Methyl ketones from carboxylic acids as valuable target molecules in the biorefinery

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The fine chemical 2-undecanone was chosen as model compound and ketonic decarboxylation and reketonization evaluated by Green Chemistry matrices, namely the carbon atom efficiency and the e-factor. The e-factor of the reaction of decanoic acid with acetic acid was less than five and, therewith, in the acceptable range for bulk chemicals, when valorizing acetone (e.g., as a solvent) and considering a 90% solvent recycling. The reketonization of decanoic acid with acetone provided a different main product, namely 10-nonadecanone, with a detrimental effect on atom efficiency.

By means of labeling experiments it was shown that ketonic decarboxylation is significantly faster than the reketonization reaction. The transformation of acetic acid into acetone was studied by in-situ and operando IR spectroscopy. Thereby it was found that the surface was covered by acetic acid. The lack of adsorption of acetone is a clear drawback for the reketonization of carboxylic acids. To improve the reaction outcome, and therewith, its sustainability a possibility has to be found to stabilize the ketone molecules on the surface in the presence of carboxylic acids.

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Methyl ketones from carboxylic acids as valuable target molecules in the biorefinery

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Abstract

For the preparation of methyl ketones, cross Ketonic Decarboxylation, i.e., the formation of a ketone from two different carboxylic acids, and the reketonization, i.e., the transformation of a carboxylic acid into a ketone employing a ketone as alkyl transfer agent, may be interesting alternatives to classical pathways involving metal-organic reagents.

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By means of labeling experiments it was shown that ketonic decarboxylation is significantly faster than the reketonization reaction. The transformation of acetic acid into acetone was studied by \textit{in-situ} and \textit{operando} IR spectroscopy. Thereby it was found that the surface was covered by acetic acid. The lack of adsorption of acetone is a clear drawback for the reketonization of carboxylic acids. To improve the reaction outcome, and therewith, its sustainability a possibility has to be found to stabilize the ketone molecules on the surface in the presence of carboxylic acids.
Methyl ketones are interesting fine chemicals. Methyl ethyl ketone (MEK, butanone) and methyl isobutyl ketone (MIBK, 4-methyl-2-pentanone) are employed as solvents for paints, coatings, adhesives, inks and other applications [1]. Several methyl ketones with a longer, linear second-alkyl chain such as 2-heptanone, 2-octanone, 2-nonanone, 2-undecanone, and 2-tridecanone are commercialized in the fragrance and flavor industry [2]. In addition, 2-undecanone is applied as an insect and animal repellant [3–5].

Applying classical Organic Chemistry, methyl ketones may be produced by the means of metalorganic reagents such as Grignard reagents, reacting carboxylic acid esters with MeMgBr. However, this reaction does not stop at the ketone stage, but goes further to the tertiary alcohol due to double addition of the Grignard reagent [6–11]. To avoid the transformation of the intermediary ketone, a special technique has to be employed: the Weinreb ketone synthesis. In a first step, an amide with N,O-dimethylhydroxylamine has to be prepared that allows only a single addition of the Grignard reagent [12–16]. Such a synthesis pathway is thus possible, but tedious and, in addition, Grignard reagents are not welcome in chemical industry. Special safety requirements have to be adopted due to their reactivity.

The ketonic decarboxylation of two carboxylic acid molecules into a ketone can be considered as an alternative pathway [17]. Thereby, the cross-coupling version with acetic acid and any carboxylic acid leads to methyl ketones. From the two different reactants, three products are obtained: the two homo-coupling products (acetone and a symmetrical ketone involving a longer alkyl chain) and the cross-coupling product (methyl ketone). Therefore, the maximum selectivity towards the methyl ketone is 50% for statistical reasons when the two carboxylic acids are employed in a one to one molar ratio.

It should be noted that neither one of the two extreme cases – exclusive formation of an unsymmetrical ketone, or a mixture of two symmetrical ketones - have been reported in literature. Some acids, which do not have alpha protons, such as pivalic, benzoic acid, etc., are not able to enolize. Therefore, such acids cannot form symmetrical ketones and they are spent entirely for the preparation of a methyl ketone in their reaction with acetic acid. The problem of the cross-ketone selectivity dependence on the ratio of two acids as well as on the type of metal oxide catalyst has been studied in details [18]. Both positive and negative deviations from statistically expected values for the selectivity towards methyl iso-propyl ketone from a mixture of acetic and isobutyrlic acids have been found.

For the reaction between a mixture of two enolizable acids, the selectivity to one of the symmetrical ketones can be reduced while the selectivity to the cross-ketone, such as methyl ketone, can be increased on a purely statistical basis by using an excess of the second acid. From the economical point of view, it may make sense to carry out the reaction with an excess of acetic acid. In general, this carboxylic acid is much cheaper than the higher homologue. Then, the formation of the long chain ketone is suppressed and the formation of the cross-coupling product, i.e., the methyl ketone, is increased together with that of acetone. If only the long-chain carboxylic acid is taken into account for the calculation of the yield, and the acetic acid considered a reactant employed in excess, the yield of the methyl ketone can be significantly increased. The penalty for the improved yield is the coproduction of acetone in excess. This is a clear disadvantage from the sustainability point of view.
A second alternative to produce methyl ketones consists in reacting acetone with carboxylic acids (eq. 1 and 2). This reaction has been first reported in the patent literature in 1989 and recently rediscovered [19,20]. The reaction sequence has been described postulating a 1,3-diketone as key intermediate (eq. 2) and the sequence named “reketonization”. In the first step, acetone is acylated to produce the 1,3-diketone. The latter compounds are known to be prone to cleavage reactions. Hence, surface hydroxyl groups assist this transformation and form part of an adsorbed carboxylate product after the reaction. The selectivity of the decomposition of the diketone is governed by thermodynamic means: the more stable products, i.e., the more substituted ketones, are favored [20].

\[
\begin{align*}
\text{Acetone} + \text{acid} & \rightarrow \text{1,3-diketone} + \text{CO}_2 + \text{H}_2\text{O} \quad \text{(eq. 1)} \\
\text{1,3-diketone} & \rightarrow \text{ketone} + \text{acid} \quad \text{(eq. 2)}
\end{align*}
\]

Taking into account the Green Chemistry principle, the reketonization is an outstanding reaction, provided that the ketonic decarboxylation is also taking place under the reaction conditions. This is quite likely, since reaction conditions and catalyst are identical. Then, the spent reagent is reconverted into fresh reagent (dashed arrow, eq. 2), producing two innocuous by-products, namely one molecule of carbon dioxide and one of water.

Herein, we will compare the production of methyl ketones by ketonic decarboxylation with acetic acid and by reketonization with acetone by Green Chemistry metrics, namely by carbon efficiency and e-factor [21,22]. We will show by isotopic labeling that the ketonic decarboxylation proceeds much faster than the reketonization reaction. Furthermore, we will identify by operando IR spectroscopy a low level of acetone adsorption on surface, under reaction conditions, as a clear impediment to the reketonization reaction.
2. Materials and Methods

2.1 Materials

Monoclinic zirconium oxide was obtained from ChemPur, Germany, as pellets with a surface area of 103–104 m² g⁻¹. Thermal treatment at 650 °C and 750 °C for 6 h (heating rate 3 K/min) provided samples with surface areas of 53.4 m²/g and 35.4 m²/g, respectively [23]. XRD measurements were performed by means of a PANalytical Cubix’Pro diffractometer equipped with an X’Celerator detector and automatic divergence and reception slits using Cu-Kα radiation (0.154056 nm). The mean size of the ordered (crystalline) domains (d) was estimated using the Scherrer equation. The equation can be written as d=(0.9 λ)/(β cosθ), where λ is the X-ray wavelength, β is the line broadening at half the maximum intensity (FWHM), after subtracting the instrumental line broadening, in radians, and θ is the Bragg angle [23]. Nitrogen physisorption isotherms were obtained using a Micromeritics ASAP 2420 analyzer. The metal oxide was out-gassed in vacuum at 400 °C for 12 h prior to the analysis. The Brunauer–Emmett–Teller (BET) method was used to calculate the surface area in the range of relative pressures between 0.01 and 0.20 Pa.

Titanium oxide was also received from ChemPur, Germany, as pellets with a surface area of 149 m²/g. The X-ray diffraction pattern showed that the titanium oxide was crystallized as anatase phase and broad signals were in accordance with surface area measured by nitrogen adsorption (i.e., with the relatively small crystal size). For further information on this material see reference [24]. Cerium oxide was obtained from Aldrich with an average particle size of 43 nm and a BET surface area of 63 m²/g. For further information on this material see reference [25].

2.2 Catalytic reactions

All reactions were carried out in a tubular fixed-bed continuous flow reactor. The set-up has been described in a previous work [26]. The catalyst (1.0 g) was employed as pellets of 0.4 to 0.6 mm, diluted with silicon carbide and a gentle nitrogen carrier gas flow applied during the reaction. The reagents were fed to the reactor by the means of syringe pumps in two different solutions. A solution of decanoic acid (25 wt%) in hexadecane was prepared and introduced with WHSV = 4.29 h⁻¹. Acetic acid was diluted with water, either in a 3 : 1 ratio (wt/wt) or a 7 : 1 ratio (wt/wt), and placed in a second syringe pump. Acetone was diluted with water in a 7 : 1 (wt/wt) and also fed separately from the decanoic acid. At the reactor outlet the liquids were condensed with ice-bath cooling. On standing, the liquid separated into an organic phase (upper layer) and an aqueous phase (lower layer). The aqueous layer was supposed to contain only a very minor amount of product which was not considered for the product balance.

Labeled acetic acid was purchased from Aldrich with a ¹³C content at the 2-position of 99%. For the reaction of labeled acetic acid and non-labeled acetone, the second feed was composed by acetone, acetic acid and water in a 9 : 1 : 3 ratio (wt/wt/wt) and introduced to the reactor at a rate of 8.4 mL/min.

2.3 IR experiments

Interaction with the catalyst surface has been studied by in situ FT-IR spectroscopy of adsorbed acetic acid and acetone. The Fourier transform infrared (FTIR) spectra were recorded at room temperature on a Nicolet Nexus FTIR 5700 spectrometer (Thermo Scientific) equipped with a DTGS KBr detector and an extended KBr beam splitter at a spectral resolution of 4 cm⁻¹.
accumulating 128 scans. The powdered samples were pressed into thin self-supporting pellets of around 10 mg/cm² and placed in a vacuum quartz cell equipped with KBr windows, where they underwent all activation and adsorption treatments. Before the measurements, the samples were activated at 723 K for 1.5 h under high vacuum (p = ~10⁻⁶ mbar) and treated with oxygen (5 min and 22 min) at the same temperature. Known amounts of either acetic acid or acetone were further introduced in the infrared cell using increasing aliquots until surface saturation was reached.

For the IR operando experiments, the catalyst powder was again pressed into a self supported pellet that was further inserted into an IR cell reactor. The so called sandwich cell was then connected to the gas manipulation apparatus, consisting of mass flow controllers and thermoregulated saturator filled with liquid acetic acid. The reaction conditions were set to a total flow rate of 8 mL/min with an acetic acid molar fraction of 3%. The reaction was studied under a heating program specified in Figure S5b. In addition, an IR gas cell (Thermo Scientific Nicolet iS50 GC-IR) allowed the analysis of the gaseous phase leaving the reactor. Infrared spectra (32 scans per spectrum) of both the catalyst and the gas phase were recorded alternately with an acquisition frequency of one spectrum every 87 s by means of a Thermo Scientific Nicolet iS50 FT-IR equipped with an MCT detector.
3. Results and Discussion

3.1 Evaluation of the synthesis of methyl ketones by Green Chemistry metrics

The formation of methyl ketones starting from the carboxylic acid and either acetic acid or acetone should be evaluated employing Green Chemistry metrics, namely by the carbon (atom) efficiency and the environmental e-factor [21,22]. Atom efficiency (including heteroatoms) may be considered a less suitable metric for this reaction because elimination of oxygen, and therewith loss of certain classes of atoms, is desired and welcome in biorefinery. In this evaluation, the main question to be answered is whether the reketonization may outperform the classical ketonic decarboxylation from the ecological point of view under industrially relevant conditions.

The ketonic decarboxylation of carboxylic acid mixtures is a well-studied transformation for mixtures. Standard conditions with monoclinic zirconia were employed to set the benchmark for the reketonization. Water was used as co-feed in two different concentration as it has been observed that it can successfully suppress the aldol condensation reaction[27] that may occur in parallel and consume the acetic acid.

In a fixed-bed continuous-flow reactor two feeds were introduced in parallel, an organic one with decanoic acid (25 wt%) in hexadecane and an aqueous one containing acetic acid and water in a 7 : 1 (wt/wt) or a 3 : 1 (wt/wt) ratio. The feed rates were set at WHSV = 4.29 h⁻¹ and WHSV = 8.90 h⁻¹ for the organic and aqueous one, respectively, to achieve a 1 : 18 molar ratio of decanoic acid and acetic acid. It was found that at a reaction temperature of 400 °C, both, acetic acid and decanoic acid were converted completely. From Figure 1a and Scheme 1, it can be seen that the 2-undecanone desired product was obtained with 85 to almost 90% selectivity in the organic liquid product. Further products were 10-nonadecanone, 2-nonanone, 3,5-dimethyl-1-nonyl-benzene and 1,3-dinonyl-5-methyl-benzene. One molecule of acetic acid is incorporated into the 2-undecanone desired product. However, most of the acetic acid is converted into acetone. The latter is produced with 90% selectivity in the organic liquid (with respect to the acetic acid as starting material; Figure 1b and Scheme 1).

Figure 1. Selectivities in the organic liquid for products derived from a) decanoic acid and b) acetic acid. The reaction was carried out in a fixed-bed continuous-flow reactor and the times refer to time on stream and the ratios, i.e., 3 : 1 and 7 : 1, to the acetic acid to water ratios (wt/wt) in the aqueous feed.
Scheme 1. Ketonic decarboxylation of decanoic acid with acetic acid in a 1:18 molar ratio. Selectivities for 2-undecanone and 10-nonadecanone in the organic liquid were calculated based on decanoic acid as starting material and the selectivities for acetone, mesitylene, dimesitone and 3,5-dimethylphenol from acetic acid.

![Scheme 1 Diagram]

Molar ratio: 1 : 18 : 20

Selectivity%: 6.1 + 85.3

Selectivity%: 90.8 + 1.5 + 1.6 + 0.4

Although the selectivity towards 2-undecanone in the liquid was good, the mass balance for the liquid itself was only moderate with 84 and 75% for 3:1 and 7:1 acetic acid to water ratios, respectively, after accounting for the noncondensable CO₂ gas loss (Table S1). This might be due to inefficient condensation of low weight products in the nitrogen flow such as water, acetone, etc. In addition, methane might be produced from acetic acid or acetone since the former has been observed when submitting a mixture of acid and ketone to the reaction conditions [28]. Hence, taking into account decanoic acid as starting material and 2-undecanone as product the carbon efficiency was 79% (with a 3:1 acetic acid/water ratio; see Table S1, Suppl. Data). However, this carbon efficiency is not meaningful, since the acetic acid reactant is not considered.

The carbon efficiency for the transformation of acetic acid into acetone is already limited by stoichiometry to 75% since one carbon atom out of four is transformed into carbon dioxide that has to be considered as a loss. Side product formation and non-quantitative mass balance lowered the carbon efficiency to the 50 to 60% range (Table S1, Suppl. Data). When taking into account both carboxylic acids and both ketones, the carbon efficiency was 62% (Table S1, Suppl. Data). This is the most reasonable value for the carbon efficiency of the reaction, provided that acetone is valorized as solvent or in other applications.

The second measurand, i.e., the e-factor, was calculated as the quotient of the sum of by-products and the mass of produced product (Table S2, Suppl. Data). When considering 2-undecanone as the only product, the e-factor was 11–13. Valorizing acetone lowers the e-factor to below 10 and considering a 90%-recovery of the solvent provides an e-factor below 5 (Table S2, Suppl. Data). The latter value makes the procedure suitable for bulk-chemical industry since in this respect, an e-factor of 5 is the upper limit. This means that, from the ecological point of view, it is reasonable to produce 2-undecanone on the multi-ton scale by the cross-ketonization of decanoic acid with an excess of acetic acid.

The alternative procedure selected for the production of 2-undecanone utilizes a reketonization reaction of acetone with decanoic acid [19,20]. Apart from the zirconia
employed in the cross-ketonization above, two further standard commercial catalysts were
chosen, namely titania (anatase) and ceria. The latter two are also well known for good
performance in the ketonic decarboxylation of carboxylic acids [29,30]. From Scheme 2 it can
be seen that all three materials catalyze the formation of the desired 2-undecanone. However,
in all cases it is only the minor product. For ceria and zirconia, the 10-nonadecanone homo-
coupling product was observed in almost 85% and 2-undecanone only in approximately 15%
yield. Titania performed a bit better producing the desired ketone in 33 to 36% selectivity and
the long-chain ketone with only 45% selectivity.

Due to the low selectivity observed with all three catalysts, carbon efficiency was low and the
e-factor was high. The exact values were not calculated since they were considered to be of
preliminary nature. Catalytic performance towards the desired product has to be improved
prior to a realistic evaluation of the transformation from the ecological point of view. Further
efforts were made to reveal the mechanism on molecular scale and to identify the bottleneck
of the reketonization. Therefore, the reketonization was studied by isotopic labeling. From the
results above, it seemed that the ketonic decarboxylation was by far faster than the
reketonization reaction and that this could be the reason for the unfavorable selectivity.

Scheme 2. Reketonization of acetone with decanoic acid in a 16 : 1 molar ratio. Selectivities for 2-undecanone and
10-nonadecanone in the organic liquid were calculated from decanoic acid after 10 h time on stream. Values in
parenthesis for 2-undecanone refer to selectivities after 2 h time on stream.

Molar ratio: 1 : 16 : 7

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>m²/g</th>
<th>10-Nonadecanone [%]</th>
<th>2-Undecanone (2 h) [%]</th>
<th>Acetone conversion [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO₂</td>
<td>149</td>
<td>45</td>
<td>36 (33)</td>
<td>46</td>
</tr>
<tr>
<td>ZrO₂</td>
<td>103</td>
<td>83</td>
<td>14 (29)</td>
<td>29</td>
</tr>
<tr>
<td>CeO₂</td>
<td>61</td>
<td>84</td>
<td>15 (16)</td>
<td>27</td>
</tr>
</tbody>
</table>

3.2 Isotopic labeling experiments
With the aim to estimate the relative reaction rates for ketonic decarboxylation and
reketonization, an experiment involving acetic acid, isotopically labeled with carbon-13 in 2-
position, and non-labeled acetone was performed (Scheme 3). From this mixture, two different
2-undecanone derivatives can be expected, the 1-¹³C ketone, with the molecular ion detected
by mass spectrometry as m/z 171, prepared from the reaction of decanoic acid with acetic acid
and the unlabeled one, m/z 170, from the reaction of decanoic acid with acetone.
Scheme 3. Formation of 2-undecanone from decanoic acid with $^{13}$C-labeled acetic acid or non-labeled acetone. Isotope distribution for 2-undecanone was determined by GC-MS. For more details on the calculation, see Suppl. Data.

Monoclinic zirconia was selected as catalyst and 400 °C as reaction temperature. Under these conditions, the conversion of decanoic acid was complete. In the product mixture, 2-undecanone was observed in a 1.2 : 1 mixture of the labeled and the non-labeled derivative (Figure S1, Suppl. Data). The high percentage of the labeled atom incorporation showed that an unexpectedly large portion of 2-undecanone was obtained from the acetic acid relative to that from acetone, despite the fact that acetone was employed in the 20-fold excess. This result clearly confirms the direct incorporation pathway via cross-coupling ketonic decarboxylation instead of some hypothetical indirect incorporation.

Scheme 4. Catalytic pathways to the formation of ketones:

a) enolization of acetone and its condensation with decanoic acid yielding unlabeled 2-undecanone and a competing degenerate reaction of acetone with acetic acid leading to the scrambling of 13-C label,

b) enolization of acetic acid followed by its condensation with itself and with decanoic acid leading to the formation of doubly labeled acetone and labeled 2-undecanone, respectively, and
c) enolization of decanoic acid and its condensation with acetic acid and with itself providing another path to the labeled 2-undecanone and to 10-nonadecanone.
The mechanism for the formation of ketones from the above mixture is shown in Scheme 4.

There are two reaction pathways consuming the enolized acetone (Scheme 4a), one leading to the formation of unlabeled 2-undecanone, m/z 170, while the other one is a degenerate reaction with acetic acid leading to the label scrambling and formation of acetone with the molecular ion m/z 59. At the same time, two pathways can lead to the formation of the labeled 2-undecanone, m/z 171, starting from the adsorption on surface and enolization of either acetic (Scheme 4b) or decanoic acid (Scheme 4c). Assuming that all three reagents, two carboxylic acids and acetone, compete for the same catalytic sites on surface, the molar ratio of decanoic acid : acetic acid : acetone = 1 : 1 : 1 should provide 2-undecanone molecular ions m/z 171 : m/z 170 in the 2 : 1 ratio on a purely statistical basis. For the applied ratio of reagents, 1 : 1.3 : 26, the statistically expected ratio of m/z 171 : m/z 170 is 1 : 10 (for details see Suppl. Data). However, the actual experimental result is different by a factor of 12 (1.2 vs. 0.1) which can be attributed to the difference between the rates of the three competing reaction pathways, two of which are condensations between decanoic acid and acetic acid, while the third one is acetone condensation with decanoic acid. It could be due to the difference in the reaction rate constants of the rate limiting condensation step, or due to the concentration of the three enolized species on the active sites. Because alpha protons in ketones are more acidic compared to that in carboxylates, the difference in the concentration of the enolized species must be explained by a weaker adsorption of acetone compared to carboxylic acids.
Decarboxylative condensation of acetic acid with itself produced acetone isotopologue with two $^{13}$-C labels, m/z 60, which was blended with the starting acetone, m/z 58, and with another isotopologue, m/z 59, providing the statistical ratio of labeled atoms in the methyl groups below 5% (Figure S1). The by-products derived from side reactions of the mixture of acetone isotopologues, such as mesityl oxide or isophorone, had the same distribution of the $^{13}$-C label. Therefore, the post-distribution of the $^{13}$-C label and its incorporation into 2-undecanone could not exceed 5% for statistical reasons.

In conclusion, the isotopic labeling experiments confirm unambiguously that the ketonic decarboxylation reaction of decanoic acid with acetic acid is significantly faster under reaction conditions than the reketonization of the same carboxylic acid with acetone.

### 3.3 In-situ IR spectroscopy for adsorption/desorption sequences of acetic acid and acetone

The DFT calculations revealed an adsorption energy of $-193 \text{ kJ/mol}$ for acetic acid onto the zirconia surface and less than half of this value for acetone desorption, namely $84 \text{ kJ/mol}$ [31]. These values indicate that acetic acid should be adsorbed preferentially compared to acetone and that the surface should be covered by the acid during the reaction. Indeed, from the above values and assuming similar adsorption entropies for acetic acid and acetone, it can be estimated from the equation

$$e^{\left(\frac{\Delta H_{\text{ads,acetone}} - \Delta H_{\text{ads,acid}}}{R\theta}\right)} \text{ (eq. 3)}$$

that a surface ratio $\frac{\text{acetic acid}}{\text{acetone}}$ of about $2.9 \times 10^8$ would be reached when submitting the catalyst to similar reactant partial pressure. The lack of adsorbed acetone on the surface may thus be one reason for the moderate performance of the reketonization reaction with respect to the ketonic decarboxylation. With the aim to support the theoretical data and this hypothesis, in-situ and operando FT-IR spectroscopic experiments were carried out.

Zirconia was pressed into a self-supported wafer and placed in an in-situ IR cell [32]. After catalyst pre-treatment and evacuation of the cell, acetic acid was admitted to the cell successively in small amounts at room temperature. After each addition, an IR spectrum was recorded of the surface. From Figure 2a it can be seen that the aliquots are adsorbed onto the surface and that all bands are growing constantly in the region of 2000 to 800 cm$^{-1}$. The main shape is a doublet with the maxima at 1552 cm$^{-1}$ and 1459 cm$^{-1}$, and with shoulders at 1424 cm$^{-1}$ and 1386 cm$^{-1}$. The two most intense peaks are tentatively assigned to $v_{\text{OCS}}$ and $v_{\text{S}}$ (OCO) of adsorbed acetates [33–35], most probably as bidentate species [36]. No new bands were observed until surface saturation revealed by the appearance of physisorbed acetic acid, indicated by the band at 1712 cm$^{-1}$.

Interestingly, a very similar behavior was observed when zirconia samples with BET surface areas of 53 or 35 m$^2$/g were employed (Figure S2, Suppl. Data) instead of the sample with a BET surface area of 100 m$^2$/g. Bands were observed at the same wavenumbers and the composed signal had a very similar shape (Figure S2c, Suppl. Data). The sample with higher surface area had a smaller average crystal size and, therefore, a higher ratio of active sites at corners and edges with respect to planar surface sites [23]. When no difference is observed for different ratios of sites, it can be concluded that the adsorption mode is little influenced by the surface geometry of the catalyst material, i.e., there is no preference for the adsorption at the edges.
Figure 2. In situ IR-spectra of a) acetic acid and b) acetone adsorbed successively onto the zirconia wafer with a BET surface area of 104 m$^2$/g, and c) of both compounds at high surface saturation.

DFT calculations were carried out placing two acetic acid molecules on a 111 zirconia surface. The intensities of the different vibration modes are depicted in Figure 3. Considering a red shift of approximately 30 cm$^{-1}$ to lower wavenumbers (with respect to the experimental data), the shape of the composed spectrum (with a broader peak width) resembles the experimental one. Therefore, this study further corroborates a bidentate coordination mode to two different zirconium atoms, even with acetate molecules in the neighborhood. In contrast, when the same study is done for the 111 zirconia surface the match is not evident (Figure S3). This is explained by a mismatch of the surface plane, but no experimental support can be provided for this argument.
Figure 3. Composite spectrum of the IR simulated vibrations obtained by the previously described DFT method [A. V. Ignatchenko, J.P. McSally, M.D. Bishop, J. Zweigle, Ab initio study of the mechanism of carboxylic acids cross-keitonization on monoclinic zirconia via condensation to beta-keto acids followed by decarboxylation, Mol. Catal. 441 (2017) 35–62, doi:10.1016/j.mcat.2017.07.019] for a model which includes two acetate molecules and two protons adsorbed on 111 surface of monoclinic zirconia (Wavenumbers and relative intensities are listed in Table S3 and vibration modes are depicted in Figure S4).

The successive adsorption procedure in the in-situ IR spectroscopy experiment was repeated with acetone and a fresh zirconia sample with a BET surface area of 100 m²/g (Figure 2b). Three major signal ranges were observed: from 1730 to 1525 cm⁻¹ with two maxima at 1680 and 1600 cm⁻¹, from 1395 to 1340 cm⁻¹, and from 1270 to 1150 cm⁻¹, with three maxima at 1250, 1223, and 1170 cm⁻¹. The last range is suitable to distinguish between adsorbed acetone and adsorbed acetic acid, and to confirm the presence of acetone on a surface covered with an excess of acetic acid, since the spectrum of adsorbed acetic acid does not involve any band in this region (Figure 2c). Vice versa, the band at a wavenumber of 1552 cm⁻¹ is indicative for acetic acid, which exhibits a strong intensity (as part of a doublet), whereas the signal of acetone consists of a smooth decline without any shoulder.

In conclusion, in-situ IR spectroscopy of acetic acid and acetone adsorbed onto a zirconia surface demonstrated that both compounds are unambiguously distinguishable by this method. Therefore, IR spectroscopy is a method of choice to study the ketonic decarboxylation of acetic acid and the reketonization of acetic acid with acetone in operando conditions.

3.4 Operando IR spectroscopy for the ketonic decarboxylation of acetic acid to acetone

3.4.1 Influence of the temperature on the signal shape

For the FTIR operando experiment, a zirconia (BET surface area of 100 m²/g) wafer was placed in an operando IR reaction chamber [37]. An acetic acid stream was passed through the chamber and the gas effluent was also monitored by IR spectroscopy. The complete experiment is depicted in a 3D image in Figure S5a with the corresponding temperature profile in Figure S5b. Temperature was raised successively from 215 °C to 315, 338, 363, 387 and 411 °C (Figure S5b). Figure S6 shows a 2D image of the same experiment.

From the Figures S3a and S4a is can be seen that the surface is immediately covered and only minor changes occur during the first 100 min on stream. In Figure 4a a comparison is shown between a spectrum recorded at 215 °C under operando conditions and one of adsorbed acetic acid recorded at room temperature under in-situ conditions. Both spectra show the same bands. Additional bands were not observed in either one of them. Therefore, it can be
concluded that at 215 °C the surface of zirconia is only covered by acetic acid mostly as acetates.

From the 2D image (Figure S6a) it seems that the $v_S$ (OCO) bands for adsorbed acetates broaden after 30 min on stream, that is when starting to increase the temperature from 215 to 315 °C. For a better understanding of the occurrence, single spectra recorded at different temperatures, i.e., at 215, 315, 338, and 363 °C were selected and presented in Figure 4a. From this illustration, it becomes evident that the signal suffers a change: when increasing temperature the two shoulders at a wavenumber of approximately 1400 cm$^{-1}$ disappear (Figure 4a). This can be seen even better in Figure 4b, in which the signal is compared for the temperatures of 215 and 387 °C. The doublet signal becomes symmetrical at higher temperature and, therewith a bit broader towards lower wavenumbers (Figure 4b). This is the reason for the widening of the right red line after 30 min in Figure S6a.

Figure 4. a) operando IR-spectra of the surface of monoclinic zirconia (BET surface area or 104 m$^2$/g) when passing acetic acid a) at increasing temperature, compared with the in-situ spectrum of acetic acid adsorbed onto the same material and recorded at room temperature; b) comparison of two operando IR-spectra recorded at different temperature.

Several hypothesis for the reason for the change in the signal shape can be taken into account. If the shoulders are due to different vibration modes, as the DFT study suggests, then the increase of the temperature should cause a variation in the intensities for these modes. If the shoulders are due to different species, e.g., with slightly different geometry or activation, these species may be more reactive. As a consequence, they are converted first and the corresponding sites are unoccupied. However, experimental support could not be found for either one of the two hypotheses.
3.4.2 Influence of the temperature on the reaction outcome at constant flow

The exhaust flow from the reaction chamber was monitored by IR spectroscopy and the spectra are depicted as 2D image in Figure S6b. For the interpretation of the experiment, it has to be taken into account that carboxylic acids, when increasing their concentration in the gas phase, aggregate and form dimers. At very low concentration, the molecules are present as monomers.

This concentration-dependent monomer-dimer equilibrium in the gas-phase has an influence on the IR interpretation since both species have different IR spectra, i.e., they can be differentiated by IR spectroscopy. Figure S7 depicts the IR spectra of acetic acid in the gas phase, in Figure S7a at increasing concentration and in Figure S7b comparing the spectra for the lowest and the highest concentrations (of the series) with the same height of the strongest band.

At higher concentration (dark purple line), the spectrum is characterized by two sharp single bands at wavenumbers of 1734 and 1294 cm⁻¹ (Figure S7b). These two bands are assigned to the ν(C=O) and ν(C-O) modes for the acetic acid dimer respectively [38]. At lower concentration (dark green line), peaks already present in the former spectrum become more relevant, namely at 1790 and 1180 cm⁻¹. The latter two are characteristic for the monomer species of acetic acid in the gas phase.

The comparison of the IR spectra of the gas phase involving a low acetic acid concentration and of the gas phase of the exhaust gas after passing acetic acid over zirconia at 215 °C revealed that both are very similar and the major bands are identical (Figure S8). Therefore, it can be concluded that when passing acetic acid at 215 °C no chemical transformation takes place. The surface coverage is maximum and excess acetic acid leaves the reactor chamber without catalytic conversion.

When having a closer look on Figure S6b at the zone of the first temperature increase (30 to 50 min), it becomes evident that a change occurs at a temperature of approximately 260 °C (marked with a dashed line). The single spectra of this range from 265 to 315 °C are depicted in Figure 5. The acetic acid bands started to fade in the reactor effluent, whereas new bands appeared at wavenumbers of 2400 cm⁻¹. The latter are characteristic for carbon dioxide.

Hence, this temperature range was considered as that at which the reaction initiates. This is in accordance with the observation that in a pulse reactor coupled with mass spectrometry, the ketonic decarboxylation started already at a temperature as low as 180 °C [39]. The other IR peaks position remain similar to what was detected in the lower temperature range while their intensity ratio changed: the proportion of monomeric acetic acid increased which is consistent with both a lowering of the CH₃COOH concentration (being partly converted to CO₂) and an increase of the reaction temperature favoring the dimer dissociation.

After 70 min, the period of change in the product mixture ended: no more acetic acid was detected, i.e., the conversion was complete. This can be seen in the two-dimensional image (Figure S6b) and the transformation of the product composition can be tracked in Figure 6 based on several selected spectra. When comparing the spectra at full conversion, i.e., for the temperature range from 363 to 411 °C (75 to 130 min), with the spectrum of acetone and the one of a mixture of carbon dioxide and water, it was confirmed that these three compounds are the sole products of acetic acid conversion (Figure 7).
The analysis of the gas phase proved unambiguously the formation and the presence of acetone. However, when going back to the surface (Figure S6a), no evidence at all was found for adsorbed acetone onto the surface. As discussed above, a signal at wavenumbers of 1200 cm\(^{-1}\) should arise (Figure 2). This is clearly not the case. When reaching 387 and 411 °C, the coverage with acetic acid decreased (Figure S6a). However, no new signals arose. This was a clear proof for the hypothesis that the adsorption of acetone at temperatures around 400 °C was not favored, although the surface was not fully covered by acetic acid. Hence, if the residence time of the acetone on the surface was short, reketonization was disfavored, whereas ketonic decarboxylation can proceed smoothly due to the presence of plenty of carboxylic acid.

Figure 5. Gas-phase IR-spectra after passing acetic acid over monoclinic zirconia at increasing temperature in the range from 265 to 315 °C.

Figure 6. Gas-phase IR-spectra after passing acetic acid over monoclinic zirconia at increasing temperature in the range from 265 to 411 °C.
Figure 7. Gas-phase IR-spectra after passing acetic acid over monoclinic zirconia at increasing temperature in the range from 265 to 411 °C.

4. Conclusions

The synthesis of methyl ketones was targeted from carboxylic acids without metalorganic reagents. When employing decanoic acid as model compound, 2-undecanone was obtained either by cross-coupling ketonic decarboxylation with acetic acid or by reketonization with acetone. However, fundamental differences were observed when the transformations were evaluated for their sustainability.

The cross-coupling ketonic decarboxylation provided an e-factor below five, which is acceptable for production even as a bulk chemical. In contrast, for the reketonization of decanoic acid with acetone, the 10-nonadecanone ketonization product was always obtained as main product. This frustrated any positive evaluation when 10-nonadecanone was considered as an undesired product.

The relative reaction rate of both transformations was studied by an isotopic labeling experiment. Acetic acid with a $^{13}$C-carbon atom in 2-position was reacted with decanoic acid in presence of 20-fold excess of acetone. Nevertheless, approximately the same amounts of labeled and unlabeled methyl groups were detected in the 2-undecanone product. This indicated that the ketonic decarboxylation was significantly faster than the reketonization.

It was hypothesized that the reason for the lower rate was the low concentration of acetone on the surface and in-situ and operando IR experiments were carried out. It was shown that indeed the surface was covered by acetic acid, whereas adsorbed acetone was not detected under reaction conditions, i.e., at 400 °C, although the coverage of the surface by acetic acid was not complete at this temperature and gaseous acetone was produced. The above results thus confirm that the reketonization reaction is limited by the absence of acetone activation through adsorption and that consequently the reketonization reaction would take place through a Langmuir Hinshelwood mechanism involving both adsorbed acid and adsorbed ketone.

In order to improve the performance of the reketonization, catalyst properties should thus be modified to improve the adsorption of acetone along with carboxylic acids.
5. Acknowledgement

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6. References


Methyl ketones from carboxylic acids as valuable target molecules in the biorefinery

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Supplementary Data

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Calculations and Tables

Green Chemistry Metrics calculation

For the *mass balance* the mass of liquid was taken into account for the product side. For the starting material the two feeds were summed up and the amount of carbon dioxide that has to be co-produced at full conversion of the carboxylic acids was subtracted:

\[
m_b = \frac{(m_{\text{liquid}})}{(m_{\text{feed1}} + m_{\text{feed2}} - m_{\text{CO2}})}
\]

The *selectivity* of a ketone product was calculated taking into account the concentration of the substance in the liquid that was related to the corresponding substrate from which it has to be formed. Yields for 2-undecanone, 10-nonadecanone, 2-nonanone, 3,5-dimethyl-1-nonyl-benzene and 1,3-dinonyl-5-methyl-benzene were related to the initial amount of decanoic acid and yields for acetone, mesitylene, isophorone and 3,5-dimethylphenol to the initial amount of acetone. Conversion was complete in all cases since neither decanoic acid nor acetic acid were observed in the liquid crude reaction mixture.

\[
\text{selectivity} = \frac{n_{\text{substance in the crude reaction mixture}}}{n_{\text{initial carboxylic acid amount}}}
\]

Calculation of the statistical probability for the isotope distribution

We estimate the probabilities of pairing two compounds. The first one is the enolic, and the second one is the carbonyl compound counted in that order. When the mixture consists of 26 parts of acetone, 1.3 parts of acetic acid, and 1 part of decanoic acid, the probability of forming a pair is the product of the two concentrations. Each concentration is calculated as the ratio of parts of that molecule divided by the sum of all parts in the mixture. For example, for the pair of reagents in the first row of the table below, we multiply parts of each reagent, acetone and acetic acid and divide by the square of the total sum of all parts: \(26 \times 1.3/(28.3)^2 = 0.0422\).

The same formula is used for all other combinations of molecule pairs. The result is shown in the last column. To verify the correctness of calculations, the summation of all probabilities has to give 1.0, that is 100%.

There are two combinations that give the m/z 171, that is acetic acid + decanoic acid or decanoic acid + acetic acid. However, only one combination gives m/z 170. It is acetone + decanoic acid. The other combination, decanoic acid (enolic component) + acetone (carbonyl component) does not give m/z 170 since the ketone product is not formed. Instead, a possible intermediate can dehydrate or go back to the starting materials.

So, on purely statistical reasons, m/z 170 has an advantage over m/z 171. When we calculate the ratio of m/z 170 to m/z 171 it is the ratio of probabilities from the last column:

\[
0.0325/(0.00162+0.00162) = 10.0
\]
The experimental ratio of m/z 170 to m/z 171 is 1/1.2 = 0.833. So, it is a factor of 10.0/0.833 = 12.0 times, which characterizes the reduction of the expected ratio from 10 down to the observed value 0.833. In other words, we did not get as much m/z 170 as we expected for statistical reasons, because m/z 171 was formed relatively 12 times faster.
<table>
<thead>
<tr>
<th>Enolized:</th>
<th>Fraction</th>
<th>Reacted with</th>
<th>Fraction</th>
<th>Product</th>
<th>Calculation</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone m/z 58</td>
<td>26</td>
<td>Acetic Acid m/z 61</td>
<td>1.3</td>
<td>Acetone m/z 59</td>
<td>$26 \times 1.3/(28.3)^2$</td>
<td>0.0422</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>Decanoic Acid</td>
<td>1</td>
<td>2-Undecanone m/z 170</td>
<td>$26 \times 1.0/(28.3)^2$</td>
<td>0.0325</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>acetone m/z 58</td>
<td>26</td>
<td>condensation products</td>
<td>$(26/28.3)^2$</td>
<td>0.844</td>
</tr>
<tr>
<td>Acetic Acid m/z 61</td>
<td>1.3</td>
<td>Acetic Acid m/z 61</td>
<td>1.3</td>
<td>Acetone m/z 60</td>
<td>$1.3 \times 1.3/(28.3)^2$</td>
<td>0.00211</td>
</tr>
<tr>
<td></td>
<td>1.3</td>
<td>Decanoic Acid</td>
<td>1</td>
<td>2-Undecanone m/z 171</td>
<td>$1.3 \times 1.0/(28.3)^2$</td>
<td>0.00162</td>
</tr>
<tr>
<td></td>
<td>1.3</td>
<td>acetone m/z 58</td>
<td>26</td>
<td>product not detected</td>
<td>$1.3 \times 26/(28.3)^2$</td>
<td>0.0422</td>
</tr>
<tr>
<td>Decanoic Acid</td>
<td>1</td>
<td>Acetic Acid m/z 61</td>
<td>1.3</td>
<td>2-Undecanone m/z 171</td>
<td>$1.0 \times 1.3/(28.3)^2$</td>
<td>0.00162</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Decanoic Acid</td>
<td>1</td>
<td>10-Nonadecanone</td>
<td>$1.0 \times 1.0/(28.3)^2$</td>
<td>0.00125</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>acetone m/z 58</td>
<td>26</td>
<td>product not detected</td>
<td>$1.0 \times 26/(28.3)^2$</td>
<td>0.0325</td>
</tr>
<tr>
<td>Total</td>
<td>28.3</td>
<td>28.3</td>
<td></td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>
The carbon efficiency was calculated by taking into account mass balance and selectivity. The calculation was done for 2-undecanone in two different manners: with respect to the decanoic acid employed and with respect to both carboxylic acids. The carbon efficiency for acetone was calculated with respect to acetic acid. Finally, the total carbon efficiency was calculated taking into account 2-undecanone and acetone as products and both carboxylic acids as starting material.

Table S1. Detailed calculation of the carbon efficiency for the reaction of decanoic acid with acetic acid.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Acetic acid/water ratio</th>
<th>Initial carbon atom number</th>
<th>Product selectivity b/%</th>
<th>m.b./wt% c</th>
<th>Carbon atoms in product d</th>
<th>Carbon atoms obtained e</th>
<th>Carbon efficiency f/%</th>
<th>Total carbon efficiency g/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decanoic acid</td>
<td>3:1</td>
<td>10</td>
<td>85.3</td>
<td>83.8</td>
<td>11</td>
<td>7.9</td>
<td>78.6 (17.2)</td>
<td>61.8</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>36 (2 x 18)</td>
<td>90.8</td>
<td>83.8</td>
<td>27 (3 x 9)</td>
<td>20.5</td>
<td>57.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decanoic acid</td>
<td>7:1</td>
<td>10</td>
<td>85.8</td>
<td>75.1</td>
<td>11</td>
<td>7.1</td>
<td>70.9 (15.4)</td>
<td>55.9</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>36 (2 x 18)</td>
<td>91.8</td>
<td>75.1</td>
<td>27 (3 x 9)</td>
<td>18.6</td>
<td>51.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Carbon atom number based on the molar ratio; reaction stoichiometry is taken into account, i.e., the 18 fold excess of acetic acid with respect to decanoic acid. b Concentration in the organic liquid of 2-undecanone with respect to other products produced from decanoic acid and of acetone with respect to other products produced from acetic acid. c Calculated as described in the Materials and Method section of the manuscript. d Decanoic acid is converted into 2-undecanone, i.e., from ten carbon atoms eleven are produced, incorporating one carbon atom from acetic acid; acetic acid is converted into acetone, i.e., from two molecules with two carbon atoms each, one acetone molecule with three carbon atoms is produced; the forth carbon atom is incorporated into a carbon dioxide molecule. e Number obtained by the following calculation: carbon atoms in product x product selectivity x m.b. f Calculated by the equation: carbon atoms obtained / initial carbon atom numbers x 100; in parenthesis the carbon efficiency is stated for 2-undecanone with respect to both substrates. g Calculated by the equation: (carbon atoms obtained in 2-undecanone and acetone) / (initial carbon atom numbers for both substrates) x 100.
Table S2. Detailed calculation of the e-factors for the reaction of decanoic acid with acetic acid.

<table>
<thead>
<tr>
<th>Acetic acid/ water ratio</th>
<th>total feed+ catalyst/g</th>
<th>mass yield(^a)/g</th>
<th>90% of solvent(^b)/g</th>
<th>non-product mass(^c)/g</th>
<th>2-undecanone(^d)</th>
<th>2-undecanone + acetone(^e)</th>
<th>2-undecanone + acetone; 90% of solvent recovered(^f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:1</td>
<td>263.2</td>
<td>21.5 (119)</td>
<td>57.9 (39.7)</td>
<td>242</td>
<td>11.2</td>
<td>5.7</td>
<td>1.19</td>
</tr>
<tr>
<td>7:1</td>
<td>263.2</td>
<td>19.4 (108)</td>
<td>57.9 (19.8)</td>
<td>244</td>
<td>12.6</td>
<td>8.0</td>
<td>4.02</td>
</tr>
</tbody>
</table>

\(^a\) Mass yield of 2-undecanone and in parenthesis of acetone. \(^b\) Amount of hexadecane solvent recovered when 90% of the solvent is recycled (in parenthesis the water solvent is specified for the aqueous feed). \(^c\) Difference of the total mass employed (starting materials and catalyst) and the product (2-undecanone) obtained. \(^d\) e-factor for the production of 2-undecanone considering this ketone as only product and without solvent recycling. \(^e\) e-factor for the production of 2-undecanone considering acetone as product that can be commercialized, but without solvent recycling. \(^f\) e-factor for considering both ketones as products for commercial valorization and a 90% recycling rate of the solvents hexadecane and water.
DFT results

Table S3. Frequencies obtained by DFT calculations placing two molecules on a 111 zirconia surface and the corresponding relative intensity.

<table>
<thead>
<tr>
<th>Frequency (cm⁻¹)</th>
<th>Relative intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1343.9</td>
<td>163</td>
</tr>
<tr>
<td>1368.4</td>
<td>677</td>
</tr>
<tr>
<td>1400.4</td>
<td>487</td>
</tr>
<tr>
<td>1417.0</td>
<td>1252</td>
</tr>
<tr>
<td>1424.6</td>
<td>156</td>
</tr>
<tr>
<td>1448.0</td>
<td>124</td>
</tr>
<tr>
<td>1454.1</td>
<td>119</td>
</tr>
<tr>
<td>1475.5</td>
<td>371</td>
</tr>
<tr>
<td>1522.8</td>
<td>2615</td>
</tr>
<tr>
<td>1534.5</td>
<td>263</td>
</tr>
</tbody>
</table>
Figures

Isotopic labeling

Figure S1. Mass spectra for a) non-labeled 2-undecanone and b) of 2-undecanone from the reaction mixture obtained with $^{13}$C-labeled acetic acid; mass spectra for c) non-labeled mesityl oxide and d) mesityl oxide from the reaction mixture obtained with $^{13}$C-labeled acetic acid; mass spectra for e) non-labeled isophorone and f) isophorone from the reaction mixture obtained with $^{13}$C-labeled acetic acid.
IR spectroscopy

Figure S2. *In situ* IR-spectra of acetic acid adsorbed successively onto the zirconia wafer with a BET surface area of a) 53.4 m²/g and b) 35.4 m²/g; c) comparison of spectra for the three samples with different BET surface areas at similar loadings (similar molar amount of acetic acid per weight of metal oxide).

DFT Results

Figure S3. Composed spectrum obtained by DFT simulation of the IR vibrations with a model including one acetate molecule and one proton adsorbed to a TiO₂ zirconia surface.
Figure S4. Vibration modes of two acetate molecules adsorbed to the zirconia surface for the stated wavenumbers (theoretical values involve a redshift to lower wavenumbers with respect to the experimental numbers.

1534 cm$^{-1}$

1522 cm$^{-1}$

1475 cm$^{-1}$

1454 cm$^{-1}$
IR spectroscopy

Figure S5. a) 3D image of the Operando IR-spectroscopy of the surface of monoclinic zirconia with a BET surface area of 100 m$^2$/g reaction when passing a flow of acetic acid at increasing temperature; b) Temperature profile of the reaction with vertical lines indicating the time for the spectra depicted in Figure 4.
Figure S6. a) 2D image of the *Operando* IR spectroscopy of the surface of *monoclinic zirconia* with a BET surface area of 100 m²/g under acetic acid reaction flow at increasing temperature; b) 2D image of the *Operando* IR-spectroscopy of the vapor phase acetic acid passed over a surface of *monoclinic zirconia* with a BET surface area of 100 m²/g reaction at increasing temperature.
Figure S7. *In-situ* IR-spectra of the acetic acid in the gas phase a) at increasing concentrations, and b) compared at low (dark green) and high (dark purple) concentration. (The same colors are used for the same concentrations in both Figures.)

Figure S8. Comparison of the gas phase IR-spectrum of the acetic acid at low concentration with the *operando* IR spectrum of the gas phase after 34 min passing acetic acid over zirconia at 215 °C.