Experimental and theoretical assessment of the mechanism and site requirements for ketonization of carboxylic acids on oxides

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Abstract

Ketonization of carboxylic acids removes O-atoms and forms new C–C bonds, thus providing routes from sustainable carbon feedstocks to fuels and chemicals. The elementary steps involved and their kinetic relevance, as well as the number and nature of the active sites on active TiO2 and ZrO2 catalysts, remain matters of active discourse. Here, site titrations demonstrate the requirement for coordinatively-unsaturated M-O-M sites (M = Ti, Zr) with specific geometry and intermediate acid-base strength. The measured site densities allow rigorous reactivity comparisons among catalysts based on turnover rates and activation free energies, as well as the benchmarking of mechanistic proposals against theoretical assessments. Kinetic, isotopic, spectroscopic, and theoretical methods show that C2–C4 acids react on anatase TiO2 via kinetically-relevant C–C coupling between 1-hydroxy enolate species and coadsorbed acids bound at vicinal acid-base pairs saturated with active monodentate carboxylates. Smaller Ti–Ti distances on rutile TiO2 lead to the prevalence of unreactive bidentate carboxylates and lead to its much lower ketonization reactivity than anatase. The prevalent dense monolayers of chemisorbed acid reactants reflect their strong binding at acid-base pairs and their stabilization by H-bonding interactions with surface OH groups derived from the dissociation of the carboxylic acids or the formation of 1-hydroxy enolates; these interactions also stabilize C–C coupling transition states preferentially over their carboxylate precursors; high coverages favor sequential dehydration routes of the α-hydroxy-γ-carboxy-alk oxide C–C coupling products over previously unrecognized concerted six-membered-ring transition states. Infrared spectra show that ubiquitous deactivation, which has precluded broader deployment of ketonization in practice and unequivocal mechanistic inquiries, reflects the gradual formation of inactive bidentate carboxylates. Their dehydration to ketene-like gaseous species is faster on anatase TiO2 than on ZrO2 and allows the effective scavenging of bidentate carboxylates via ketene hydrogenation to alkanals/alkanols on a Cu function present within diffusion distances. These strategies make anatase TiO2, a more effective catalyst than ZrO2, in spite of its slightly lower initial turnover rates. This study provides details about the mechanism of ketonization of C2–C4 carboxylic acids on TiO2 and a rigorous analysis of the sites required and of active and inactive bound species on TiO2 and ZrO2. The preference for specific distances and for intermediate acid-base strength in M-O-M species is consistent with the structure and energy of the proposed transition states and intermediates; their relative stabilities illustrate how densely-covered surfaces, prevalent during ketonization catalysis, represent an essential requirement for the achievement of practical turnover rates.

1. Introduction

Carboxylic acids form new C–C bonds via bimolecular ketonization reactions to give alkanones, CO2, and H2O [1]:

\[
R_1\text{COOH} + R_2\text{COOH} \rightarrow R_1C(=O)R_2 + CO_2 + H_2O \quad (R_1, R_2 = \text{alkyl})
\]

Such reactions remove three O-atoms and form a new C–C bond from two acid molecules, thus providing an attractive route for oxygen removal using the C-atoms within reactants, instead of added H2, in upgrading biomass-derived feedstocks into fuels and chemicals [2–6]. The alkanone products can be used in subsequent aldol condensation reactions to increase their chain length and remove additional O-atoms [7,8].

Ketonization is catalyzed by metal oxides (e.g. MgO, BaO, MnO2, CeO2, ZrO2, and TiO2) [6–22], with ZrO2 and TiO2 among the most effective oxides [2,3]. Ketonization elementary steps and their
Ketonization requires the presence of a H-atom at an α-position with respect to the −COOH group in one of the acid reactants [2]. For instance, pivalic acid (C(CH3)3COOH), which lacks an α-H-atom, reacts with valeric acid (CH3(CH2)2COOH, two α-H-atoms) to form 2,2-dimethylpentan-3-one in cross-ketonization, but cannot undergo self-ketonization to form 2,2,4,4-tetramethylpentan-3-one [19]. Similarly, aldol condensation reactions of carbonyl compounds require two α-H-atoms in one of the reactants, because such reactions involve enolate species formed by cleavage of α-C−H bonds and subsequent dehydration of aldols formed to α,β-unsaturated carbonyl compounds [23,24]. These C−H bonds exhibit lower heterolytic dissociation energies than those at other locations within the molecules; their cleavage is mediated by acid-base pairs of intermediate strength, which stabilize the transition states required for enolate formation [5,7,24]. The enolates formed from the carbonyl reactants then couple with another carbonyl species to form unstable aldols with a new C−C bond, which subsequently dehydrate to α,β-unsaturated carbonyl aldol condensation products (Scheme 1).

It seems plausible that the ketonization of carboxylic acids is also mediated by enolate-like species, in this case, in the form of 1-hydroxy enolates. The species formed from C−C bond formation via reactions of 1-hydroxy enolates with another acid reactant ultimately decompose via CO2 and H2O elimination, instead of the H2O elimination route in condensation reactions, because neither dehydration nor decarboxylation steps alone can form stable products (Scheme 1). 13C tracer studies show that the CO2 molecule from the carbonyl group in the acid reactant that undergoes α-C−H bond cleavage and then nucleophilically attacks a coadsorbed acid reactant [10,25]; this is consistent with 1-hydroxy enolates as reaction intermediates, but excludes ketene-mediated routes, which would form CO2 from the carbonyl group in the coadsorbed acid instead of that in the acid that undergoes α-C−H bond cleavage [2,9].

Here, we report turnover rates and selectivities for ketonization of C−C4 carboxylic acids on anatase and rutile TiO2 (TiO2(a), TiO2(r)) and on monoclinic and tetragonal ZrO2 (ZrO2(m), ZrO2(t)). This study exploits the benefits of gaseous H2 and a Cu function to confer unprecedented catalyst stability, thus allowing detailed mechanistic inquiries on stable catalysts. These mechanistic studies include kinetic, isotopic, spectroscopic, and theoretical methods, which are combined here to probe plausible ketonization elementary steps and their kinetic relevance on TiO2(a), an active and stable catalyst for these reactions, and on TiO2(r), the least active catalyst among those examined. A parallel examination of such ketonization pathways on ZrO2 has confirmed the involvement of elementary steps similar to those reported here on TiO2. Reactivities are reported here as ketonization turnover rates, using the number of acid-base M−O (M = Ti, Zr) pairs determined by titration with propanoic acid during catalysis; such rates allow comparisons of the intrinsic properties of acid-base pairs on different metal oxides and rigorous benchmarking of theoretical methods against experiments. These data provide compelling evidence for the involvement of acid-base pairs in ketonization steps and for the consequences of their acid-base properties and geometry on the intrinsic ketonization reactivity of metal oxide surfaces.

These experimental and theoretical methods show that acid-base pairs are saturated with monodentate carboxylates on TiO2(a) and with bidentate carboxylates on TiO2(r) during ketonization catalysis. Monodentate carboxylate structures form from dissociation of the carboxylic acid on a Ti−O pair via interactions of their two O-atoms with the Ti center and the abstracted proton bound at the O site, while bidentate configurations place the two O-atoms at Ti centers of two vicinal Ti−O pairs. Such near-saturation coverages by acid-derived species prevent the re-adsorption and secondary condensation of primary alkanoic products along the catalyst bed, thus maintaining the high ketonization selectivities typical of TiO2 (and ZrO2) catalysts. Infrared spectra during catalysis show that monodentate carboxylates and molecularly adsorbed acids are reactive intermediates on TiO2(a) and TiO2(r) surfaces, respectively; bidentate carboxylates, in contrast, act as unreactive spectators on both surfaces. These bidentate carboxylates can be scavenged via hydrogenation of ketene, present as trace gaseous species in equilibrium with bidentate carboxylates; such reactions are mediated by a Cu function present within diffusion distances from TiO2 surfaces, leading to much slower deactivation for TiO2 (and ZrO2) catalysts when H2 and Cu are present.

The form of the measured rate equations for all carboxylic acids, the observed (H/D) kinetic isotope effect values near unity, the infrared evidence for near saturation coverages of monodentate or bidentate carboxylates, and the effects of alkyl substituents on ketonization turnover rates are consistent with C−C bond formation between a 1-hydroxy enolate and a coadsorbed acid as the sole kinetically-relevant step. These conclusions are confirmed by DFT treatments on densely-covered TiO2(a) and TiO2(r) surfaces, which lead to activation free energy barriers and kinetic isotope effects in excellent agreement with experiments, while also

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**Scheme 1.** Analogous elementary steps involved in ethanal condensation and ethanoic acid ketonization on acid-base pairs (shown for TiO2 catalysts as an illustrative example).

(a) Aldol condensation

(b) Ketonization

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confirming the prevalence of monodentate or bidentate carboxylates. High coverages of monodentate carboxylates are essential for ketonization turnovers on TiO2(a), because the kinetically-relevant C–C coupling transition state (TS) is stabilized by H-bonding interactions with vicinal surface OH groups, formed upon dissociation of coadsorbed acids to carboxylates; such stabilization decreases the free energy difference between the C–C coupling TS and the two monodentate carboxylate precursors. The Ti–Ti distances in Ti–O–Ti structures are shorter on TiO2(r) than on TiO2(a) surfaces. Such shorter distances bring more effective orbital overlap between Ti centers and O-atoms in bidentate carboxylates, leading to their prevalence over the monodentate modes, for which closer Ti–Ti centers lead to steric repulsion.

Steric hindrance also destabilizes C–C coupling TS structures on TiO2(r) surfaces, rendering such surfaces essentially inactive in ketonization catalysis. The intermediacy of monodentate carboxylates present at near saturation coverages, the unreactive nature of bidentate carboxylates, and the kinetic relevance of the C–C coupling TS involving 1-hydroxy enolates and coadsorbed acid reactants appear to be general mechanistic features of ketonization reactions on practical oxide catalysts.

2. Methods

2.1. Catalyst preparation and characterization

Anatase TiO2 (TiO2(a), 99.7%, 240 m2 g−1, Alfa Aesar) and rutile TiO2 (TiO2(r), 99.5%, 160 m2 g−1, Aldrich) were treated in flowing air (99.999%, 1.67 cm3 g−1 s−1, Praxair) by heating to 673 K (at 0.167 K s−1) and holding for 3 h. Monoclinic ZrO2 (ZrO2(m), 131 m2 g−1) was prepared using hydrothermal methods [26], ZrO(NO3)2 (Zr(NO3)2·2H2O, 99.5%, Sigma-Aldrich) and urea (99%, Aldrich) were dissolved in 60 cm3 deionized water (0.40 mmol cm−3 Zr4+, urea/Zr4+ = 10 mole). This solution was placed in a Teflon-lined stainless-steel autoclave (100 cm3) and held stagnant at 383 K for 20 h under its autogenous pressure. The resulting solids were washed with deionized water until the filtrate reached a neutral pH, then treated in stagnant ambient air at 383 K (0.167 K s−1) overnight and in flowing air (1.67 cm3 g−1 s−1, 99.999%, Praxair) at 673 K (0.167 K s−1 heating rate, 4 h hold). Tetragonal ZrO2 (ZrO2(t), 167 m2 g−1) was prepared via hydrolysis of ZrOCl2 (ZrOCl2·8H2O, 99.5%, Sigma-Aldrich) in an aqueous solution (0.40 mmol cm−3 Zr3+, 333 K) at a constant pH of 10 adjusted by 5.0 M NH4OH (99.99%, Sigma-Aldrich) [27]. The precipitate was washed with deionized water until the rinse solution was free of Cl− ions, as determined using 0.2 mmol cm−3 aqueous AgNO3 (>99%, Sigma-Aldrich). The samples were then treated at 383 K (0.167 K s−1) overnight in stagnant ambient air and at 723 K (0.167 K s−1) for 2 h in flowing air (1.67 cm3 g−1 s−1, 99.999%, Praxair). The identity and phase purity of these ZrO2 samples were examined by powder X-ray diffraction (XRD) measurements (Cu Kα radiation, λ = 0.15418 nm, 40 kV, 40 mA, Bruker D8 Advance; diffractograms shown in Fig. S1 of Supporting Information [S1]).

H2 and Cu/SiO2 catalysts (ca. 20 wt.% Cu) were used to improve the stability of TiO2 and ZrO2 ketonization catalysts. The Cu-based catalysts were prepared using homogeneous deposition-precipitation methods [24]. Cu(OH)2 was deposited onto colloidal silica (30 wt.%, LUDOX SM-30) from an aqueous solution of Cu(NO3)2·3H2O (99.99%, Sigma-Aldrich) via a urea hydrolysis (CO(NH2)2, 99%, Aldrich) at 363 K (urea/Cu2+ = 3 mole). The resulting suspension was kept at 363 K (0.167 K s−1) for 20 h while stirring (12 Hz) and then filtered and washed with deionized water until the filtrate gave a neutral pH value. The recovered powders were treated in stagnant ambient air by heating to 383 K (at 0.167 K s−1) and holding overnight and in flowing dry air (1.67 cm3 g−1 s−1, 99.999%, Praxair) by heating to 723 K (at 0.167 K s−1) and holding for 5 h. These samples were then treated in flowing 10% H2/He (5.56 cm3 g−1 s−1, 99.999%, Praxair) at 573 K (0.033 K s−1) for 2 h, and passivated in flowing 1% O2/He (0.83 cm3 g−1 s−1, 99.999%, Praxair) at ambient temperature for 1 h before exposure to ambient air. The mean Cu crystallite size (d) in Cu/SiO2 (7.9 nm) [24] was measured from the breadth of the most intense (111) reflection in diffractograms (2θ = 43.3°) using the Scherrer equation and Cu Kα radiation (0.15418 nm wavelength).

2.2. Catalytic rate measurements

The reactions of gaseous C2–C4 carboxylic acids (ethanoic acid (CH3COOH, >99.7%, Sigma-Aldrich), propionic acid (C3H7COOH, >99.5%, Sigma-Aldrich), and butanoic acid (C4H9COOH, >99%, Sigma-Aldrich)) were carried out in an isothermal packed-bed reactor (1.0 cm I.D.) with plug-flow hydrodynamics at temperatures between 503 K and 533 K. Experiments were carried out on TiO2(a), TiO2(r), ZrO2(m), and ZrO2(t) and on their respective physical mixtures with 20 wt.% Cu/SiO2 co-catalysts (oxide/Cu/SiO2) = 0.5–2 mass); these mixtures were prepared by crushing and mixing the mixtures with a mortar and pestle and then pressed into wafers, crushed, and sieved to retain 125–180 μm aggregates. The mixtures were then treated in flowing 10% H2/He (5.56 cm3 g−1 s−1, 99.999%, Praxair) by heating to 543 K (at 0.0833 K s−1) and holding for 2 h within the reactor before catalytic measurements. Liquid carboxylic acids were introduced using a syringe pump (Cole Parmer, 74900 series) at 433 K into a flow of H2-He mixtures (20 kPa H2, 99.999%, Praxair) metered using electronic mass flow controllers (Porter, Inc.). All lines were kept at 433 K to prevent condensation of reactants and products. Isotopic data were obtained using the same procedures and ethanoic acid-d4 (CD3COOD, >99%, Sigma-Aldrich) and D2 (>99%, Praxair) as reactants.

Reactor and product concentrations were determined by online gas chromatography (Agilent 6890). Carboxylic acids, anhydrides, alkanones, and other oxygenates were detected by a flame ionization detector after separation in a capillary column (Agilent, HP-1, methyl silicone, 50 m, 0.32 mm ID × 1.05 μm). H2, H2O, CO, and CO2 were detected by measuring thermal conductivity after chromatographic separation in a packed column (Porapak-Q, 4.8 m, 80–100 mesh). Molecular speciation was confirmed using known standards and mass spectrometry (HP 5972 mass spectrometer). A carbon basis was used to calculate all conversions and selectivities. For catalytic rate measurements, reactant conversions were kept below 5% to ensure the absence of axial reactant concentration gradients.

2.3. Titration of acid-base pairs during catalysis

Acid-base pairs on oxide surfaces can be titrated with carboxylic acids during aldol condensation, because acids strongly bind at such pairs and convert via ketonization at much lower rates than aldol condensation turnovers of carbonyl compounds [24]. These acid-base pairs are involved in both condensation and ketonization reactions, as shown in this study, thus allowing the rigorous reporting of the reactivity of each catalyst as turnover rates. These titrations were carried out on TiO2(a), TiO2(r), ZrO2(m), and ZrO2(t) catalysts using propanoic acid titrants (20 Pa) during acetone condensation reactions (0.8 kPa, 453 K) [24]. The titrant and product concentrations in the effluent were measured using the chromatographic protocols described above. The number of accessible acid-base pairs on the oxides was determined from the amount of adsorbed propanoic acid required to fully suppress con-
densation rates and the specific titrant stoichiometry inferred from infrared evidence and DFT treatments for each oxide. These studies showed that TiO$_2$(a) favors dissociated acids bound in a monoden-
tate form on a single Ti$-$O pair via respective interactions of the
two O-atoms in the formed carboxylates with the Ti center and
the abstracted proton bound at the O-atom in the Ti$-$O pair (Sec-
tions 3.3 and 3.4), leading to a titrant stoichiometry of one acid per
Ti$-$O pair. In contrast, TiO$_2$(r) (Sections 3.3 and 3.4), ZrO$_2$(m) [3],
and ZrO$_2$(t) [3] favor dissociated acids interacting with two vicinal
M$-$O pairs (M = Ti, Zr) via interactions of each of the two O-atoms
in the carboxylate structures with one of the M centers and in-
teraction of the abstracted H-atom and one of the lattice O-atoms,
to give a stoichiometry of one acid for each two M$-$O pairs.

Measured titration values for these TiO$_2$ and ZrO$_2$ oxides are in
reasonable agreement with their low-index-plane site densities
except for TiO$_2$(r) (Table 1). The fast prevalent deactivation of
TiO$_2$(r), caused by desorption hurdles of condensation products,
accounts for its lower measured Ti$-$O pair densities [24]. These
densities of acid-base pairs (Table 1) were used to report ketoniza-
tion reactivity as turnover rates, a measure of intrinsic reactivity
that allows rigorous comparisons among oxides and between the-
ory and experiment for each oxide catalyst.

2.4. Infrared spectroscopy measurements

Transmission infrared (IR) spectra were measured using a Nico-
let 8700 FT-IR spectrometer equipped with a Hg-Cd-Te (MCT)
detector. Samples were pressed into self-supporting wafers (5–
15 mg cm$^{-2}$) and placed in a cell with KBr windows. The samples
were treated at 573 K (0.0833 K s$^{-1}$) in He (5.56 cm$^3$ g$^{-1}$ s$^{-1}$, 99.999%, Praxair) for 2 h and then cooled to 523 K before collecting
spectra. Ethanoic acid (>99.7%, Sigma-Aldrich; 0.2–1.6 kPa) was
injected using a syringe pump using the same procedures as for
rate measurements (Section 2.2). All spectra were collected by
averaging 64 scans in the 4000–650 cm$^{-1}$ range with a 2 cm$^{-1}$ res-
olution and normalized by the C$=$O stretching band intensity of
gaseous ethanoic acid (1900–1600 cm$^{-1}$) at 1.6 kPa.

2.5. Density functional theory methods

Theoretical treatments of the elementary steps involved in
ketonization of ethanoic acid on TiO$_2$(a) and TiO$_2$(r) surfaces were
carried out using periodic plane-wave density functional theory
(DFT) methods [31–34] with the Perdew-Burke-Ernzerhof (PBE)
exchange-correlation functional [35,36] as implemented in the
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exchange-correlation functional [35,36] as implemented in the

Table 1

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Crystallographic acid-base pair density$^a$ (nm$^{-2}$)</th>
<th>Measured areal density of site pairs (nm$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO$_2$(a)</td>
<td>(101) 5.2, (100) 5.6, (001) 7.0, (010) 5.6</td>
<td>3.7$^b$</td>
</tr>
<tr>
<td>TiO$_2$(r)</td>
<td>(110) 5.2, (100) 7.4, (001) 7.4, (011) 8.0</td>
<td>1.6$^b$</td>
</tr>
<tr>
<td>ZrO$_2$(m)</td>
<td>(−111) 6.8, (111) 8.1, (−101) 5.7, (011) 5.3</td>
<td>6.0$^b$</td>
</tr>
<tr>
<td>ZrO$_2$(t)</td>
<td>(101) 8.6, (011) 7.5, (100) 5.2, (111) 3.3</td>
<td>5.8$^b$</td>
</tr>
</tbody>
</table>

$^a$ Selected planes are the most stable ones present on each metal oxide [28–30].
$^b$ Adapted from Ref. [24].
$^c$ Titration data shown in Section S2, SL.
characteristic of the molecular vibration along the reaction coordinate.

Vibrational frequencies for the optimized structures of reactive species and transition states were determined from the Hessian matrix using the same k-point mesh and convergence criteria for the geometric optimizations, while the bottom three layers of each unit cell were all frozen during the frequency analysis in order to reduce computational cost; these frequencies were not corrected by any factors. The enthalpies, entropies, and Gibbs free energies of reactants, transition states, and products were calculated for each elementary step from these frequencies using vibrational partition functions derived from the rigid-rotor harmonic oscillator approximation [48]. Weakly-bound adsorbates contain fewer than three low-frequency modes (<60 cm⁻¹). These modes were treated as rotations similar to gaseous molecules, instead of treating as harmonic oscillators, because the latter treatments lead to significant errors in the magnitude of the vibrational partition functions [49].

Hydroxide anion affinity (E_HA) for an acid site (A) is defined as the energy released from binding of a gaseous hydroxide anion (OH⁻), initially present at non-interacting distances, onto the acid site A:

\[ E_{HA} = E_{AH} - E_A - E_{OH} \]  

where \( E_i \) represents the electronic energy of species \( i \); these \( E_{HA} \) values are used as energy-based descriptors of the strength of a Lewis acid site. Proton affinity (E_PA) for a basic site (B) is defined in a similar way in order to describe the strength of the basic site B:

\[ E_{PA} = E_{HB} - E_B - E_H \]  

where \( E_i \) represents the electronic energy of species \( i \). These affinities for the acid-base pairs present on TiO₂(a) (101) surfaces were estimated using a Ti₄O₁₈H₇₆ cluster model instead of the above slab models, because dipole and quadrupole energy corrections cannot be calculated correctly for periodic systems with a net charge [42]. This cluster was extracted from a TiO₂(a) (101) surface with H-atoms attached to terminal O-atoms to maintain charge neutrality (structure shown in Section S3, SI). Similarly, a Ti₆O₁₂₀H₈₀ cluster (Section S3, SI) was constructed in order to estimate \( E_{HA} \) and \( E_{PA} \) for the Ti−O pairs present on TiO₂(r) (110) surfaces.

3. Results and discussion

3.1. Ketonization turnover rates of carboxylic acids on TiO₂ and ZrO₂ catalysts

Ketonization reactions of C₂−C₄ carboxylic acids (\( \text{C}_n\text{H}_{2n-1}\text{COOH}, n = 1–3 \)) take place with high selectivity on anatase TiO₂ (TiO₂(a)), rutile TiO₂ (TiO₂(r)), monoclinic ZrO₂ (ZrO₂(m)), and tetragonal ZrO₂ (ZrO₂(t)) catalysts. Carbon selectivities to ketonization products were above 95% (at 9–11% acid conversion, 48–72 h on all TiO₂ and ZrO₂ catalysts by extended treatments in flowing He at 523 K (Section S6, SI), suggesting that the site blockage occurs via the gradual formation of unreactive species that can be desorbed slowly, but without the need for a reactive environment (i.e. H₂ or O₂ treatments). Infrared spectra showed that such unreactive residues consist of bidentate carboxylates formed via dissociative adsorption of carboxylic acids on two vicinal acid-base pairs (Scheme 3; Section 3.3); the timescale for the appearance and disappearance of bidentate carboxylate vibrational features coincides with that for deactivation and regeneration, respectively (Section 3.3). DFT treatments of ketonization elementary steps on TiO₂(a) and TiO₂(r) surfaces also indicate that bidentate carboxylates are not involved in ketonization turnovers (Section 3.4); they act instead as unreactive spectators that occupy acid-base pairs, thus rendering them inaccessible for catalytic turnovers.

Ethanoic acid ketonization rates on TiO₂(a) and TiO₂(r) catalysts remained essentially constant with time in the presence of gaseous H₂ and a Cu function (\( k_d \approx 0.002 \text{ ks}^{-1} \); 20 kPa H₂, \( \text{Cu/SiO}_2 \)/oxide = 1 (mass); Fig. 1b). These conditions and catalyst mixtures led to the concurrent appearance of ethanolic and ethanol, which form via hydrogenolysis of ethanoic acid or hydrogenation of its ketene derivatives (\( \text{CH}_2=C=\text{O} \); from dehydration of ethanoic acid [14]) on Cu surfaces (Scheme 4). The combined formation rates of these hydrogenation products were much lower than ketonization rates (Section S7, SI). Ketonization rates of propanoic acid and...
butanoic acid were also rendered stable over time by these bifunctional strategies ($k_d < 0.002$ ks$^{-1}$ on TiO$_2$(a); Fig. 2).

We surmise that the bidentate carboxylates can dehydrate to form gaseous ketenes in trace amounts (Scheme 3), as evident from DFT calculations (Section S8, SI); these ketene concentrations are set by their unfavorable formation thermodynamics and are well below detection limits. Steady-state coverages of bidentate carboxylates can thus be decreased by the continuous slow scavenging of ketene species to form ethanal and ethanol[4,50] on a Cu function present within diffusion distances from Ti—O centers. Such scavenging into stable products prevents ketene re-adsorption and the re-formation of the unreactive bidentate carboxylates. These stable ketonization rates on TiO$_2$(a) and TiO$_2$(r) allow the rigorous assessment of the ketonization mechanism through combined kinetic and isotopic methods, as described in Section 3.2.

The deactivation of ZrO$_2$(m) and ZrO$_2$(t) catalysts in ketonization of ethanoic acid was suppressed less effectively by the gaseous
H₂ (20 kPa) and the Cu function ((Cu/SiO₂)/oxide = 1 mass) than on TiO₂(a) or TiO₂(r). The kₙ values decreased from 0.094 to 0.061 ks⁻¹ on ZrO₂(m) and from 0.082 to 0.040 ks⁻¹ on ZrO₂(t) (Fig. 1), in contrast to the essential suppression of deactivation processes on TiO₂(a) and TiO₂(r) using similar strategies and conditions (kₙ ≤ 0.002 ks⁻¹; Fig. 1b). Higher (Cu/SiO₂)/oxide mass ratios did not lead to further stabilization of these ZrO₂ catalysts (0.060 ks⁻¹ on ZrO₂(m) at (Cu/SiO₂)/oxide = 2 (mass); Section S9, SI). Such findings appear to indicate that desorption of bidentate carboxylates from ZrO₂(m) and ZrO₂(t) exhibits kinetic hurdles that inhibit their equilibration with gaseous ketene and thus the continuous scavenging of bidentate carboxylates via irreversible ketene hydrogenation on the Cu function. DFT treatments show that the conversion of bidentate carboxylates to ketenes on ZrO₂(m) (−111) and TiO₂(a) (101) surfaces is limited by the C=O bond cleavage in bidentate carboxylates; its free energy barrier is higher on ZrO₂(m) (−111) than on TiO₂(a) (101), because Zr centers on ZrO₂(m) are weaker Lewis acids than Ti centers on TiO₂(a) (Section S8, SI); as a result, the C=O cleavage TS that mediates ketene formation is less stable on ZrO₂(m) because its two O-atoms interact more weakly with Zr than they do with Ti centers on TiO₂(a).

3.2. Effects of reactant pressure on ketonization rates and implications for elementary steps and their kinetic relevance on anatase and rutile TiO₂

All rates reported hereinafter were obtained on stable TiO₂(a) and TiO₂(r) catalysts, present as mixtures with Cu/SiO₂ and in the presence of 20 kPa H₂ (Fig. 1b). These rates were not influenced detectably by the prevalent pressure of the ketonization products (i.e. alkanones, H₂O and CO₂; 0.02–0.2 kPa), which was varied by changes in space velocity (Section S10, SI), consistent with the weak binding of such product molecules on Ti−O pairs of moderate acid-base strength [24]. These product concentrations do not therefore appear as terms in the denominator of the ketonization rate equations derived below.

Fig. 3a shows ketonization turnover rates for ethanoic acid-d₀ and ethanoic acid-d₄ reactants as a function of their respective pressures (0.1–3.0 kPa) on TiO₂(a)+Cu/SiO₂ mixtures (523 K, 20 kPa H₂/D₂). Rates increased with increasing reactant pressure, but became less sensitive to the concentration of reactants at higher ethanoic acid pressures. Similar trends were observed for propanoic and butanoic acids (Fig. 3a) and for ethanoic acid at other temperatures (503–533 K; Fig. 3b). The nearly zero-order kinetic dependences at higher reactant pressure (>1.2 kPa) are consistent with the strong adsorption and monolayer coverages of surface carboxylates derived from acid reactants on TiO₂(a) at the conditions of catalysis.

A plausible sequence of ketonization elementary steps on TiO₂(a) is shown for the specific case of ethanoic acid in Scheme 5. This sequence leads to rate equations consistent with the rate data and isotope effects shown in Fig. 3 and with theoretical assessment of free energies for these elementary steps shown in Section 3.4. The kₙ and kᵣ parameters in Scheme 5 represent the rate constants for the forward and reverse directions of Step x, respectively, and Kₓ is the corresponding equilibrium constant for each step (Kₓ = kᵣ / kₙ).

These elementary steps involve the dissociation of ethanoic acid at a Ti−O pair (AcO'); monodentate carboxylate; Step 1, Scheme 5), with an O-atom in the carboxylic group bound to the Ti center and the other one H-bonded to the H-atom that is abstracted from the acid and bound at the Ti−O pair. These carboxylates can also bind to two vicinal Ti−O pairs (‘AcO’; bidentate carboxylate; Step 2, Scheme 5), with each of its two O-atoms bound at one of the two Ti centers and the abstracted H-atom bound at a lattice O-atom. Infrared spectra during ketonization catalysis show that AcO’ species are the most abundant surface intermediates (MASI) (Section 3.3) during ketonization on TiO₂(a). Ethanoic acid is not preferentially bound as bidentate carboxylate species (’AcO”), a configuration previously proposed as the prevalent MASI during
catalysis and claimed as the reactive intermediate in ketonization reactions on TiO$_2$(a) \cite{16,17,22}, ZrO$_2$(m) \cite{19,21}, CeO$_2$ \cite{14,18,22}, and ZnO-Cr$_2$O$_3$ \cite{20} based on infrared spectra of pre-adsorbed ethanoic acids at conditions removed from practical ketonization catalysis \cite{21,22} and on DFT-derived estimates of electronic energies at low surface coverages \cite{19}. The explicit treatments of these densely-covered surfaces and of the thermal corrections and entropy effects required for accurate energies and free energies at low surface coverages \cite{19}. The explicit treatments of these densely-covered surfaces and of the thermal corrections and entropy effects required for accurate energies and free energies in DFT calculations lead to the conclusion that monodentate carboxylates, instead of bidentate species, prevail as adsorbed species and that they act as the reactive intermediates in ketonization catalytic sequences on TiO$_2$(a) (Section 3.4) and also on ZrO$_2$ surfaces, as we shall report separately.

In Scheme 5, 1-hydroxy enolates form from acids via $\alpha$-$\text{C}$$\text{--H}$ cleavage in AcO$^-$ species at Ti–O pairs (Step 3, Scheme 5); these enolates nucleophilically attack the carboxyl C-atom in a neighboring AcO$^-$ to form $\alpha$-hydroxy $\gamma$-carboxy alkoxides containing a new C–C bond (Step 4, Scheme 5); these steps resemble those involved in aldol condensation of carboxyl compounds on acid-base pairs (Scheme 1; Ref. \cite{24}). Aldol condensation turnovers involve cleavage of $\alpha$-$\text{C}$$\text{--H}$ bonds to form enolate species and subsequent C–C bond formation between the enolate and a coadsorbed carboxyl reactant bond at a vicinal Ti center to form $\gamma$-keto alkoxide species, as the precursors to the aldol products. In contrast to these $\gamma$-keto alkoxide intermediates prevalent in condensation reactions, the alkoxides formed via C–C coupling between species derived from two carboxylic acids (Step 4, Scheme 5) retain the $\text{OH}$ group at the $\alpha$-C-atoms and the $-\text{COOH}$ group at the $\gamma$-C-atom; dehydra-
tion of these groups can be catalyzed by a vicinal lattice O center to form $\beta$-keto carboxylates (Steps 5–7, Scheme 5), which then reproto-
tonate to $\beta$-keto acids (Step 8, Scheme 5). These $\beta$-keto acid inter-
mediates are very reactive and decarboxylate to form C$_3$ enolates (i.e. propen-2-olates) and CO$_2$ (Steps 9–11, Scheme 5). The propen-2-olate species subsequently reprotonate to form acetone, completing a ketonization turnover (Steps 12–13, Scheme 5). The lack of space velocity effects on rates (Section S10, SI) indicates that the adsorption constants ($K_1$; Scheme 5) for H$_2$O (K$_{10}$), CO$_2$ (K$_{11}$), and acetone (K$_{12}$) are very small and that the coverages of these species are thus kinetically-negligible on TiO$_2$(a) surfaces during ketonization catalysis.

Significant kinetic H/D isotope effects would indicate that bonds containing a H-atom form or cleave in kinetically-relevant steps. For instance, enolate formation, the kinetically-relevant step in aceto-condensation on TiO$_2$(a), gives a H/D isotope effect of 2.4 (523 K; Ref. \cite{24}). The ketonization rates measured for ethanoic acid-d$_8$ and ethanoic acid-d$_4$ are, however, very similar ($r_8/r_4$ = 1.1 ± 0.1 at 0.6–2.2 kPa, TiO$_2$(a); Fig. 3a) and rule out the kinetic relevance of the $\alpha$-$\text{C}$$\text{--H}$ cleavage step that forms 1-hydroxy enolates from monodentate carboxylates (Step 3, Scheme 5). Such small observed H/D isotope effects would also be inconsistent with the kinetic relevance of any other step involving activation or cleavage of a C–H–O–H bond in Scheme 5 (i.e. Steps 5, 6, 8, 9, and 12). Thus, C–C coupling between 1-hydroxy enolates and coadsorbed AcO$^-$ (Step 4, Scheme 5) and decarboxyla-
tion of $\beta$-keto carboxylates (Step 10, Scheme 5) are the only plaus-
ible kinetically-relevant elementary steps consistent with measured H/D kinetic isotope effects.

The elementary steps in Scheme 5, taken together with (i) the pseudo-steady-state approximation for all bound species; (ii) the quasi-equilibrated nature of all steps except C–C coupling (Step 4, Scheme 5) and decarboxylation (Step 10, Scheme 5) steps; (iii) an irreversible decarboxylation step; and (iv) AcO$^-$ and * (bare Ti–O pairs) as the most abundant surface intermediates (MASI; from infrared spectra; Section 3.3) give the rate equation:

$$\frac{r}{[L]} = \frac{k_4K_{10}K_2^2(P_{\text{acid}})^2}{k_4P_{\text{H2O}}(1 + K_1P_{\text{acid}})^2}$$

(6)

Here, $k_3$, $k_4$, and $K_2$ are the respective forward and reverse rate constants and equilibrium constant for Step x in Scheme 5, and $[L]$ is the concentration of catalytically relevant acid-base pairs on oxide surfaces (derivation in Section S11, SI). The weak effects of conversion and of H$_2$O pressure (0.02–0.2 kPa) on ketonization rates (Section S10, SI) indicate that the $k_4P_{\text{H2O}}(1 + K_1P_{\text{acid}})^{-1}$ term in Eq. (5) is much smaller than the $k_{10}$ constant, which indicates, in turn, that the C–C coupling step (Step 4, Scheme 5) is irreversible and the sole kinetically-relevant step. Eq. (6) then becomes:

$$\frac{r}{[L]} = \frac{k_4K_2^2(P_{\text{acid}})^2}{(1 + K_1P_{\text{acid}})^2}$$

(7)

The functional form of Eq. (7) accurately describes all rate data for ethanoic acid at 503–533 K (Fig. 3), regressed parameters shown in Tables 2 and 3) and leads to isotopic effects near unity for the
1. Dissociation of ethanoic acid on a Ti-O pair to form AcO*:

\[
\begin{align*}
\text{CH}_3 & + \quad \text{O} \rightarrow \text{Ti} \xleftrightarrow[k_1]{k_1} \text{H} \quad \text{O} \rightarrow \text{Ti} \quad \text{(AcO*)} \\
\text{H} & \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

2. Dissociation of ethanoic acid on two Ti-O pairs to form *AcO*:

\[
\begin{align*}
\text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_2]{k_2} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{(AcO*)} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

3. α-C-H cleavage from AcO* to form 1-hydroxy enolate:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_3]{k_3} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{1-hydroxy enolate} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

4. C-C coupling between 1-hydroxyl enolate and co-adsorbed AcO* to form α-hydroxy γ-carboxy alkoxide:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_4]{k_4} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{(α-hydroxy γ-carboxy alkoxide)} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

5. Dissociation of O-H bond in α-hydroxy γ-carboxy alkoxide to form γ-hydroxy γ-oxido carboxylate:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_5]{k_5} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{(γ-hydroxy γ-oxido carboxylate)} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

6. H₂O elimination from γ-hydroxy γ-oxido carboxylate to β-keto carboxylate:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_6]{k_6} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{(β-keto carboxylate)} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

7. H₂O desorption:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_7]{k_7} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{+ H₂O} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

8. Protonation of β-keto carboxylate to form β-keto acid:

\[
\begin{align*}
\text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 & \quad \text{O} \quad \text{C} \quad \text{H}_3 \xleftrightarrow[k_8]{k_8} \text{H} \quad \text{O} \quad \text{C} \quad \text{H}_3 \quad \text{(β-keto acid)} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

9. Dissociation of β-keto acid on a Ti-O-Ti structure:

\[
\begin{align*}
\text{O} \quad \text{Ti} \quad \text{O} & \quad \text{Ti} \quad \text{O} \quad \text{Ti} \xleftrightarrow[k_9]{k_9} \text{O} \quad \text{Ti} \quad \text{O} \quad \text{Ti} \\
\text{O} & \quad \text{Ti} \quad \text{O} \\
\text{O} & \quad \text{Ti} \\
\text{O} & \quad \text{Ti}
\end{align*}
\]

Scheme 5. Proposed elementary steps for carboxylic acid ketonization on acid-base pairs of TiO₂(a) (shown for ethanoic acid as an illustrative example).
\(k_4^*K_3\) and \(K_1\) terms in Eq. (7) \((k_4^*K_3H/(k_4^*K_3)D = 1.1, (K_1)H/(K_1)D = 1.0,\) 523 K, Table 2), consistent with the kinetic relevance of the C–C coupling step (Step 4, Scheme 5) and with the involvement of H-atoms only in quasi-equilibrated steps, a conclusion confirmed by DFT treatments in Section 3.4, as also inferred above from the magnitude of the rates with perdeuterated and undeuterated reactants.

The \(K_1\) term in Eq. (7) determines the fractional coverage \(\theta_{AcO^-}\) of monodentate AcO\(^{-}\) species bound at a Ti–O pair (\(\theta_{AcO^-}\); Step 1, Scheme 5):

\[
\theta_{AcO^-} = \frac{K_1P_{AcO^-}}{1 + K_1P_{AcO^-}}
\]

(8)

The \(\theta_{AcO^-}\) values range from 0.70 to 0.99 ML (523 K, 0.1–3.0 kPa ethanoic acid) when using \(K_1\) values from ketonization rates and the functional form of Eq. (7) (24 ± 2 kPa; Table 2). These values indicate that ketonization turnovers occur on TiO\(_2\)(a) surfaces nearly saturated with AcO\(^{-}\) species, a conclusion confirmed by in-situ infrared data (Section 3.3) and by DFT-derived adsorption energies (Section 3.4).

Ketonization rates of propanoic and butanoic acids are also described accurately by Eq. (7) (Fig. 3a). The regressed \(K_1\) values for propanoic and butanoic acids \((13 ± 2, 7.9 ± 0.6\) kPa\(^{-1};\) 523 K, Table 2) also lead to near saturation coverages \(\theta_{AcO^-}\) of 0.56–0.97, propanoic acid; 0.44–0.96, butanoic acid; 523 K, 0.1–3.0 kPa acid). Thus, the kinetic relevance of the C–C coupling step (Step 4, Scheme 5) and the high coverages of monodentate carboxylates prevalent during catalysis seem to apply for the ketonization of C\(_2\)–C\(_4\) carboxylic acids on TiO\(_2\)(a) surfaces.

Ketonization rates for ethanoic acid-d\(_0\) and ethanoic acid-d\(_4\) on rutile TiO\(_2\) powders (TiO\(_2\)(r)) are also consistent with the functional form of Eq. (7) (Fig. 4; Table 2); these reactants give H/D isotope effects near unity for both \(k_4^*K_3\) and \(K_1\) \((k_4^*K_3H/(k_4^*K_3)D = 1.1,\) \((K_1)H/(K_1)D = 1.0,\) Table 2), indicative of similar pathways and active Ti–O pairs on TiO\(_2\)(r) and TiO\(_2\)(a). The regressed values of \(K_1\) (5.4

Table 2

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reactant</th>
<th>(K_1^0) (kPa(^{-1}))</th>
<th>(\Delta G_{AcO^-}) (kJ mol(^{-1}))</th>
<th>(k_4^*K_3^0) (10(^{-6}) (Ti-O(^{-})) (^{-1}) s(^{-1}))</th>
<th>(\Delta G_{CC,Ac}) (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO(_2)(a)</td>
<td>CH(_3)COOH</td>
<td>24 ± 2</td>
<td>−33 ± 1</td>
<td>269 ± 3</td>
<td>166 ± 1</td>
</tr>
<tr>
<td></td>
<td>CD(_3)COOH</td>
<td>24 ± 2</td>
<td>−33 ± 1</td>
<td>236 ± 4</td>
<td>167 ± 1</td>
</tr>
<tr>
<td></td>
<td>C(_2)H(_5)COOH</td>
<td>13 ± 2</td>
<td>−30 ± 1</td>
<td>102 ± 3</td>
<td>170 ± 1</td>
</tr>
<tr>
<td></td>
<td>C(_3)H(_7)COOH</td>
<td>7.9 ± 0.6</td>
<td>−28 ± 1</td>
<td>41 ± 1</td>
<td>175 ± 1</td>
</tr>
<tr>
<td>TiO(_2)(r)</td>
<td>CH(_3)COOH</td>
<td>5.4 ± 0.3</td>
<td>−27 ± 1</td>
<td>34 ± 1</td>
<td>175 ± 1</td>
</tr>
<tr>
<td></td>
<td>CD(_3)COOH</td>
<td>5.4 ± 0.3</td>
<td>−27 ± 1</td>
<td>30 ± 1</td>
<td>176 ± 1</td>
</tr>
</tbody>
</table>

a 523 K; fitted data adopted from Fig. 3a for TiO\(_2\)(a) and Fig. 4 for TiO\(_2\)(r).
b Fitted using Eq. (7).
c Fitted using Eq. (9).
d Fitted using Eq. (13).
Table 3
Regressed $K_1$, $\tilde{k}_1K_2$, $\Delta G_{AcO}$, and $\Delta G_{CC,a}$ values (to the functional form of Eq. (7)) for ketonization of ethanoic acid on TiO$_2$(a) at temperatures between 503 K and 533 K and corresponding enthalpy and entropy components of free energies.$^a$

<table>
<thead>
<tr>
<th>$T$ (K)</th>
<th>$K_1$ (kPa$^{-1}$)</th>
<th>$\Delta G_{AcO}^a$ (kJ mol$^{-1}$)</th>
<th>$\Delta H_{AcO}^a$ (kJ mol$^{-1}$)</th>
<th>$\Delta S_{AcO}$ (J mol$^{-1}$ K$^{-1}$)</th>
<th>$\tilde{k}_1K_2$ (10$^{-6}$ (Ti-O)$^{-1}$ s$^{-1}$)</th>
<th>$\Delta G_{CC,a}^e$ (kJ mol$^{-1}$)</th>
<th>$\Delta H_{CC,a}$ (kJ mol$^{-1}$)</th>
<th>$\Delta S_{CC,a}$ (J mol$^{-1}$ K$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>503</td>
<td>71 ± 7</td>
<td>−36 ± 1</td>
<td>−114 ± 3</td>
<td>−155 ± 6</td>
<td>77 ± 1</td>
<td>165 ± 1</td>
<td>137 ± 1</td>
<td>−56 ± 1</td>
</tr>
<tr>
<td>513</td>
<td>39 ± 4</td>
<td>−35 ± 1</td>
<td>−113 ± 3</td>
<td>−154 ± 6</td>
<td>145 ± 3</td>
<td>166 ± 1</td>
<td>138 ± 1</td>
<td>−56 ± 1</td>
</tr>
<tr>
<td>523$^b$</td>
<td>24 ± 2</td>
<td>−33 ± 1</td>
<td>−110 ± 3</td>
<td>−153 ± 6</td>
<td>269 ± 3</td>
<td>166 ± 1</td>
<td>139 ± 1</td>
<td>−57 ± 1</td>
</tr>
<tr>
<td>533</td>
<td>15 ± 2</td>
<td>−32 ± 1</td>
<td>−108 ± 3</td>
<td>−152 ± 6</td>
<td>488 ± 7</td>
<td>167 ± 1</td>
<td>140 ± 1</td>
<td>−58 ± 1</td>
</tr>
</tbody>
</table>

$^a$ Fitted data adopted from Fig. 3b.
$^b$ Adopted from Table 2.
$^c$ Fitted using Eq. (7).
$^d$ Fitted using Eq. (9).
$^e$ Fitted using Eq. (13).

Fig. 4. Effects of ethanoic acid pressure on ketonization turnover rates (ethanoic acid and ethanoic acid-d$_4$; TiO$_2$(r) + 20 wt.% Cu/SiO$_2$ (1:1 mass), 523 K, 20 kPa H$_2$ for undeuterated reactants, 20 kPa D$_2$ for deuterated reactants). Dashed lines represent the regressed fits to the mechanism-based functional form of Eq. (7).

Here $G_{AcO}$, $G_{AcO}^{eb}$, and $G_{Ti-O}$ are the free energies of the bound monodentate carboxylate (Step 1, Scheme 5), the gaseous carboxylic acid, and the Ti–O pair. The $\tilde{k}_1K_2$ numerator term in Eq. (7) reflects, in turn, the free energy difference between the C–C coupling TS ($G_{CC}^e$; Step 4, Scheme 5) and two gaseous acid reactants and two bare Ti–O pairs ($G_{CC,a}$; Scheme 6):

$$\tilde{k}_1K_2 = \frac{kbT}{h} \exp(-\Delta G_{CC}^e/RT)$$ (11)

$$\Delta G_{CC}^e = G_{CC}^{eb} - 2G_{AcO} - 2G_{Ti-O}$$ (12)

The $\tilde{k}_1K_2$ term, determined from measured $\tilde{k}_1K_2$ (Eq. (11)) and $K_1$ (Eq. (8)) values, represents the maximum ketonization turnover rate ($r_{\text{max}}$); it is achieved as monodentate AcO$^*$ species reach saturation coverages:

$$r_{\text{max}} = \tilde{k}_1K_2 = \frac{kbT}{h} \exp(-\Delta G_{CC,a}^e/RT)$$ (13)

Here $\Delta G_{CC,a}^e$ represents the free energy of the C–C coupling TS (Step 4) with respect to two bound AcO$^*$ species on TiO$_2$(a) surfaces (Scheme 6):

$$\Delta G_{CC,a}^e = G_{CC}^{eb} - 2G_{AcO}$$ (14)

Table 2 reports $\Delta G_{AcO}$ and $\Delta G_{CC,a}$ values from the $K_1$ and $\tilde{k}_1K_2$ parameters from all rate data regressed to the functional form of Eq. (6) for C$_3$–C$_4$ carboxylic acids on TiO$_2$(a). The $\Delta G_{AcO}$ values (523 K; Table 2) become less negative as the alkyl chain in the carboxylic acid lengthens ($\sim 33 \pm 1$ kJ mol$^{-1}$, ethanoic acid; $\sim 28 \pm 1$ kJ mol$^{-1}$, butanoic acid), indicative of steric effects that weaken AcO$^*$ binding at the nearly saturated TiO$_2$(a) surfaces present during ketonization catalysis.

$\Delta G_{CC,a}$ values (523 K; Table 2) became more positive with increasing alkyl chain length ($\sim 166 \pm 1$ kJ mol$^{-1}$, ethanoic acid; $\sim 175 \pm 1$ kJ mol$^{-1}$, butanoic acid). These trends reflect, in part, the stronger steric hindrance imposed by the larger alkyl groups in the 1-hydroxy enolate and coadsorbed AcO$^*$ components of the C–C coupling TS than for its two AcO$^*$ precursors (Step 4, Scheme 5); they also arise, to some extent, from electron-donating alkyl substituents that make the α-C-atom in 1-hydroxy enolate a weaker nucleophile [51]. Alkyl substituents have the opposite effects on the decarboxylation of β-keto carboxylates (Step 10, Scheme 5) than on the C–C coupling step. Stronger repulsion between the larger alkyl groups at the α-C and β-C positions of β-keto carboxylates favors CO$_2$ elimination. The alkyl group at the α-C position also stabilizes the decarboxylation TS via p–p conjugation with the incipiently formed C═C bond. The consequent higher decarboxylation rates as alkyl chains lengthen provide additional evidence for the kinetic irrelevance of this step, because measured $\Delta G_{CC,a}$ values increase with increasing alkyl substitution (Table 2).
The enthalpy and entropy components of measured $\Delta G_{\text{AcO}}$ and $\Delta S_{\text{AcO}}$ values for ethanoic acid were obtained by regressing the rate and equilibrium constants in Eq. (7) from rate data at different temperatures (503–533 K; $\Delta G = \Delta H - T \Delta S$; Table 3). The $\Delta H_{\text{AcO}}$ and $\Delta S_{\text{AcO}}$ values for the adsorption of ethanoic acid as monodentate carboxylates on TiO$_2$(a) are $-114 \pm 3 \text{ kJ mol}^{-1}$ and $-155 \pm 6 \text{ J mol}^{-1} \text{ K}^{-1}$, respectively (Table 3), reflecting the predominant enthalpic component in $\Delta G_{\text{AcO}}$ values at these temperatures. Measured $\Delta H_{\text{C,a}}$ and $\Delta S_{\text{C,a}}$ values for ethanoic acid ketonization on TiO$_2$(a) are $137 \pm 1 \text{ kJ mol}^{-1}$ and $-56 \pm 1 \text{ J mol}^{-1} \text{ K}^{-1}$ (Table 3). These enthalpy and entropy values, taken together with the respective free energies, allow accurate benchmarking of experimental and theoretical methods in determining the preferred ketonization pathways and the kinetic relevance of the steps and intermediates that mediate ketonization turnovers on TiO$_2$(a) surfaces (Section 3.4).

The evidence presented above indicates that ketonization of C$_2$–C$_4$ carboxylic acids proceeds via kinetically-relevant C–C coupling transition states on Ti–O pairs of TiO$_2$(a) surfaces essentially saturated with monodentate carboxylates bound at acid-base pairs. These conclusions are confirmed below by the infrared detection of the adsorbed species prevalent during ketonization catalysis (Section 3.3) and by theoretical assessments of the stability of adsorbed species and transition states over a broad range of surface coverages (1/8–1 ML) (Section 3.4).

### 3.3. Infrared study of adsorbed species derived from ethanoic acid adsorption on anatase and rutile TiO$_2$ catalysts

Infrared spectra were collected during ethanoic acid ketonization on TiO$_2$(a) and TiO$_2$(r) at 523 K and 0.2–1.6 kPa ethanoic acid in order to assess the type, coverage, and kinetic involvement of adsorbed species. Ethanoic acid (AcOH) can dissociate to form monodentate (AcO$^-$; Step 1, Scheme 5) or bidentate (AcO$^{2-}$; Step 2, Scheme 5) carboxylates at one or two Ti–O pairs; it can also bind molecularly via H-bonding at a Ti–O pair (AcOH$^*$) [3]. DFT-derived binding energies show that the relative coverages of AcO$^-$ and AcOH$^*$ depend on the strength of the basic lattice O-atom (Section 3.4). AcO$^-$ is much more stable than AcOH$^*$ on Ti–O pairs in TiO$_2$(a); in contrast, AcOH$^*$ is the most stable monodentate form on TiO$_2$(r), because its coordinatively-unsaturated O-atoms are more weakly basic than those on TiO$_2$(a) ($E_{ox} = -1097$ vs. $-1175$; Section 3.4). These carboxylate and molecular forms can be distinguished by stretching modes of their respective carboxyl or carboxylate moieties (–C(=O)OH, –C(=O)O–). AcOH$^*$ binds with its O-atom at the Ti center of a Ti–O pair and its hydroxy H-atom at the O-atom of this Ti–O pair (Scheme 7a). AcO$^-$ species binds in monodentate form with its two O-atoms at the Ti center of a Ti–O pair and at the abstracted H-atom, which is bound at the O-atom in the Ti–O pair (Scheme 7b). In contrast, ‘AcO’ species binds in bidentate form with each of its two O-atoms at one Ti center in two vicinal Ti–O pairs (Scheme 7c).

DFT-derived vibrational frequencies for these modes were used to assign these bands and to determine the relative stability of these species as a function of coverage on TiO$_2$ surfaces. Surface coverages ($\theta_{\text{acid}}$) are defined here based on Ti–O pairs:

$$\theta_{\text{acid}} = \frac{n_{\text{acid}}}{n_{\text{Ti,O}}}$$

where $n_{\text{acid}}$ is the number of adsorbed carboxylic acid molecules and $n_{\text{Ti,O}}$ is the number of exposed Ti–O pairs. The maximum $\theta_{\text{acid}}$ value for each form is set by their respective binding stoichiometries (1 for AcOH$^*$ and AcO$^*$, 1/2 for ‘AcO’). DFT-derived frequencies for C=O and C–O stretches of AcOH$^*$ on TiO$_2$(a) are 1641–1659 cm$^{-1}$ and 1480–1493 cm$^{-1}$, respectively (at 1/6–1 ML; Table 4). The antisymmetric $\nu_{\text{C=O}}$ ($\nu_{\text{C=O,as}}$) and symmetric $\nu_{\text{C=O}}$ ($\nu_{\text{C=O,s}}$) vibrations in AcO$^*$ on TiO$_2$(a) appear at 1540–1564 cm$^{-1}$ and 1379–1409 cm$^{-1}$, respectively (at 1/6–1 ML; Table 4); these frequencies are at 1529–1531 cm$^{-1}$ ($\nu_{\text{C=O,as}}$) and 1435–1437 cm$^{-1}$ ($\nu_{\text{C=O,s}}$) for ‘AcO’ (at 1/8–1/2 ML; Table 4).

The infrared spectra on TiO$_2$(a) after treatments of He at 573 K for 2 h exhibit O–H bands (3667 cm$^{-1}$; Fig. 5a), assigned to titanol species at surface defects ubiquitous on oxide crystallites [52,53]. Contact with ethanoic acid (1.0 kPa) at 523 K caused these O–H stretches to shift to lower wavenumbers and to merge with a broader and more intense band centered at 3150 cm$^{-1}$, which is assigned to OH species derived from the dissociation of ethanoic acid to form either AcO$^*$ or ‘AcO’ (Schemes 7b and c); such a frequency shift relative to isolated...
Ti–OH species reflects the effects of H-bonding [22] at the prevalent dense adlayers. These isolated titanos are present as minority species and are thus not explicitly considered as active structures in the DFT treatments of ketonization elementary steps (Section 3.4).

Three distinct bands appeared upon contact of TiO2(a) with ethanoic acid at 523 K (2936, 1548, and 1385 cm−1) together with those for the gaseous reactants (3596, 3581, 3566, 1796, 1776 cm−1) [53] and the CO2(g) ketonization product (2362 cm−1) [54]. DFT treatments show that the bands at 1548 and 1385 cm−1 correspond to νCDO,as and νCDO, vibrations in AcO−, respectively (DFT: 1540–1564 cm−1, 1379–1409 cm−1; Table 4). The band at 2936 cm−1 corresponds to the –CH3 stretch (νCH3) in AcO− (DFT: 2982–2990 cm−1; Table 4) [55]. The frequencies of these νCDO,as and νCDO, bands were essentially unperturbed by changes in ethanoic acid pressure (0.2–1.6 kPa; Fig. 6a), indicating that AcO− is the predominant carboxylate and that it is present at near-saturation coverages on TiO2(a) at all conditions. The intensity of the –CH3 stretch band increased with increasing ethanoic acid pressure in a Langmuir manner (Fig. 6a; Eq. (8)) with a K1 value (24 ± 2 kPa−1, Fig. 6a) that is similar to that derived from ketonization rate data and Eq. (6) (24 ± 2 kPa−1, Table 2; Fig. 3a). These K1 values show that monodentate carboxylates (AcO−) are present at high coverages (θAcO− 0.83–0.97 ML) as the predominant adsorbed species on TiO2(a) at all conditions of relevant ketonization catalysis.

The removal of ethanoic acid from the contacting gas phase led to the gradual disappearance of the bands for AcO− and CO2(g) on TiO2(a) samples (Fig. 5a) over 2 h at 523 K and to the concurrent appearance of bands at 1538 and 1428 cm−1 (Fig. 5a); these bands correspond to νCDO,as and νCDO, stretches in bidentate carboxylates (AcO−) according to DFT estimates (1529–1531 cm−1, 1435–1437 cm−1; Table 4). The intensity of these AcO− bands decreased very gradually with time and the bands became undetectable after treatment in He at 523 K for 26 h. These treatments in He at 523 K also led to the full recovery of initial ketonization rates on TiO2(a) samples deactivated for 22 h to 0.76 of initial rates; 523 K, 1.0 kPa ethanoic acid; Section 3.1). The recombative desorption of the active AcO− species leads to a decrease in their coverage with time; the concomitant increase in vacant sites (°) then allow the gradual formation of AcO− as the stable form of adsorbed ethanoic acid on TiO2(a) surfaces. The slow removal of these AcO− species in an inert environment is consistent with the nature of the regeneration treatments that led to the recovery of initial ketonization rates on deactivated samples and also with the proposal that bidentate carboxylates act as unreactive spectator species that prevent access to the Ti–O pairs required for ketonization turnovers.

Exposure of TiO2(r) to gaseous ethanoic acid (1.0 kPa, 523 K; Fig. 5b) led to bands similar to those observed on TiO2(a), but at lower frequencies (1522, 1401 cm−1). These bands correspond to νCDO,as and νCDO, stretches in bidentate carboxylates (AcO−), an assignment based on DFT-derived frequencies (1514–1522 cm−1, 1432–1444 cm−1, Table 4) and on spectroscopic and theoretical evidence for the prevalence of AcO− over AcOH and AcO− on TiO2(r) [3,52]. These νCDO,as and νCDO, frequencies did not change with ethanoic acid pressure (0.2–1.6 kPa; Fig. 6b) or after removal of ethanoic acid from contact with the catalysts for 0.5 h (Section S12.1); thus, we conclude that bidentate carboxylates (AcO−) are the MASI on TiO2(r) during ketonization catalysis, in distinct contrast to the prevalence of monodentate AcO− species on TiO2(a) surfaces. The integrated intensity of the νCDO,as band (2932 cm−1) on TiO2(r) was unaffected by the ethanoic acid pressure (0.2–1.6 kPa; Fig. 6b), indicative of the presence of AcO− species at near saturation coverages. The regressed fits of these coverages on TiO2(r) to the Langmuir form of Eq. (8) give a K1 value of 190 ± 3 kPa−1 (Fig. 6b), a value that differs markedly from that derived from the rate data and Eq. (7) on TiO2(a) (5.4 ± 0.3 kPa−1; Table 2; Fig. 4). Thus, the species detected in the infrared spectra on TiO2(r) sur-

![Scheme 7. DFT-derived adsorption modes for ethanoic acid on Ti-O pairs (PBE + D3BJ, PAW, TiO2(a) (101) surfaces).](image)

<table>
<thead>
<tr>
<th>Oxide</th>
<th>Mode</th>
<th>θacid range (ML)</th>
<th>Frequency (cm−1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO2(a)</td>
<td>AcOH−</td>
<td>1/6–1</td>
<td>νCDO,as 1641–1659, νCDO, 1480–1493, νOH 2985–2991</td>
</tr>
<tr>
<td></td>
<td>AcO−</td>
<td>1/6–1</td>
<td>1540–1564, 1379–1409, 1435–1437</td>
</tr>
<tr>
<td></td>
<td>‘AcO−</td>
<td>1/8–1/2</td>
<td>1529–1531</td>
</tr>
<tr>
<td></td>
<td>AcOH−</td>
<td>1/4–1</td>
<td>1584–1604, 1473–1485</td>
</tr>
<tr>
<td></td>
<td>AcO−</td>
<td>1/8–1/2</td>
<td>1514–1522, 1432–1444</td>
</tr>
<tr>
<td>TiO2(r)</td>
<td>AcOH−</td>
<td>1/4–1</td>
<td>νCDO,as 1584–1604, νCDO, 1473–1485, νOH 2989–2997</td>
</tr>
<tr>
<td></td>
<td>‘AcO−</td>
<td>1/8–1/2</td>
<td>1514–1522, 1432–1444</td>
</tr>
</tbody>
</table>

*PBE + D3BJ, PAW, using TiO2(a) (101) and TiO2(r) (110) surfaces as the respective models; computational details described in Section 2.4.

b No stable AcO− structures can be isolated during energy and geometry optimizations because of the weakly basic nature of the O-atoms on TiO2(r) surfaces.
faces differ from those that account for the denominator term in Eq. (7). These different $K_1$ values can only be reconciled by considering the carboxylate species that occupy the Ti—O pairs responsible for catalytic turnovers to be present only as minority species, with the bidentate carboxylates prevalent in the infrared spectra as the majority species but without their detectable catalytic involvement.

We conclude based on this evidence that ketonization reactivity reflects such minority sites and that they are likely to reflect the presence of anatase-like structures in these TiO$_2(r)$ samples. Ultraviolet Raman spectra have shown that the phase transformation from anatase to rutile TiO$_2$ requires a higher temperature at the surface than in the bulk crystal (973 vs. 823 K)\cite{56}, indicating that anatase-like structures may be retained at the surface of some of the crystallites present in TiO$_2(r)$ samples even after the bulk of most crystals has converted to the rutile structure. These conclusions are consistent with the lower turnover rates observed on TiO$_2(r)$ compared with TiO$_2(a)$ and with DFT-derived energetics that would lead to areal ketonization rates on TiO$_2(r)$ (110) surfaces even lower than those measured on TiO$_2(r)$ powders (Section 3.4).

These spectra and their theoretical analysis indicate that monodentate AcO$^-$ species predominate on TiO$_2(a)$ and act as reactive intermediates in ketonization turnovers. Bidentate “AcO” species prevail on TiO$_2(r)$ but are not involved in ketonization turnovers. These data and conclusions contradict the previously proposed involvement of bidentate carboxylates (“AcO”) as reactive intermediates in ketonization turnovers on TiO$_2$ and ZrO$_2$ surfaces\cite{14,16–21}. These unreactive bidentate species desorb slowly as gaseous ketene molecules; their scavenging by hydrogenation on Cu sites accounts for both the formation of ethanal and ethanol and for the inhibition of deactivation brought forth by the presence of gaseous H$_2$ and a Cu function during ketonization of ethanoic acid on TiO$_2$ and ZrO$_2$ (Section 3.1).

3.4. Theoretical assessment of ketonization elementary steps and adsorbed species on anatase and rutile TiO$_2$ surfaces

TiO$_2(a)$ and TiO$_2(r)$ surfaces preferentially expose their most stable (101) and (110) planes, respectively\cite{40}. These surface planes are used here as periodic slab models in DFT estimates of the binding and reactive properties of Ti—O pairs. We address the involvement of Ti—O pairs in the stabilization of adsorbed species and transition states involved in the elementary steps that mediate ethanoic acid ketonization turnovers (Scheme 5). In doing so, we also assess the influence of the strength of the acid and base sites and the Ti—O distances on adsorption and activation free energies.
TiO$_2$(a) (101) surfaces exhibit sawtooth-like corrugations that expose two types of Ti cations and two types of O anions (Scheme 8a and b) [22]. One of the Ti centers exhibits sixfold coordinative saturation, as the Ti atoms do in the anatase bulk (Ti$_{6c}$, coordination number (CN) of 6), while the other Ti center is five-coordinate and is coordinatively-unsaturated (Ti$_{5c}$, CN 5). Their connecting O-atoms have either twofold (O$_{2c}$, CN 2) or threefold (O$_{3c}$, CN 3) coordination.

The affinity of a gaseous OH$^-$ anion ($E_{HA}$; Eq. (3)) can be used to assess the acid strength of these two types of Ti Lewis centers. The affinity of a gaseous proton ($E_{PA}$; Eq. (4)) can be used, in turn, to assess the strength of the basic O-anions. These OH$^-$ and H$^+$ affinities are more negative on Ti and O centers with lower coordination numbers (Table 5), as expected from their coordinative unsaturation, which allows effective orbital overlap with adsorbed molecules. In fact, the OH$^-$ affinity of coordinatively-saturated Ti$_{6c}$ centers ($E_{HA}(Ti_{6c})$) is nearly zero (<1 kJ mol$^{-1}$, Table 5); they cannot bind intermediates and transition states, thus rendering Ti$_{6c}$ sites inactive in ketonization catalysis, as also concluded in the case of condensation reactions on TiO$_2$(a) surfaces [24]. We surmise, and then show below, that Ti$_{5c}$ sites ($E_{HA}$ = 246 kJ mol$^{-1}$, Table 5) are the only Ti centers able to stabilize adsorbed acid molecules and the transition states that mediate their reactions; therefore, they are the Ti centers in the Ti–O pairs responsible for ketonization turnovers on TiO$_2$(a) (101) surfaces. In contrast, the $E_{PA}(O_{2c})$ and $E_{PA}(O_{3c})$ values are less negative on TiO$_2$(r) (110) surfaces (1093 kJ mol$^{-1}$, Table 5) than on TiO$_2$(a) (101) surfaces ($1175$ kJ mol$^{-1}$ vs. 1138 kJ mol$^{-1}$, Table 5), indicative of much stronger Lewis acid centers. In contrast, the $E_{PA}(O_{2c})$ and $E_{PA}(O_{3c})$ values are less negative on TiO$_2$(r) (110) surfaces (1093 kJ mol$^{-1}$, Table 5) than on TiO$_2$(a) (101) surfaces ($1175$ kJ mol$^{-1}$ vs. 1138 kJ mol$^{-1}$, Table 5), indicating that O-atoms are less basic on TiO$_2$(r). Not unexpectedly, these differences in Ti–O distances and acid-base strength lead to very different binding modes and reactivity of adsorbed acid molecules on TiO$_2$(a) and TiO$_2$(r), as discussed in detail below.

Ethanoic acid can form molecular AcOH or dissociated AcO$^-$ at Ti$_{5c}$–O$_{2c}$/3c pairs on TiO$_2$(a) (101) surfaces. Their relative abundance depends on the basicity of the accessible lattice O-atoms that must interact with the –OH group in ethanoic acid. The
weaker O$_{3c}$ site preserves the O–H bond intact upon adsorption (O–H distance: 0.105 nm vs. 0.099 nm in AcOH (g), Scheme 9a) and forms weakly-adsorbed AcOH$^+$ species at Ti$_{5c}$–O$_{3c}$ pairs. The O–H bond in AcOH is cleaved to form AcO$^-$ (O–H distance: 0.139–0.143 nm, Scheme 9b and c) at Ti$_{5c}$–O$_{2c}$ pairs consisting of Ti$_{5c}$ centers with O$_{2c}$ sites at either the first or second coordination shell (Ti$_{5c}$–O$_{2c}$ distance: 0.184 vs. 0.413 nm, Scheme 9b and c); this is also evident from the nearly-formed H–O$_{2c}$ bond on both Ti$_{5c}$–O$_{2c}$ pairs.

### Table 5

<table>
<thead>
<tr>
<th>Surface</th>
<th>$E_{\text{HA}}$ (kJ mol$^{-1}$)</th>
<th>$E_{\text{PA}}$ (kJ mol$^{-1}$)</th>
<th>$d_{\text{Ti5c-Ti5c}}$ (nm)</th>
<th>$d_{\text{Ti5c-O2c}}$ (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO$_2$(a) (1 0 1)</td>
<td>246</td>
<td>&lt; -1</td>
<td>0.383</td>
<td>0.184</td>
</tr>
<tr>
<td>TiO$_2$(r) (1 1 0)</td>
<td>369</td>
<td>&lt; -1</td>
<td>0.299</td>
<td>0.360</td>
</tr>
</tbody>
</table>

* PBE + D3BJ, PAW.

scheme 9. DFT-derived adsorption modes for ethanoic acid on TiO$_2$(a) (1 0 1) and TiO$_2$(r) (1 1 0) surfaces (PBE + D3BJ, PAW, $\theta_{\text{acid}}$ = 1/2 ML). Only one acid molecule is shown on the surface for clarity; distances are given in nm.
DFT-derived adsorption free energies ($\Delta G_{\text{ads}}$; 1/2 ML, 523 K, 1 bar) for the AcO$^*$ modes at these two Ti$_{5c}$–O$_{2c}$ structures were nearly identical (−52 and −51 kJ mol$^{-1}$; Section S13, SI) and much more negative than for AcOH$^*$ at the Ti$_{5c}$–O$_{3c}$ pair (−15 kJ mol$^{-1}$; Section S13, SI), thus making AcO$^*$ species the predominant monodentate form of adsorbed ethanoic acid on TiO$_2$(a). The most stable “AcO$^*$” structure on TiO$_2$(a) (1 0 1) surfaces is also located at Ti$_{5c}$–O$_{2c}$ pairs, with the two carboxylate O-atoms each bound to one of two neighboring Ti$_{5c}$ centers and the dissociated H-atom coordinated to the basic O$_{2c}$ site (Scheme 9d). These stronger acid-base Ti$_{5c}$–O$_{3c}$ pairs are used in the DFT treatments of ketonization elementary steps that are described next.

The DFT-derived $\Delta G_{\text{ads}}$ values for AcO$^*$ species bound at Ti$_{5c}$–O$_{2c}$ pairs on TiO$_2$(a) (1 0 1) surfaces vary from $-$55 to $-$50 kJ mol$^{-1}$ (525 K, 1 bar) (Eq. (2)) as the acid coverage ($\theta_{\text{acid}}$) increases (1/6–1 ML, Fig. 7a); the respective adsorption enthalpies ($\Delta H_{\text{ads}}$) vary from $-$132 to $-$140 kJ mol$^{-1}$ (Fig. 7b). These small differences in $\Delta G_{\text{ads}}$ and $\Delta H_{\text{ads}}$ values indicate that the distances between Ti$_{5c}$ centers at TiO$_2$(a) (1 0 1) surfaces ($d_{\text{TiO}_2\text{--TiO}_2}$ 0.383 nm, Table 5) do not lead to strong lateral repulsion among AcO$^*$ species, even at the saturation coverages prevalent during ketonization catalysis.

In contrast, DFT-derived $\Delta G_{\text{ads}}$ values for bound “AcO$^*$” species at these Ti$_{5c}$–O$_{2c}$ pairs become much less negative ($-$82 to $-$43 kJ mol$^{-1}$) with increasing acid coverage (1/8 to saturation 1/2 ML) (Fig. 7a). Such destabilization predominantly reflects the $\Delta H_{\text{ads}}$ component in $\Delta G_{\text{ads}}$ (Fig. 7b). Similarly, the Ti$_{5c}$–Ti$_{5c}$ distances in TiO$_2$(a) (1 0 1) preclude repulsive interactions among alkyl groups in vicinal “AcO$^*$” species, as in the case of AcO$^*$ above. These Ti$_{5c}$–Ti$_{5c}$ distances at the two vicinal Ti$_{5c}$ centers linked to the O atoms in the bound “AcO$^*$” (Scheme 9d) increase slightly from 0.381 nm to 0.384 nm as acid coverage increases (1/8 to saturation 1/2 ML), while the O–O distances in “AcO$^*$” remain nearly unchanged ($d_{\text{O-O}}$ 0.231–0.232 nm, Scheme 9d). These changes with coverage lead to somewhat less effective overlap between Ti and O orbitals in “AcO$^*$” and to the concomitant “AcO$^*$” destabilization as coverage increases (Fig. 7a).

The above effects of acid coverage on $\Delta G_{\text{ads}}$ values for AcO$^*$ and “AcO$^*$” species (Fig. 7a) indicate that “AcO$^*$” species dominate at acid coverages below 1/4 ML but become minority species at higher coverages, when “AcO$^*$” and AcO$^*$ are equilibrated (Step 3 in Scheme 5). Rate and infrared data showed that $K_1$ values did not depend on coverage (Sections 3.2 and 3.3), consistent with the prevalence of AcO$^*$ species and their slow interconversion to “AcO$^*$” during ketonization catalysis.

DFT treatments were also used to assess the relative rates of AcO$^*$ conversion to “AcO$^*$” (via Step 2, Scheme 5) and to ketonization products (via Steps 3–13, Scheme 5). The rate of formation of “AcO$^*$” from AcO$^*$ ($r_{\text{keto}}$) is given by

$$\frac{r_{\text{keto}}}{[L]} = k_2 \theta_{\text{AcOH}} \theta_{\text{AcO}}$$

where [L] is the number of catalytically relevant Ti–O pairs, $\theta_{\text{AcOH}}$ and $\theta_{\text{AcO}}$ are the respective fractional coverages of AcO$^*$ and unoccupied Ti–O pairs (“), and $k_2$ is the forward rate constant for Step 2 in Scheme 5. Ketonization rates ($r_{\text{keto}}$) in contrast, involve bimolecular reactions between vicinal AcO$^*$ species at rates limited by C–C coupling between AcO$^*$ and a 1-hydroxy enolate (Step 4, Scheme 5), as shown by kinetic and isotopic data (Section 3.2) and DFT methods (shown next). Ketonization rates are given by

$$\frac{r_{\text{keto}}}{[L]} = k_4 K_1 K_2 \theta_{\text{AcO}} \theta_{\text{AcOH}}$$

As shown in Scheme 10, these ($r_{\text{keto}}$/$r_{\text{AcOH}}$) ratios reflect the free energy difference ($\Delta G_{\text{keto--AcOH}}$; Eqs. (19) and (20)) between the TS for the C–C coupling step (G$_{\text{C-C}}$, Step 4 in Scheme 5) and the sum of the TS for “AcO$^*$” formation from AcO$^*$ (G$_{\text{AcO, AcO}}$, Step 2 in Scheme 5) and a gaseous ethanoic acid (G$_{\text{AcOH}}$):

$$\frac{r_{\text{keto}}}{r_{\text{AcOH}}} = \exp(-$$

$$\Delta G_{\text{keto--AcOH}}/RT) [\text{AcOH}]$$

$$\Delta G_{\text{keto--AcOH}} = G_{\text{C-C}} - G_{\text{AcO, AcO}} - G_{\text{AcOH}}$$

(20)

The DFT-derived $\Delta G_{\text{keto--AcOH}}$ value for AcO$^*$ bound at Ti$_{5c}$–O$_{2c}$ pairs on TiO$_2$(a) (1 0 1) is 45 kJ mol$^{-1}$ (523 K, 1 bar ethanoic acid). The TS for “AcO$^*$” formation and its free energy are shown in Sec-

![Fig. 7. DFT-derived (a) adsorption free energy ($\Delta G_{\text{ads}}$) and (b) its enthalpy component ($\Delta H_{\text{ads}}$) as a function of acid fractional coverage ($\theta_{\text{acid}}$; Eq. (15)) for AcO$^*$ (●) and “AcO$^*$” (Δ) on TiO$_2$(a) (1 0 1) surfaces (PBE + D3BJ, PAW, 523 K, 1 bar ethanoic acid). Dashed lines indicate qualitative trends.]
tion S14 (SI), while the structure and free energy of the C–C coupling TS are shown below. These free energies lead to ($I_{\text{ket}}/I_{\text{AcO}}$) ratios much smaller than unity at all pressures and temperatures of interest (Section S15, SI). Thus, DFT methods indicate that “AcO”–AcO” equilibration should occur in the timescale of ketonization turnovers, in contradiction to the slow formation and desorption of ‘AcO’ evident from infrared spectra (Section 3.3), the formation of acetaldehyde and the inhibition of deactivation when H2 and a Cu function are used (Section 3.1), and the nature of the treatments required to fully recover initial rates after significant deactivation (in the absence of Cu and H2; Section 3.1).

The Grimme’s D3BJ dispersion component in the PBE functionals [43,44] used in these DFT treatments to account for long and intermediate range van der Waals attractive interactions tends to overestimate the binding of adsorbed species, in this case the binding of acid-derived species at TiO2 overtemperatures of interest (Section S15, SI). Thus, DFT methods indicate that these free energies lead to $\Delta G_{\text{ads}}$ values show that bidentate “AcO” species at Ti5c–O2c pairs on TiO2(r) (110) become less stable with increasing acid coverage (θ_acid) up to saturation coverages (1/2 ML) (Fig. 8a; ΔHads components depicted in Fig. 8b), as found also on TiO2(a) (101) (Fig. 7a). These ΔGads values for “AcO” are more negative on TiO2(r) (110) than on TiO2(a) (101) (e.g. -82 vs. -43 kJ mol$^{-1}$, 1/2 ML “AcO”, 523 K, 1 bar, Figs. 7a and 8a), as a result of shorter Ti5c–Ti5c distances on TiO2(r) (110) than on TiO2(a) (101) surfaces (d_{Ti5c–Ti5c} 0.299 vs. 0.383 nm, Table 5); these Ti5c–Ti5c distances on TiO2(r) (110) match more closely the O–O distances in “AcO” species (d_{O–O} 0.230 nm, Schemes 9f), thus providing more effective orbital overlap.

The DFT-derived ΔGads values for AcOH* species on TiO2(r) (110) also become less negative from -59 kJ mol$^{-1}$ (1/4 ML) to -53 kJ mol$^{-1}$ (1/2 ML) and then to -11 kJ mol$^{-1}$ at saturation coverages (1 ML, Fig. 8a), in contrast to the much smaller ΔGads change on TiO2(a) (101) in the same range of coverages (-54 to -50 kJ mol$^{-1}$, Fig. 7a). This stronger influence of coverages on the stability of monodentate modes on TiO2(r) (110), especially at θ_acid above 1/2 ML, is indicative of strong steric repulsion between monodentate species bound to vicinal Ti5c–O2c pairs in TiO2(r) (110), with its shorter Ti5c–Ti5c distances than in TiO2(a) (101). As expected from such repulsion, the effect of acid coverage predominantly reflects the enthalpic component of ΔGads (Fig. 8b). The preference for “AcO” over AcOH* on TiO2(r) surfaces at all acid concentrations for the “AcO” formation TS. As a result, the free energy for the “AcO” formation TS ($G_{\text{AcO}}$) is expected to be underestimated more than that for the C–C coupling TS ($G_{\text{CC}}$), leading to the overestimation for ΔGads values (Eq. (20)). As shown next, such overbinding tendencies influence the C–C coupling TS and the bound reactants (two adjacent AcO*) similarly; their free energy difference (ΔG_{CC}, Eq. (11)) is thus nearly independent of the overbinding tendencies and can be used for the benchmarking between experiment and theory.

The DFT-derived ΔGads values show that bidentate “AcO” species at Ti5c–O2c pairs on TiO2(r) (110) become less stable with increasing acid coverage (θ_acid) up to saturation coverages (1/2 ML) (Fig. 8a; ΔHads components depicted in Fig. 8b), as found also on TiO2(a) (101) (Fig. 7a). These ΔGads values for “AcO” are more negative on TiO2(r) (110) than on TiO2(a) (101) (e.g. -72 vs. -43 kJ mol$^{-1}$, 1/2 ML “AcO”, 523 K, 1 bar, Figs. 7a and 8a), as a result of shorter Ti5c–Ti5c distances on TiO2(r) (110) than on TiO2(a) (101) surfaces (d_{Ti5c–Ti5c} 0.299 vs. 0.383 nm, Table 5); these Ti5c–Ti5c distances on TiO2(r) (110) match more closely the O–O distances in “AcO” species (d_{O–O} 0.230 nm, Schemes 9f), thus providing more effective orbital overlap.
coverages (Fig. 8a) is consistent with the absence of detectable AcOH bands in the infrared spectrum of TiO2(r) during ethanoic acid ketonization reactions (Fig. 5b, Section 3.3).

The proposed elementary steps for ethanoic acid ketonization (Scheme 5) were examined on TiO2(a) (101) surfaces at 1 ML AcO\(^{−}\) coverages (\(\theta_{\text{AcO}}\), Eq. (15)) using DFT methods; such high coverages seek to rigorously account for the saturated surfaces prevalent during catalysis. The first step involves the cleavage of the \(\alpha\)−\(\mathrm{H}\) bond in AcO\(^{−}\) to form 1-hydroxy enolates (Step 3 in Scheme 5). The \(\mathrm{H}\)-atom is abstracted by the vicinal \(\mathrm{O}_{2c}\) site; the \(\alpha\)-\(\mathrm{H}\)−\(\mathrm{O}_{2c}\) distance is 0.113 nm and the \(\alpha\)-\(\mathrm{C}\)−\(\mathrm{H}\) distance is 0.150 nm at the TS that mediates the formation of the 1-hydroxy enolate (Scheme 11a). The similar \(\alpha\)-\(\mathrm{H}\)−\(\mathrm{O}_{2c}\) distances at the TS and in the bound 1-hydroxy enolate (0.113 vs. 0.110 nm) demonstrate the late nature of the enolate formation TS on TiO2(a) (101); such a late TS reflects the strong \(\alpha\)-\(\mathrm{C}\)−\(\mathrm{H}\) bond in carboxylic acids and the endothermic nature of such elementary steps. The transition states for enolate formation from carbonyl compounds in aldol condensation reactions on TiO2(a) (101) occur earlier along the reaction coordinate than for acid reactants because the \(\alpha\)-\(\mathrm{C}\)−\(\mathrm{H}\) bonds are weaker in carbonyl compounds than in carboxylic acids [24].

1-Hydroxy enolates can attack the carboxylic C-atom in a vicinal AcO\(^{−}\) via its nucleophilic \(\beta\)-\(\mathrm{C}\)-atom to form a new \(\mathrm{C}\)−\(\mathrm{C}\) bond (Step 4, Scheme 5). The two \(\mathrm{C}\)-atoms lie farther apart at the TS (0.234 nm, Scheme 11b) than in the product state (0.150 nm), but are closer than their combined van der Waals radii (0.340 nm), although the \(\mathrm{C}\)-\(\mathrm{O}\) bond lengths in the reactant and the TS (0.104 vs. 0.105 nm, Scheme 11c). The \(\mathrm{H}\)-shift TS is stabilized by interactions with the bound \(\mathrm{OH}\) and \(\mathrm{H}_{2}\mathrm{O}\) species derived from coadsorbed AcO\(^{−}\) (Step 4, Scheme 5). The two \(\mathrm{C}\)-atoms lie farther apart at the TS (0.234 nm, Scheme 11b). DFT-derived free energies along the reaction coordinate (Section S18, SI) show that AcO\(^{−}\) is formed in the decarboxylation of \(\alpha\)-\(\mathrm{H}\)-\(\mathrm{O}_{2c}\) (0.114 vs. 0.113 nm, respectively). Acetone desorption (Step 13, Scheme 5) then completes the catalytic ketonization turnover on TiO2(a) surfaces.

Conversely, the propen-2-olate product formed in the decarboxylation of \(\beta\)-\(\mathrm{C}-\)ketonates (Step 10, Scheme 5) reprotoenonates to form acetone (Step 12, Scheme 5). The TS structure (Section S16, SI) resembles that for enolate formation from AcO\(^{−}\) in its ketonization reactions (Scheme 11a), but with a shorter \(\alpha\)-\(\mathrm{C}\)−\(\mathrm{H}\) and a longer \(\alpha\)-\(\mathrm{H}\)−\(\mathrm{O}_{2c}\) bond (0.148 vs. 0.150 nm, 0.114 vs. 0.113 nm, respectively). Acetone desorption (Step 13, Scheme 5) then completes the catalytic ketonization turnover on TiO2(a) surfaces.

Fig. 9 depicts free energies along the reaction coordinate for the ketonization elementary steps in Scheme 5 (523 K, 1 bar ethanoic acid, 1 ML AcO\(^{−}\)) relative to two gaseous ethanoic acids and a bare TiO2(a) surface (enthalpies and entropies; Section S17, SI). AcO\(^{−}\) species exhibit the lowest free energy among adsorbed species, consistent with AcO\(^{−}\) as the most abundant surface intermediate (MASI). DFT-derived adsorption free energies for AcO\(^{−}\) (\(\Delta\text{G}_{\text{AcO}^{\cdot\cdot}}\) = 50 kJ mol\(^{-1}\), Eq. (10); Fig. 9) are slightly more negative than measured values (−33 ± 1 kJ mol\(^{-1}\), Table 3), a trend that reflects the overbonding tendencies of the Grimme’s D3BJ dispersion corrections in PBE functionals [43,44]; this is also evident from the more negative \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) values derived from theory (−140 kJ mol\(^{-1}\), Table 6) compared with those obtained from the regression of the temperature dependence of measured \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) (−114 ± 3 kJ mol\(^{-1}\), Table 3).

The C−C coupling TS (\(T_{\text{AcO}}\) in Fig. 9; Step 4, Scheme 5) gives the highest free energy along the reaction coordinate, consistent with its kinetic relevance in ketonization reactions on TiO2(a). The DFT-derived \(\Delta\text{G}_{\text{AcO}^{\cdot\cdot}}\) value (Eq. (14)), given by the difference between the free energies of the C−C coupling TS and two bound AcO\(^{−}\) species, is 160 kJ mol\(^{-1}\) (523 K, 1 bar ethanoic acid, 1 ML AcO\(^{−}\), Table 6); its respective enthalpy and entropy components (\(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}, \Delta\text{S}_{\text{AcO}^{\cdot\cdot}}\)) are 128 kJ mol\(^{-1}\) and −63 J mol\(^{-1}\) K\(^{-1}\) (Table 6). Measured \(\Delta\text{G}_{\text{AcO}^{\cdot\cdot}}\), \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) and \(\Delta\text{S}_{\text{AcO}^{\cdot\cdot}}\) values are 166 ± 1 kJ mol\(^{-1}\), 137 ± 1 kJ mol\(^{-1}\), and −56 ± 1 J mol\(^{-1}\) K\(^{-1}\) (Tables 2 and 3), in good agreement with these DFT estimates. The \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) difference between DFT-derived and measured values (9 kJ mol\(^{-1}\)) is much smaller than for \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) (27 kJ mol\(^{-1}\)), because overbonding tendencies influence the bound reactant and TS for \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\), but only the product state in the case of \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\). DFT-derived kinetic isotope effects for the C−C coupling step (\(k_{\text{AcO}}\), Eq. (13)) and thermodynamic isotope effects for ethanoic acid dissociation to AcO\(^{−}\) (K, Eq. (9)) are both near unity (\(k_{\text{AcO}}/k_{\text{AcOH}} = 1.1\)), in agreement with experiments (\(k_{\text{AcO}}/k_{\text{AcOH}} = 1.1\)). DFT-derived free energies along the reaction coordinate (Section S18, SI) show that AcO\(^{−}\) remains the MASI and the C−C coupling remains the kinetically-relevant step at both coverages. The \(\Delta\text{G}_{\text{AcO}^{\cdot\cdot}}\) value, however, is larger at lower coverages (181 vs. 160 kJ mol\(^{-1}\), Table 6), a difference that predominantly reflects the stabilizing effects of H-bonding on \(\Delta\text{H}_{\text{AcO}^{\cdot\cdot}}\) at higher coverages (149 vs. 128 kJ mol\(^{-1}\), Table 6). We conclude that the prevalent high acid coverages are requisite for ketonization catalysis because of the preferential stabilization of the C−C bond formation TS over its relevant precursors on TiO2(a) (101) by H-bonding, which become most evident at near-saturation coverages. Such coverage effects provide yet another demonstration of how dense monolayers allow facile turnovers for reactions that would proceed much more slowly, or not at all, at lower coverages, because crowded surfaces favor TS structures over those of the relevant precursors [57].

A concerted form of the two-step H\(_{2}\)O elimination reaction (Steps 5–6, Scheme 5) of \(\alpha\)-hydroxy \(\gamma\)-carboxy alkoxide species (formed in the C−C coupling step) to \(\beta\)-\(\mathrm{C}\)-ketonates becomes kinetically accessible only at low acid coverages (1/3 ML AcO\(^{−}\), Scheme 12). This concerted route is mediated by a six-membered ring TS (Scheme 11f) and involves a direct shift of the carboxyl \(\mathrm{H}\)-atom to the leaving \(\alpha\)-\(\mathrm{OH}\) group. This route exhibits a slightly lower free energy at the TS than for the \(\mathrm{H}_{2}\)O formation TS involved in the two-step route (Step 6, Scheme 5), but only at acid coverages much lower than those prevalent during practical ketonization catalysis (65 vs. 69 kJ mol\(^{-1}\), 1/3 ML, Section S18, SI). The concerted
route becomes favored at low coverages, which cannot provide the H-bonding interactions that favor the sequential two-step pathways. This concerted route, however, was not considered in previous studies [3,19], in which theoretical treatments were implemented on essentially bare surfaces.

The ketonization elementary steps in Scheme 5 were also examined on coordinatively-unsaturated Ti5c–O2c pairs at TiO2(r) (110) surfaces. AcOH is the stable monodentate form of adsorbed ethanoic acid at Ti5c–O2c pairs on TiO2(r) surfaces (Scheme 9e), in contrast to the dissociated AcO species that prevail on TiO2(a) (101) (Schemes 9b and c). These AcOH species are much less stable, however, than bidentate carboxylates (\(\text{AcO}^+\)) on TiO2(r) (110) (Fig. 8). TiO2(r) surfaces thus prefer to saturate with \(\text{AcO}^+\). The free energies for \(\text{AcO}^+\) on TiO2(r) (110) (−72 kJ mol\(^{-1}\), 523 K, 1 bar ethanoic acid, with respect to gaseous ethanoic acid reactants and a TiO2(r) surface henceforth) were more negative than those for other intermediates or transition states along the ketonization coordinate (Fig. 10; discussed in detail below), indicating that \(\text{AcO}^+\) is the MASI on TiO2(r) (110) at ketonization conditions.

These theoretical conclusions are consistent with the infrared spectra obtained from TiO2(r) samples during ethanoic acid ketonization catalysis (Section 3.3).

The formations of 1-hydroxy enolates from monodentate and bidentate forms of adsorbed ethanoic acids on TiO2(r) (110) (AcOH and \(\text{AcO}^+\) in this case) were both examined. The enolization of AcOH at a Ti5c–O2c pair on TiO2(r) (110) involves TS structures (Scheme 13a) similar to those on TiO2(a) (110) (Scheme 11a).

Scheme 11. DFT-derived transition state structures involved in ethanoic acid ketonization on TiO2(a) (101) surfaces (PBE + D3BJ, PAW). Spectator coadsorbed acids are not shown for clarity; distances are given in nm.

The abstracted a-H-atom at the TS on TiO2(r) (110) is slightly closer to the O2c site and farther from the a-C atom than on TiO2(a) (101) (0.109 vs. 0.113 nm, 0.162 vs. 0.150 nm, Schemes 11a and 13a). This later TS on TiO2(r) (110) is consistent with the weaker basicity of O2c sites on TiO2(r) (110) than on TiO2(a) (101) (Table 5). In contrast to AcOH, \(\text{AcO}^+\) binds to two neighboring Ti5c centers via its two O-atoms before its a-H-atom is abstracted by a vicinal O2c site (Scheme 13b). The enolization TS of \(\text{AcO}^+\) has a more negative enthalpy than for AcOH (−45 vs. −33 kJ mol\(^{-1}\), 523 K, 1/2 ML \(\text{AcO}^+\), Section S19, SI), but also a larger entropy loss (−229 vs. −192 J mol\(^{-1}\).}
K, Section S19, SI); these differences lead to a higher free energy for the enolization TS of \(\text{\textit{AcO}}\) relative to that of \(\text{\textit{AcOH}}\) (75 vs. 67 kJ mol\(^{-1}\)), indicating the more strongly bound \(\text{\textit{AcO}}\) species are less reactive than \(\text{\textit{AcOH}}\) in the formation of 1-hydroxy enolates.

The 1-hydroxy enolates nucleophilically attack another \(\text{\textit{AcOH}}\) coadsorbed at a vicinal Ti5c\(\text{\textit{AcO}}\) pair to form a new C–C bond (Step 4, Scheme 5). The incipient C–C bond at the C–C coupling TS on TiO\(_2\)(r) (110) has a distance of 0.238 nm (Scheme 12c), similar with that on TiO\(_2\)(a) (101) (0.234 nm, Scheme 10b). DFT-derived enthalpies for this TS, however, are much less negative on TiO\(_2\)(r) (110) than on TiO\(_2\)(a) (101) (−116 vs. −152 kJ mol\(^{-1}\), 523 K, referenced to two gaseous \(\text{\textit{AcOH}}\) reactants and a bare TiO\(_2\)(a) surface, Sections S16 and S18, SI); these less favorable enthalpies lead, in turn, to much higher TS free energies on TiO\(_2\)(r) (110) (97 kJ mol\(^{-1}\), Fig. 10) than on TiO\(_2\)(a) (101) (61 kJ mol\(^{-1}\), Fig. 9). The less stable C–C coupling TS structures on TiO\(_2\)(r) (110) reflect, in part, stronger repulsive interactions between the bound

![Fig. 8. DFT-derived (a) adsorption free energy (\(\Delta G_{\text{ads}}\)) and (b) its enthalpy component (\(\Delta H_{\text{ads}}\)) as a function of acid fractional coverage (\(\theta_{\text{acid}}\); Eq. (15)) for \(\text{\textit{AcOH}}^*\) and \(\text{\textit{AcO}}^*\) (\(\Delta\)) on TiO\(_2\)(r) (110) surfaces (PBE + D3BJ, PAW, 523 K, 1 bar ethanoic acid). Dashed lines indicate qualitative trends.](image)

![Fig. 9. DFT-derived free energy reaction coordinate diagram for ethanoic acid ketonization on TiO\(_2\)(a) (101) surfaces (PBE + D3BJ, PAW; 523 K, 1 bar ethanoic acid, 1 ML \(\text{\textit{AcO}}^*\)). All energy values are reference to two gaseous ethanoic acid reactants and a bare TiO\(_2\)(a) surface, which defines the zero energy point in the ordinate. Only key surface intermediates and transition states are shown for clarity. TS\(_x\) and P\(_x\) represent the transition state and product of Step \(x\) in Scheme 5, respectively.](image)

### Table 6

<table>
<thead>
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<th>(\theta_{\text{acid}}) (ML)</th>
<th>(\Delta H_{\text{ads}}) (kJ mol(^{-1}))</th>
<th>(\Delta S_{\text{ads}}) (J mol(^{-1}) K(^{-1}))</th>
<th>(\Delta G_{\text{ads}}) (kJ mol(^{-1}))</th>
<th>(\Delta H_{\text{CC,a}}) (kJ mol(^{-1}))</th>
<th>(\Delta S_{\text{CC,a}}) (J mol(^{-1}) K(^{-1}))</th>
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<td>−172</td>
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<td>128</td>
<td>−63</td>
<td>160</td>
</tr>
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<td>−135</td>
<td>−160</td>
<td>−51</td>
<td>149</td>
<td>−60</td>
<td>181</td>
</tr>
</tbody>
</table>

\(\Delta\) PBE + D3BJ, PAW, 523 K, 1 bar ethanoic acid.

K\(^{-1}\), Section S19, SI); these differences lead to a higher free energy for the enolization TS of \(\text{\textit{AcO}}^*\) than that of \(\text{\textit{AcOH}}^*\) (75 vs. 67 kJ mol\(^{-1}\)), indicating the more strongly bound \(\text{\textit{AcO}}^*\) species are less reactive than \(\text{\textit{AcOH}}^*\) in the formation of 1-hydroxy enolates.
1-hydroxy enolate and the coadsorbed AcOH\(^{-}\) reactants at the TS, because of the closer Ti\(_{5c}\) centers on TiO\(_2\)(r) (110); they also reflect the absence of H-bonding between the C\(_{A}\)C coupling TS and surface OH species derived from AcO\(^{-}\) bound at neighboring Ti\(_{5c}\)−O\(_{2c}\) pairs, as a result of the longer Ti\(_{5c}\)−O\(_{2c}\) distance on TiO\(_2\)(r) (110), which places surface OH species farther from the C\(_{A}\)C coupling TS (Scheme 13c).

The subsequent dehydration of the C\(_{A}\)C coupling products (\(\alpha\)-hydroxy \(\gamma\)-carboxy alkoxide species) to \(\beta\)-keto carboxylates preferentially occurs via the concerted six-membered ring TS route (Scheme 12) on TiO\(_2\)(r) (110) (Scheme 13d; free energy 94 kJ mol\(^{-1}\), 523 K, 1 bar ethanoic acid, Fig. 10), as also found, but only at 1/3 ML coverages, on TiO\(_2\)(a) (101) (Scheme 11f). In contrast, the two-step intramolecular H-shift pathway (Steps 5–6, Scheme 5), mediated by O\(_{2c}\) sites, is unfeasible on TiO\(_2\)(r) (110), as shown by the high TS free energies for the H-shift from the carboxyl group in alkoxides to a vicinal O\(_{2c}\) site (>150 kJ mol\(^{-1}\), 523 K, 1 bar ethanoic acid; Step 5, Scheme 5). Such high free energies reflect the lack of H-bonding stabilization by neighboring surface OH species, which also leads to the high TS free energies for the C–C coupling steps on TiO\(_2\) (r) as discussed above (Scheme 13c).

Decarboxylation and reprotonation of the \(\beta\)-keto carboxylate dehydration products form acetone and CO\(_2\) (Steps 10–14, Scheme 5), which complete the ketonization turnover on TiO\(_2\)(r) surfaces. DFT-derived structures of reactants, transition states, and products involved in these steps also resemble those on TiO\(_2\)(a) (101).

The C–C coupling TS (Step 4, Scheme 5) has the highest free energy along the ketonization pathway on TiO\(_2\)(r) (110) (523 K, 1 bar ethanoic acid, with respect to two gaseous ethanoic acid reactants and a bare TiO\(_2\) surface, Fig. 10), indicating that the ketonization rates on TiO\(_2\)(r) (110) are limited by the C–C coupling step between 1-hydroxy enolates and coadsorbed acids.

Ketonization rates on saturated TiO\(_2\)(r) (110) surfaces, prevalent at ketonization conditions as evident from infrared spectra (Section 3.3), can thus be described as:

\[
\frac{r}{[L]} = \frac{k_0T}{2\pi} \exp\left(-\frac{\Delta G_{CC,r}}{RT}\right)P_{\text{acid}}
\]  

where \([L]\) is the number of catalytically-relevant Ti−O pairs on TiO\(_2\)(r) (110); \(\Delta G_{CC,r}\) represents the free energy of the C–C coupling TS (\(\Delta G_{CC}\)) on TiO\(_2\)(r) (110) with respect to a bound “AcO” species (\(G_{\text{AcO}}\)) and a gaseous acid reactant (\(G_{\text{acid}}\)):

\[
\Delta G_{CC,r} = \Delta G_{CC} - G_{\text{AcO}} - G_{\text{acid}}
\]  

DFT-derived \(\Delta G_{CC,r}\) value is 169 kJ mol\(^{-1}\) (523 K, 1 bar ethanoic acid, Fig. 10), leading to ketonization turnover rates that linearly increase from \(7.3 \times 10^{-8}\) to \(2.2 \times 10^{-6}\) (Ti−O)\(^{-1}\) s\(^{-1}\) as the pressure
of ethanoic acid increases within 0.1–3.0 kPa at 523 K (Eq. (21)). Such a first-order kinetic dependence on ethanoic acid pressure is inconsistent with the functional form of Eq. (7), which accurately describes the measured ketonization rates on TiO$_2$(r) within the same pressure range (Fig. 4); the respective ketonization turnover rates ($7.3 \times 10^{8}/$C$_2$10$/C_0^{8}/C_0^{2.2}/C_2^{10}/C_0^{6}$ (Ti$A_O$)$/C_0^{1}$ s$^{-1}/C_0^{1}$) estimated from the DFT treatments are also much lower than the experimentally-measured values ($4.3 \times 10^{8}/$C$_2$10$/C_0^{6}/C_2^{10}/C_0^{5}$ (Ti$A_O$)$/C_0^{1}$ s$^{-1}/C_0^{1}$), Fig. 4). These DFT calculations thus provide evidence that the majority TiO$_2$(r) surfaces are inactive for ketonization and that the minority sites or residual TiO$_2$(a) surfaces present in the TiO$_2$(r) powders account for the measured ketonization rates.

The above theoretical treatments and their accurate benchmarking with experiments shed light into the underpinning geometric factors that lead to marked reactivity differences between rutile and anatase TiO$_2$ surfaces. Specifically, the identity and binding properties of the prevalent forms of dissociated acid reactants and their reactivity in ketonization depend on the local extended coordination of coordinatively-unsaturated Ti$_{5c}$A$_{O_{2c}}$ pairs. The concerted stabilization of the relevant C–C bond formation transition states leads to compensation effects that attenuate the differences in acid strength of the Ti$_{5c}$ centers and in basicity of the O$_{2c}$ centers between Ti$_{5c}$–O$_{2c}$ pairs on TiO$_2$(r) (110) and TiO$_2$(a) (101). Consequently, Ti$_{5c}$–O$_{2c}$ and Ti$_{5c}$–Ti$_{5c}$ distances are the most accurate descriptors of reactivity for ketonization of carboxylic acids on TiO$_2$ and account for the very different reactivity of anatase and rutile surfaces.

4. Conclusions

C$_2$–C$_4$ carboxylic acids undergo selective ketonization to alkanones, CO$_2$, and H$_2$O on TiO$_2$ and ZrO$_2$ catalysts at 503–533 K. Coordinatively unsaturated acid-base M–O (M = Ti, Zr) pairs on these oxides are catalytically relevant for ketonization reactions; the numbers of these pairs were titrated by carboxylic acids during aldol condensation reactions. Ketonization turnover rates are higher on monoclinic ZrO$_2$ than on tetragonal ZrO$_2$ and anatase TiO$_2$ but are much lower on rutile TiO$_2$. The more active oxides, however, show larger deactivation rate constants. Unreactive bidentate carboxylates, formed gradually from dissociation of carboxylic acids on M–O pairs, account for the deactivation during steady-state catalysis. Cu co-catalysts and added H$_2$ scavenge trace levels of gaseous ketene species, present in equilibrium with bidentate carboxylates, via hydrogenation of these ketene species to alkanals and 1-alkanols and thus inhibit deactivation significantly.

Infrared spectra and theoretical treatments show that dissociation of carboxylic acids on anatase TiO$_2$ surfaces forms monodentate carboxylates each bound on one Ti$_{5c}$A$_{O}$ pair and bidentate carboxylates each bound on two vicinal Ti$_{5c}$A$_{O}$ pairs. The stability of the monodentate carboxylates on anatase TiO$_2$ surfaces is slightly influenced by the surface coverage, because of the absence of strong repulsive interactions between carboxylates bound to Ti–O pairs with large distances between nearest Ti centers. The bidentate carboxylates, in contrast, become less stable with increasing acid coverages, as a result of the mismatch between the distances of the Ti–Ti centers and of the O–O atoms in the bidentate carboxylates. This difference in the stability dependence on the surface coverage for monodentate and bidentate carboxylates drives a strong preference to crowd anatase TiO$_2$ surfaces with monodentate carboxylates, which are prevalent at ketonization conditions. In contrast to anatase TiO$_2$, the closer Ti–Ti centers on rutile TiO$_2$ lead to more efficient binding of the two O-atoms in each bidentate carboxylate at these Ti centers and to stronger...
meric repulsion between monodentate adsorbed acids bound at vicinal Ti–O pairs. These effects combine to make bidentate carboxylates the predominant adsorbed species on rutile TiO$_2$.

The C–C coupling of 1-hydroxy enolate species, formed from α,β-unsaturated carboxylates, provides a common, kinetically-relevant step for ketonization on anatase and rutile TiO$_2$ surfaces. The C–C coupling transition state (TS) on anatase TiO$_2$ becomes more stable relative to its monodentate carboxylate precursors as the coverage of the precursors increases, because of H-bonding between this C–C coupling TS and vicinal surface OH species derived from dissociation of coadsorbed carboxylic acids. Such stabilization via H-bonding also renders a surface-mediated two-step route favorable for the subsequent intramolecular dehydration of the C–C coupling products (α-hydroxy-γ-carboxy alkoxides) at high acid coverages. In contrast, a concerted route through a six-membered ring TS prevails for this dehydration reaction at low acid coverages. These H-bonding interactions are absent on rutile TiO$_2$ surfaces, because of the longer distance between Ti and O sites in Ti–O–Ti pairs in rutile TiO$_2$ than in anatase TiO$_2$, making bound TS structures and surface OH species farther apart from each other. The closer Ti–Ti centers on rutile TiO$_2$ lead to steric hindrance between the coreactants at the C–C coupling TS, further rendering rutile TiO$_2$ much less reactive than anatase TiO$_2$ in ketonization catalysis. These differences in the stability of surface intermediates and transition states between anatase and rutile TiO$_2$ surfaces unveil the necessity of moderate distances of acid-base and acid–acid centers for ketonization of carboxylic acids on metal oxides.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.jcat.2016.11.006.

References