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THESIS

STRUCTURE AND REACTION MECHANISMS OF PEPTIDE FORMATION OVER NANOSTRUCTURED ZEOLITE

ORANIT PHUAKKONG

A Thesis Submitted in Partial Fulfillment of
the Requirements for the Degree of
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Oranit Phuakkong 2009: Structure and Reaction Mechanisms of Peptide Formation over Nanostructured Zeolite. Master of Science (Chemistry), Major Field: Chemistry, Department of Chemistry. Thesis Advisor: Assistant Professor Piboon Pantu, Ph.D. 48 pages.

The peptide bond formation between two glycine molecules over acidic FAU zeolite was theoretically investigated using the ONIOM2 method. The H-FAU zeolite was modeled with the 120T cluster to include the unique supercage structure of this zeolite. The active region, the 14T cluster of the zeolite acid site, and the reactive molecules were treated with the B3LYP/6-31G(d,p) method. The rest of the 120T model was treated with the UFF force field, to represent the confinement effect of the zeolite pore channel. Three adsorption configurations of two glycine molecules over acidic FAU zeolite, namely Amino-bound, Carboxyl-bound and Hydroxyl-bound, were considered as starting points for the reaction. By comparing the activation energies of various reaction paths, it was appeared that the reaction preferentially proceeds through the concerted mechanism. In the pathway via the most stable adsorption configuration, the Amino-bound, the Brønsted acid site bound strongly with the first glycine molecule but did not involve in the reaction. Therefore, the high activation energy of 51.7 kcal/mol was observed. In the pathway via the Hydroxyl-bound configurations, the Brønsted acid site directly involved in the proton transfer and facilitated the peptide bond formation and, thus, the activation energy was greatly reduced to 11.2 kcal/mol. The results of this study may be helpful for understanding the fundamentals of how peptide formation of amino acid occurs over zeolite.

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Student's signature Thesis Advisor's signature

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Oranit Phuakkong

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LIST OF ABBREVIATIONS

AM1	=	The Austin model 1
B3LYP	=	Becke's three parameter hybrid functional using the LYP correlation functional
DFT	=	Density Functional Theory
FAU	=	Faujasite zeolite
HF	=	Hartree-Fock
kcal	=	kilocalories
kcal/mol	=	kilocalorie per mol
KS	=	Kohn-Sham
LCAO	=	Linear Combination of Atomic Orbitals
MNDO	=	The Modified Neglect of Diatomic Overlap method
MP	=	Møller-Plesset
MP2	=	Møller-Plesset theory at second order
MP3	=	Møller-Plesset theory at third order
NBO	=	Natural bond orbital
ONIOM	=	Our-own-N-layer Integrated molecular Orbital + molecular Mechanics
QM/MM	=	Quantum Mechanical/Molecular Mechanical calculations
SCF	=	self-consistent field
STO	=	Slater type orbital
STO-3G	=	Slater type orbital approximated by 3 Gaussian type orbitals
UFF	=	Universal Force Field

STRUCTURE REACTION MECHANISMS OF PEPTIDE FORMATION OVER NANOSTRUCTURED ZEOLITE

INTRODUCTION

The peptide bond formation is important to protein chemistry and biological chemistry. In addition, understanding the synthesis of peptides from amino acids may help to reveal the evolution of protein synthesis in the prebiotic period. Bernal (1951) reported the early speculative about synthesis of peptides from amino acid in pre-biotic conditions. It was mentioned that mineral surfaces such as clays may have played an important role on catalytic peptide bond formation on primitive Earth. Smith, (1998) and Parsons *et al.*, (1998) suggested that some silica-rich surface of feldspars and zeolites might be able to generate biopolymers such as polypeptide because of the presence of acid sites and hydroxyl species in the pore channels. There are many researchers have studied peptide bond formation in a series of well-designed experiments on a variety of inorganic materials. Recent experimental reports (Bujdák *et al.*, 1996a, 1996b, 1997, 1999, 2003) showed that peptide bond formation can be catalyzed by clay minerals such as montmorillonite, smectite and kaolinites under simulating prebiotic conditions.

The reaction between amino acids occurs via lone-pair electron of the α-amino nitrogen atom of one amino acid which attacks the α-carboxyl carbon of another amino acid in a nucleophilic acyl substitution reaction. In several previous theoretical studies, the model system of ammonia and formic acid was employed as a representative of the peptide bond formation system because they had similar geometries and energetics (Oie *et al.*, (1982); Jensen *et al.*, (1992); Chalmet *et al.*, (2001); Rimola *et al.*, (2005)). The uncatalyzed reaction in the gas phase can proceed via both stepwise and concerted mechanisms but the stepwise process requires slightly less energy than the concerted mechanism (Jensen *et al.*, 1992). Ab initio calculations showed that hydrogen fluoride and trifluoroaluminum can act as Brønsted and Lewis catalysts, respectively, to reduce the activation barrier for the amide bond

formation. More recently, catalytic roles of Brønsted and Lewis site on feldspar surface for peptide bond formation have been reported by Rimola *et al*., (2007). The Lewis sites can strongly attach the glycine molecule to the surface and the Brønsted sites can efficiently catalyze the reaction.

Zeolites are alumino-silicates which have a well define, 3-dimensional crystalline with uniform pore and channel sizes unlike, clays that have a layered crystalline. The Brønsted acid sites in zeolites are protons associated with negatively charged framework oxygens linked into alumina tetrahedral. Zeolites are solid acid and are often used as catalysts. The catalytic activity of zeolites is related to strength of the acid sites, which depends on chemical composition and topology of zeolite frameworks. Zeolites have void and space that can host cations, water or other molecules.

Boekfa *et al*., (2008) have reported the adsorption of glycine and L-alanine on the H-ZSM-5 zeolite. The interactions with the Brønsted acid site of the zeolite, the interactions with the nearby oxygen framework and van der Waals interactions with the zeolite walls are also found to be important for stabilizing the adsorbed amino acids and zwitterions. However, the effect of nanoporous of zeolites on peptide bond formation has not been studied yet.

In this study, the peptide bond formation from two glycine molecules over acidic zeolite was theoretically investigated. The stepwise and concerted mechanisms were considered. In the former, the first step of reaction is the C-N bond formation and the second step is dehydration to produce dipeptide and a water molecule. In the concerted mechanism, during the C-N bond formation, one hydrogen atom of amino group of first glycine is transferred to hydroxyl group of the other glycine with subsequent release of water. The effect of the nanoporous structure of the zeolite on the catalytic reaction is determined

LITERATURE REVIEW

Since Bernal (1951) suggested that mineral surfaces such as clays may have played an important role on catalytic peptide bond formation on primitive Earth. Peptide bond formation has attracted much attention. The objective in the peptide bond formation study is to identify the significant events in the evolution of protein synthesis. In order to approach this objective, numerous attempts, both from experimental and computational points of view, were rigorously performed to examine the basic step of peptide bond formation.

In several theoretical studies, Most of the widely studied model system was ammonia and formic acid to represent the peptide bond formation system because they had similar geometries and energetic (Oie *et al*., 1982, 1983; Jensen *et al*., 1992; Chalmet *et al*., 2001; Rimola *et al*., 2005). For example, Oie *et al*. (1982) studied the S_N2 reaction between ammonia and formic acid using the semi-empirical MNDO and *ab initio* molecular orbital methods. Two reaction mechanisms were examined, stepwise and concerted reaction. The results of MNDO and *ab initio* calculations revealed that the stepwise mechanism is more favorable than the concerted one. In stepwise mechanism, C-N bond formation is the rate-determining step. Furthermore, In 1983, they studied the S_N2 reaction between formic acid and two ammonia molecules with the second ammonia as a catalyst for model reaction of amine-catalyzed peptide bond formation using an *ab initio* molecular orbital method. A comparison with uncatalyzed amide bond formation (Oie *et al*., 1982) indicates that the participation of the second ammonia molecule reduces the internal activated energy but increases the entropy contribution to the free energy of activation, with a net decrease in free energy of activation about 10 kcal/mol for the stepwise reaction and only 2 kcal/mol for the concerted reaction. The ammonia catalyzed stepwise reaction was found to be more favorable than the concerted one, and for the former the free energy of activation of the second step was slightly higher than that of the first step.

Jensen *et al.*, (1992) studied the peptide bond on uncatalyzed reaction in the gas phase using AM1 and *ab initio* methods. The results showed that stepwise mechanism required slightly less energy than the concerted mechanism and the two proton transfer step, from nitrogen to oxygen and the C-N bond formation step required nearly the same energy.

Antonczak *et al.*, (1994) studied the water-assisted hydrolysis of formamide at the MP3/6-31G**//3-21G *ab initio* level for neutral and H_3O^+-promoted processes. The computations predict an important catalytic effect through O-protonation. Assistance by a water molecule lowers the free energy barriers of the neutral and the acid-promoted reactions, but the effect is especially large in the second case. The influence of electrostatic interactions with the bulk is discussed using a continuum model to represent the liquid. Substantial modifications of the transition-state geometries are predicted, but the average change in the activation barriers is rather small.

Several experimentally researchs in peptide bond formation have been reported by Bujdák and co-workers (Bujdák *et al*., 1996a, 1996b, 1997, 1999, 2003). Their researchs include: Bujdák *et al.*, (1996) studied the effect of smectite composition on the catalysis of peptide bond formation. Two trioctahedral smectites (hectorite and saponite), three pure montmorillonites, a ferruginous smectite, an Fe(II)-rich smectite and three smectites containing goethite admixture were used to catalzed glycine and diglycine oligomerizations as drying/wetting cycles at 80°C. Highest peptide bond formation was found with trioctahedral smectites. About 7% of glycine was converted to diglycine and diketopiperazine on hectorite after 7 days. In the case of dioctahedral smectites, highest yields were achieved using clays with a negative-layer charge localized in the octahedral sheets (up to 2% of converted glycine after 7 days). The presence of Fe(II) in clay is reflected in a higher efficiency in catalyzing amino acid dimerization (about 3.5% of converted glycine after 7 days). The possible significance of the results for prebiotic chemistry is discussed.

Bujdák *et al.*, (1996a) studied the effect of exchangeable cations, namely, alkali and alkaline metal, ammonium and aluminum ions, on montmorillonite catalyzed peptide formation. Amino acid dimerization and peptide chain elongation proceed with relatively low yields on macroscopically swelling montmorillonites (Li-, Na-) due to redistribution and insufficient concentration of reactant molecules on the clay surface. Cyclic anhydride formation, proceeding by monomolecular mechanism, is affected by the accessibility of catalytic sites for dimer activation. Weaker sorbed exchangeable cations do not block catalytic sites, and thus favour cyclic anhydride formation. Oligomerization of glyclne (gly) and diglycine (gly_2) on montmorillonite have been studied using cyclic, drying-wetting process at temperatures below 100°C under varying reaction conditions (Bujdák *et al.*, 1996b). The influence of substrate/ clay ratio, temperature and pH was found to be different for amino acid dimerization, cyclic anhydride (CA) formation and peptide chain elongation. High temperatures and neutral pH favour CA formation over diglycine production. An amino acid /catalyst ratio of 0.2 mmol/g leads to optimal yields. It revealed that amino acid dimerization and CA formation take place at the edges of clay particles. Peptide chain elongation, starting from gly_2, produces higher yields at higher temperatures and neutral pH.

Additionally, Bujdák *et al.*, (1997) studied Oligomerization of glycine (gly) and diglycine (gly_2) on silica and alumina in wetting-drying cycles at 80°C. Glycine produces less than 1% total yield of gly_2 and diketopiperazine (DKP) after one week. In experiments starting from gly_2, more than 10% DKP is formed. Formation of higher oligomers (gly_3-gly_6) proceeded as well, with 3.8% and 5.l% total yields on silica and alumina surfaces respectively. The effect of clay structures on peptide bond formation include reactions of glycine (gly), diglycine (gly_2), glycine+alanine (ala), gly_2+ala was investigated (Bujdák and Rode, 1999). The results showed as following (i) Clay composition influences the activation of reactant molecules at clay particle edges. (ii) Acidity (basicity) of the clay surface can change state of reactant. (iii) The clay structure is related to suspension stability and thus accessibility of clay catalytic sites. Mg-rich trioctahedral clays hectorite (smectite) and talc are the most efficient catalysts. Oligomerization of gly and gly_2 proceeds on all clays, whereas

oligopeptides including ala units are formed with much lower yields and only on the most efficient catalysts.

Furthermore, The reactions of the dipeptides (gly_2, ala_2) themselves and in combination with a variety of amino acids (glycine, alanine, valine, leucine, proline) and glycine oligopeptides (gly_3, gly_4, gly_5) on activated alumina surface were studied (Bujdák and Rode, 2003). Reactions of glycine oligopeptides led to the formation of oligomers up to gly_{11}. Combinations of gly_2 with other amino acids led to various reactions proceeding by different reaction mechanisms. In the reactions of gly_2 with other amino acid, cyclic anhydride ($cyc(gly_2)$) formation was followed by amino acid addition and molecular rearrangement led to the formation of gly-gly-AA (amino acid) tripeptides. In the reaction of ala_2 with glycine, this type of reaction apparently does not proceed readily, although very high yields of $cyc(ala_2)$ are formed. The reactivities of the individual components are not always reflected in reactions of their mixtures.

From Bujdák's works, they attempted to study the peptide bond formation under simulating prebiotic conditions or high temperature. Basiuk *et al*., (2001) attempted to find mild conditions for peptide formation and they reported catalytic activity of three forms of alumina (which proved to be an efficient catalyst for this process) in the intermolecular condensation of L-alanine. They expanded the temperature interval down to 55°C and used the simplest permanent heating procedure, without employing fluctuating drying/wetting conditions. The finding result is that even under the lowest temperature considered (i.e. 55°C) short peptide formation can be detected already after 10-30 days of heating. This fact implies that the abiotic peptide formation might occur in a wide variety of planetary environments, without need for high temperatures, given the presence of amino acid building blocks and alumina-containing minerals.

On the other hand, Chalmet *et al*., (2001) reported a theoretical study on ester aminolysis reaction mechanisms in aqueous solution. It is believed that the formation of a zwitterionic intermediate plays a key role in the aminolysis process whose rate

determining step is the formation or breakdown of such an intermediate, depending on pH. Stepwise and concerted processes were studied. Static and dynamic solvent effects were analyzed by using a dielectric continuum model in the first case and molecular dynamics simulations together with the QM/MM method in the second case. The results show that a zwitterionic structure is always formed in the reaction path although its lifetime appears to be quite dependent on solvent dynamics.

Some investigators have pointed out the effect of divalent cations on peptide formation (Remko and Rode, 2001; Rimola *et al.*, 2007). Remko and Rode (2001) studied model reactions between glycine and ammonia and the dimerization of glycine with and without Mg^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} cations as catalysts for peptide bond formation using the B3LYP functional with 6-311+G(d,p) and 6-31+G(d) basis sets. The B3LYP method was also used to characterize the 12 gas-phase complexes of neutral glycine, its amide and glycylglycine with Lewis acids Mg^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}, respectively. The results showed that the presence of divalent cations (i.e. Mg^{2+}, Cu^{2+} and Zn^{2+}) can enhance the formation of peptide bond reaction compared with those of the uncatalyzed reaction. The formation of a dipeptide is a more exothermic process than the creation of simple amide from glycine. The catalytic effect of the transition metal ions Ni^{2+} Cu^{2+} and Zn^{2+} is more pronounced than that of the Mg^{2+} cation. Interaction enthalpies and Gibbs energies of metal ion-base complexes increase as $Mg^{2+}<Zn^{2+}< Cu^{2+}<Ni^{2+}$. However, there is sufficient evidence for the presence of Cu^{2+} on the primitive earth. They concluded that Cu^{2+} ions might played a significant role in the formation of the first proteins in the origin of life.

Base on the previos results, Rimola and co-workers (Rimola *et al.*, 2007) studied the catalytic role of Cu^{2+} play in the peptide bond formation using density functional calculations. First, the Cu^{2+}-$(glycine)_2 \rightarrow Cu^{2+}$-(glycylglycine) + H_2O reaction was investigated since mass spectrometry low collision activated dissociation (CAD) spectra of Cu^{2+}-$(glycine)_2$ led to the elimination of a water molecule, which suggested that an intracomplex peptide bond formation might have occurred. Results show that this intracomplex condensation is associated to a very high free energy barrier (97 kcal/mol) and reaction free energy (66 kcal/mol) because of the loss of

metal coordination during reaction. Second, the condensation reaction between two glycines was studied in aqueous solution using discrete water molecules and the conductor polarized continuum model (CPCM) continuous method. It is found that the synergy between the interaction of glycines with Cu^{2+} and the presence of water molecules acting as proton-transfer helpers significantly lower the activation barrier (from 55 kcal/mol for the uncatalyzed system to 20 kcal/mol for the Cu^{2+} solvated system) which largely favors the formation of the peptide bond.

Due to the presence of acid sites and hydroxyl species in the pore channels of feldspar and zeolite (Smith, 1998; Parsons *et al.*, 1998). The catalytic role of Brønsted and Lewis site on peptide bond formation was investigated (Aquino *et al.*, 2004; Rimola *et al.*, 2005; Rimola *et al.*, 2007). Aquino *et al.*, (2004) studied the catalysis of the amide-bond formation for the concerted reaction of acetic acid and methylamine on clay mineral surfaces using density functional theory calculations. Two typical cluster models for surface defects representing hydrogen-bonded interactions and a Lewis acid defect have been selected. Additionally, a series of catalysts of varying strength (e.g. $AlCl_3$, $Al(OH)_3$, $[Al(H_2O)_5]^{3+}$, H^+, H_3O^+, H_3O^+-H_2O, H_2O and $(H_2O)_2$) which can act as Lewis or Brønsted acids was investigated as well. The results suggested a strongly asynchronous mechanism with the prior formation of C-N bond followed by a proton transfer from nitrogen to oxygen and activation barrier was reduced by the interaction with clay. Additionally, the amide bond formation between ammonia and formic acid using hydrogen fluoride and trifluoroaluminum as model systems of Brønsted and Lewis catalysts have been studied (Rimola *et al.*, 2005). It was found that the combination between Brønsted and Lewis catalysts greatly lowered the activation barrier for the amide bond formation.

More recently, Rimola *et al.*, (2007) studied the catalytic role of Brønsted and Lewis site on feldspar surface on peptide bond formation. They reported that the Lewis site alone reduced the energy barrier to 40 kcal/mol and the Brønsted site alone reduced the energy barrier to 18 kcal/mol comparing to the activation energy barrier of 50 kcal/mol for uncatalyzed gas phase reaction. Both acid sites on feldspar surface

had important role in the reaction. The Lewis sites can strongly attach the glycine molecule to surface and the Brønsted sites can efficiently catalyze the reaction.

In regarding, the adsorption of amino acid on silica rich surfaces have been studied (Rimola *et al.*, 2006; Boekfa *et al.*, 2008), Rimola and co-workers (2006) studied the periodic B3LYP simulation of glycine adsorption on a surface silica model terminated by isolated hydroxyl groups using either a 2D slab or a single polymer strand cut out from the (001) surface of an all-silica edingtonite. A number of B3LYP optimized structures have been found by docking glycine on the silica surface exploiting all possible hydrogen bond patterns. Whereas glycine is adsorbed in its neutral form, two structures show glycine adsorbed as a zwitterion, the surface playing the role of a “solid solvent” whereas intrastrand hydrogen bond cooperativity stabilizes the zwitterions. The adsorbed zwitterionic structures are no longer formed at a lower glycine coverage as simulated by enlarging the unit cell so as to break intrastrand hydrogen bonds, showing the importance of H-bond cooperativity in stabilizing the zwitterionic forms. The NH_2 group plays only a minor role as a weak hydrogen bond donor.

From previous work of our research group, The adsorption of glycine and L-alanine on the H-ZSM-5 zeolite has been studied using an embedded ONIOM (MP2/6-31G(d,p):UFF) level of theory (Boekfa *et al.*, 2008). The adsorption energy is computed to be -31.3 and -34.8 kcal/mol for glycine and L-alanine, respectively. Two hydrogen bonded complexes are identified: one is the cyclic double hydrogen bonded complex via the interactions of the carboxyl group and the zeolite acid site having adsorption energies of -25.4 and -30.0 kcal/mol for glycine and L-alanine, respectively. The second is the hydrogen bonded complex via the interactions of the hydroxyl group and the zeolite acid site having weak interaction energies, -20.7 and -23.9 kcal/mol for glycine and L-alanine, respectively. The zwitterion form is not found in the acidic H-ZSM-5 but the glycine zwitterion is found to be stably adsorbed on the Na-ZSM-5 with the adsorption energy of -24.8 kcal/mol. In addition to the interactions with the Brønsted acid site of the zeolite, the interactions with the nearby

oxygen framework and van der Waals interactions with the zeolite walls are also found to be important for stabilizing the adsorbed amino acids and zwitterions.

METHODS OF CALCULATIONS

1. Computational method

The ONIOM (Our-own-N-layer Integrated molecular Orbital + molecular Mechanics) method was developed by Morokuma and co-workers (1996). The method is “onion-like”. The model system is generally divided into shells. The aim is to perform a high-level calculation on just a small part of the system and to include the effects of the reminder at lower levels of theory. In principle, the extrapolation result could have similar accuracy to a high-level calculation on the full system.

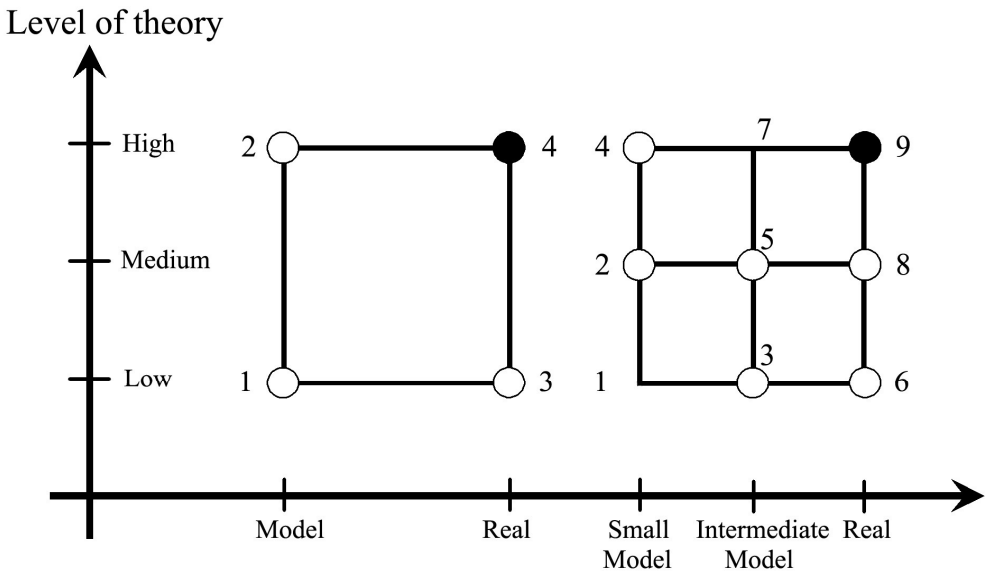


Figure 1 The ONIOM extrapolation scheme for a molecular system partitioned into two (left) and three (right) layers.

The concept of the ONIOM method is represented schematically in Figure 1, The goal is to describe the real system at the highest level of theory, i.e. the approximation of the target E_4 (point 4) in a system partitioned into the two layer ONIOM or E_9 (point 9) in a system partitioned into the three layers. In the case of two

layers, the total energy of the system (E_{ONIOM2}) is obtained from three independent calculations:

$$E_{ONIOM\,2} = E_3 - E_1 - E_2 \qquad (1)$$

Where E_3 is the energy of the real system calculated at the low level of theory. E_1 and E_2 are the energies of the model system calculated at the low and high level of theory, respectively.

The extrapolated energy E_{ONIOM2} is an approximation to the true energy of the real system E_4:

$$E_4 = E_{ONIOM} + D \qquad (2)$$

Thus, if the error D of the extrapolation procedure is constant for two different structure (e.g. between reactant and transition state), their relative energy ΔE_4 will be evaluate correctly by using the ONIOM energy ΔE_{ONIOM2}.

For a system consist of the three layers, For a three-layer ONIOM scheme, the energy expression can be written as:

$$E_{ONIOM\,3} = E_6 - E_3 + E_5 - E_2 + E_4 \qquad (3)$$

Since the evaluation of E_1 (the smallest model system at the lowest level of theory) does not require much computational effort, its value can be used to determine the effect of the three-layer approach as compared to a two-layer partitioning with points 1, 4 and 6. If the energy different between the two and three-layer extrapolation is constant, a two layer partitioning with the intermediate layer omitted would give comparable accurate results.

It should be noted that the layers need not be inclusive or contiguous. The so-called ‘inner layer’ does not have to be physically inside the ‘outer layer’. The layers can be any part of the system. Each layer does not have to be contiguous; it can consist of several separate regions of the system.

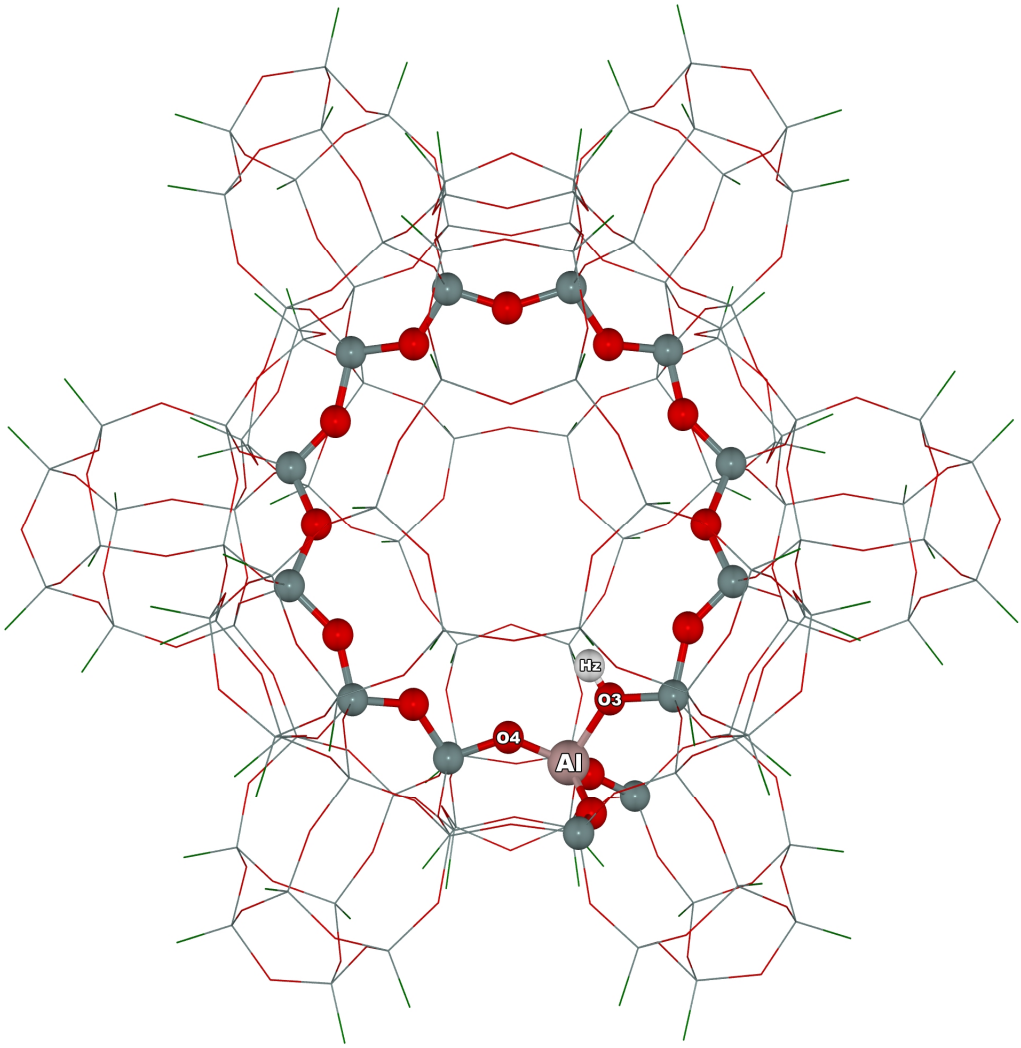
2. Computational Models and Details of Calculations

The structure of acidic faujasite zeolite, including two supercages, is modeled with the 120T cluster. The cluster model was obtained from the crystal lattice structure of faujasite zeolite. One of the silicon atom in model was substituted by an aluminum atom and a proton is added to the oxygen atoms bonded directly to the aluminum atom. The ONIOM2 method was used to calculate the peptide bond formation over acidic FAU zeolite. In the 120T ONIOM model (Figure 2), the 14T active region which included the Brønsted acid site on the 12T window of the FAU supercage was treated with B3LYP/6-31G(d,p) level of theory. The 120T extended framework which covered two supercages of FAU was treated with Universal Force Field (UFF). The reaction coordinates according to the stepwise and concerted mechanisms of the peptide bond formation were proposed. Structures of stationary points along the reaction coordinates were optimized and characterized by the analytical calculation of harmonic frequencies as minima (for intermediates) or saddle points (for transition states). During the optimization, only the 5T of Brønsted acid site, [(≡SiO)$_3$Al(OH)Si≡] and the interacting probe molecules were allowed to relax. All calculations were performed by using Gaussian 03 code (Frisch ***et al.***, 2003).

The total energy of the whole system can be expressed within the framework of the ONIOM methodology developed by Morokuma and coworkers (1996).

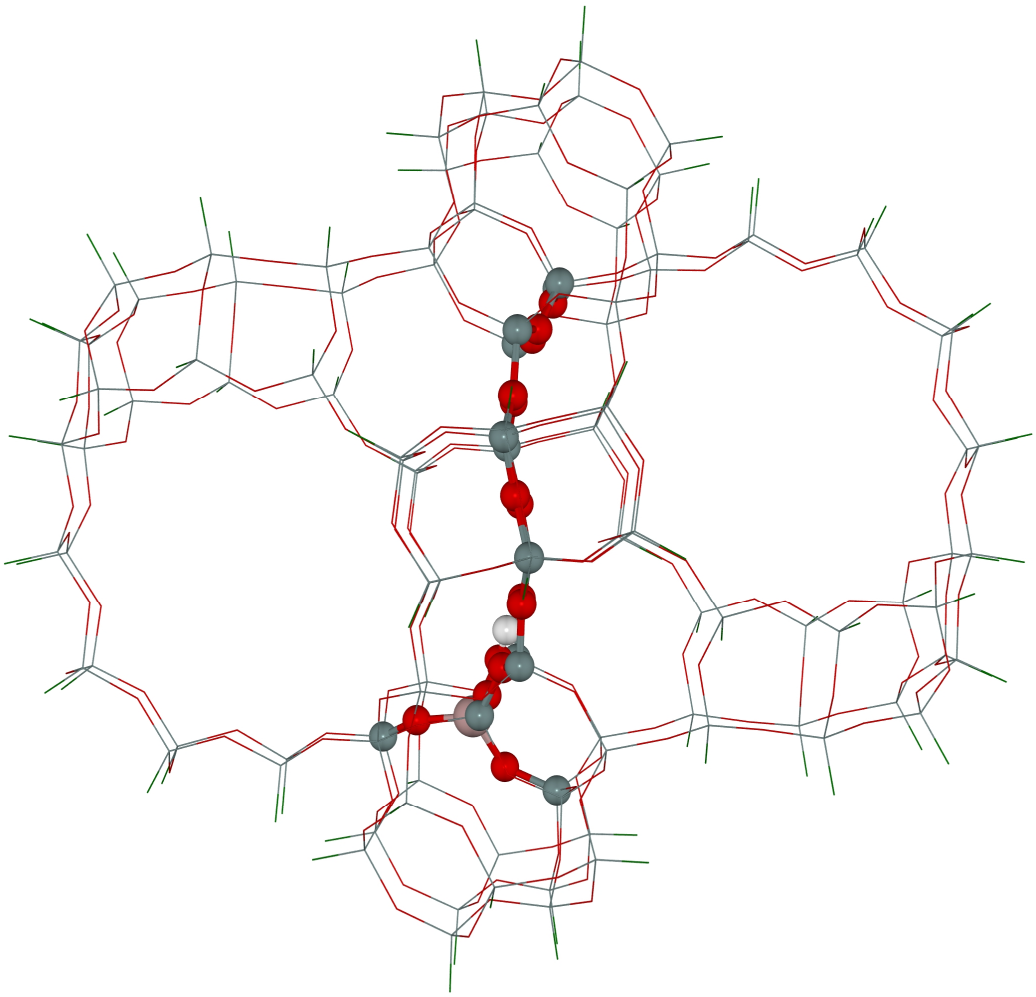
$$E_{ONIOM\,2} = E_{low}^{real} + \left(E_{high}^{cluster} - E_{low}^{cluster} \right) \qquad (4)$$

where the superscript ***real*** means the whole system and the superscript ***cluster*** means the 14T active region. The subscript ***high*** and ***low*** mean high- and low-levels of calculations used in the ONIOM calculation.



(a)

Figure 2 120 T cluster used to model the H-FAU zeolite. The 14T cluster which was treated at the higher level in the ONIOM method was shown by balls and sticks. The extended 120T structure was shown by thin lines: viewed from (a) the front view (b) the side view.



(b)

Figure 2 (Continued)

The adsorption energy (E_{ads}) is defined as the energy difference between the adsorption complex (E_{A-B}) and its constituent components (E_A and E_B), i.e.,

$$E_{ads} = E_{A-B} - (E_A + E_B) \qquad (5)$$

The binding energy is defined as the negative value of the adsorption energy. Thus bound molecules have positive binding energy and negative adsorption energy.

RESULTS AND DISCUSSIONS

Part A: Adsorption of two glycine molecules on H-FAU.

Three possible configurations of the adsorption of the first glycine molecule on H-FAU were optimized and shown in Figure 3.

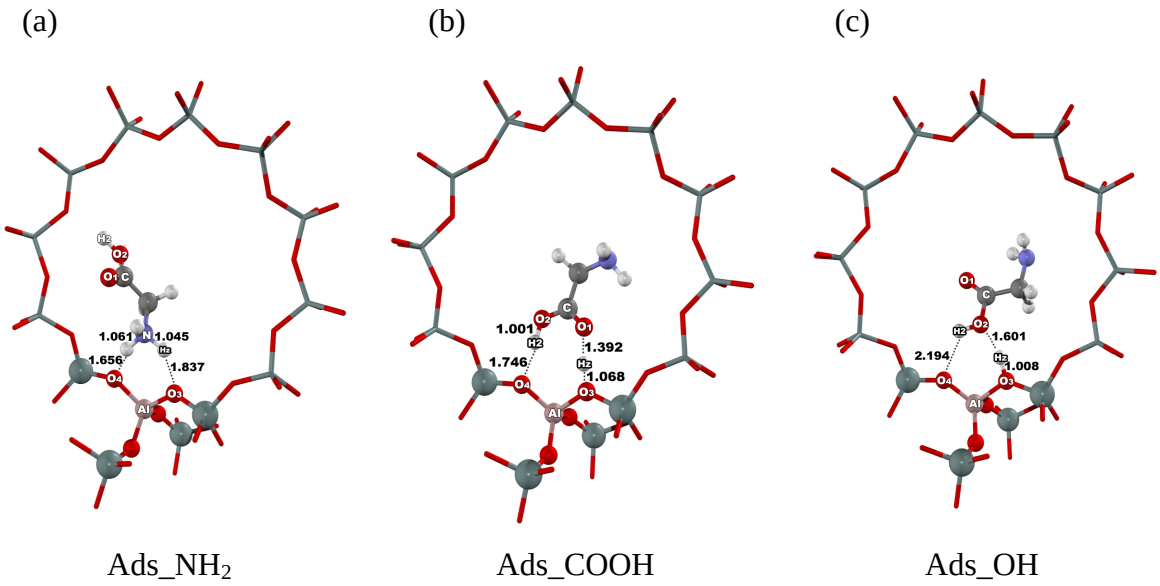


Figure 3 Adsorption of Glycine on H-FAU via (a) amino group, (b) carboxylic group and (c) hydroxyl of carboxylic group (distances in Å).

The glycine molecule can interact with the Brønsted acid site via the amino group, the carboxyl group and the hydroxyl group. The selected parameters (bond lengths, bond angles) and adsorption energies obtained in the calculation are tabulated in table 1.

Table 1 The geometrical parameters, adsorption energies, E_{ad} (kcal/mol) of the glycine molecule adsorbed on H-FAU (distances are in angstroms and angles are in degrees)

Parameter	Glycine	H-FAU	Ads_NH_2	Ads_COOH	Ads_OH
Distance (Å)					
r (O3-Hz)	-	0.971	1.837	1.068	1.008
r (C-O1)	1.211	-	1.214	1.240	1.202
r (C-O2)	1.354	-	1.327	1.311	1.381
r (O2-H2)	0.972	-	0.983	1.001	0.982
r (Al-O3)	-	1.954	1.794	1.878	1.916
r (Al-O4)	-	1.714	1.799	1.758	1.736
Angle (°)					
∠ O3-Al-O4	-	99.0	102.2	100.4	99.9
$E_{ad\ (kcal/mol)}$	-	-	-42.8	-27.5	-18.8
$E_{rel\ (kcal/mol)}$	-	-	0.0	15.4	24.0

The most stable adsorption complex is via amino group (Figure 3a). The amino group abstracts the Brønsted acidic proton of zeolite to produce the $–NH_3^+$ cation. The adsorption energy is -42.8 kcal/mol (relative to gas phase glycine and isolated zeolite). The second most stable adsorption complex is the adsorption of glycine on H-FAU via carboxyl group (Figure 3b). The adsorbed glycine molecule forms two hydrogen bonds with the Brønsted acid site. The O3–Hz Brønsted bond distance is increased from 0.971 to 1.068 Å and the C–O1 bond distance is increased from 1.211 to 1.240 Å as a result of the interaction between the proton of zeolite and the carbonyl group. The hydroxyl group of the adsorbed glycine molecule also interacts with the nearby oxygen atom (O4) on the zeolite framework. The adsorption energy is -27.5 kcal/mol. The least stable complex is the adsorption of glycine on H-FAU via hydroxyl group (Figure 3c). The hydroxyl group forms a hydrogen bond interaction with the Brønsted acidic proton of the zeolite. The adsorption energy is -18.8 kcal/mol.

Three adsorptions of two glycine molecules on H-FAU were optimized and shown in Figure 4. Then, another glycine was added to the systems. The second glycine molecule adsorbs by interacting with the first adsorbed molecule and zeolite framework.

The adsorption energies of two glycine molecules in different configurations and selected parameters (bond lengths, bond angles) obtained in the calculation are tabulated in table 2.

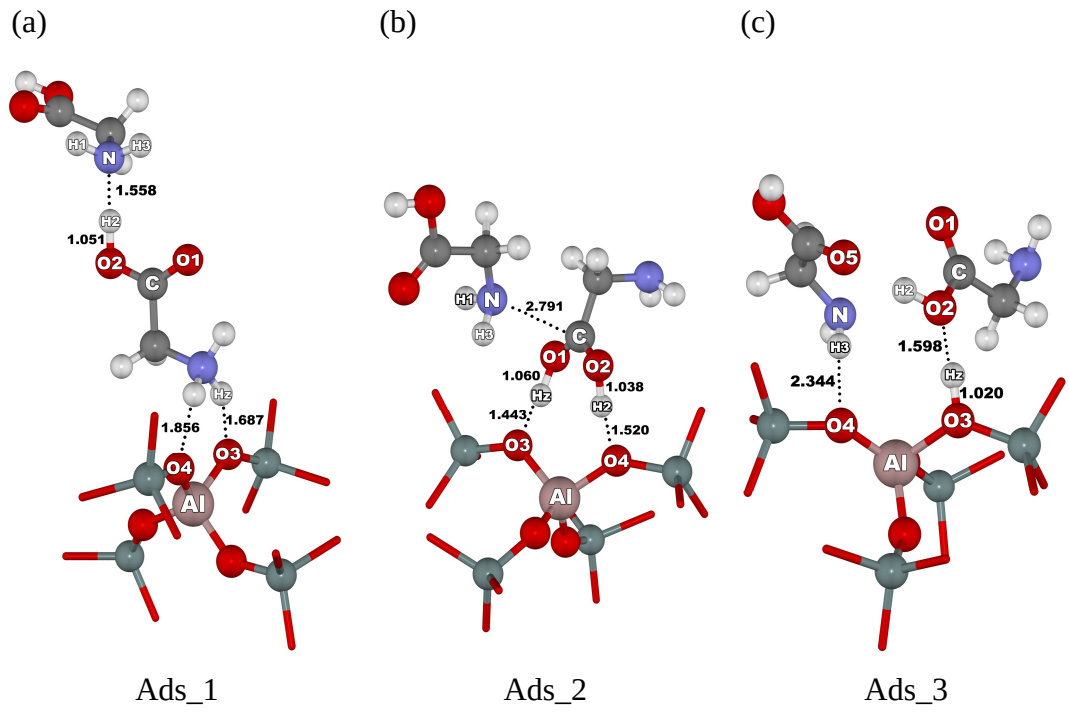


Figure 4 Glycine molecules adsorbed on H-FAU via (a) amino group (Ads_1), (b) carboxylic group (Ads_2) and (c) hydroxyl of carboxylic group (Ads_3) (distances in Å).

Table 2 The geometrical parameters, adsorption energies, E_{ad} (kcal/mol) of the glycine molecules adsorbed on H-FAU (distances are in angstroms and angles are in degrees) and atomic charges on carbon atom of Carboxyl group of glycine reaction center (charges in $|e|$).

Parameter	Glycine	H-FAU	Ads_1	Ads_2	Ads_3
Distance (Å)					
r (O3-Hz)	-	0.971	1.687	1.443	1.020
r (C-O1)	1.211	-	1.223	1.279	1.206
r (C-O2)	1.354	-	1.308	1.286	1.369
r (C-N)	-	-	3.316	2.791	3.204
r (N-H1)	1.018	-	1.021	1.019	1.017
r (O2-H1)	-	-	3.128	3.203	3.800
r (O2-H2)	0.972	-	1.051	1.038	1.003
r (Al-O3)	-	1.954	1.800	1.813	1.908
r (Al-O4)	-	1.714	1.786	1.795	1.725
Angle (°)					
∠ O3-Al-O4	-	99.0	102.7	100.6	101.7
q C	0.807	-	0.819	0.895	0.833
$E_{ad\ (kcal/mol)}$		-	-60.9	-40.3	-36.3
$E_{rel\ (kcal/mol)}$	-	-	0.0	20.6	24.6

The most stable adsorption structure of two glycine molecules on H-FAU is the ion-pair adduct (Ads_1). The first adsorbed glycine molecule is protonated by Brønsted acid site. The computed adsorption energy is -60.9 kcal/mol (relative to gas phase molecules and isolated zeolite). In the carboxyl-bound configuration (Figure 4b), the carbonyl oxygen (O1) of the carboxylic group interacts with the Brønsted acidic proton of zeolite and the acidic proton of zeolite induces the lengthening of O3–Hz bond distance to increase from 0.971 to 1.443 Å. The C=O1 bond distance is increased from 1.211 Å to 1.279 Å, indicating that the adsorption weakens the C=O bond. As a result, the positive charge on the C carbonyl atom increases from 0.807 to 0.895. The hydroxyl of carboxylic group also interacts with oxygen framework, H2-

O4 bond distance is 1.520 Å. The second glycine molecule weakly interacts with the first adsorbed molecule over the intermolecular N---C distance of 2.791 Å. This adsorption complex has the adsorption energy about -40.3 kcal/mol compared to the gas phase but it is destabilized by 20.6 kcal/mol compared to the first adsorption configuration, Ads_1.

In hydroxyl-bound configuration (Figure 4c), the hydroxyl oxygen (O2) of carboxylic group forms a hydrogen bond interaction with the Brønsted acidic proton of the zeolite and also forms hydrogen bond interaction with the carbonyl oxygen of the second glycine molecule with a distance of 1.673 Å and an angle of O2H2O5 of 174.3^{o}. The C-O2 bond is slightly increased from 1.354 Å to 1.369 Å leading to the increase in the positive charge of the C atom at the reaction center from 0.807 to 0.833 as compared to the isolated glycine molecule. The adsorption energy is calculated to be -36.3 kcal/mol. This adsorption complex is relatively destabilized by 24.6 kcal/mol compared to the Ads_1 complex.

Part B: Peptide bond formation

Two possible pathways for the peptide bond formation of two glycine molecules are presented. The reaction can be considered to proceed through either a concerted reaction mechanism or a stepwise reaction.

1. Concerted reaction mechanism

The schemes of concerted reactions starting from three adsorption configurations are presented in Figure 5. The peptide bond formation is carried out through the protonation of the Brønsted acidic proton to the amino group (in path a, Figure 5a), to the oxygen atom of Carboxyl group (in path b, Figure 5b) and the hydroxyl of carboxyl group (in path c, Figure 5c) of the glycine molecule, respectively. The reactions are simultaneously involving the nucleophilic attack of the amino group on the Carboxyl carbon atom and the indirect transfer of a hydrogen atom from the amino group to the hydroxyl group of another glycine molecule, which result in an adsorbed Diglycine and a water molecule.

a) Amino-bound configuration

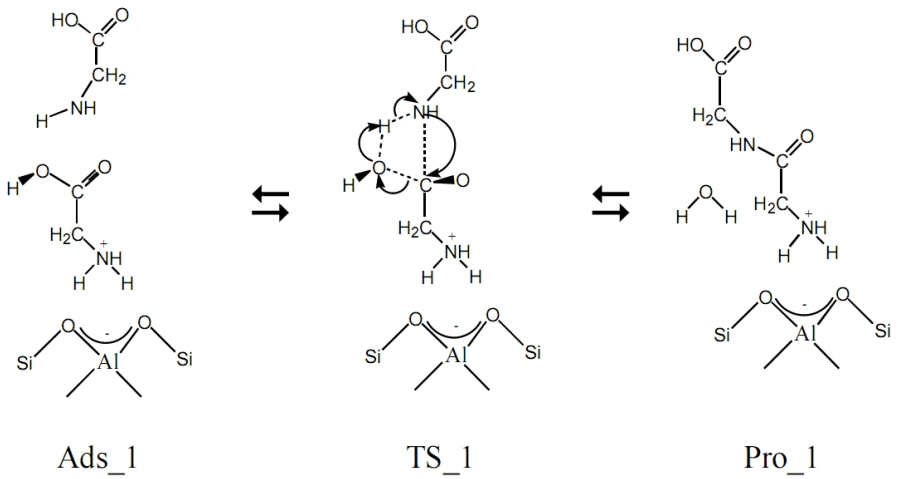
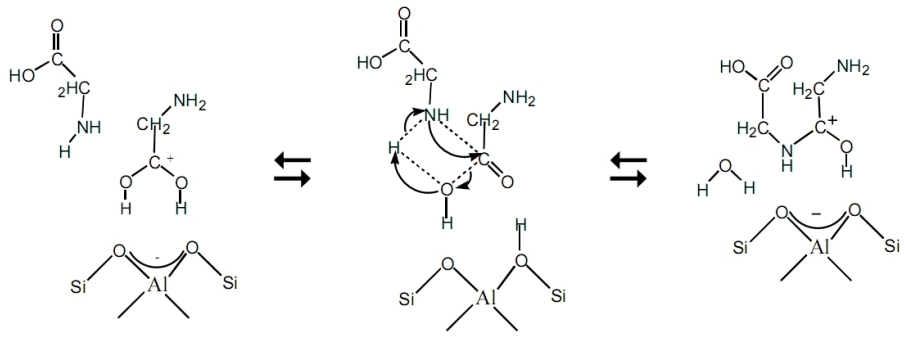


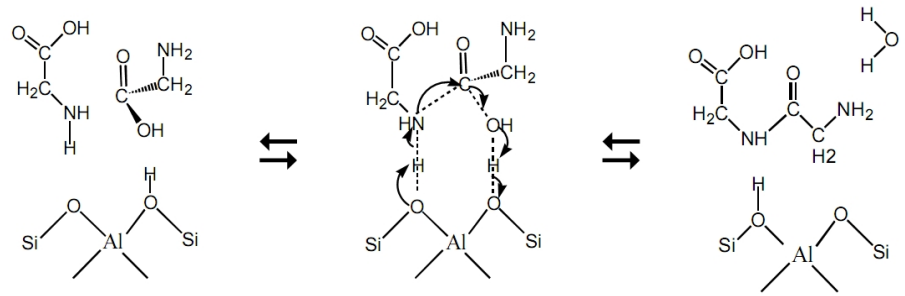
Figure 5 Concerted reaction mechanism of two glycine molecules over H-FAU zeolite via (a) amino bound, (b) carboxyl bound and (c) hydroxyl bound.

b) carboxyl -bound configuration



Ads_2 TS_2 Pro_2

c) hydroxyl -bound configuration



Ads_3 TS_3 Pro_3

Figure 5 (Continued)

It is noticed the adsorbed products of the three pathways are in different configurations. In path a, the diglycine product is protonated at its amino group. In the path b, the diglycine product is protonated at its oxygen atom of the formed amino group. In the last pathway, the diglycine is not protonated but is adsorbed via hydrogen bond interaction with the acid site.

The reaction profiles for the three different starting configurations are shown in Figure 6. The selected geometrical parameters are shown in Table 3 and optimized structures of intermediates and transition state of the three pathways are shown in Figure 7-9.

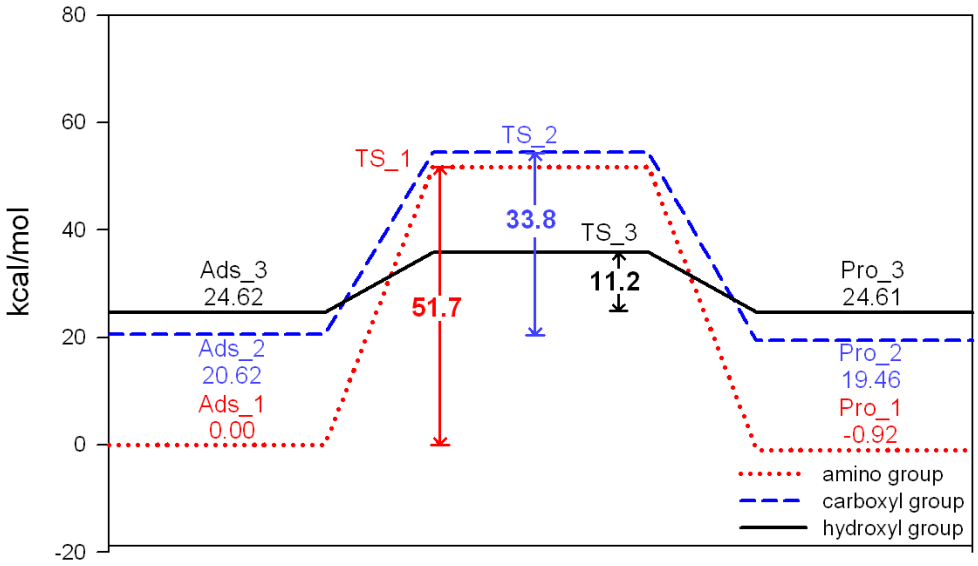


Figure 6 Relative energy profile (kcal/mol) of the concerted mechanism of peptide formation on H-FAU by using ONIOM (B3LYP/6-31G (d,p):UFF). Dotted line refers to amino-bound configuration, dashed line refer to carboxyl-bound configuration and dark line refer to hydroxyl-bound configuration.

Table 3 The ONIOM(B3LYP/6-31G(d,p):UFF) geometrical parameters of the adsorption complexes, transition states and products for concerted reaction mechanism of peptide bond formation from two glycine molecules over H-FAU (distances are in angstroms and angles are in degrees).

Parameter	Amino-bound			Carboxyl-bound			Hydroxyl-bound		
	Ads_1	TS_1	Pro_1	Ads_2	TS_2	Pro_2	Ads_3	TS_3	Pro_3
Distance (Å)									
r (O3-Hz)	1.687	1.673	1.898	1.443	1.654	1.419	1.020	1.733	2.081
r (C-O1)	1.223	1.226	1.228	1.279	1.339	1.283	1.206	1.197	1.215
r (C-O2)	1.308	1.822	3.598	1.286	1.570	2.800	1.369	2.053	5.101
r (C-N)	3.316	1.559	1.347	2.791	1.519	1.318	3.204	1.614	1.407
r (N-H1)	1.021	1.197	3.143	1.019	1.315	1.022	1.017	1.042	1.794
r (O2-H1)	3.128	1.330	0.966	3.203	2.825	3.502	3.800	2.661	3.384
r (O2-H2)	1.051	0.973	0.981	1.038	1.015	0.977	1.003	0.974	0.969
r (Al-O3)	1.800	1.807	1.800	1.813	1.810	1.830	1.908	1.781	1.747
r (Al-O4)	1.786	1.775	1.784	1.795	1.782	1.756	1.725	1.776	1.899
Angle (°)									
∠ O3-Al-O4	102.7	102.6	103.3	100.6	101.8	103.1	101.7	104.1	99.4
$E_{a\ (kcal/mol)}$		51.7			33.8			11.2	

The optimized transition state structures are confirmed by the corresponding imaginary frequencies which indicate the concerted mechanism of the peptide formation over H-FAU zeolite. The nucleophilic attack of the lone pair electron of the amino group to the carbonyl carbon atom of the carboxyl group and, simultaneously, the proton transfer from the amino group to one of the oxygen atoms of the hydroxyl group. Then, the adsorbed diglycine and a water molecule are formed.

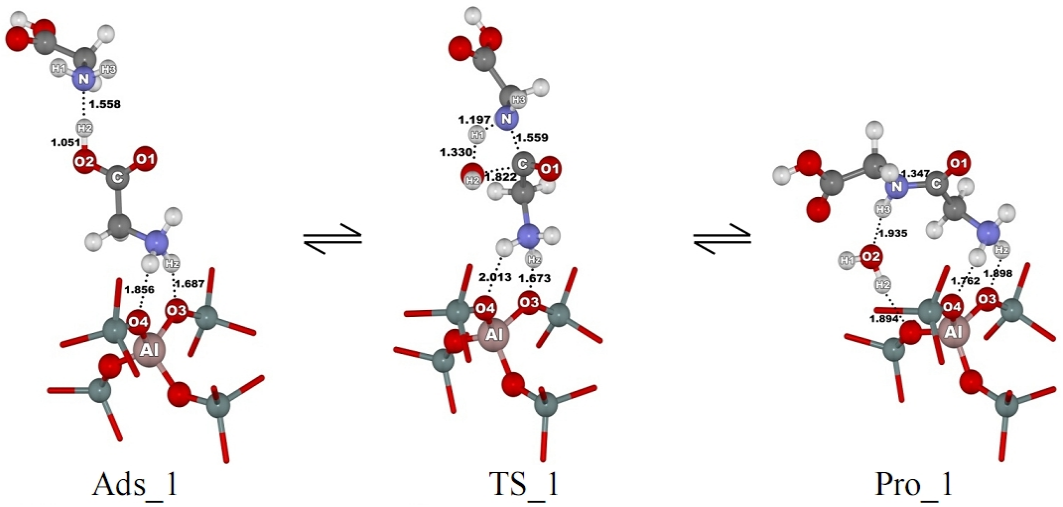


Figure 7 Optimized geometry of adsorption complex, transition state and products of concerted reaction mechanism via amino-bound configuration.

The transition state of the Ads_1 (amino-bound) configuration (Figure 7) corresponds to the following movements: The N atom moves forward the C atom (the N-C distance decreased from 3.316 Å to 1.559 Å) to form a peptide bond, while the H1 proton is transferred from the amino group to the oxygen atom (O2) of the hydroxyl group (the N-H1 bond is elongated from 1.021 Å to 1.197 Å and the O2-H1 distance is decreased from 3.128 Å to 1.330 Å). The activation barriers of this pathway is 51.7 kcal/mol which is very close to that of the reported uncatalyzed reaction of two glycine molecules in the range of 47.7-52.7 kcal/mol (Jensen *et al.*, 1992). This is not unexpected because the reaction center is far away from the Brønsted acid site. The protonated amino group also does not significantly affect the electrophilicity of the carbonyl carbon atom, which indicate by the slight change of positive charge at the C atom (0.819) compared to the isolated glycine (0.807) molecule in Table 2. The Brønsted acidic proton only function to strongly bound the glycine molecule to zeolite surface but does not catalyze the reaction.

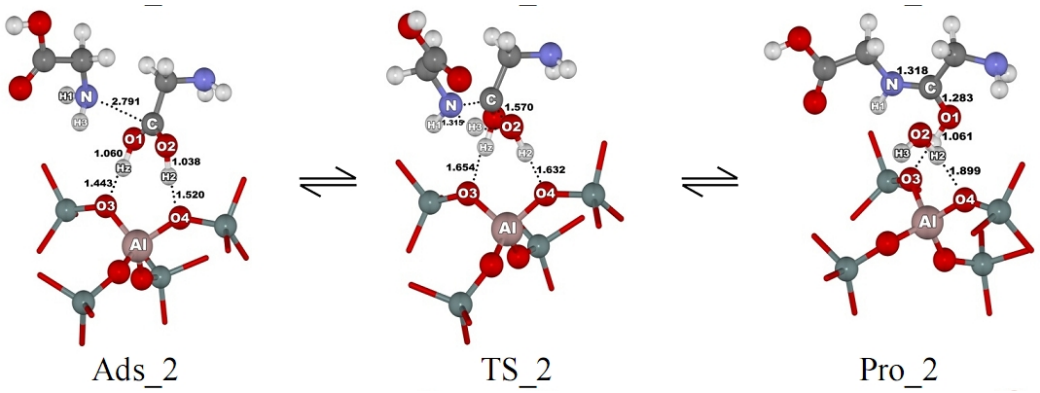


Figure 8 Optimized geometry of adsorption complex, transition state and products of concerted reaction mechanism via carboxyl-bound configuration.

In the case of Ads_2 (carboxyl-bound) configuration (Figure 8), a more favorable reaction path is found and the total activation barrier is reduced to 33.8 kcal/mol (Table 3). Unlike the amino-bound configuration, the peptide bond formation occurs on the adsorbed (activated) carboxyl group. The oxygen atom (O1) of the carboxyl of glycine is protonated by the Brønsted acidic proton, leading to an increase in electron deficiency on the carbon atom which is facilitating the nucleophilic attack by lone pair electron of nitrogen and reduce the activation barrier.

The most favorable reaction path is found with the total activation barrier being only 11.2 kcal/mol (Table 3) when the reaction begins with the Ads_3 (hydroxyl-bound) configuration. The reason for such a dramatic barrier lowering is the presence of an eight-membered ring of the transition structure in which a double proton transfer occurs: the Brønsted acidic proton from the H-FAU zeolite is protonating to the glycine OH group and, simultaneously, the proton from NH_3 is being abstracted by the adjacent oxygen atom of the H-FAU zeolite. The proton transition state (shown in Figure 9) clearly demonstrates the C–N bond formation between the two glycine molecules and the C-O bond breaking to release the water molecule. The C-O2 bond distance of the glycine is elongated from 1.369 Å to 2.053 Å and the peptide bond is

generated by the C-N bond formation with the decreasing of the C-N distance form 3.204 Å to 1.614 Å.

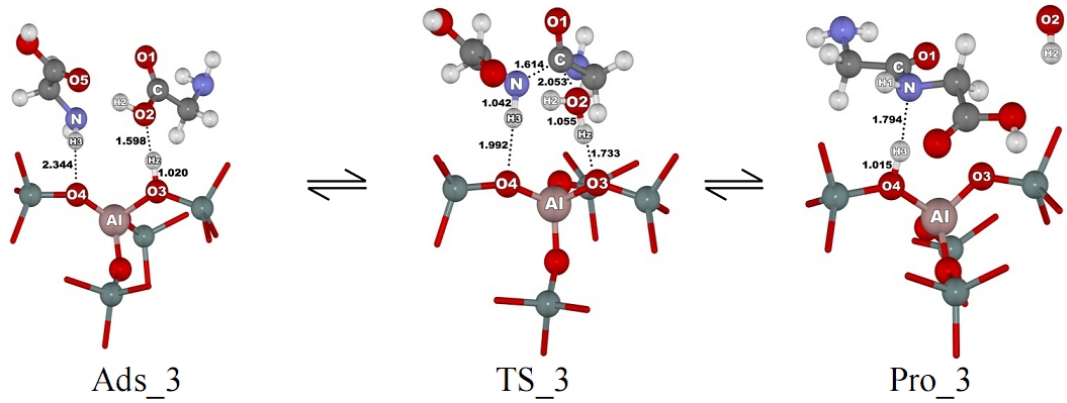


Figure 9 Optimized geometry of adsorption complex, transition state and products of concerted reaction mechanism via hydroxyl-bound configuration.

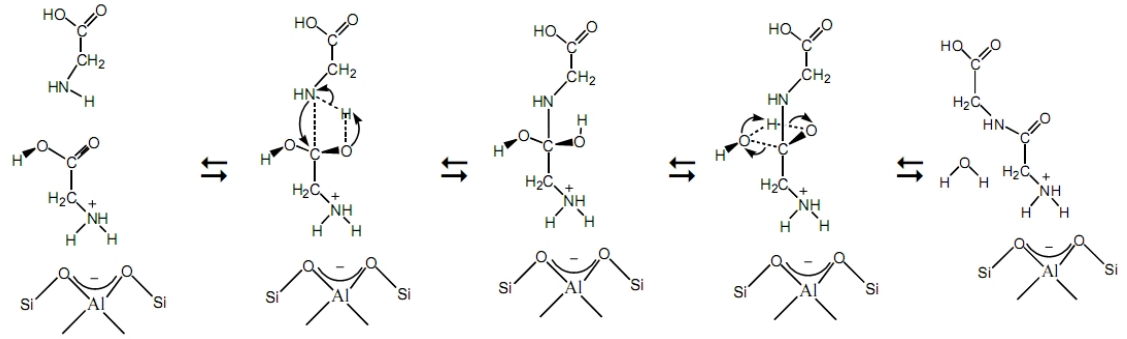
Although the Ads_3 is the least stable adsorption complex, the reaction in this path proceeds through the most stabilized transition state. Thus, the activation energy is greatly reduced. The synergistic effect of Brønsted acidic proton to protonate the leaving -OH group and adjacent oxygen lewis base to abstract proton from $–NH_2$ group is attributed to the facile peptide bond formation. The reaction energy (relative to the starting co-adsorption complex) is almost thermo neutral in all cases.

2. Stepwise reaction mechanism

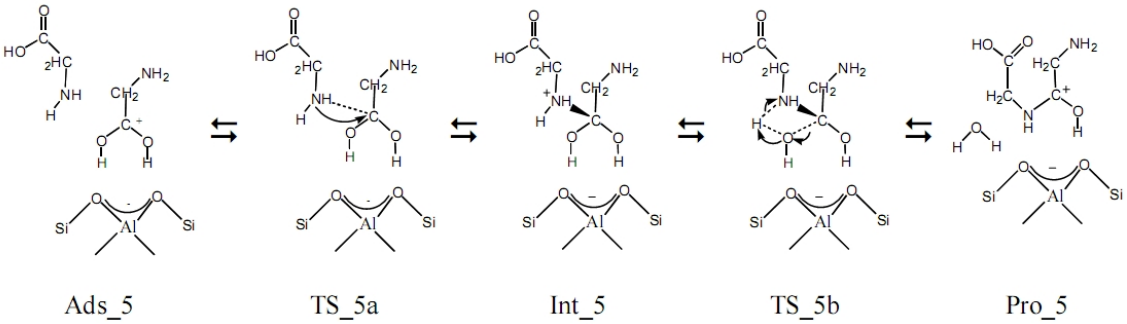
The peptide bond formation of two glycine molecules can also proceed via the stepwise reaction mechanism. The first step is the C-N bond formation by the nucleophilic attack of the amino group on the carboxyl carbon atom to form a diolic intermediate. The second step involves the dehydration of diolic intermediate to form the diglycine and the water molecule adsorbed over H-FAU.

The reaction schemes are presented in Figure 10. Similar to concerted mechanism, the reaction is considered to begin with three adsorption configurations. In path (a) the Brønsted acid site protonate the amino group (Figure 10a) and strongly binds the amino acid via the ion-pair interaction. In path (b) and (c), the Brønsted proton catalyzes the reaction by interacting with the carbonyl oxygen atom and the hydroxyl group of the carboxylic group, respectively. The first step of the reaction is the C-N bond formation which involves the nucleophilic attack of the amino group on the carboxyl carbon atom and the indirect transfer of a hydrogen atom from the amino group to the carbonyl oxygen atom to form the diolic intermediate. The next step is dehydration to produce adsorbed Diglycine and a water molecule.

a) Amino-bound configuration



b) carboxyl -bound configuration



c) hydroxyl -bound configuration

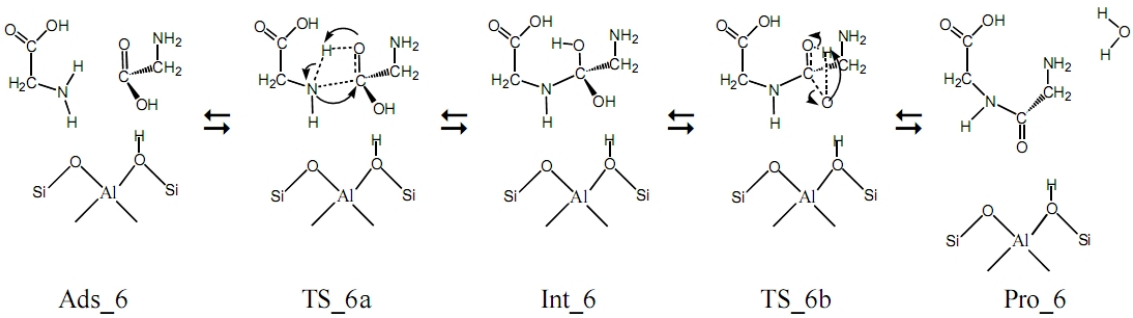


Figure 10 Stepwise reaction mechanism of two glycine molecules over H-FAU zeolite via (a) amino bound, (b) carboxyl bound and (c) hydroxyl bound.

The calculated energy profiles of the stepwise reaction mechanism for the three different starting configurations are shown in Figure 11 and the selected geometrical parameters of the transition state are shown in Table 4.

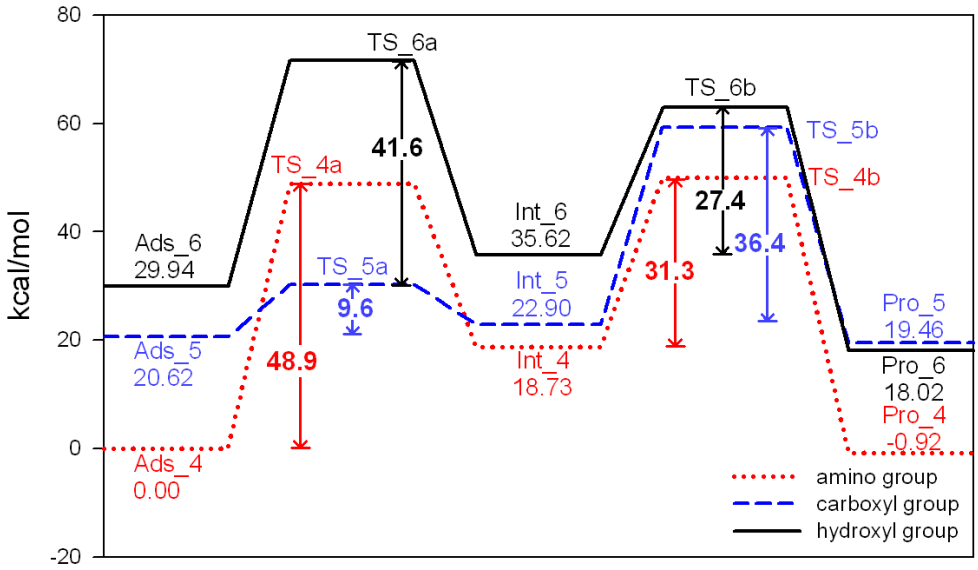


Figure 11 Relative energy profile (kcal/mol) of the stepwise mechanism of peptide formation on H-FAU by using ONIOM (B3LYP/6-31G(d,p): UFF). Dotted line refers to amino-bound configuration, dashed line refer to carboxyl-bound configuration and dark line refer to hydroxyl-bound configuration.

Table 4 The ONIOM(B3LYP/6-31G(d,p):UFF) geometrical parameters of the adsorption complexes, transition states and products for stepwise reaction mechanism of peptide bond formation from two glycine molecules over H-FAU (distances are in angstroms and angle are in degrees).

			Amino-bound					Carboxyl-bound					Hydroxyl-bound				
Parameters	Glycine	H-FAU	Ads_4	TS_4a	Int_4	TS_4b	Pro_4	Ads_5	TS_5a	Int_5	TS_5b	Pro_5	Ads_6	TS_6a	Int_6	TS_6b	Pro_6
Distance (Å)																	
r (O3-Hz)	-	0.971	1.687	1.740	1.765	1.656	1.898	1.443	1.686	1.659	1.617	1.419	1.003	1.035	1.029	1.309	1.434
r (C-O1)	1.211	-	1.223	1.353	1.410	1.320	1.228	1.279	1.343	1.351	1.331	1.283	1.208	1.331	1.392	1.523	2.944
r (C-O)	1.354	-	1.308	1.390	1.404	1.905	3.598	1.286	1.350	1.359	1.544	2.800	1.376	1.466	1.463	1.439	1.278
r (C-N)	-	-	3.316	1.581	1.437	1.357	1.347	2.791	1.706	1.645	1.512	1.318	3.307	1.561	1.449	1.405	1.327
r (N-H1)	1.018	-	1.021	1.026	1.012	1.016	3.143	1.020	1.039	1.036	1.036	1.022	1.017	1.027	1.017	1.025	1.035
r (N-H3)	1.018	-	1.019	1.240	2.406	2.671	1.024	1.019	1.025	1.026	1.364	3.720	1.018	1.250	2.415	2.470	3.247
r (O2-H1)	-	-	3.128	2.403	2.288	3.056	0.966	3.882	2.554	2.514	2.654	3.502	4.244	2.485	2.347	2.507	2.554
r (O2-H2)	0.972	-	1.051	0.974	0.973	0.972	0.981	1.038	0.998	0.994	1.006	0.977	0.990	0.972	0.969	1.164	3.423
r (O2-H3)	-	-	3.080	2.732	2.573	1.309	1.935	3.203	2.581	2.544	1.200	0.977	3.894	2.518	2.698	2.788	3.423
r (O1-H3)	-	-	3.052	1.326	0.974	1.171	5.247	3.386	3.292	3.275	2.849	3.904	2.352	1.341	0.981	0.989	0.970
r (Al-O3)	-	1.954	1.800	1.801	1.797	1.811	1.800	1.813	1.795	1.797	1.786	1.830	1.923	1.899	1.904	1.836	1.814
r (Al-O4)	-	1.714	1.786	1.782	1.793	1.766	1.784	1.795	1.766	1.765	1.775	1.756	1.737	1.717	1.718	1.734	1.732
Angle (°)																	
∠ O3-Al-O4	-	99.0	102.7	102.7	102.4	102.7	103.3	100.6	104.1	104.1	104.0	103.1	99.6	102.1	102.0	103.7	105.3
$E_{a\ (kcal/mol)}$	-	-		48.9		31.3			9.6		36.4			41.6		27.4	

In the first case, the first amino acid is protonated at its amino group and bound strongly on the acid site. Then, it is attacked at its carboxylic group by lone pair electron of another glycine molecule. The peptide bond is generated by the subsequent four-membered transition state which consists of the hydrogen transfer simultaneously with the intermolecular bond formation (Figure 12).

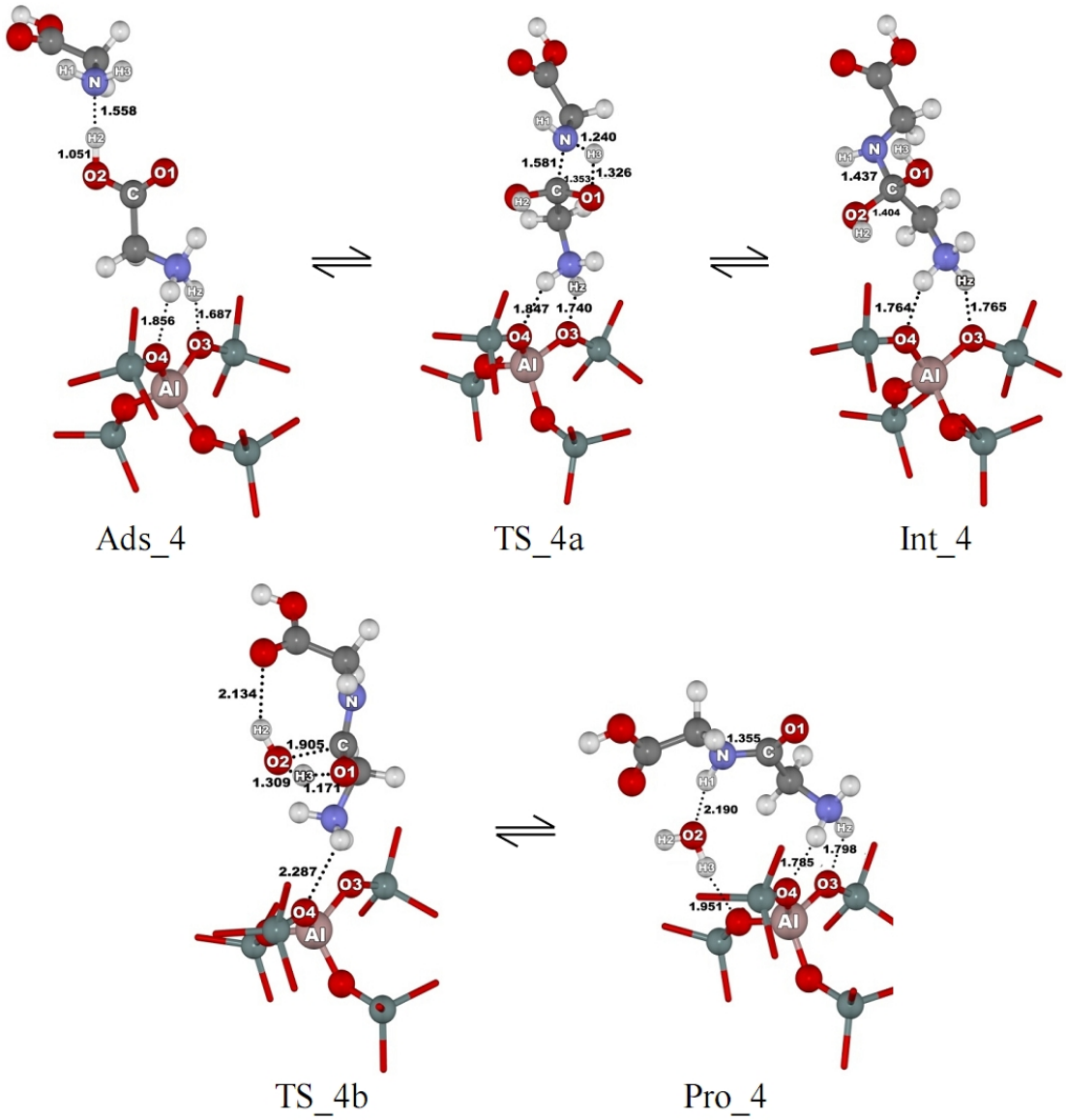


Figure 12 Optimized geometry of adsorption complex, transition states and products of stepwise reaction mechanism via amino-bound configuration.

The amino hydrogen atom (H3) from second glycine is moved to the carboxyl oxygen atom (O1) on first glycine as the C-N bond is formed. At the transition state (TS_4a), the intermolecular distance (C-N) is 1.581 Å and the N-H3 is elongated to 1.240 Å. The H3 proton is moving toward the carbonyl oxygen atom (H3-O1 = 1.326 Å) causing the C=O double bond to be increased to 1.353 Å. The calculated activation barrier is 48.9 kcal/mol which is comparable to that of the concerted reaction mechanism (51.7 kcal/mol). The diolic intermediate which has an sp^3 tetrahedral configuration around the carbon atom at the peptide bond, is produced and adsorbed over the deprotonated active site. The diolic intermediate is close to from the framework by 1.764 Å and the binding energy is 42.2 kcal/mol. At the second transition state (TS_4b), the dehydration proceeds via the planar four-membered ring transition state in which the tetrahedral configuration around the carbon atom of the diolic intermediate is distorted. The energy barrier is 31.3 kcal/mol. As the hydroxyl cleavages from the diolic intermediate, C-O2 distance is extended from 1.404 Å to 1.905 Å, the C-N bond is contracted from 1.437 Å to 1.357 Å and the protonic H3 from O1 is moved forward to O2 with the distance of 1.171 Å and 1.309 Å, respectively. The calculated binding energy of the products (Pro_4) is found to be 61.8 kcal/mol.

From the Carboxyl-bound configuration (Figure 13), the first transition state (TS_5a) of the peptide formation involves only nucleophilic attack of the amine nitrogen on the carboxyl carbon which has been protonated by the Brønsted proton. The activation energy of 9.6 kcal/mol is required for the transition state of the C-N bond formation. The binding energy of the intermediate with zeolite is 38.0 kcal/mol. The intermediate subsequently looses a water molecule through the hydrogen transfer from the amino group to the leaving group with the energy barrier estimated to be 36.4 kcal/mol. The four-membered transition state (TS_5b) shows the elongated N-H3 bond length of 1.364 Å and contracted O2-H2 distance of 1.200 Å. The elongated C-O2 bond length of 1.544 Å corresponds to the departure of the hydroxyl group. The obtained products are the coadsorption of protonated diglycine and water molecules over the zeolitic framework.

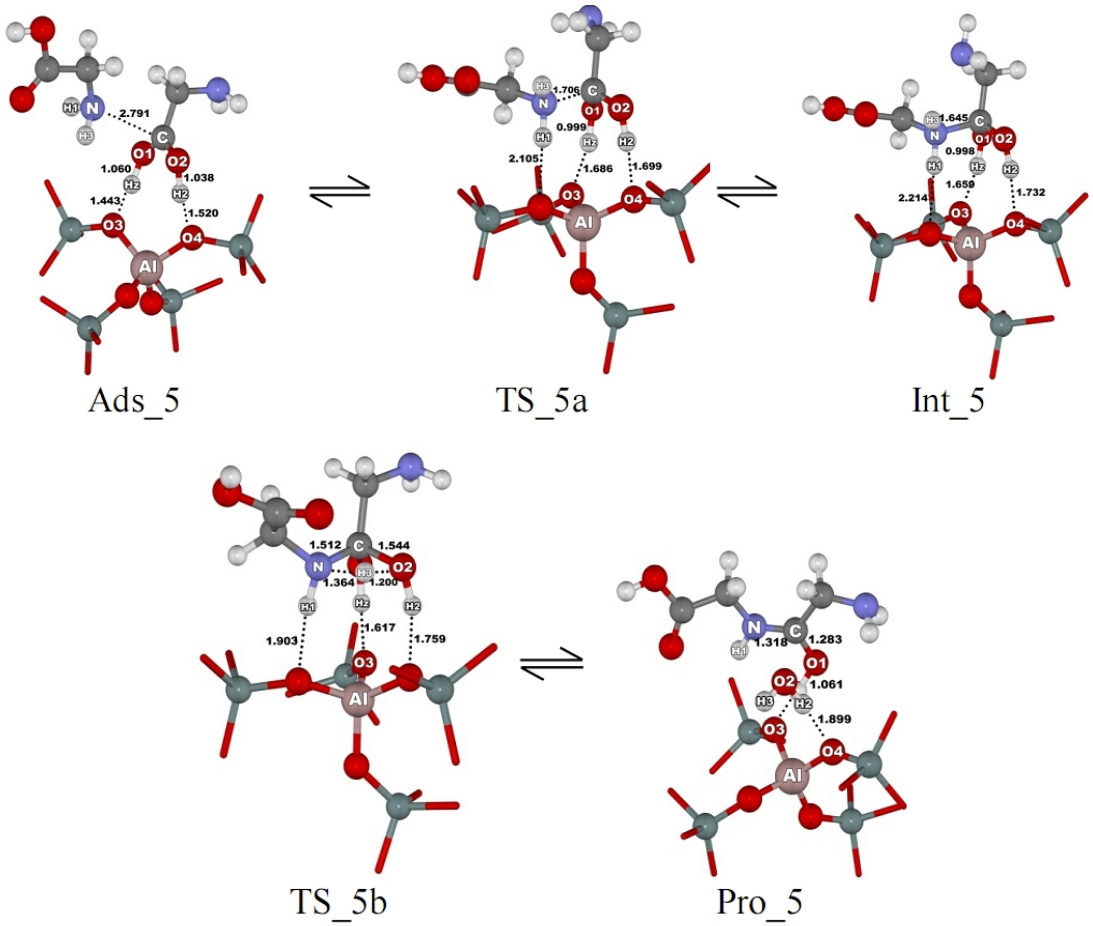
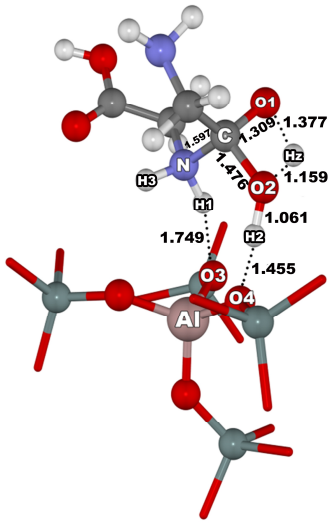


Figure 13 Optimized geometry of adsorption complex, transition states and products of stepwise reaction mechanism via carboxyl-bound configuration.

In addition, another transition state is found. It involves the hydrogen transfer between hydroxyl group of diolic intermediate (TS_5c) but it requires higher activation energy than the previous mentioned transition state (TS_5b) by 9.91 kcal/mol. The optimized geometry of transition state is shown in Figure 14



TS_5c

Figure 14 Optimized geometry of second transition states of stepwise reaction mechanism via carboxyl-bound configuration.

In the last case, the reaction starts from the Hydroxyl-bound configuration (Figure 15). This adsorption configuration (Ads_6) is slightly different from the Ads_3 that was used in the concerted mechanism. The second glycine molecules placed farther away from the framework to be in a position suitable to interact with the carbonyl group of the first adsorbed glycine. The complex structure shows a non-protonated form between the hydroxyl group and the Brønsted acidic proton. The positive charge of the C atom at the reaction center increasing from 0.807 to 0.828 compared to that of the isolated glycine molecule which is less positive than the charge on the same C atom (0.833) in the Ads_3 that was used in the concerted reaction mechanism. The adsorption complex Ads_6 is less stable than the Ads_3 complex by 5.4 kcal/mol.

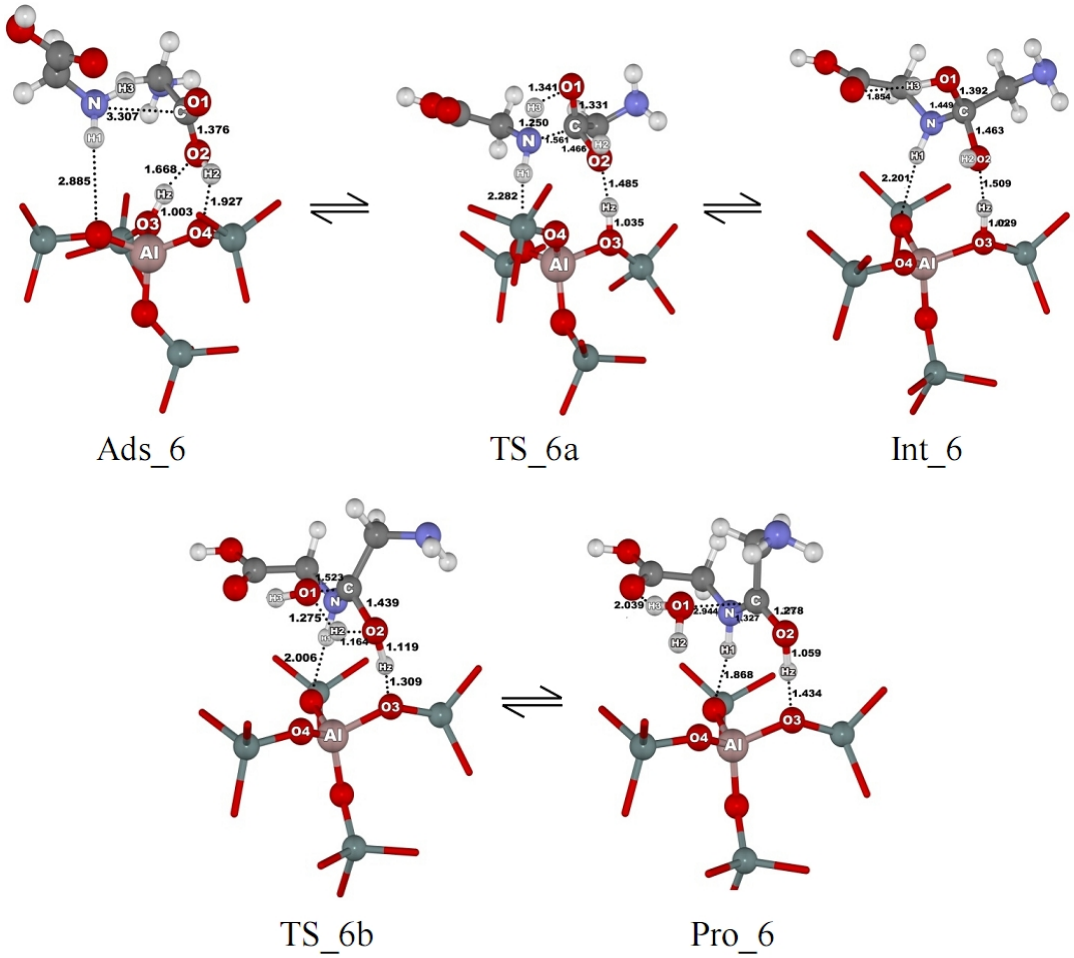


Figure 15 Optimized geometry of adsorption complex, transition states and products of stepwise reaction mechanism via hydroxyl-bound configuration.

The first step is the C-N bond formation. Similar to the Amino-bound case, the reaction does not involve the proton transfer from the Brønsted acid site. The lone pair electron of the amino group of the second glycine molecule attacks the carbonyl carbon atom of the first adsorbed glycine and, simultaneously, a proton on the amino group is transferred to the carbonyl oxygen atom. The transition state is a the four-membered transition state. The proton H3 from N atom of second glycine moves toward cabonyl oxygen of first glycine (O1) as shown in the distances of N-H3 and O1-H3 of 1.331 Å and 1.341 Å, respectively. The carbonyl C-O double bond length is elongated to 1.250 Å as the O atom receives the H3 proton. The intermolecular

distance of C-N is shortened from 3.307 Å to 1.561 Å. The generated diolic intermediate (Int_6) adsorbs over the active site with two hydrogen bond interactions. The binding energy is computed to be 25.3 kcal/mol. In the dehydration step, the zeolitic proton is transferred to the leaving hydroxyl group of the reacting molecule. The Brønsted O3-Hz bond distance is increased to 1.309 Å and the O2-Hz distances is decreased to 1.119 Å. The C-N bond is contracted to 1.439 Å, The leaving hydroxyl group is departing from the carbonyl carbon atom as the C-O1 distance is increased to 1.523 Å. This transition state has an activation energy of 27.4 kcal/mol. The products are diglycine and water molecules located over the active region of the zeolite.

It is appeared that the stepwise mechanism is at best having comparable activation energies to the concerted mechanism and having much higher activation energy in some cases. It is interesting to note that when the reaction starts from the carboxyl-bound configuration, the Brønsted acid site can greatly catalyzed the C-N bond formation and reduce the activation energy to only 9.6 kcal/mol The results from both mechanisms show that the roles of Brønsted acid site depend strongly on the orientation of the adsorbed molecules. The Brønsted acid site can play an important role in catalyzed the peptide bond formation when the amino acids adsorbed in a suitable configuration

CONCLUSION

The catalysis of peptide bond formation of two glycine molecules on H-FAU zeolite has been studied by the ONIOM2 scheme. The reaction are assumed to start from three possible adsorption configurations of co-adsorbed glycine molecules by having the first molecule interacting with the zeolite Brønsted acid site via amino-bound, carboxyl-bound and hydroxyl-bound, respectively. Two possible mechanisms have been investigated, namely, the concerted and the stepwise reaction mechanisms.

In the concerted mechanism both C-N bond formation and the release of water take place simultaneously in one step. Depending the orientation of the starting co-adsorbed molecules, the role of Brønsted acid site is varied. The interaction with the Brønsted acidic proton increases the positive charge of the carbonyl carbon atom of first adsorbed molecule. This means that the interaction with the catalyst increases the electron deficiency on that carbon atom and, thus, facilitates nucleophilic attack by the lone pair of the amine.

In the first pathway (starting from Amino-bound configuration), the role of the acid site is just to hold the first glycine molecule in place but does not participate in the reaction. The high activation energy closed to the uncatalyzed gas phase reaction is observed. In the second pathway, the interaction between the carboxyl group and the Brønsted acid site increase the positive charge on the carbonyl carbon atom and, thus, reduce the activation energy significantly. In the third pathway, the synergistic effects of Brønsted acid to protonate the leaving hydroxyl group and of adjacent oxygen lewis base to abstract proton from amine group result in a marked reduction of the activation energy. The activation energies from the three pathways are in the order of Amino-bound 〉 Carboxyl-bound 〉 Hydroxyl-bound (51.7, 33.8 and 11.2 kcal/mol, respectively).

In the stepwise reaction mechanism, the reactions take place in two steps having a stable diolic intermediate. The first step is the C-N bond formation

through a nucleophilic attack of the nitrogen on a carbon atom to form the diolic intermediate. The second step is the dehydration of the diolic intermediate to produce the dipeptide product and a water molecule adsorbed on the active site.

Similar to the concerted mechanism, the roles of Brønsted acid are varied with the starting orientation of the adsorbed molecules. In all cases, the stepwise mechanism has comparable or higher activation energies. It is interesting to note that in pathway starting from the carboxyl-bound adsorption complex, the strong interactions with the acid site greatly reduce the activation energy for the C-N bond formation to 9.6 kcal/mol but in second step, the dehydration of the diolic intermediate requires a high activation energy of 36.4 kcal/mol.

In conclusion, the catalytic role of the Brønsted acid site of H-FAU zeolite have been elucidated. The Brønsted acid can actively catalyzed the peptide bond formation and markedly reduce the activation energy provided that the adsorbed glycine is oriented to have the reaction center strongly interacting with the Brønsted acid site. However, the probability to find adsorbed glycine molecules in the right orientations depends on several factors which has not been included in this study. For example, the presence of more than one Brønsted acid sites or the presence of Lewis acid sites in proximity could strongly affect the orientation and the stability of the adsorbed molecule. It is very interesting to study these factors but it is outside the scope of this study.

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APPENDIX

Oral Presentation to Conferences

- **Oral presentation: Structure and Reaction Mechanisms of Peptide Formation over Nanostructured Zeolite.**

Oranit Phuakkong, Karan Bobuatong, Bundet Boekfa, Saowapak Choomwattana, Pipat Khongpracha, Piboon Pantu and Jumras Limtrakul**.** Abstract of paper Congress on Pure and Applied Chemistry International Conference (PACCON 2009), Naresuan University, Phisanulok, Thailand, January 14 –16, 2009

S4-OR-5

Structure and Reaction Mechanisms of Peptide Formation over Nanostructured Zeolite

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The peptide bond formation from two glycine molecules over acidic FAU zeolite is theoretically investigated. The structure of the 120T cluster, including two supercages is taken from the lattice structure of H-FAU zeolite. The ONIOM2 scheme, in which the whole model is subdivided into two layers, is adapted for computational efficiency. The active region of 14T cluster to represent the acid site of zeolite and the reactive molecules are treated with the B3LYP/6-31G (d,p) method. In addition, to represent the confinement effect of the zeolite pore structure, the rest of the 120T cluster is treated with the UFF force field. Two reaction pathways, the concerted and the stepwise reaction mechanism are considered. Three possible adsorption configurations of two glycine molecules over acidic FAU zeolite have been found, namely Amino-bound, Carboxyl bound and Hydroxyl-bound. A comparison of the relative energies of the various reaction paths indicates that the catalytic reaction is preferentially proceeds through the concerted mechanism. The least stable adsorption configuration, the Hydroxyl-bound configuration has the lowest energy barrier for the peptide bond formation which is estimated to be 11.2 kcal/mol. Whereas, the most stable adsorption configuration, the Amino-bound configuration, has the highest activation energy of 51.7 kcal/mol. The results of this study may be helpful for understanding the fundamentals of how peptide formation of amino acid over zeolite works.

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S4-OR-6

Theoretical Study of Mechanism and Kinetics for the Reaction of Chlorine Atoms with Toluenes

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The mechanism and kinetics for the hydrogen abstraction reaction of chlorine atoms with chlorotoluenes from the methyl groups were studied theoretically. Potential energy profile was calculated at the hybrid BH&HLYP level of density functional theory with the cc-pVDZ basis set. The refined barrier height and reaction energy was further calculated at the CCSD (T)/cc-pVDZ. Thermal rate constants in the temperature range of 200 – 400 K were evaluated by the canonical variational transition state theory (CVT) incorporating corrections from tunneling using the multidimensional semiclassical small-curvature tunneling (SCT) method. The hinder rotation effect was also taken into account to correct the thermal rate constants. The calculated values of the thermal rate constants are in good agreement which less than a hundred times differ from the available experimental results.

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