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Role of synergic interaction in transition state formation of aldol reaction on metal oxide catalyst: A DFT investigation

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This contribution highlights a eight-member ring transition state for aldol reaction of propanal on O-terminated ZrO₂(111) and CeO₂(111) surfaces. The relative heights of activation barriers for α -H abstraction and nucleophilic addition are controlled by surface acid-base pair strength. We report the first theoretical evidence of the alternative to Zimmerman-Traxler model.

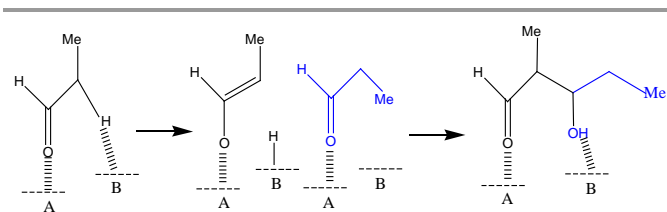
Aldol condensation is a valuable C–C bond formation reaction that provides an efficient way of increasing carbon chain length of molecules containing a carbonyl group, such as aldehydes, ketones, carboxylic acids and esters. This reaction has been intensively studied for more than five decades as a synthesis method of great importance in stereochemistry and synthesis of organic products, mostly via homogeneous catalysis.^{1–13} Due to its efficiency in forming new C–C bonds, the aldol reaction has found renewed interest in recent years in the field of bio-oil upgrading via heterogeneous catalysis.^{14–19} For this application, stereochemistry is not a major concern.

The reaction mechanism for the homogeneously catalyzed aldol reaction is well established.^{3–9} It is widely accepted that enolization is the first step, i.e., either an enol or an enolate is formed by either acid- or base-catalyzed reaction; the nucleophilic addition of enol or enolate to the carbonyl carbon of an aldehyde or ketone is the second step. Several transition state models have been proposed to explain the observed stereoselectivity of the product.^{3–9} The well-known Zimmerman-Traxler model³ features a cyclohexane-chair-like (six-member ring) transition state (TS), in which the stereochemistry of enolate controls the stereochemistry of the product (e.g., β -hydroxyaldehydes or β -hydroxyketone). In general, (E)-enolates lead to *anti* products, whereas (Z)-enolates lead to *syn* products. Due to steric constraints,

substituents are preferentially placed at equatorial position in cyclohexane-chair-like TS and thus the *syn*-pentane interaction is avoided. This explanation, based on the structure of the TS, accurately predicts the stereoselectivity observed experimentally in many homogeneous aldol reactions. In the case of heterogeneous catalyzed aldol reactions, a conventional bimolecular surface reaction mechanism has been typically proposed for solid acid-base catalysts, e.g. metal oxides.^{20–21} This mechanism includes the following two reaction steps: (i) the α -H abstraction of the aldehyde (or ketone) is initiated on a basic O site, forming an enolate-like species adsorbed at the Lewis acid site; (ii) the C–C bond formation takes place via enolate nucleophilic attack of the carbonyl carbon of another aldehyde or ketone (Scheme 1). In contrast to the homogeneous mechanism, the heterogeneous mechanism proceeds via a bifunctional pathway, which requires the presence of bifunctional surface acid-base pair sites. Nonetheless, detailed information on the TS structure and on the bifunctional pathway at the acid-base sites is still lacking.

Herein, we report a theoretical study of the two-step Langmuir-Hinshelwood (LH) mechanism of the aldol reaction of propanal on O-terminated cubic ZrO₂(111) and CeO₂(111) surfaces using a density-functional theory (DFT) method [see Supporting Information (SI) for computational details]. It is known that propanal has rotational isomers, or rotamers.²² Figure 1 shows the two rotamers A and B considered in our model study. Rotamer A (C_s symmetry) has an eclipsed conformation with two α -H and carbonyl O facing opposite directions, while rotamer B has a skew conformation with two α -H and carbonyl O facing to the same direction. B is slightly higher in energy (1.2 kcal/mol) compared to A, which is the global-minimum energy structure. The calculated rotational barrier is 2.2 kcal/mol for A \rightarrow B and 1.0 kcal/mol for B \rightarrow A (Figure 1). Our results agree well with previous work.²² These small rotational barriers can easily be overcome at room temperature and thus make rotamer A and B equally available for aldol reaction under experimental conditions.

^a College of Chemistry and Chemical Engineering, Shanghai University of Engineering Science, Shanghai 201620, China. *E-mail: weian@sues.edu.cn. Electronic Supplementary Information (ESI) available: Computational details, projected-DOS, geometrical information along MEP, transition state search on O-terminated CeO₂(111) surface, and comparison of adsorption of two rotamer A and B are included. See DOI: 10.1039/x0xx00000x



Scheme 1. Heterogeneous aldol reaction (propanal as a representative) on bifunctional surface Lewis acid (A)-base (B) pair sites.

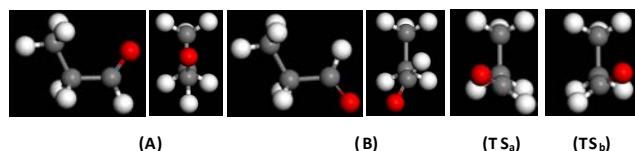
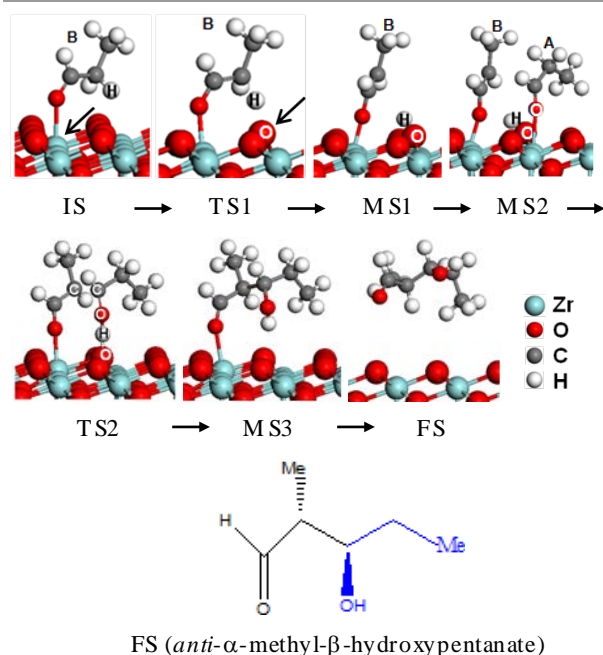


Figure 1. Optimized structures of two rotamers (A and B) of propanal and two TSs between their interconversion depending on clockwise or anti-clockwise rotation. Torsion angle (α): $\alpha_A=0^\circ$, $\alpha_B=147.9^\circ$, $\alpha_{TS(a)}=55.7^\circ$ and $\alpha_{TS(b)}=304.3^\circ$, respectively.



FS (*anti*- α -methyl- β -hydroxypentanoate)

Figure 2. Evolution of geometrical structures along minimum energy pathway (MEP) for the aldol reaction of propanal on O-terminated $ZrO_2(111)$ surface during one catalytic turnover. IS: initial state; TS: transition state; MS: metastable state. Imaginary frequencies: $i1331.7\text{cm}^{-1}$ (TS1), $i683.6\text{cm}^{-1}$ (TS2). The labeled H, O, and C atoms are those involved in transition state formation in α -H abstraction (TS1) and nucleophilic addition (TS2). The arrows representatively point to the slightly protruded Zr and O atoms on the surface.

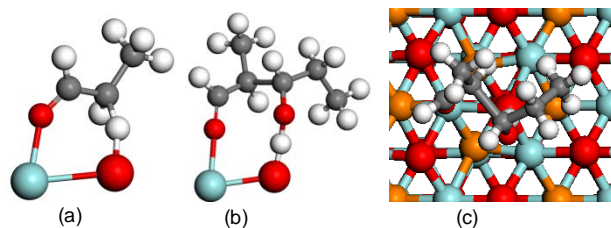


Figure 3. Transition states for aldol reaction on a metal oxide catalyst (a) six-member ring TS1, (b) eight-member ring TS2; (c) Top view of TS2; Yellow: second-layer of O atoms.

However, we found that the orientation of carbonyl O and α -H has a major impact on how the aldol reaction is initiated. The binding of rotamer B on the surface is much stronger than that of rotamer A (e.g., -8.7 vs -1.8 kcal/mol on $ZrO_2(111)$ surface) because both carbonyl O and α -H of rotamer B can readily interact with the surface sites (IS in Figure 2 and Figure S3). Such a η^1 -adsorption mode for carbonyl O has been recently verified by experiment.²³ The lone-pair of carbonyl O interacts with Lewis-acid Zr (or Ce) site while the α -H interacts with the nearest-neighboring Lewis-base O, forming a suitable geometry for the subsequent α -H abstraction step. The α -H abstraction step leads to the formation of a resonance-stabilized (E)-enolate (MS1 in Figure 2), with both C=O and C=C α bonds having identical bond lengths (1.344 and 1.345 Å, respectively. See also Table S1) in a planar structure, a noted feature for carbon 2p π -bonding. As a contrast, the adsorption of the rotamer A experiences a severe geometry frustration, which makes the subsequent α -H abstraction unfavorable. That is, the aldol reaction of propanal is initiated by rotamer B, or E-isomer in enolate form. The α -H abstraction has a TS featuring a six-member ring structure (Figure 3(a) and TS1 in Figure 2).

In a typical LH mechanism (bimolecular), it is mandatory that a second reactant molecule must be co-adsorbed in its proximity. We identified that rotamer A is an *ideal* candidate for co-adsorbed reactant in the subsequent aldol reaction than rotamer B (MS2 in Figure 2) because of its less severe steric hindrance and better matched orientation than the latter. In homogeneous aldol reaction, both carbonyl reactant molecules and molecular catalyst are able to move freely in three dimensions adjusting their orientations in solution and therefore, one adsorbed carbonyl molecule and one enolate are able to be bound to the exact *same* metal (M) site forming six-member ring enolate-metal complex transition state. This is in stark contrast to a solid catalyst surface where the metal and oxygen sites are confined with a rigid lattice and therefore little mobility. The surface active sites can only be accessed by co-reactant molecules either from the gas phase above or by diffusion from adjacent sites. This geometrical restriction greatly limits the possibilities that co-adsorbed reactant molecules can have any configurations for reaction without energetic penalty. For any given elementary reaction step, a specific orientation is needed for the formation of lower-energy TS. This is particularly critical for a reaction as complex as aldol reaction in which complex intermediates are involved. Therefore, only those configurations that lead to a good fit with other coadsorbed-molecules on the surface can result in TS having a lower

activation barrier and proceed with higher probability, the so-called minimum energy pathway (MEP). In a recent study of *n*-butanal aldol reaction on cluster model of isolated titanol and Ti Dimer, the exact same six-member ring TS as in homogeneous aldol reaction was proposed.²⁴ However, a TS bound to the same Lewis acid (Zr or Ce) site was not observed in our model study, neither for MS2 in which two propanal molecules never co-adsorbed at the same Ce or Zr site. We speculate that using a small-size cluster model would be equivalent to mimic a homogeneous metal-complex catalyst, against commonly employed nanoparticles with the size in the range of several nanometers ideally represented by slab model. This manifests the importance of employing appropriate model for valid results.

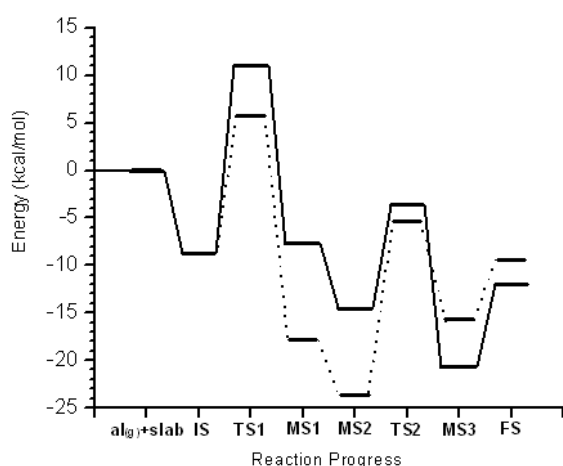


Figure 4. Energy profile for the two-step Langmuir-Hinshelwood mechanism along the minimum-energy pathway for the aldol reaction of propanal on O-terminated $\text{ZrO}_2(111)$ (dashed line, $E_{a1}/E_{a2}=14.5/18.4$ kcal/mol) and O-terminated $\text{CeO}_2(111)$ (solid line, $E_{a1}/E_{a2} = 19.7/10.9$ kcal/mol). The zero line represents the gas-phase propanal(s) and a clean slab.

Energy profile in Figure 4 shows that the adsorption of the second propanal rotamer A (MS2) at the nearest-neighboring Lewis-acid Zr (or Ce) site is also quite strong, which makes the LH mechanism feasible. The stronger bound (E)-enolate is approached by the strong bound rotamer A in TS2 formation, which is facilitated by $\text{C}_B \bullet \bullet \bullet \text{C}_A$ bond formation via nucleophilic addition and $\text{O} \bullet \bullet \bullet \text{H}$ bond formation of β -hydroxyl group in a concerted fashion. This clearly shows the crucial role of synergic interaction that has played in transition state formation of aldol reaction on metal oxide catalyst (Figure 2). The structure of TS2 features an eight-member ring, which contrasts six-member ring TS of homogeneous aldol reaction and leads to surface aldol formation of *anti*- α -methyl- β -hydroxypentanal (MS3 in Figure 2). The projected-density of states (DOS) of labeled H, C, O atoms of TS1, MS1, TS2, MS2 (Figure S) also suggest moderate to strong electronic interactions among $\text{O} \bullet \bullet \bullet \text{H} \bullet \bullet \bullet \text{O}$ and $\text{C}_B \bullet \bullet \bullet \text{C}_A$ when bonds are being formed.

The aldol product can easily desorb from the solid surface due to its weak binding (-0.7 kcal/mol on $\text{ZrO}_2(111)$ surface and -3.3 kcal/mol on $\text{CeO}_2(111)$ surface) and the desorption process

is aided by relaxation of gas-phase *anti*- α -methyl- β -hydroxypentane and entropy increase. One can also see that the surface active sites undergo certain reconstruction from IS to MS3 where both Lewis-acid Zr (or Ce) site and Lewis-base O site (arrows in Figure 2) are slightly protruded above the surface, but are eventually recovered in FS at the end of one catalytic turnover (Figure 2).

Table 1. Calculated Bader charge (e^-)²⁵ for surface active sites

Bader Charge	M^{q+}	O^{q-}
$\text{ZrO}_2(111)$	2.38	1.12
$\text{CeO}_2(111)$	2.09	1.08

Table 1 shows that Lewis acid-base pair strength on $\text{ZrO}_2(111)$ surface is stronger than that on $\text{CeO}_2(111)$ surface. This leads to stronger (E)-enolate binding at the (Zr + O) pair site and therefore lowered activation barrier of E_{a1} for α -H abstraction step. On the other hand, the much stabilized MS2 on $\text{ZrO}_2(111)$ makes the E_{a2} of nucleophilic addition almost twice of that on $\text{CeO}_2(111)$, a manifestation of the Sabatier principle. Still, the fact that the rate-limiting step is determined by the highest activation barrier along MEP (Figure 4) would render cubic ZrO_2 a higher turnover frequency for aldol reaction than cubic CeO_2 . Therefore, the relative activation barrier for α -H abstraction and C-C formation can be altered by engineering the surface acid-base pair strength via rational catalyst design.

Conclusions

We have examined the detailed reaction mechanism of aldol reaction of propanal on metal oxide surfaces, namely cubic $\text{ZrO}_2(111)$ and $\text{CeO}_2(111)$ surface. An eight-member ring transition state for C-C bond formation has been identified and bifunctional surface acid-base pair strength can be beneficial to α -H abstraction but detrimental to nucleophilic addition at the same time. The implication is to design optimal acid-base pair strength for catalyst's better selectivity and activity. We hope our theoretical predictions will stimulate experimental verifications.

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