Theoretical insights in to the selective oxidation of steroidal alcohol over heterogeneous catalysis

Dehbi Atallah[1]*, Lounis Zoubida[1,2], Farouk Hamza Reguig[3] and Abdelkader Bengueddach[1]

[1]*Laboratory of Chemistry of Materials LCM, University of Oran 1 Ahmed Ben Bella, Algeria*
[2]*Laboratory of Engineering of Industrial Safety And Suitable Development LISIDD, University of Oran 2 Mohamed Ben Ahmed, Algeria*
[3]*Laboratory of Physical Chemistry Macromolecular LCPM, University of Oran 1 Ahmed Ben Bella, Algeria*

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ABSTRACT

The adsorotion and selective oxidation mechanism of steroidal alcohol 5α-cholestan-3β-ol by H_2O_2 over Chromium exchanged zeolites Cr-ZSM5 represented by a model clusters [(SiH3)4-AlO4-Cr], has been studied by using the ONIOM2 (B3LYP/6-31G(d,p):LANL2DZ) methodology. The computation results show that the adsorption and dissociation process of H_2O_2 followed by five step mechanism for selective oxidation of 5α-cholestan-3β-ol to 5α-cholestan-3-one, and the decomposition of grafted species ($OC_{28}H_{47}$) is the most difficult reaction due to relatively high activation barriers (E_{act}= 39.2 kcal.mol^{1-}). The major role of Cr-ZSM5 as catalyst is the decomposition of O-H bonde of 5α-cholestan-3β-ol, this energy calculated to be 10.3 kcal.mol^{1-}. The theoretical calculations performed in this study obviously indicate that Cr^{1+}site in Cr-ZSM5 catalyst has a significant an important role on the catalytic oxidation of 5-alpha-cholestanol to 5-alpha-cholestanone by H_2O_2.

Keywords : Cr-zsm5, zeolite, 5-alpha-cholestan-3β-ol, 5α-Cholestan-3-one, selective oxidation, ONIOM2 methodology, catalyst.

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INTRODUCTION

In the past few decades, Selective oxidation of alcohols is the most popular reaction transformation in steroid chemistry [1]. this specific reaction is generally employed as an intermediary step in the synthesis of a large variety of bioactive steroid compounds [2]. For this important reason, experimental and theoretical studies have been developed during the years. Lounis, Z et al. have investigated the 5α-cholestan-3-one formation reactions on Cr-MFI via the oxidation of 5α-cholestan-3β-ol by tert-butyl hydroperoxide as oxidant and reported that 5α-cholestan-3β-ol selectivity is higher than 83 % at temperatures above 80 C° [3] , Honghan Fei et al. have reported that Metal Organic Framework shows good performance in selective oxidation of this steroidal alcohol on the surface of the catalyst [4]. There has been significant research activity to improve new method for producing 5α-cholestanone. However neither experimental nor theoretical literature has an investigation for 5α-cholestan-3β-ol selective oxidation to 5α-cholestan-3-one by H_2O_2 on Cr-ZSM5 catalysts.

metal exchanged ZSM-5 catalysts have several catalytic activities and selectivity for a lot of reactions. It has been experimentally reported [5-6] that M-ZSM5 MFI gives good performance in the selective oxidation of alcools to corresponding carbonyls. The oxygen on metal atoms created by dissociation of oxidizing agents (H_2O_2, t-Butyl Hydroperoxide, N_2O, Na_2CO_3, ...), plays an important role in the selective oxidation of alcools to their corresponding carbonyls on M-ZSM5 that is confirmed by both theoretical [7-8] and experimental [9] literature.

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Furthermore, In our previous study [5], it is confirmed that iron and copper exchanged ZSM5 zeolite have an excellent activity catalytic for oxidation of phenol and P-cresols by different oxidizing agents .

Moreover, The increasing demand for environmental chemical processes and the need of bioactive steroid molecules required in medicinal and pharmaceutical industries have impelled many researchers to investigate really green technologies. On the other hand, catalytic oxidations with aqueous hydrogen peroxide H_2O_2 is a very attractive process, which is inexpensive, safe, environmentally friendly, and H_2O is the only by-product. [6-10].

The aim of this study is to investigate adsorption and selective oxidation of 5α-cholestan-3β-ol by H_2O_2 over Chromium exchanged zeolites cluster, and demonstrate the active sites and reaction mechanism patch way by used the two-layer ONIOM 2 scheme, which was described by two different methods. DFT (density functional theory) [11] with B3LYP (three-parameter hybrid method involving the Lee, Yang, and Parr correlation) formalism for high level of theory [12] including all of atoms : catalyst, axidant and reactant exept Chromium atom calciated with Los Alamos LANL2DZ (effective core potential (ECP) basis set).

CLUSTER MODEL AND COMPUTATIONAL DETAILS
II.1. Cluster model :
The catalytically active center and a portion which are located at the main channel of the zeolite framework are displayed with a $[(SiH_3)4-AlO_4-V]$ cluster. As shown in figure 1, by substitution isomorphoc of one aluminium atom for a silicon atom which contain the 5 T site of ZSM5 zeolithe, the negative charge created and compensated by H^+. next, this brønsted acid was echanged by metal atoms (Chromium atoms), the addition of transition metals ions into the framework zeolithe increased the activity of the catalyst [13] in this study we ineerst pratyclay to Chromium echanged ZSM5 due to highest activity catalytic and selctiviy for alcohol oxidation, on the other hand to obtain a neutral cluster, we terminated the dangling bonds of the terminal silicon atoms with H atoms and kept fixed at their crystallographic coordinates. The rest atoms of steroidal alcohol, oxidant and Cr-ZM5were kept relaxed.
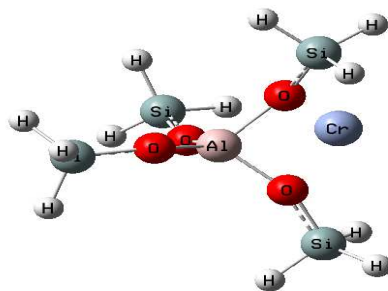

Figure 1. Final optimized geometry of Cr-ZSM5 catalyst

II.2. Computational details
In this study, and for computational efficiency, we used two layer ONIOM (ONIOM2) methodology [14-15]. All calculations are based on DFT (B3LYP) For best description of reaction profiles, the standard 6-31G(d,p) basis set level of theory for Steroidal Alcohol, the oxidant H_2O_2 and 5T full quantum cluster ZSM5 zeolithe witch represent the preferable active sites of metal-ctalysts [16] and LANL2DZ for chrmoium atom (Figure 1), which is implemented in the Gaussian 09 suite of programs . The geometrcrical and structural parameters of the ZSM-5 framework unit cell consists five crystallographically distinct tetrahedral (T) site were designed according to the crystal structure of Cr-ZSM5 lattice with unit cell parameters a= 20,0276A˚, b= 19,8243A˚ and c= 13,4034 A˚ reported by Lounis et al. in a X-Ray diffraction study [17]. were fully optimized without any symmetry. At the same theoretical levels of theory, vibrational frequencies were computed to verified all the stationary points and transition states which confirms the minimum on the potential energy surface.

Recent studies show that the ONIOM methodology has been successfully used to investigate various oxidative transformation onto alcohols and olefins moleculs on catalysts [18].

The computational strtegy used in this study is as follows. At first, single point energy were calculated with deferents spin multiplicity (SM) numbers for the clusters system and adsorbing molecules, and lowest single point energy (SPE) was accepted as the correct SM for all calculation. The Cr-ZSM5 and the adsorbing molecules, H_2O_2 and steroidal alcohol 5-alpha-cholestanol, were then thoroughly optimized geometrically by means of equilibrium geometry (EG) calculations. In the second step we located the adsorbing molecules at predefined distance of the active site of Cr-ZSM5 catalyses. Moreover, to find the lowest energy for final equilibrium geometry and the highest energy for transition state geometry, an energy profile as a function of the selected reaction coordinate distance was

performed by coordinate driving calculation. The resulting relative energies for the Cr-ZSM5 and 5α-cholestan-3β-ol molecules were created against the reaction coordinate.

The relative energy is illustrated as the following formula :

$$\Delta E = E_{System} - (E_{Cluster} + E_{Adsorbate})$$

where E_{System} is the calculated energy of the optimized structure , $E_{Cluster}$ included energy of the cluster zeolithe-5-alpha-cholestanol. and $E_{Adsorbate}$ inclose the adsorbing substrat. Finally, to get the final geometry for the single reaction step, we reoptimize the geometry with the minimum energy on the energy profile without fixynig reaction coordinate. The geometry with the highest energy from the energy profile is chosen as the input geometry for the transition state (TS) geometry calculations. the transition structures were acquired by employing the synchronous quasi-Newtonian method (QST3) [19] implemented in Gaussian software. The intrinsic reaction coordinate (IRC) [20] calculations for the system used to confirm that the reaction links the correct products with reactants.
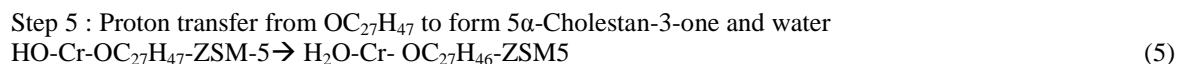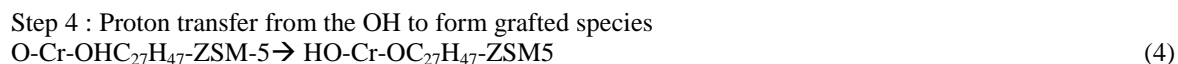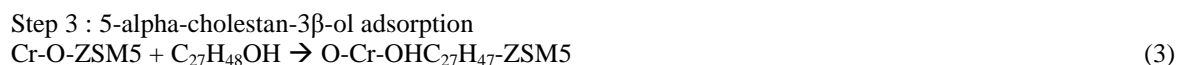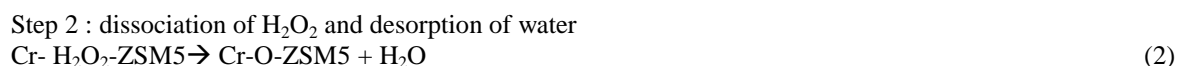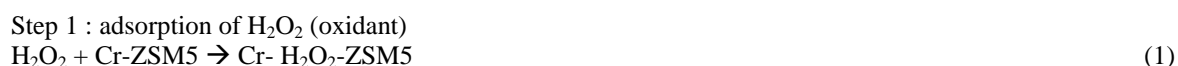
RESULTS AND DISCUSSION

III.1. Results
Single point energy values for all SM numbers of the Cr-ZSM-5 cluster are shown in Table 1, the lowest SPE was determined to be 6 for Cr-ZSM5 cluster and Cr-ZSM5 cluster including 5-alpha-cholestan-3β-ol and H_2O_2 molecules, meaning there are five unpaired electrons. This lowst single point energy was accepted for all calculation. The optimized geometries for the Cr-ZSM5 cluster modeled as $[(SiH_3)_4\text{-}AlO_4\text{-}Cr]$ and calculated for the neutral charge, see Figure 1. Silicon–Oxygen distances vlaues of a Cr-ZSM5 cluster were calculated to be 1.54 Å.

Table 1 : Single Point energy values of an Cr-ZSM-5 Cluster for SM=2,4,6, and 8.

Spin Multiplicity	Energy (au)
2	-3915.2533871
4	-3975.3437156
6	**-3975.3568151**
8	-3975.3158055
10	-3975.3144364

3.1.2. Selective oxidation of 5-alpha-cholestan-3β-ol to 5α-Cholestan-3-one by H_2O_2 on Cr-ZSM5 cluster :

The following is multistep reaction (namely step1 to step7) were employed to represante the reaction mechanism for selective oxidation of 5-alpha-cholestan-3β-ol to 5α-Cholestan-3-one by H_2O_2 on Cr-ZSM5 cluster :

Step 1 : adsorption of H_2O_2 (oxidant)
H_2O_2 + Cr-ZSM5 → Cr- H_2O_2-ZSM5   (1)

Step 2 : dissociation of H_2O_2 and desorption of water
Cr- H_2O_2-ZSM5→ Cr-O-ZSM5 + H_2O (2)

Step 3 : 5-alpha-cholestan-3β-ol adsorption
Cr-O-ZSM5 + $C_{27}H_{48}OH$ → O-Cr-OH$C_{27}H_{47}$-ZSM5   (3)

Step 4 : Proton transfer from the OH to form grafted species
O-Cr-OH$C_{27}H_{47}$-ZSM-5→ HO-Cr-O$C_{27}H_{47}$-ZSM5   (4)

Step 5 : Proton transfer from O$C_{27}H_{47}$ to form 5α-Cholestan-3-one and water
HO-Cr-O$C_{27}H_{47}$-ZSM-5→ H_2O-Cr- O$C_{27}H_{46}$-ZSM5   (5)

Step 6 : Desorption of water
H_2O-Cr- O$C_{27}H_{46}$-ZSM5→ Cr- O$C_{27}H_{46}$-ZSM5+ H_2O (6)

Step 7 : desorption of 5α-Cholestan-3-one
Cr- O$C_{27}H_{46}$-ZSM5   →   Cr-ZSM5 + $C_{27}H_{46}O$ (7)

As given in equation 1, the reaction is initiated by the physical adsorption of H_2O_2 molecule on the zeolithe surface. The dissociation of H_2O_2 on the Cr-ZSM5 active sites after first tarnsition state building the reactive centre CrO in zeolite, this step represented by equation 2, The optimized geometry of $[CrO]^+ZSM5^-$ cluster is shwen in Figure 2.
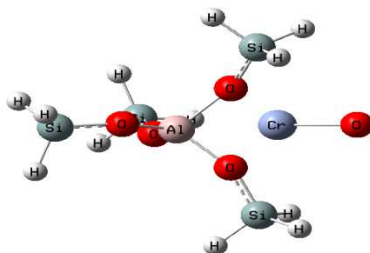
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Figure 2. Optimized geometry of [CrO]1+-ZSM5 cluster

The optimized geometry of adsorbing 5-alpha-cholestan-3β-ol molecul is depicted in Figure 3. The process of steroidal alcohol adsorption (step 3) schow an exotermic reaction (-23.42 kcal.mol[1-]) and have no activation barrier. The next step is favored thermodynamically (Step A4, ΔE=-28.91 Kcal.mol[1-]) and leads to the formation of grafted species $C_{27}H_{47}O$, the moved proton of 5-alpha-cholestan-3β-ol towards the oxygen atom located on Chromium atom forme hydroxyle molecule, this tread have a high activation barrier (E_{act}=10.28 kcal.mol[1-]). The transition stat and equilibrium geometry structures for this step shwen in Figure 4. as described in equation 5 the proton transfer frome $OC_{27}H_{47}$ to hydroxyle to produce $OC_{27}H_{46}$ and H_2O, (ΔE=41.58 kcal.mol[1-]) witch main the reaction is endothermic, and shows a very important activation barrier (E_{act} =40.63 kcal.mol[1-]) The corresponding transition stat and equilibrium geometry structure of this step is shown in Figure 5. in the last two steps, 5α-Cholestan-3-one formed on the clusters will desorb from the surfaces with desorption barrier value 36.56 kcal.mol[1-], then 17.45 kcal.mol[1-] for water. The intrinsic reaction coordinate (IRC) calculations were performed to demonstrate the transition stat TS and equilibrium geometry EG structures for step 5, the results are depicted in Figure 5.
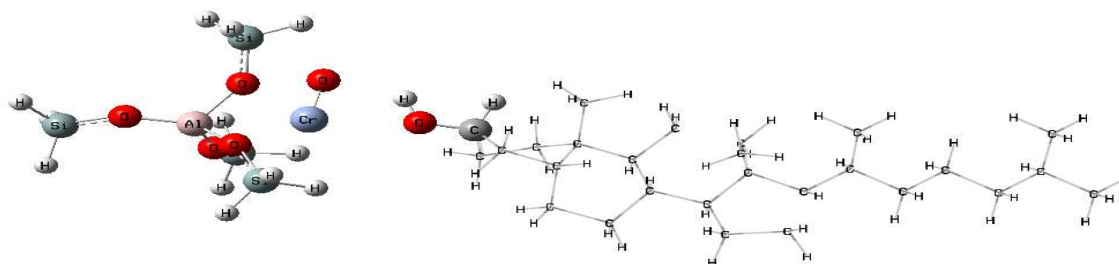

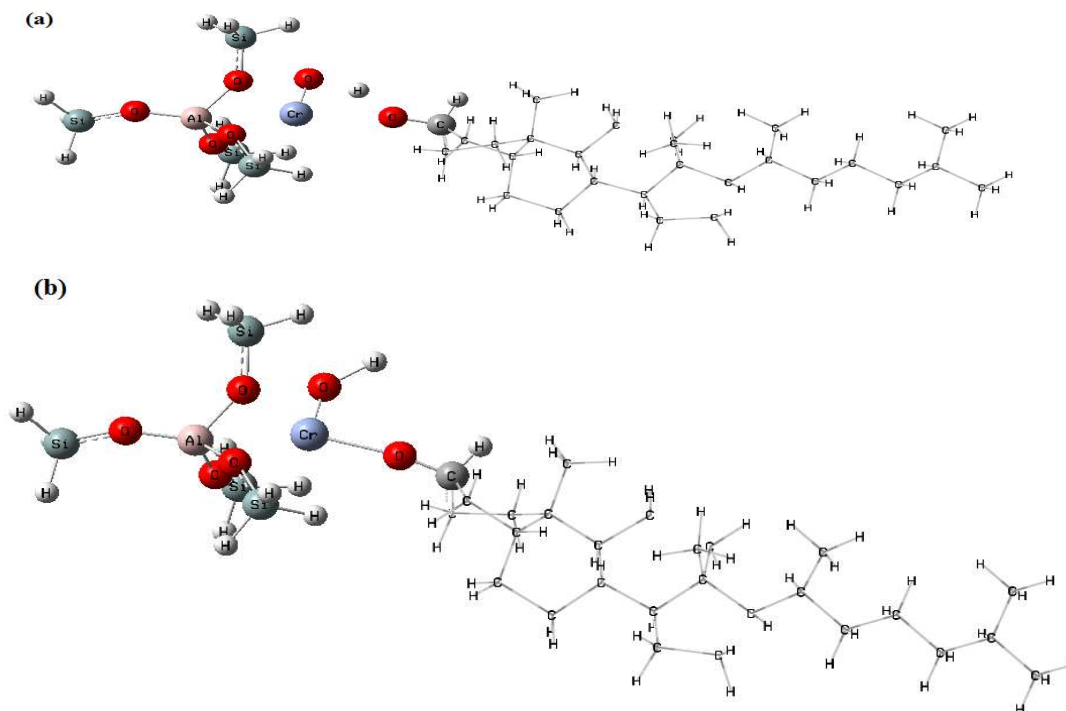**Figure 3. Equilibrium geometry for 5-alpha-cholestan-3β-ol adsorption on Cr-ZSM5 (step 3)**

Figure 4. (a) transition state TS and (b) equilibrium geometry EG for proton transfer from the OH of 5-alpha-cholestan-3β-ol to form grafted species on Cr-ZSM5 (step 4)
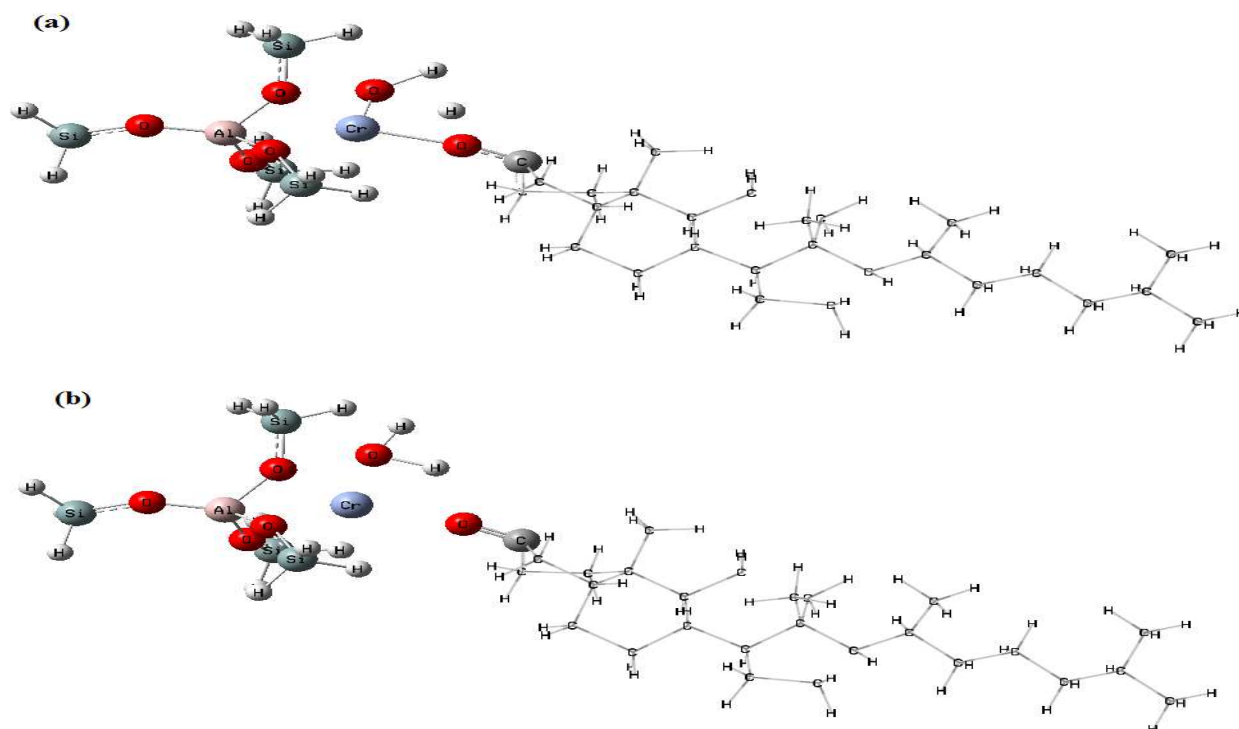
Figure 5. (a) transition state TS and (b) equilibrium geometry EG proton transfer from CH₃O of grafted species to form water and 5α-cholestan-3-one on Cr-ZSM5 (step 5)

DISCUSSION

The catalytic oxidation of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one by hydrogen peroxide H_2O_2 on $[Cr]^{1+}$ site in Cr-ZSM5 zeolite modeled as a $[(SiH_3)_4-AlO_4-Cr]$ has been investigated theoretically in this study. The spin multiplicity number of six (6) calculated in this work for the $[Cr]^{1+}$-ZSM5$^-$ clusters is the selfsame as the spin multiplicity number employed in the literature [16-21-22]. A five tetrahedral ZSM5 cluster model was utilized to generate 5-alpha-cholestan-3-one from 5-alpha-cholestan-3β-ol by hydrogen peroxide in this work since very identical structural and energetic characteristics of many adsorption complexes have been achieved in 5T [23-24], as mentioned above, Table 2 report the spin densities and Mulliken atomic charges, of Chromium atom of the cluster for all steps for equilibrium geometry and transition state geometries. As can be seen from this table, the Chromium atoms have a high spin density, which mean that the unpaired electrons are centralized on Chromium atoms. moreover, the atomic charges of Chromium atom for the clusters after the reactions are slightly higher than those of the initial ZSM5 clusters, which offer a more positive sign on Chromium atoms in the cluster throughout the reactions in analogy to the initial ZSM5 clusters. Figure 7 displays a summary the calculated reaction energy diagram for the oxidation of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one by hydrogen peroxide on reactive sites of Cr-ZSM5 zeolite (include zero-point energy (ZPE) corrections). Activation barriers for the respective reaction path involved in the 5-alpha-cholestan-3β-ol oxidation to 5-alpha-cholestan-3-one are also tabulated in Table 2. before to the 5-alpha-cholestan-3β-ol oxidation, [Cr] sites promote the hydrogen peroxide dissociation resulting in the formation of [Cr-O] sites. The formed extraframework oxygen species on the ZSM5 clusters are the reactive centers for the following oxidation of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one. Dissociation of hydrogen peroxide molecule on $[Cr]^{1+}$ sites has been investigated on the same cluster models and discussed in previous theoretical studies [25-26]. The most important reaction for the 5-alpha-cholestan-3β-ol oxidation is the activation of O-H bond of 5-alpha-cholestan-3β-ol. In this work, the activation barrier value for the proton transfer from OH of adsorbed 5-alpha-cholestan-3β-ol on [CrO] site to form grafted species (step 4) is calculated to be 10.28 kcal.mol^{1-}. This value is basically lower than the value of dissociation energy of C-H bond of grafted species $OC_{27}H_{47}$. also indicate that Cr-ZSM5 catalyst has a positive impact on 5-alpha-cholestan-3β-ol oxidation to 5-alpha-cholestan-3-one. In the next step, the activation of grafted species $OC_{27}H_{47}$ to form 5-alpha-cholestan-3-one and water on the surface (step 5) has required a very high energy barrier (Eact = 39.19 kcal.mol^{1-}), this is possibly due to the fact that the formation of grafted species of $[HO-Cr-OC_{27}H_{47}]$ (step 4) is a reaction step which is highly favored thermodynamically on the site (ΔE = -134.08 kcal.mol^{1-}). After the formation of 5-alpha-cholestan-3-one and H_2O on the catalyst, water firstly desorbs with a desorption barrier value of 17.45 kcal.mol^{1-} from the surface since 5-alpha-cholestan-3-one desorption from the surface of catalyst has a higher desorption barrier (36.56 kcal.mol^{1-}).

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All of the 5-alpha-cholestan-3-one formation steps (step 1- step 7) over $[Cr]^{1+}$ resulted in the formation of a oxygenated $[Cr-O]^{1+}$ species, which can also act as the reactive center for 5-alpha-cholestan-3-ol oxidation to 5-alpha-cholestan-3-one by hydrogen peroxide. These steps are similar to the steps oxidation of alcohols reported in the literature [8-27].
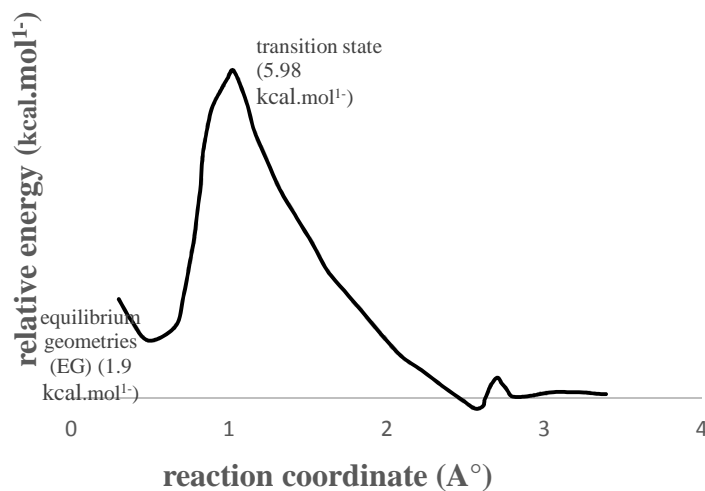

Figure 6. Energy profile for proton transfer from CH$_3$O of grafted species OC$_{28}$H$_{47}$ to to form 5-alpha-cholestan-3-one and H$_2$O$_2$ (step 5)

Table 2 : Mulliken atomic charges, spin densities, and Activation barriers for EG and TS structures of selective oxidation mechanism of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one by H$_2$O$_2$ on Cr-ZSM5 catlyst

| Steps number	geometry	Charge	Spin density	Activation barriers (kcal.mol^{1-})
Cr^{1+}-ZSM5$^-$	EG	+0.54	4.931	0
step 1 : adsorption of H$_2$O$_2$	EG	1.21	4.141	0
step 2 : dissociation of H$_2$O$_2$	EG	+1.01	4.068	25
step 3 : 5-alpha-cholestan-3β-ol adsorption	EG	+1.3	4.291	0
step 4 : Proton transfer from the OH to form grafted species	EG	+1.25	4.689	31
	TS	+1.17	4.478	
step 5 : Proton transfer from OC$_{28}$H$_{47}$ to form 5-alpha-cholestan-3-one and water	EG	+0.87	3.762	185
	TS	1.03	3.974	
step 6 : Desorption of water	EG	+0.57	4.971	59
step 7 : desorption of 5-alpha-cholestan-3-one	EG	+0.76	4.856	168
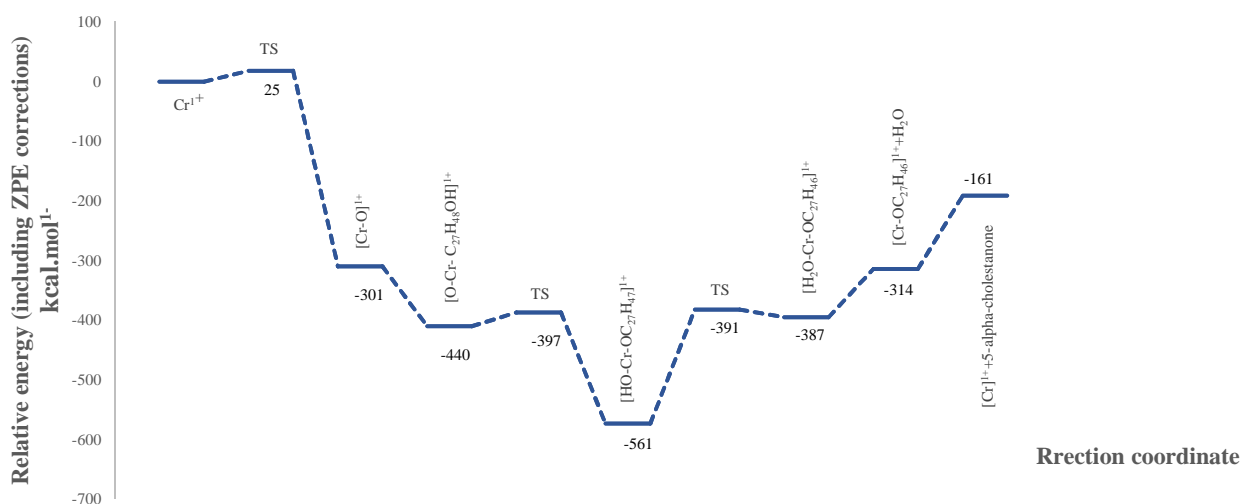
Figure 7 : Relative energy profile kcal.mol^{1-} for Selective oxidation of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one by H$_2$O$_2$ on Cr-ZSM5 cluster

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CONCLUSION

The essential reaction steps involved in the catalytic selective oxidation of 5-alpha-cholestan-3β-ol to 5-alpha-cholestan-3-one by H_2O_2, over Chromium sites in Cr-ZSM5 zeolite represented by a $[(SiH_3)_4\text{-}AlO_4\text{-}Cr]$ cluster model have been investigated by means of ONIOM2 (B3LYP/6-31G(d,p): LANL2DZ) calculations. The choice of reactive center was based on a previous investigation of H_2O_2 dissociation on metal echanged ZSM-5. Activation and interaction energies of reaction intermediates are presented. It is found that the reactive centre Cr^{1+} cation interacts with steroidal alcohol more strongly than the Brönsted acid H^{1+}, and the 5-alpha-cholestan-3-one formation step (step 5) is the most difficult reaction among seven steps due to highly activation barrier (Eact = 39.19 kcal.mol^{1-}) for grafted species decomposition. these feature show that this type of catalyst may have good performance and efficiency for selective oxidation of Steroidal Alcohol to bioactive steroid molecules.

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