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Insights into Ethanol Coupling over Hydroxyapatite using Modulation Excitation *Operando* Infrared Spectroscopy

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Abstract: The coupling of biomass-derived ethanol to *n*-butanol is a topic of contemporary interest. Indeed, *n*-butanol can not only be used as a higher energy-density fuel additive, it is also a key component in perfumes and serves as a solvent for paints and dyes. Hydroxyapatite (HAP) emerged in the literature as a promising catalysts for this transformation, with *n*-butanol selectivity reaching ~75% at 10% ethanol conversion. However, the molecular-level mechanism for this reaction is still unclear and several mechanistic questions remain unanswered. Here, we use diffuse reflectance infrared Fourier Transform spectroscopy, coupled with mass spectrometry following a modulation excitation approach (ME-DRIFTS-MS) that enables us to better understand the dynamic processes involved. Our approach allows for a vibrational characterization of the active surface species and the formulation of a consistent mechanism. Based on our experimental observations, Ca^{2+}/OH^- can be put forward as the main active site for the aldol condensation. POH/OH^- acid-base pair is proposed as the active site for the Meerwein-Ponndorf-Verley (MPV) direct hydrogen transfer of the aldol condensation product, crotonaldehyde.

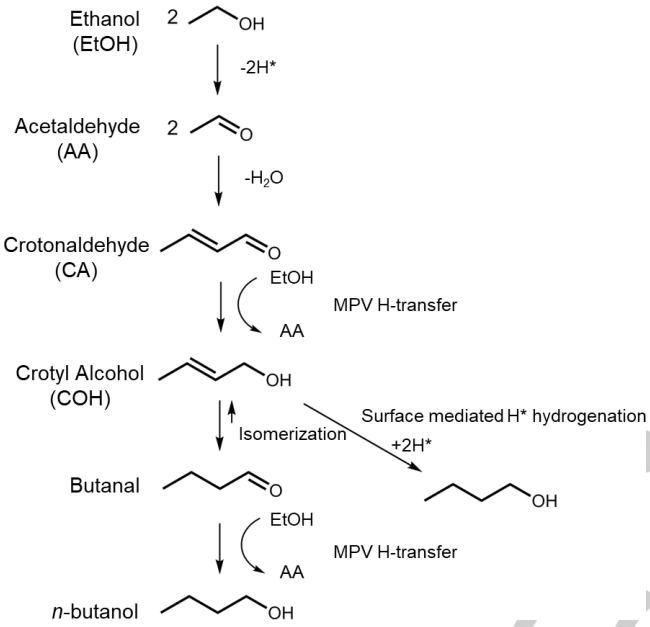
Introduction

With the increased corn-based bio-ethanol production in the United States, the catalytic upgrading of ethanol to more valuable chemicals such as higher alcohols and alkenes has drawn renewed interest. Special attention is geared towards *n*-butanol – the simplest upgrading product, formed from condensation of two ethanol molecules – because of its wide range of applications such as a fuel additive, a solvent, and additive in perfumes, amongst others.[1] When used as a fuel additive, *n*-butanol is superior to ethanol because of its higher energy density, and the fact that it is less corrosive and less water soluble.[2] The conventional petrochemical route for synthesizing *n*-butanol is hydroformylation of propylene to butanal, and the subsequent hydrogenation of butanal to *n*-butanol. The hydroformylation process to synthesize *n*-butanol requires high pressures and uses homogeneous cobalt, rhodium, palladium, or ruthenium catalysts,[3] which are expensive and create separation issues. Hence, there exists an interest to explore alternative approaches to produce *n*-butanol under milder conditions using heterogeneous catalysts, and preferably starting from a biomass-derived feedstock. The Guerbet reaction offers one attractive alternative route for producing *n*-butanol from ethanol through C-C bond formation and hydrogenation.[4]

Several heterogeneous catalysts have been investigated for the Guerbet reaction including metal oxides, zeolites, hydroxyapatite, and supported metals.[5] Those studies indicate that hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAP) shows promising conversion (10%) and selectivity toward *n*-butanol (75%) under atmospheric condition because of its favorable acid-base properties.[6] The widely accepted description of the reaction involves four main steps as depicted in Scheme 1.[4b, 5a, 6b, 7] Ethanol first dehydrogenates/oxidizes into acetaldehyde, followed by acetaldehyde self-aldol condensation. Under the reaction conditions, the aldol addition product dehydrates very rapidly to form crotonaldehyde. Crotonaldehyde is then transformed to crotyl alcohol in a first hydrogenation. Finally, crotyl alcohol is converted to *n*-butanol through a second hydrogenation. This reaction pathway has been established using conventional kinetics and steady-state isotopic transient kinetic analysis (SSITKA). The latter revealed that acetaldehyde, obtained from ethanol dehydrogenation, remains on the surface to undergo consecutive reactions to generate *n*-butanol.[8] However, there is still a debate on the second hydrogenation step from crotyl alcohol to *n*-butanol. Two different hydrogenation pathways have been suggested in the literature and are summarized in Scheme 1. The first pathway is a surface-mediated hydrogenation of the C=C bond of crotyl alcohol, where the surface hydrogen comes from ethanol dehydrogenation in the first step.[9] In an alternative mechanism, crotyl alcohol first isomerizes and tautomerizes to butanal. The C=O can then be directly hydrogenated by ethanol *via* the Meerwein-Ponndorf-Verley (MPV) reaction to form *n*-butanol.[10] We propose to take another approach to investigate ethanol coupling over HAP to clarify the second hydrogenation step and gain a deeper understanding of the reaction mechanism in general that could potentially benefit future catalyst design.

Ho *et al.* reported Ca-O species to be responsible for ethanol dehydrogenation and direct hydrogen transfer, while the self-aldol condensation of acetaldehyde is proposed to occur on CaO/PO_4^{3-} as an acid-base pair as identified in CO_2 titration experiments.[10a] On the other hand, the OH^-/POH acid-base pair was suggested to be the active site for ethanol coupling over HAP by applying the amphoteric probe molecule, acetylene, using IR spectroscopy.[11] Hill *et al.* also investigated

the surface sites on HAP using CO_2, pyridine, acetylene, and glycine adsorption, and found that it is possible to have Ca^{2+} and POH as acid sites and OH^- as a basic site on HAP.[12] Recently, Ca^{2+}/OH^- and POH/OH^- were reported as acid-base pairs responsible for ethanol dehydrogenation and aldol condensation, respectively, by using *operando* DRIFTS measurement.[13] Although there are already various studies that point out the importance of the acid-base pair on HAP during ethanol coupling to *n*-butanol, the role of the specific sites on HAP during each step, including hydrogenation, is still unclear. Therefore, direct spectroscopic evidence from *operando* experiments is needed to elucidate the relationship between each step and surface site.



Scheme 1. Generally accepted pathways of ethanol coupling to *n*-butanol over hydroxyapatite (HAP), MPV stands for Meerwein-Ponndorf-Verley reaction.

Here, we investigate ethanol coupling to *n*-butanol over hydroxyapatite (HAP) using diffuse reflectance infrared Fourier transform spectroscopy coupled with mass spectrometry (DRIFTS-MS) to simultaneously monitor the surface species and the product distribution in the gas phase.[14] In addition, we use modulation excitation (ME) to intensify the signal for active species and enhance the signal-to-noise ratio.[15] Moreover, by operating with phase-sensitive detection (PSD), the spectroscopic signatures of consecutive reaction intermediates can be revealed in the phase-domain, providing micro-kinetic information.[16] Our *operando* DRIFTS-MS with ME experiments show spectroscopic evidence to support the generally accepted reaction mechanism of ethanol coupling over HAP *via* the Guerbet pathway. In addition, Ca^{2+}/OH^- pair sites are proposed as main active site for aldol condensation and POH/OH^- pair sites are proposed to be responsible for Meerwein-Ponndorf-Verley (MPV) direct hydrogen transfer for hydrogenation. Spectroscopic evidence for the isomerization of crotyl alcohol supports direct hydrogen transfer as the second hydrogenation step during ethanol coupling. Interactions between surface species and different reaction intermediates are discussed to guide further catalyst design for ethanol upgrading.

Results and Discussion

In this work we use modulation excitation (ME) with diffuse reflectance infrared Fourier Transform spectroscopy coupled with mass spectrometry (DRIFTS-MS). Modulation excitation spectroscopy works similarly to a lock-in amplifier which is used to enhance the signal-to-noise ratio and extract the desired signals from noisy condition.[16-17] The same concept can also apply to a spectroscopic technique by periodically perturbing the system with one variable such as reactant concentration, temperature, pressure, or radiation.[15a] When a catalytic system is perturbed under quasi steady-state conditions, reaction intermediates will oscillate with the same frequency. After averaging several periods, the signal from active species will be enhanced while the spectator species will not respond to the stimulation and can thus be easily distinguished. In addition, the signal-to-noise ratio will increase because of the averaging. Moreover, by operating with phase sensitive detection (PSD) to transform from time-domain to phase-domain, different active species will show distinct phase-delays compared to the starting reactant. These different phase shifts contain kinetic information.

The transmission IR spectrum of the commercial HAP sample dehydrated at 600°C is shown in Figure S1. The peak at 3572 cm^{-1} corresponds to the columnar hydroxyl group (OH^-) on HAP. The band at 3648 cm^{-1} is attributed to bulk POH group; 3674 and 3706 cm^{-1} correspond to surface POH site which coincide with previous reports. The combination bands and overtone of P-O feature can also be observed at 2200-1900 cm^{-1}. The bands between 1550 and 1250 cm^{-1} are attributed to carbonate species.[10a, 18] The wavenumbers of POH peaks discovered here are slightly higher than in the literature. Although the recording temperature may affect the IR peak position, the room temperature HAP reference IR spectrum (Figure S1) is similar to a previous study.[18b] In *operando* condition, we recorded the IR spectra at 330°C compared to 350°C in previous report.[13] Given the closeness of the recording temperatures, we attribute POH peak position discrepancies mainly to the higher dehydration temperature (600°C) in this study. The X-ray diffraction pattern is presented in Figure S2 and is identical to previous literature and shows no signs of impurities.[10a]

Modulation experiments with ethanol

We first introduce the starting reactant, ethanol, to the system to understand the formation of reaction intermediates. Before starting the modulation experiment, HAP was treated under pure Ar flow and heated to 330 °C, followed by periodic switching between ethanol and pure Ar. The outlet is monitored by mass spectrometry. The chosen m/z values correspond to unique MS fragments of each intermediate and product and some signals are scaled for better reading (Figure 1a). When ethanol is introduced into the system, the signals from the reaction intermediates and product such as acetaldehyde (m/z=44), crotyl alcohol (m/z=57), and *n*-butanol (m/z=56) can be observed. During ethanol coupling, 1,3-butadiene (m/z=54) occurs as the side product obtained *via* the dehydration of crotyl alcohol by Lewis acid site on HAP.[12] Only trace amounts of butanal (m/z=72) and crotonaldehyde (m/z=70) are observed, implying that hydrogenation of the carbonyl group on both species occurs rapidly. The product distribution (*i.e.* the selectivity) is in line with a previous kinetic study.[10a]

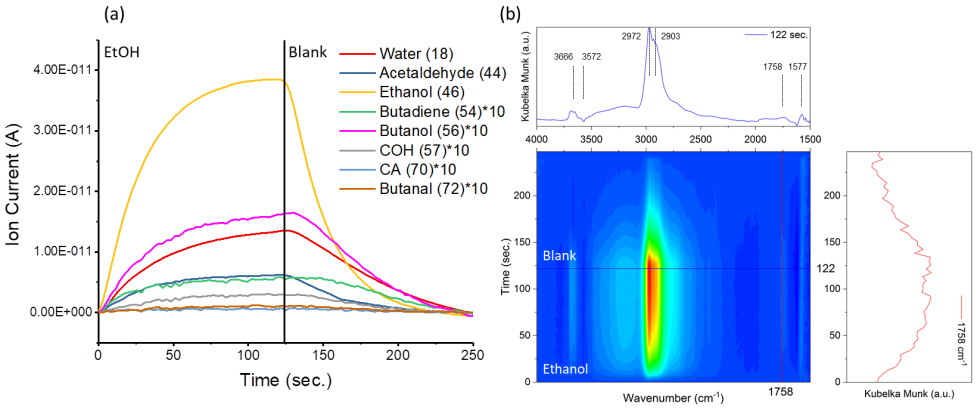


Figure 1. Modulation experiment between ethanol (5.0%) in Ar and pure Ar (20 mL min^{-1}) over 5 mg hydroxyapatite (HAP) at 330°C, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas (a) selected m/z signals from mass spectrometry response (b) Time-domain DRIFT spectra and the line at 122 sec. indicates gas channels switch.

In the first half period of the experiment, the surface is covered by ethanol as indicated by the features at 3666, 2972, 2933 and 2903 cm^{-1} for υ(O-H), υ(CH_3, asymmetric stretching), υ(CH_2, asymmetric stretching), and υ(CH_3, symmetric stretching), respectively (Figure 1b). This observation corroborates the conclusion of a previous study that shows high ethanol coverage on HAP comparing to MgO at reaction temperature by using steady-state isotopic kinetic transient analysis (SSITKA).[8] Aside from the intense ethanol signals in the spectra, a small band at 1758 cm^{-1} indicates the formation of acetaldehyde, an intermediate in ethanol coupling following the Guerbet pathway. In contrast, a band at 1577 cm^{-1} corresponds to aromatic coke acting as spectator species that does not respond to the modulation, showing the capability of modulation excitation to discriminate active and spectator species. Moreover, to the best of our knowledge, acetaldehyde has not been directly observed before in ethanol coupling using *in-situ* spectroscopy. The intensity of columnar hydroxyl group (OH^-) at 3572 cm^{-1} on HAP[18b, 19] (Figure S1) decreases during the reaction (Figure 1b) suggesting an interaction of ethanol with the OH^-. The importance of the columnar hydroxyl group is supported by a previous kinetic study which shows that HAP($Ca_{10}(PO_4)_6(OH)_2$) with OH^- is more selective to *n*-butanol than beta-tricalcium phosphate (β-$Ca_3(PO_4)_2$) and fluoride-substituted phosphate ($Ca_{10}(PO_4)_6F_2$),[20] since the OH^- group could be responsible for base-catalyzed aldol condensation.

Modulation experiment with ethanol/acetaldehyde and ethanol

To investigate the aldol condensation reaction, we added acetaldehyde to the reagent stream while keeping the ethanol concentration constant at 2.5%. The HAP surface was first saturated with 2.5% ethanol in Ar and the background was taken before starting periodic modulation in which the first half period was ethanol/acetaldehyde with 3:1 molar ratio and ethanol was maintained at 2.5% in the feed. After averaging and operating phase sensitive detection (PSD) for five periods of MS responses and DRIFT spectra, the changing signals are attributed to the perturbation by acetaldehyde. The response MS signals show an enhancement for the aldol condensation product, crotonaldehyde (m/z=70) (Figure 2a). The result is in line with previous observations that the rate of C-C bond formation increases linearly with co-fed acetaldehyde.[9] In addition to the increase of crotonaldehyde, other intermediates and side products including butanal (m/z=72), crotyl alcohol (m/z=57) and 1,3-butadiene (m/z=54) are observed. The final product, *n*-butanol (m/z=56), appears with 17 seconds time-delay in the gas phase compared to acetaldehyde and other intermediates, suggesting that desorption of product may be slow over HAP.

The time-domain infrared spectra show a negative peak at 2980 cm^{-1} indicating partial desorption and/or reaction of surface-bound ethanol. The other significant peaks in the C-H region at 2736, 3026, and 2960 cm^{-1} correspond to acetaldehyde, crotyl alcohol, and *n*-butanol, respectively, showing a sequential time-delay in each species, which is in line with the proposed Guerbet pathway (Figure 2b). Notably, the co-fed acetaldehyde (2736 cm^{-1}) can be first seen at 8 sec. and the consecutive intermediate crotyl alcohol (3026 cm^{-1}) appears at 25 sec. suggesting aldol condensation and direct hydrogen transfer from ethanol *via* Meerwein-Ponndorf-Verley (MPV) pathway proceed rapidly. The strong signal at 1761-1720 cm^{-1} is due to υ(C=O) from gas phase acetaldehyde. The emergence of a feature at 1645 cm^{-1} corresponding to υ(C=C) from the aldol product, crotonaldehyde, shows a time-delay compared to υ(C=O) from acetaldehyde. The features from the other intermediate butanal are barely observed in the IR spectrum, which could be attributed to the fast desorption and/or reaction, or they are hindered by peaks from acetaldehyde, as there is a notable amount of crotonaldehyde (m/z=70) and butanal (m/z=72) in the MS response (Figure 2a). The decreasing signal of columnar hydroxyl group at 3572 cm^{-1} indicates that the OH^- group may behave as basic site to abstract α-hydrogen on acetaldehyde to form the enolate for aldol condensation.

By using phase-sensitive detection (PSD), phase-domain IR spectra show three distinct species in the C-H region: acetaldehyde with a phase delay of 10° (or 7 s) at 2736 cm^{-1}, crotyl alcohol with a phase delay of 40° (or 28 s) at 3026 cm^{-1}, and *n*-butanol with a phase delay of 70° (or 49 s) at 2960 cm^{-1} (Figure 3). We emphasize that the phase delay is corrected by 30° due to the inherent dead volume of the DRIFTS cell and

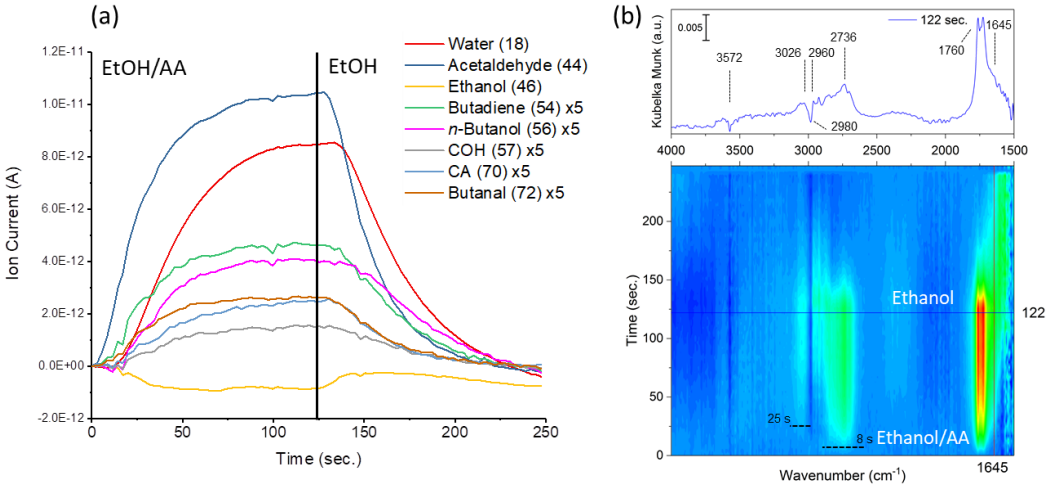


Figure 2. Modulation experiment between ethanol (2.5%)/AA with 3:1 molar mixture in Ar as carrier gas and ethanol in Ar over 5 mg hydroxyapatite (HAP) at 330°C, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas. (a) selected m/z signals from mass spectrometry response (b) Time-domain DRIFT spectra and the line at 122 sec. indicates gas channels switch.

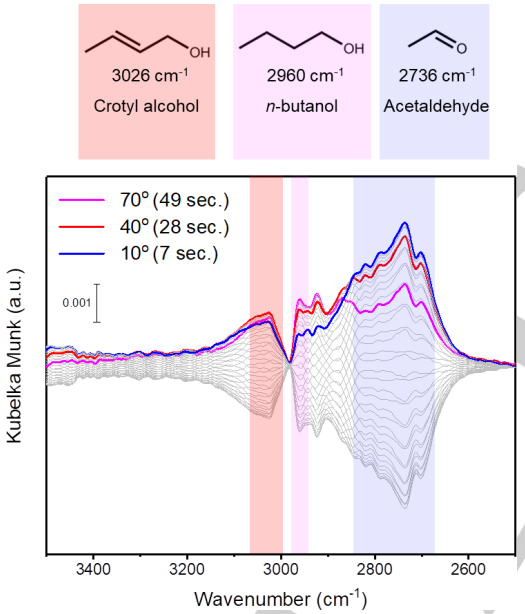


Figure 3. Phase-sensitive detection (PSD) DRIFT spectra in C-H region with modulation experiment between ethanol (2.5%)/AA with 3:1 molar mixture in Ar as carrier gas and ethanol in Ar flow over 5 mg HAP, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas. The phase-delay at 10° corresponds to acetaldehyde, 40° correlates to crotyl alcohol, and 70° indicates *n*-butanol. A full period (250s) is identical to 360°.

that phase delays of various species should therefore only be used relative to one another. The observed consecutive reaction intermediates and product agree with the generally accepted hypothesis that ethanol coupling to *n*-butanol on HAP at 330°C proceeds *via* the Guerbet pathway.

Modulation experiment with ethanol/crotonaldehyde and ethanol

To study the role of crotonaldehyde and hydrogenation products such as crotyl alcohol, butanal, and *n*-butanol, we co-fed crotonaldehyde with ethanol as described previously for acetaldehyde. In the experiment shown in Figure 4a, HAP was first equilibrated in ethanol feed, followed by periodically switching to a 3:1 molar ratio ethanol/crotonaldehyde flow. In the gas phase, acetaldehyde (m/z=44) increases dramatically when crotonaldehyde is co-fed. Crotyl alcohol (m/z=57), butanal (m/z=72) and *n*-butanol (m/z=56) are enhanced as well. The increased production of acetaldehyde in the beginning of first half period indicates that direct hydrogen transfer from ethanol to crotonaldehyde occurs rapidly. An undesired side product, 1,3-butadiene (m/z=54) also increases with co-fed crotonaldehyde, suggesting dehydration of crotyl alcohol may compete with the further hydrogenation step. Moreover, *n*-butanol (m/z=56) and water (m/z=18) appear with 11 seconds time-delay in the MS response, implying slow desorption from the HAP surface.

A similar result can also be seen in the time-domain IR spectra, (Figure 4b) where υ(C=O) from acetaldehyde emerges as a side band at 1758 cm^{-1} at the beginning, along with the υ(C-H) for crotyl alcohol at 3026 cm^{-1} with co-fed crotonaldehyde, indicating MPV hydrogen transfer is fast. More importantly, the *n*-butanol signal at 2960 cm^{-1} persists into the second half period when crotonaldehyde is removed from the feed, which is in line with MS response that the desorption rate of *n*-butanol is slow. In the phase-domain IR spectra, the co-fed crotonaldehyde can be observed at 2730 and 2815 cm^{-1} with 10° (7 s) phase delay, while crotyl alcohol appears at 3026 cm^{-1} with 40° (28 s) phase delay. The final product, *n*-butanol, can be seen at 2960 cm^{-1} with 70° (49 s) phase delay (Figure S7).

This result mirrors the behavior we observed earlier when modulating between ethanol/acetaldehyde and ethanol. The phase-domain IR spectra demonstrate that the aldol condensation product subsequently undergoes hydrogenation to form *n*-butanol. Although several studies show that the C=O

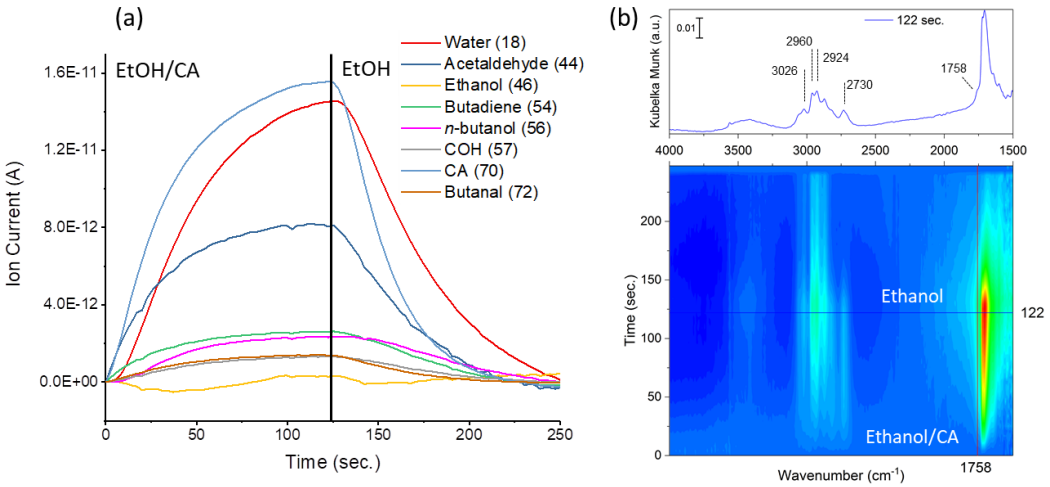


Figure 4. Modulation experiment between ethanol (2.5%)/CA with 3:1 molar mixture in Ar as carrier gas and ethanol in Ar over 5 mg hydroxyapatite (HAP) at 330°C, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas. (a) selected m/z signals from mass spectrometry response (b) Time-domain DRIFT spectra and the line at 122 sec. indicates gas channels switch.

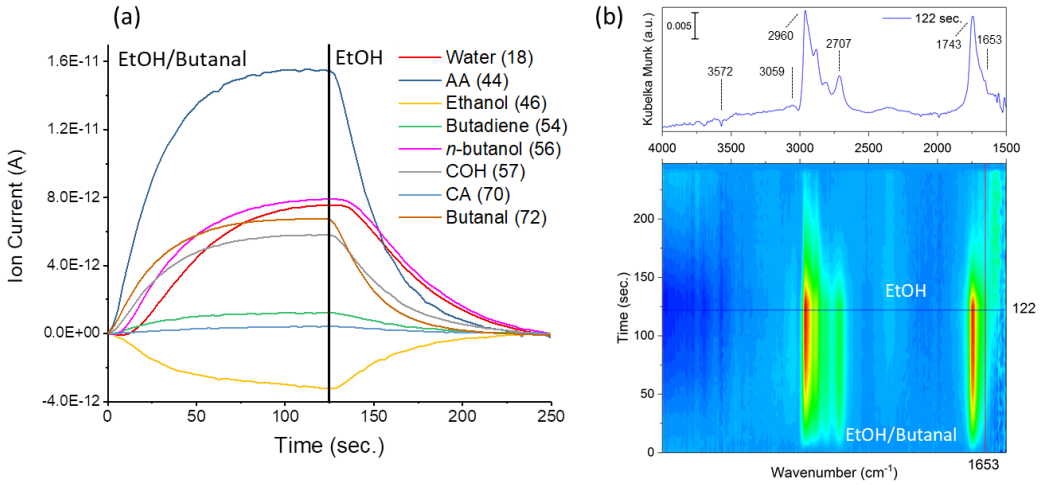


Figure 5. Modulation experiment between ethanol (2.5%)/butanal with 3:1 molar mixture in Ar as carrier gas and ethanol in Ar over 5 mg hydroxyapatite (HAP) at 330°C, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas. (a) selected m/z signals from mass spectrometry response (b) Time-domain DRIFT spectra and the line at 122 sec. indicates gas channels switch.

on crotonaldehyde will be hydrogenated by MPV direct hydrogen transfer from ethanol to form crotyl alcohol, the mechanism of the second hydrogenation step is still not well understood. Indeed, the hydrogenation can occur either to the C=C bond of crotyl alcohol through a surface-mediated pathway[9] or it can occur at the C=O bond of butanal, which is isomerized from crotyl alcohol, through the MPV direct hydrogen transfer from ethanol to obtain *n*-butanol[10] (Scheme 1). In a subsequent ME experiment, we perturbed the system with crotyl alcohol and butanal in order to obtain insights into this second hydrogenation step.

Modulation experiment with ethanol/crotyl alcohol and ethanol

When crotyl alcohol is co-fed into the system during ethanol coupling, the dehydration side products, 1,3-butadiene (m/z=54) and water (m/z=18), increase directly in MS response. On the other hand, the desired product, *n*-butanol (m/z=56), increases slightly compared to 1,3-butadiene when co-feeding crotyl alcohol (m/z=57) into the system (Figure S8a). The enhancement of 1,3-butadiene could be due to the moderate Lewis acidic site on HAP[11-12] which favors the dehydration pathway under crotyl alcohol co-feed condition. Interestingly, while 1,3-butadiene seems to increase with crotyl alcohol addition, the final product, *n*-butanol, does not increase substantially. This difference in response suggests that, *n*-butanol could predominately come from MPV direct

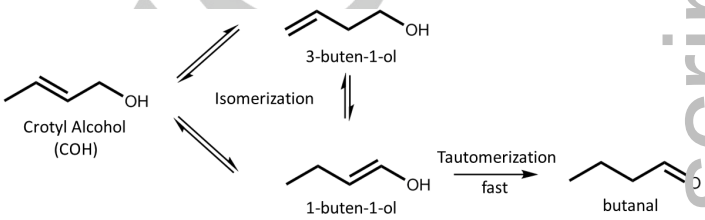
hydrogenation of C=O on butanal, obtained from crotyl alcohol isomerization; hydrogenation on C=C of crotyl alcohol through surface mediated hydrogen seems unlikely.

In the time-domain IR spectra (Figure S8b), crotyl alcohol becomes the dominant surface species on HAP with several significant features at 3026, 2923, 2879, 1676 cm^{-1}, in-line with the MS response that the increased ethanol in the first half period is due to competitive adsorption with crotyl alcohol (*viz,* ethanol desorbs from HAP surface because of the addition of crotyl alcohol). The competitive adsorption can explain the inhibition of direct hydrogen transfer due to a lower abundance of ethanol on the HAP surface, therefore enhancing the dehydration on Lewis acidic sites. The evidence for 1,3-butadiene from dehydration of crotyl alcohol can also be observed at 1817 cm^{-1}. As a result, ethanol coupling over HAP at high crotyl alcohol concentration tends to undergo the dehydration pathway due to Lewis acidity on HAP[20] and competitive adsorption with ethanol.

Modulation experiment with ethanol/butanal and ethanol

When co-feeding butanal during ethanol coupling over HAP, the MS responses show that *n*-butanol (m/z=56) increases dramatically as a main product and the ethanol (m/z=46) signal decreases in the first half period, indicating that direct hydrogen transfer from ethanol to butanal occurs rapidly (Figure 5a). The result implies that *n*-butanol stems from butanal as the last reactive intermediate by direct hydrogen transfer. The sacrificial ethanol will then dehydrogenate to acetaldehyde and subsequently undergo self-aldol condensation to crotonaldehyde which can be hydrogenated by direct hydrogen transfer to finish the autocatalytic cycle. This finding supports a previous study which stated that acetaldehyde is generated mainly from direct hydrogen transfer and ethanol is mainly a hydrogen source for direct hydrogen transfer.[10b] Furthermore, there is no significant increase in crotonaldehyde (m/z=70), rendering further support for the fast hydrogenation of C=O to crotyl alcohol (m/z=57) which we can clearly observe in MS response.

In the time-domain IR spectra, the peaks at 2960 cm^{-1} correspond to υ(C-H) from *n*-butanol which remains on the surface into the second half period compared to butanal at 2707 and 1743 cm^{-1} (υ(C-H) and υ(C=O), respectively) (Figure 5b). The slow desorption of *n*-butanol can also be observed in the MS response, where *n*-butanol (m/z=56) shows a time-delay of 6 seconds relative to the introduction of butanal. Although there is only a trace amount of crotonaldehyde observed in MS response, the peak at 1653 cm^{-1} might be the evidence of υ(C=C) in crotonaldehyde surface species from self-aldol condensation of acetaldehyde coming from direct hydrogen transfer. Interestingly, a peak appears at 3059 cm^{-1} during the butanal co-feed experiment with a 25 seconds time-delay compared to the signal from butanal. This vibrational feature is too high a frequency for υ(=C-H) in crotyl alcohol, but similar to the terminal alkene υ(=CH_2) signal in 1-butene.[21] Thus, the emergence of the peak at 3059 cm^{-1} could correspond to 3-buten-1-ol having terminal alkene feature from crotyl alcohol isomerization (Scheme 2). However, the other isomer, 1-buten-1-ol, cannot be found in the IR spectra; the less stable isomer, 1-buten-1-ol, will most likely undergo fast tautomerization to butanal. This finding supports that isomerization and tautomerization can occur on the HAP surface to generate butanal which can be further hydrogenated by direct hydrogen transfer to *n*-butanol. Although it has been suggested that the isomerization can occur on basic sites or Ca-O sites on HAP surface,[10a] there has been no spectroscopic support for the hypothesis. Here, the peak at 3059 cm^{-1} observed in IR spectra corresponds to a crotyl alcohol isomer with a higher frequency feature corresponding to a terminal alkene υ(=CH_2). Furthermore, because of the poor dehydrogenation ability of HAP,[10b] the main source of acetaldehyde may come from direct hydrogen transfer (Scheme 1); thus, the second hydrogenation most likely proceeds *via* the MPV direct hydrogenation pathway. Besides dehydrogenation of ethanol to obtain the very first acetaldehyde to proceed the reaction, the trace amount of dissolved O_2 in ethanol may also cause oxidation of ethanol to acetaldehyde, since there are barely redox properties on HAP compared to transition metal catalysts.



Scheme 2. Isomerization pathway for crotyl alcohol to butanal.

Modulation experiment with crotonaldehyde and ethanol

To better understand the hydrogenation process, we first saturated the HAP surface and reached steady state in an ethanol feed and subsequently switched to crotonaldehyde feed without ethanol. Before switching to the crotonaldehyde flow, ethanol is the predominant surface species on HAP. After switching to crotonaldehyde flow, acetaldehyde and C_4 intermediates such as crotyl alcohol and butanal increase immediately as well as *n*-butanol, indicating that direct hydrogen transfer from ethanol occurs rapidly (Figure 6a). More importantly, once the surface ethanol is fully consumed by direct hydrogen transfer, the reaction stops at crotyl alcohol and butanal. The final hydrogenation products, *n*-butanol and acetaldehyde stop producing at 30 seconds after switching to the crotonaldehyde feed. Crotyl alcohol formation also reaches its maximum around 40 seconds because of a lack of surface ethanol to hydrogenate crotonaldehyde. It is worth noting that after consuming surface ethanol species, butanal increases slightly until the end of the first half period, while crotyl alcohol slightly decreases at the same time. This finding also indicates that isomerization from crotyl alcohol to butanal takes place on HAP surface.

In the time-domain IR spectra, the negative peaks at 2977 and 2903 cm^{-1} correspond to υ(CH_3, asymmetric stretching), and υ(CH_3, symmetric stretching) from surface ethanol consumption which corroborates the finding that ethanol mostly behaves as a hydrogen donor (Figure 6b). The features from crotonaldehyde at 2815, 2730, 1720, 1697, 1645 cm^{-1} gradually dominate the HAP surface, indicating the reaction stops without adding ethanol. While the bands at 1720 and 1645 cm^{-1} correspond to υ(C=O) and υ(C=C), respectively, from gas phase crotonaldehyde, the emergence of 1697 cm^{-1} could be adsorption of carbonyl group on acid site such as Ca^{2+} or POH. Notably, a band emerges at 3059 cm^{-1} which is similar to the feature in butanal co-feed IR spectra above (Figure 5b),

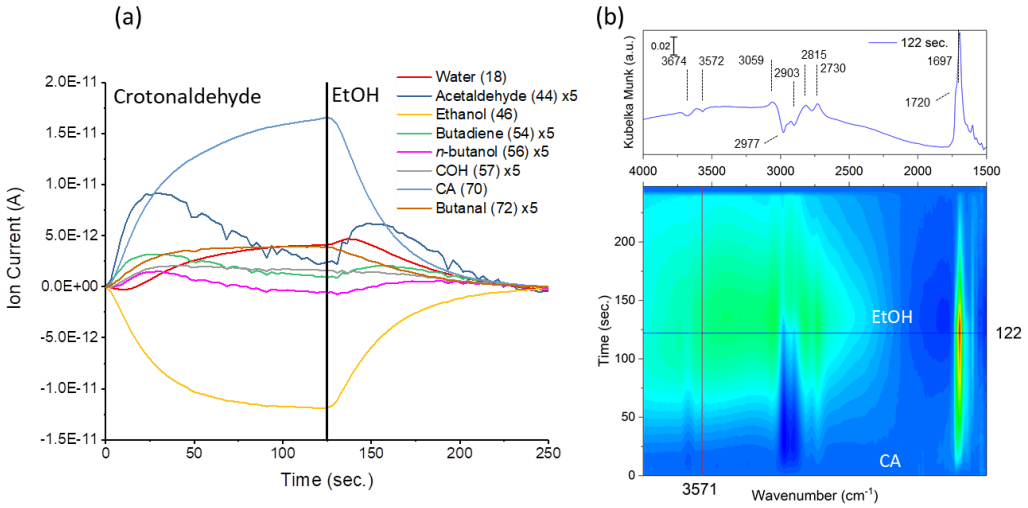
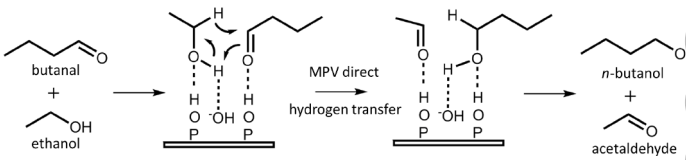


Figure 6. Modulation experiment between CA (0.8%) and ethanol (2.5%) in Ar as carrier gas over 5 mg hydroxyapatite (HAP) at 330°C, the total flow rate for both channel are 20 mL min^{-1} which Ar behaves as balance gas. (a) selected m/z signals from mass spectrometry response (b) Time-domain DRIFT spectra and the line at 122 sec. indicates gas channels switch.

suggesting a terminal alkene-like species which could form from crotyl alcohol isomerization. This inference is supported by the MS responses, as butanal increases while crotyl alcohol decreases once the sacrificial ethanol is consumed. The decreased peaks at 3572 and 3674 cm^{-1} correspond to OH^- and POH on HAP which are likely responsible for direct hydrogen transfer and isomerization. The same decreasing peaks for OH^- and POH can also be found in the butanal co-feed experiment (Figure 5b).

The possible acid and base sites on HAP have been characterized by using pyridine, CO_2, acetylene, and glycine as probe molecules.[11-12] The proposed acid sites are Ca^{2+} and protonated phosphate groups, POH, while the columnar OH^- group is the most significant basic site on the HAP surface. Therefore, Ca^{2+}/OH^- and POH/OH^- acid-base pairs are potential active sites for ethanol coupling over HAP surface. The significant decreased band at 3572 cm^{-1} corresponding to OH^- group on HAP surface in acetaldehyde co-feed experiment, indicates that OH^- is one of the active sites for base-catalyzed aldol condensation (Figure 2b). The importance of OH^- for C-C coupling is further supported by the increased selectivity towards *n*-butanol for HAP compared to calcium phosphate ($Ca_3(PO_4)_2$) without OH^- group.[20] Since we do not observe a significant signal corresponding to the POH group in acetaldehyde co-feed IR spectra, Ca^{2+}/OH^- may likely act as acid-base pair for aldol condensation over HAP. We emphasize that the background of co-feed experiments are collected under standard reaction condition when 2.5% ethanol in the feed at 330°C. Therefore, the changes in the IR and MS spectra are the responses due to the co-feed of different intermediates. When co-feeding butanal and modulating between crotonaldehyde and ethanol (Figure 5b and Figure 6b) there is a decrease in the POH/OH^- acid-base pair signal. This suggests that POH/OH^- is the active site for Meerwein-Ponndorf-Verley (MPV) direct hydrogen transfer. (Scheme 3) The findings corroborate the work by Osman *et al*. where they found no production of *n*-butanol if the POH site has been poisoned.[13]

The isomerization of crotyl alcohol to 1-butene-1-ol can occur on both acid and base site, since Bronsted acid site such as POH can protonate to C=C and subsequently, the adjacent carbon releases a proton to form a new C=C bond to finish isomerization.[21] The basic OH^- site can also isomerize crotyl alcohol to form 1-butene-1-ol. This isomerization is facile over metal oxide catalysts like MgO and CaO.[10a, 22] In the experiment where we feed crotonaldehyde over an ethanol-saturated system, a decreased peak of POH at 3674 cm^{-1} may indicate deprotonation of POH group and a decrease peak at 3572 cm^{-1} suggests the abstraction of hydrogen by the OH^- group to eliminate the columnar hydroxyl group signal (Figure 6b). Therefore, both POH and OH^- can be able to catalyze crotyl alcohol isomerization and the isomer, 1-butene-1-ol, will subsequently tautomerize to butanal and be hydrogenated *via* direct hydrogen transfer to *n*-butanol.



Scheme 3. Meerwin-Ponndorf-Verley (MPV) direct hydrogen transfer on POH/OH^- acid-base pair.

Conclusion

In this study, the mechanism for ethanol coupling to *n*-butanol over HAP is investigated using *operando* DRIFTS-MS with modulation excitation (ME) and phase sensitive detection (PSD). The enhanced signal-to-noise ratio allows us to observe the IR features from intermediates and help to elucidate the mechanism. MS results and the phase-domain spectra show the consecutive formation of reaction intermediates, supporting the Guerbet pathway as the overall mechanism for ethanol coupling over HAP. The phase-domain IR spectra from

acetaldehyde co-feed experiments demonstrate consecutive reaction intermediates during ethanol coupling. The first hydrogenation step in which crotonaldehyde converts to crotyl alcohol is attributed to direct hydrogen transfer from ethanol by the result of crotonaldehyde co-feed experiment. From the result of modulating between crotonaldehyde and ethanol experiment, the emergence of the peak at 3059 cm^{-1} corresponds to terminal-like alkene $\upsilon(=CH_2)$ indicating the appearance of 3-butene-1-ol, the isomer of crotyl alcohol. This finding implies that crotyl alcohol undergoes isomerization and tautomerization to butanal over the HAP surface and the second hydrogenation subsequently occurs on butanal by direct hydrogen transfer to produce *n*-butanol.

We also show that the Ca^{2+}/OH^- acid-base pair may be mainly responsible for aldol condensation based on acetaldehyde co-feed experiment. In addition, direct hydrogen transfer occurs on POH/OH^- acid-base pair, since hydrogen donor, ethanol, can be stabilized on HAP surface on both sites based on ethanol adsorption IR spectrum and *operando* DRIFT spectra. Finally, the active site for isomerization can be either POH or OH^-, because both sites show interaction in modulation DRIFT spectra between crotonaldehyde and ethanol. The competitive adsorption between ethanol and crotyl alcohol suggests that isomerization may be critical for the overall performance, since direct hydrogen transfer occurs rapidly. This puts forward the hypothesis that eliminating the Lewis acid site could avoid the undesired dehydration side-reaction, while increasing the POH and OH^- site density could enhance the isomerization.

Experimental Section

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAP) was purchased from Sigma-Aldrich and was calcined at 600°C with 5°C/min ramp rate for 2 hours under dry air before operating ethanol coupling reaction. Ethanol was dehydrated by molecule sieves (3Å) before using to eliminate the interference in IR spectra.

The modulation excitation DRIFTS-MS setup allows for the introduction and vaporization of liquid substrates, and switching between two different flows, effectively modulating the concentration of reactants during experiment. In short, argon was used as carrier gas and connected to two different mass flow controllers to generate two independent feed. Besides of Ar as carrier gas, Ar is also a balance gas to maintain total flow rate at 20 mL min^{-1}.Two syringe pumps were used to introduce liquids that are evaporated in a heated spiral before reaching an electronically controlled two-position-four-way valve. Depending on the position of this valve, either flow A or B enters into the DRIFTS accessory. The catalyst, HAP, is filled in ta ceramic cup in DRIFTS cell with approx. 5 mg. Finally, the gas-phase composition is monitored with an online mass spectrometer. By periodically switching between flow A and B, the influence of either component on the reaction can be analyzed in a transient manner. A single period of the complete modulation is 250 seconds in this study, unless further mentioned. The detail for ME-DRIFTS-MS setup can be found in previous study.[14]

All IR measurements are collected by a Bruker Vertex 70 spectrometer with mercury cadmium telluride (MCT) detector. Each spectrum is obtained from 64 scans with 8 cm^{-1} resolution and 4 seconds as temporal resolution in modulation experiment. The DRIFTS accessory was purchased from PIKE Technologies (DiffusIR) and approximately 5 mg HAP can be loaded in the ceramic crucible. The m/z responses are obtained from ThermoStar mass spectrometer, Pfeiffer Vacuum, attached on the outlet of DRIFTS accessory. The phase sensitive detection (PSD) transforms the DRIFT spectra from time-domain to phase domain by using the equations as follows.

$$A_k(\varphi_k^{PSD}) = \frac{2}{T}\int_0^T A(t)\sin(k\omega t + \varphi_k^{PSD})\,dt$$

T is the length of a period, ω is the stimulation frequency, ϕ_k is the phase delay, k is the demodulation index (k = 1 in the study), $A(t)$ is the active species response in the time-domain, and A_k is the response in the phase-domain. The transformation to the phase-domain leads to a dependence of the vibrational signals on the phase angle ϕ instead of the time. For example, 250 sec period can be converted to 360°. The analysis of the spectra was processed using MATLAB codes.

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Keywords: modulation excitation spectroscopy • Guerbet reaction • ethanol coupling • hydroxyapatite • butanol • DRIFTS

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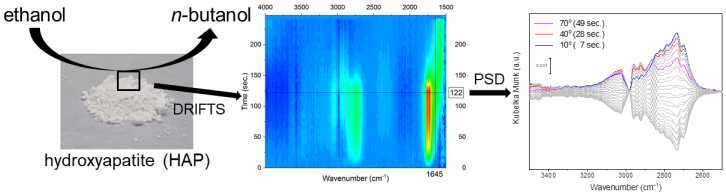

Mechanistic study of ethanol coupling to *n*-butanol over hydroxyapatite is investigated by DRIFTS and mass spectrometry following a modulation excitation approach. The approach confirms the Guerbet pathway and suggests the Ca^{2+}/OH^- acid-base pair as the main active site for aldol condensation and POH/OH^- as the major acid-base pair for direct hydrogen transfer and isomerization.

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