Aldol condensations of alkanals and alkanones form new C-C bonds and remove O-atoms via activation of C-H bonds, nucleophilic attack of carbonyls by enolates, and dehydration of aldehydes to α,β-unsaturated carbonyl compounds. Oxides, such as TiO\textsubscript{2} and ZrO\textsubscript{2}, catalyze such reactions, but unfavorable equilibria limit rates and side reactions form unsaturated residues that cause rapid catalyst deactivation. Metal functions (e.g., Cu, Pt, Pd), even when present as physical mixtures, and H\textsubscript{2} can hydrogenate unsaturated intermediates, thus removing thermodynamic bottlenecks and avoiding side reactions and deactivation. Bifunctional mixtures convert alkanols and carbonyl compounds (alkanals, alkanones) as equivalent reactants, and in doing so, allow the direct conversion of oxygenate streams of broad composition into useful products with new C-C bonds and fewer O-atoms.

Areal condensation (and esterification) rates of C\textsubscript{2}-C\textsubscript{5} oxygenates are much higher on anatase than on rutile TiO\textsubscript{2}. These rates are unaffected by CO\textsubscript{2} or 2,6-di-tert-butylpyridine, but are reversibly inhibited by pyridine and propanoic acid, consistent with the concerted involvement of Lewis acid-base site pairs of balanced strength and with the absence of strongly basic or Brønsted acidic sites. Titration with propanoic acid during catalysis gave site densities of 3.7 nm\textsuperscript{-2}, consistent with Ti densities on anatase surfaces, thus ruling out minority surface defects as active sites and allowing rigorous assessments of activation free energies and turnover rates.

C\textsubscript{2}-C\textsubscript{5} oxygenates convert on TiO\textsubscript{2} at total rates proportional to alkanal/alkanone pressures; the esterification/condensation rate ratios depend linearly on the alkanol/alkanal ratios in the equilibrated reactants. These data, taken together with normal kinetic isotope effects (2.4, ethanol-D\textsubscript{6}, 523 K) and with the skeletal structure of the products formed, are consistent with rate-limiting enolate formation steps via α-C-H cleavage on Ti-O site pairs, with O-atoms as the base and Ti centers as Lewis acid centers that coordinate enolate moieties. New C-C bonds form via subsequent coupling with alkanals (alkanones) and dehydration to α,β-unsaturated carbonyls. New C-O bonds form via reactions of alkanals-derived enolates with alkanols, via H-transfer and rate-limiting alkanal-alkoxide coupling to form unstable hemiacetals. A metal function, present within diffusion distances, hydrogenates unsaturated carbonyl and dehydrogenates hemiacetals to stable condensation and esterification products, respectively. The relative reactivity of the metal function in C=C and C=O hydrogenation influences esterification/condensation rate ratios; Pt favors C=C hydrogenation, thus inhibiting esterification, while Cu favors C=O hydrogenation, thus equilibrating alkanals-alkanol reactants and removing esterification bottlenecks. Weak H/D isotope effects on esterification/condensation ratios (1.4, ethanol-D\textsubscript{6}, 523 K) show that the formation of C-O and C-C bonds limit the rate of enolate reactions (instead of intervening hydrogen transfer steps).

These mechanistic conclusions are general to all C\textsubscript{2}-C\textsubcript{5} oxygenates examined and consistent with density functional theory (DFT) treatments on TiO\textsubscript{2} clusters extracted from extended anatase surfaces. DFT-derived activation free energies (Δ\textsubscript{A}G\textsuperscript{‡}) for enolate formation from C\textsubscript{2}-C\textsubscript{5} oxygenates are in excellent agreement with measured values, as is the case also for their relative values for esterification and condensation from each enolate. Stronger α-C-H bonds in alkanones leads to lower reactivity than for alkanals, while longer and more branched alkyls at the α-C position lead
to steric hindrance and higher enolate formation \( \Delta G^\ddagger \). DFT-derived \( \Delta G^\ddagger \) differences between C-O and C-C bond coupling transition states (TS) also agree with measured values and illustrate how alkyl substitution effects are stronger for condensation TS, because of they require more precise orbital alignment, than for esterification TS. The rates nucleophilic attack of various carbonyl compounds by a given enolate can be measured from cross-condensation reaction selectivities. For example, C₃ enolates react with acetaldehyde and propanal at similar rates; they react with acetone much more slowly than with acetaldehyde or propanal, because of the additional C-C bond at the C=O group, but with formaldehyde much faster, because it lacks C-C bonds at the carbonyl group.

These mechanistic details and their consequences for the relative reactivity of oxygenates remain unchanged for condensation and esterification reactions on acid-base site pairs at monoclinic ZrO₂ (m-ZrO₂) surfaces. Anatase TiO₂ and m-ZrO₂ gave similar turnover rates, enolate formation activation free energies (128 +/- 5 kJ/mol; from acetone), and kinetic isotope effects (2.4, acetone-D₆) for acetone reactants. Rates on m-ZrO₂ were reversibly inhibited by CO₂, but not by pyridine, because acid-base pairs on m-ZrO₂ contain stronger basic sites and weaker acid sites than anatase TiO₂, which still provide the acid-base strength balance required for the concerted \( \alpha-C-H \) bond activation [1]. These conclusions are consistent with DFT-derived interaction energies of H⁺ and OH⁻ (as probes of base and acid strength) on ZrO₂ and TiO₂ surfaces.

These mechanistic inferences and predictive kinetic models have been extended to ketonization of carboxylic acids on TiO₂ and ZrO₂ surfaces, which also involve the cleavage of \( \alpha-C-H \) bonds to form enolic species and subsequent C-C coupling reactions.

References