Possible reaction pathways including sequential aldol condensation (AC) reaction and subsequent aromatization of 2,4,6-octatrienal to form 2-MB products (black arrows), self-addition of 2-butenal to form 2- and 4-MB products (red arrows), and cross-addition of 2,4-hexadienal and a C_2 reactant to form 4-MB products (blue arrow).

significant selectivities (>95%) at the lowest conversions, which suggests that 2,4,6-octatrienal is a primary product of 2-butenal self-condensation. The selectivity to 2,4,6-octatrienal decreases as that for 2-MB=O and 2-MB-OH increases, which together with reported mechanisms for dehydrocyclization reactions,[29,30] strongly suggests that the 2-MB products form as secondary products from 2,4,6-octatrienal. Furthermore, the higher selectivity of 2-MB=O compared to 2-MB-OH within the lower range of conversion (0–50%) shows that 2-MB-OH forms from 2-MB=O via H-transfer steps that likely use ethanol as a hydrogen donor (e.g., the MPV reaction).[26] Overall, these data (Figure 1 and Figure 3) together with results from our previous study investigating sequential reactions of acetaldehyde[26] provide a nearly complete description of the series of reactions that form 2-MB=O primarily by cyclization of 2,4,6-octatrienal, which is produced by either the cross-aldol condensation between acetaldehyde and 2,4-hexadienal or by self-condensation of 2-butenal. The details of the reaction mechanism for the latter are described in the following section.

Figure 3 shows also that the self-condensation of 2-butenal appears to form 4-MB=O (initial selectivity of 4%) as a primary product. Yet this must occur in a rapid sequence of steps, because no well-accepted elementary step would form multiple C–C bonds and simultaneously eliminate both H_2O and H_2. Previous studies have proposed several different mechanisms[26–28,31–33] for the formation of 4-MB=O that proceed through distinctly structured, highly-unstable acyclic intermediates that readily react (e.g., by dehydrocyclization) to form 4-MB=O. To the best of our knowledge, neither our group, nor others, have been able to directly detect these intermediates during reactions on heterogeneous catalysts, and thus the mechanism for 2-butenal self-condensation for this step may be any one (or combination) of the multiple pathways proposed.[27,31–33] The 4-MB-OH species forms as a secondary product likely by H-transfer reactions that hydrogenate the carbonyl of 4-MB=O at rates comparable to those that form 4-MB=O, which is consistent with selectivities to 4-MB=O that are nearly constant across the full range of conversions (Figure 3). In the following section, we test several hypothesized mechanisms and propose the most plausible 4-MB=O formation pathway on HAP.

Two Potential Routes to Form 4-MB Products

Scheme 2 summarizes four possible pathways for the nucleophilic addition of carbanions (formed by deprotonation of 2-butenal) to a second molecule of 2-butenal that form intermediates capable of producing 2-MB and 4-MB structures after intramolecular C–C bond formation steps. Deprotonation of 2-butenal occurs preferentially at the γ-C rather than other C-atoms,[27,31,33] owing to the stabilizing effects of the formed allyl anion resonant structure and the difficulty of deprotonating at other C-atoms. However, within the pool of resonant structures whose formation is facilitated by the conjugated π-bonds, the negative charge can reside at multiple C-atoms or the O-atom.[27] The carbonyl-C is the most electrophilic carbon in 2-butenal (as a result of the electronegativity of the O-atom),[27] and therefore, the carbonyl-C is a likely position for nucleophilic attack. The β-C is the other possible electrophilic position and may undergo nucleophilic attack to form a C–C bond.[27] A comparison of the results of previous investigations shows that the predominant position for nucleophilic addition depends strongly on the reaction conditions, reactants, and catalysts and must be determined for each different combination of these variables.[26–28,31–33] Scheme 2 shows four routes in which C–C bonds form by addition of the two most probable



Scheme 2. Four potential 2-butenal self-addition reaction pathways: four types of nucleophilic attack of resonant anion structures to another 2-butenal (1: from γ-C to β-C, 2: from α-C to β-C, 3: from α-C to carbonyl-C, 4: from γ-C to carbonyl-C). Route 1 includes two parallel pathways (1A and 1B) to form 2-MB=O and 4-MB=O, respectively, formed via a common intermediate.[27]

nucleophiles (γ-C or α-C) to the two most electrophilic positions within 2-butenal (β-C or carbonyl-C).

Route 1 (Scheme 2) involves C–C bond formation between γ- and β-C and has been recently proposed as a pathway that can form 2- (Route 1A) but also 4-MB (Route 1B) products via a common intermediate (5-methylhept-2-enedial) after C–C bond formation and subsequent dehydrocyclization.[27] The routes 1A and 1B differ on which carbon the further deprotonation of the intermediate proceeds.[27] Route 2 (Scheme 2) forms a C–C bond between α- and β-C of 2-butenals and proceeds via an unstable intermediate (2-ethylidene-3-methyl-glutaraldehyde), which was only observed directly during 2-butenal addition reactions over TMBAF at mild conditions (reaction at room temperature over the course of two days).[31] The final pathway that may form 4-MB products involves C–C bond formation between α- and carbonyl-C (Route 3, Scheme 2) and was proposed by Kurokawa.[33] Route 4 (Scheme 2), C–C bond formation between γ- and carbonyl-C, forms 2,4,6-octatrienal.[27] Among potential 2-butenal self-condensation routes, 4-MB products likely form by either Route 1, Route 3, or both. These two pathways differ in both the position of anionic function within deprotonated 2-butenal (γ- or α-C) and in the location of the nucleophilic attack (β-C or carbonyl-C).

Pathways to Form 4-MB Products from 2-Butenal

The reactivity of distinct carbon positions within the C_4 chain in 2-butenal differ significantly from those in 2-butenol and 3-methyl-2-butenal as a consequence of the hydrogenation of the carbonyl and the addition of the methyl group, respectively. Therefore, a comparison of the product selectivities from self- and cross-addition reactions of these three species provides insight to the most plausible pathway(s) that form 4-MB species.

Figure 4 shows that the steady-state 2-butenal consumption rate over HAP catalyst is approximately 0.6 $\mu mol\, g_{catal}^{-1}\, s^{-1}$ (0.35 kPa C_4H_6O, 100 kPa H_2, 548 K), and the rate of 2-butenol consumption is more than two orders of magnitude lower at similar conditions (0.35 kPa C_4H_7OH, 100 kPa H_2, 548 K). The products formed during 2-butenol conversions include 2-butenal, 2,4,6-octatrienal, and the 2- and 4-MB species. The last three products form in ratios that closely resemble the product distribution obtained from 2-butenal. The significantly lower reaction rate together with the similarity of the products suggest that 2-butenol simply dehydrogenates to form 2-butenal (similar to dehydrogenation of ethanol to acetaldehyde during the Guerbet reaction)[7] over HAP catalyst, which subsequently undergoes self-condensation. Furthermore, self-addition of 2-butenol without dehydrogenation to form 2-butenal should undergo only two possible parallel pathways (nucleophilic attack from α- or γ-C of deprotonated 2-butenol to β-C of another 2-butenol, Scheme S1) owing to the lack of a carbonyl group. These reactions would form acyclic diols (5-methylhept-2-ene-1,7-diol and 3-methyl-2-vinylpentane-1,5-diol, Scheme S1) as final products; however, neither of these products was observed. These results suggest that, under our reaction conditions, self-condensation of 2-butenol does not contribute significantly to the formation of 2- and 4-MB products.

Figure 5 shows the differences between the formation rates of 2- and 4-MB products measured during reaction of pure 2-butenal (0.08 kPa C_4H_6O, 1 kPa C_2H_5OH, 100 kPa H_2) and during reaction of an equimolar mixture of 2-butenal and 2-butenol (0.08 kPa C_4H_6O, 0.08 kPa C_4H_7OH, 0.92 kPa C_2H_5OH, 100 kPa H_2), and the ratio of the formation rates of each MB-OH to MB=O products (Γ) over HAP catalyst at 548 K. The identity of the products detected at these two conditions are identical (2,4,6-octatrienal, 2- and 4-MB products, Figure S2), and no new terminated products were observed. If the two reactants are co-fed, in addition to the self-condensation of 2-butenal (while the self-condensation of 2-butenol does not likely occur as shown in Figure 4), the deprotonation of 2-butenol followed by its attack to 2-butenal may contribute to the formation of 2- and 4-MB-OH products (Scheme 3). The complete absence

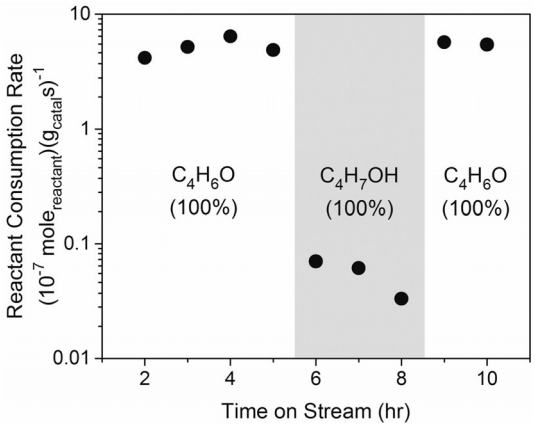


Figure 4. Comparison of the rates for the consumption of 2-butenal and 2-butenol by self-addition reactions (0.35 kPa C_4H_6O or C_4H_7OH, 100 kPa H_2) over HAP catalyst at 548 K as a function of time on stream.

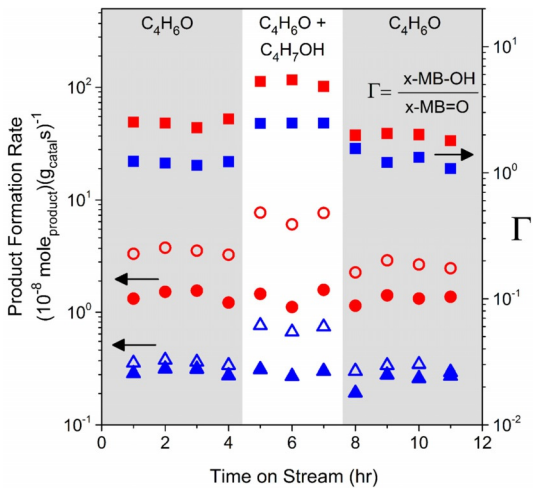


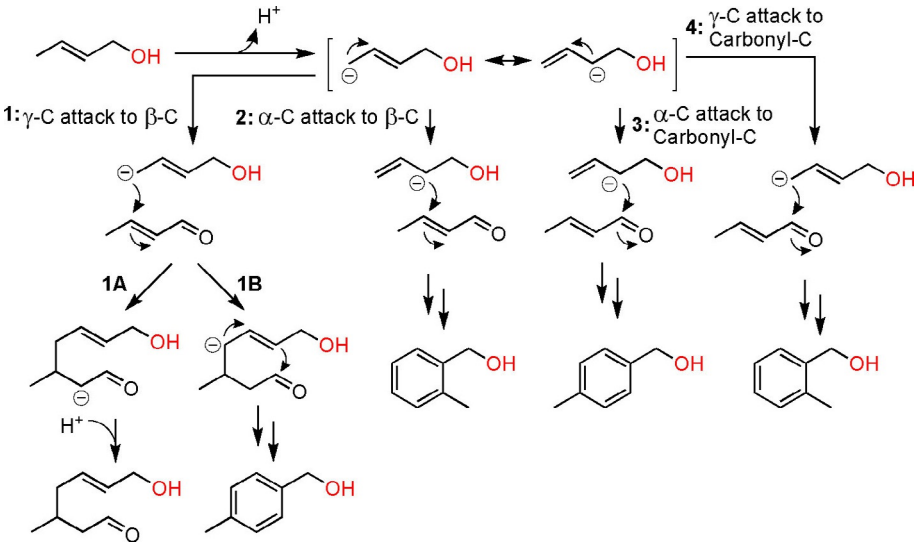
Figure 5. Product formation rate (red ●: 2-MB=O, red ○: 2-MB-OH, blue ▲: 4-MB=O, blue △: 4-MB-OH) from pure 2-butenal (0.08 kPa C_4H_6O, 1 kPa C_2H_5OH, 100 kPa H_2) and mixture of 2-butenal and 2-butenol (0.08 kPa C_4H_6O, 0.08 kPa C_4H_7OH, 0.92 kPa C_2H_5OH,100 kPa H_2), and the ratio of the formation rate of MB-OH to MB=O, Γ, (red ■: 2-MB-OH over 2-MB=O, blue ■: 4-MB-OH over 4-MB=O) over HAP catalyst at 548 K as a function of time on stream.

of the distinct and stable terminated products (7-hydroxy-5-methylhept-2-enal and 5-hydroxy-3-methyl-2-vinylpentanal, Scheme S2) that would form by the cross-reaction pathways suggests that enals formed by deprotonation of 2-butenal do not attack 2-butenol to form C–C bonds.

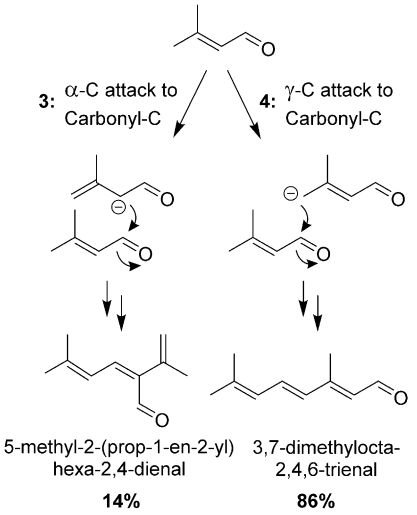
Figure 5 shows that the 2- and 4-MB-OH product formation rate (Figure 5, open symbols) nearly double when 2-butenol is introduced, while formation rates of MB=O species did not change (Figure 5, filled symbols). If 2- and 4-MB-OH products are formed via hydrogenation of 2- and 4-MB=O products,[26] the formation rates of MB=O and MB-OH products would likely be proportional to one another, and Γ would not change. However, Figure 5 shows clearly that the value of Γ increases by a factor of two when feeding the mixture, which suggests that a fraction of the 2- and 4-MB-OH species may form by a parallel pathway that involves deprotonation of 2-butenol (or the corresponding surface alkoxide) and its addition to 2-butenal by pathways depicted in Scheme 3. Four nucleophilic attack routes are possible (which are similar to those in Scheme 2) and the final products are 2- and 4-MB-OH species or an acyclic compound (7-hydroxy-3-methylhept-5-enal), which would be the terminal product formed via route 1 A (Scheme 3). Notably, we do not observe any features in GC or GC-MS data that could correspond to 7-hydroxy-3-methylhept-5-enal, and therefore we conclude that it does not form.

Route 1 has been proposed to occur over several catalysts previously.[27,31–33] Within route 1, the dominant pathway is generally accepted to form 2-MB products (route 1A, Scheme 2).[31–33] Resasco et al. experimentally observed products formed by both routes 1 A and 1 B and used density functional theory (DFT) calculations to show that the deprotonated intermediates involved in route 1 B are energetically more stable (in the gas-phase) than those in 1 A.[27] Based on these findings, nucleophilic attack of an enolate (formed here from 2-butenol) to the β-C of 2-butenal (route 1, Scheme 3) would form both an acyclic (route 1 A) and a cyclic (route 1 B) product. The lack of any detectable quantity of the acyclic product (7-hydroxy-3-methylhept-5-enal) or any new products at all (Figure S2) during these cross-addition experiments (Figure 5), suggests that route 1 A is inactive on HAP. This observation suggests (indirectly) that route 1 B also does not occur, because the previous work always found that ratio of the rates of route 1 A to route 1 B ranged from 0.2 to 4.[27] In addition, hard-soft acid-base (HSAB) theory suggests that C–C bonds are unlikely to form between the γ-C of 2-butenol (route 1B, Scheme 3) or 2-butenal (route 1 B, Scheme 2) (i.e., hard bases), and the β-C of 2-butenal (i.e., a soft acid), as a result of the mismatch of the Lewis acid-base pair.[34] Rather, HSAB theory would indicate that C–C bonds are more likely to form between the γ-C (route 4, Scheme 3) or α-C (route 3, Scheme 3) of 2-butenol, and the carbonyl-C of 2-butenal (i.e., a hard acid). These arguments are also consistent with the fact that the carbonyl-C is more electrophilic than the β-C of 2-butenal (as expected) during self-condensation reactions over the HAP catalyst. Thus, the analysis of the data in Figures 4 and 5, in conjunction with HSAB theory, strongly suggests that nucleophilic attacks from γ-C (route 4) and α-C (route 3) toward carbonyl-C atoms are most likely involved in the formation of 2-MB and 4-MB species, respectively, and C–C bond formation at the β-C (i.e., routes 1 A and 1 B) occurs rarely.

Further support for these implications (i.e., the greater probability of C–C bond formation between the γ-C or α-C, and the carbonyl-C) is given by the product distribution obtained following self-addition reactions of 3-methyl-2-butenal (0.18 kPa C_5H_8O, 100 kPa H_2) over HAP catalyst at 548 K. Scheme 4 depicts the plausible pathways that form the two predominant products, which were identified as 5-methyl-2-(prop-1-en-2-yl)hexa-2,4-dienal and 3,7-dimethylocta-2,4,6-trienal, based on GC-MS analysis and GC retention times (Figure S4 with detailed discussion). The deprotonation of 3-methyl-2-butenal gives resonant structures that resemble those for 2-butenal (Scheme 2), and these structures would enable nucleophilic attack from either the γ-C (Route 4, Scheme 4) or the α-C (Route 3, Scheme 4). Conveniently, the



Scheme 3. C–C bond formation pathways by cross-addition involving deprotonation of C-atoms within 2-butenol and addition to 2-butenal.



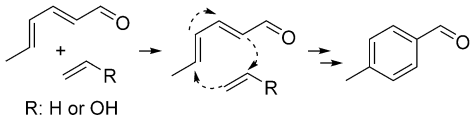
Scheme 4. Self-addition of 3-methyl-2-butenal and formation of 5-methyl-2-(prop-1-en-2-yl)hexa-2,4-dienal and 3,7-dimethylocta-2,4,6-trienal (14% and 86% in selectivity, respectively.

final products remain as acyclic C_{10} enals and can be detected directly, because the methyl group on β-C also frustrates dehydrocyclization of these species. The two products observed (5-methyl-2-(prop-1-en-2-yl)hexa-2,4-dienal and 3,7-dimethylocta-2,4,6-trienal) exactly match those expected to form by the attack of nucleophilic α-C (route 3) or γ-C atoms (route 4) to the carbonyl-C. Notably, no products originating from C–C bond formation with β-C were observed, which further supports the assertion that routes 1A and 1B are inactive. Admittedly, C–C bonds are less likely to form at the β-C, as the methyl group sterically hinders nucleophilic attack, but the additional methyl group is not likely to completely prevent this reaction pathway from proceeding if it was active for self-addition of 2-butenal. Therefore, routes 3 and 4 seem likely to occur during self-condensation of 2-butenal.

Collectively, product formation rates and selectivities from reactions of 2-butenal (Figures 3, 4, and 5), 2-butenol (Figures 4 and 5, Scheme 3), and 3-methyl-2-butenal (Scheme 4, Figure S4) strongly suggest that the dominant pathways to form 4- and 2-MB products from self-addition of 2-butenal on HAP catalysts (Scheme 2) involve the nucleophilic attack of the α-C and γ-C, respectively, to the carbonyl-C (routes 3 and 4).

Potential of Diels–Alder Chemistry to Form 4-MB via Cross-addition of C_2 and C_6 Reactants

The Diels–Alder (DA) reaction between C_6 and C_2 reactants may also contribute to 4-MB product formation rates. The DA reaction is well-known to occur within other biomass upgrading schemes[1] (e.g., *p*-xylene production from 2,5-DMF and ethylene),[35,36] and the DA reaction may occur between 2,4-hexadienal (a diene) formed by sequential addition reactions of acetaldehyde (Figure 1) and C_2 reactants containing C=C bond (i.e., dienophiles such as ethylene and vinyl alcohol) that form in situ by dehydration and tautomerization reactions. DA reaction between these species would directly form cyclic



Scheme 5. Diels–Alder type reaction of 2,4-hexadienal and C_2 intermediates (allyl alcohol or ethylene) to form 4-MB=O.

products, and subsequent dehydrogenation or dehydration reactions could contribute to the 4-MB=O observed (Scheme 5).

Figure 6 shows apparent reaction rate of aldol-type reaction between C_2–C_6 enals and acetaldehyde (0.1 kPa reactant, 0.35 kPa C_2H_4O, 1 kPa C_2H_5OH, 100 kPa H_2) and that of DA reaction between 2,4-hexadienal (C_6) and ethylene (0.1 kPa C_6H_8O,

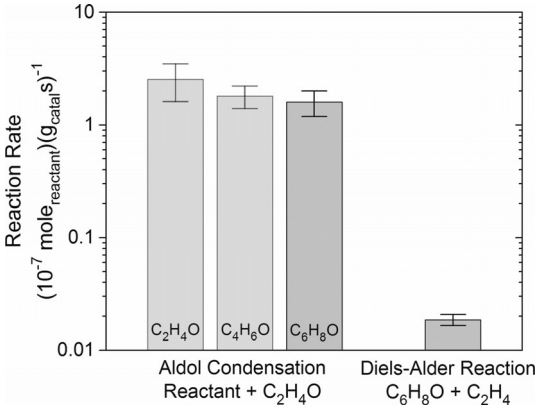


Figure 6. Reaction rates of aldol condensation of C_2–C_6 enals and acetaldehyde (0.1 kPa reactant, 0.35 kPa C_2H_4O, 1 kPa C_2H_5OH, 100 kPa H_2) and DA reaction of 2,4-hexadienal and ethylene (0.1 kPa C_6H_8O, 2 kPa C_2H_4, 99 kPa H_2) over HAP catalyst at 548 K.

2 kPa C_2H_4, 99 kPa H_2) over HAP catalyst at 548 K. The apparent rate for DA reaction with ethylene is two orders of magnitude lower than that for aldol condensation with acetaldehyde, even at an ethylene co-reactant pressure 50–100 times greater than that obtained in situ when feeding pure ethanol streams (5 kPa C_2H_5OH, 96 kPa H_2, 573 K).[7] DA reactions frequently use high reactant pressures (3–7 MPa) to drive the reaction forward.[35,36] However, the concentrations of ethylene and vinyl alcohol here are very low, because the selectivity toward ethylene over the HAP catalyst is small (less than 4% at 10% conversion of ethanol)[7] and tautomerization of acetaldehyde is highly unfavorable ($\Delta G = 59\ kJ\ mol^{-1}$ at 548 K).[26] Rates for DA reactions over heterogeneous catalysts are frequently found to be proportional to the concentration of ethylene,[37,38] therefore, the apparent rate constant for the DA reaction could be estimated (roughly) to be three to four orders of magnitude smaller than for aldol condensation in this system. Consequently, the DA reaction is not likely to contribute significantly to the formation of 4-MB at the reaction conditions used here. Other possible DA reactions, such as addition of 1,3-butadiene and 2-butenal to form 2-MB products, are also unlikely based on the combination of extremely low 1,3-butadiene concentrations and the expectation that the ap-

parent rate constants would be similar in value to those for DA between C_6 and C_2 species.

Conclusions

In the present study, the detailed formation pathways of 2- and 4-MB products from acetaldehyde were investigated over HAP catalyst using the combination of product analysis and rate measurements. Scheme 6 summarizes the proposed 2- and 4-MB=O formation routes. The 2-MB products are formed mostly via dehydrocyclization of 2,4,6-octatrienal, which is formed via either sequential aldol condensation of acetaldehyde with 2,4-hexadienal or self-condensation of 2-butenal. On the other hand, the 4-MB products are mostly formed from a highly reactive acyclic intermediate created by self-addition of 2-butenal via nucleophilic addition of α-C to the carbonyl-C. The plausible carbon positions, among which C–C bonds form, were investigated by using 2-butenol and 3-methyl-2-butenal as model C_4 reactants, which have limited reactivities on specific carbons as a result of the lack of a carbonyl group and the presence of a methyl group, respectively. The DA reaction between C_2 and C_6 reactants does not contribute to measured rates of C_8 aromatic formation, because this pathway proceeds at a rate several orders of magnitude slower than those involving aldol or Michael addition reactions. These findings provide a complete view of the reaction network that produces 2- and 4-MB species from acetaldehyde over HAP catalyst, which may be a useful strategy to produce high volume monomers (terephthalic acid and phthalic anhydride) from renewable resources.

Experimental Section

The Ca-HAP catalyst with a Ca/P ratio of 1.67 was purchased from Acros Organics (Lot: A0333466). The powders were pelletized, crushed, and sieved to obtain Ca-HAP agglomerations with diameters of 230–560 μm. Aldehyde condensation and aromatization reactions were conducted using a U-shaped, tubular glass reactor with a packed-bed configuration. The reactor was placed in a vertically-aligned temperature-controlled tubular furnace (National Element, FA-120). The temperature of the catalyst bed was controlled by a PID controller (Watlow, EZ-ZONE) connected to a variable transformer. The Ca-HAP catalysts were treated in situ by heating at 10 K min^{-1} to 773 K and holding for 2 h under He flow (20 cm^3 min^{-1}) to remove adsorbed water and other molecules (e.g., CO_2) before measuring catalytic rates. Flow rates of H_2 (SJ Smith, 99.999%) and C_2H_4 (SJ Smith, 10% C_2H_4 in He) were set by mass flow controllers (MFC, Porter, 601 series). Liquid phase reactants (ethanol, Decon Pure Ethanol 200 proof, 100%; acetaldehyde, Fluka, 99.5%, crotonaldehyde, predominantly *trans*, Sigma–Aldrich, 99%; crotyl alcohol, mixture of *cis* and *trans*, Sigma–Aldrich, 96%; *trans-trans*-2,4-hexadienal, Sigma–Aldrich, 95%; and 3-methyl-2-butenal, Sigma–Aldrich, 97%) were introduced using a syringe pump (KD Scientific, Legato 110) and were vaporized inside the 1/4" stainless steel transfer lines, which were heated to >473 K using electrical heating tape. Liquid acetaldehyde and ethanol were combined within one of the syringes and were fed as a mixture (25–50 mol% C_2H_4O). The flow rates of all reactants were controlled to maintain the intended partial pressures of each reactant species and to obtain the desired reactant conversions during experiments. The total pressure of the system was maintained at 101 kPa by co-feeding H_2, which decreases the rate of catalyst deactivation during condensation reactions of oxygenated species.[26]

The identity and concentrations of reactants and products in the reactor effluent stream were measured using a gas-chromatograph (GC, Agilent 6850) equipped with a capillary column (DB-WAX, 30 m×0.25 mm×0.25 μm) and a flame ionization detector (FID). The retention time for each component was determined using standard chemicals (*o*-tolualdehyde, Sigma–Aldrich, 97%; *p*-tolualdehyde, Sigma–Aldrich, 97%; 2-methylbenzyl alcohol, Sigma–Aldrich, 98%; 4-methylbenzyl alcohol, Sigma–Aldrich, 98%), and the molecular speciation of these and heavier products was confirmed using a gas-chromatograph mass-spectrometer (GC-MS, Shimadzu, QP2010 Ultra). Rates were measured at conversions of the limiting reactant which were less than 15% (and more frequently at conversions less than 10%) to identify primary reaction pathways and to ensure that depletion of reactants across the bed had a minimal influence on measured rates. Aldol condensation rates are calculated by dividing the conversion of the reactant aldehydes by the residence time. Selectivities are reported based on moles of carbon of the products (C-%).

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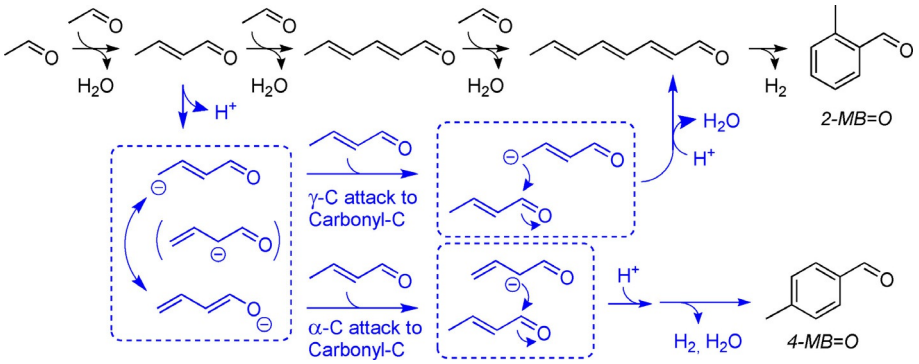

Scheme 6. Proposed 2- and 4-MB=O formation pathways including (black arrows) sequential aldol condensation and aromatization of 2,4,6-octatrienal to form 2-MB=O, (blue arrows) self-addition of 2-butenal to 2,4,6-octatrienal and 4-MB=O.

Keywords: bioethanol upgrading · crotonal · hydroxyapatite · reaction mechanism · tolualdehyde

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