Ab-Initio Computational Study : The Activation Energy Changes and Steric Effects In Peptide Synthesis Of Ac-AA-NH2 and Ac-AP-NH2

by Bambang Cahyono

Submission date: 01-Jun-2022 09:19AM (UTC+0700)
Submission ID: 1848184586
File name: document-1.pdf (856.82K)
Word count: 3671
Character count: 19757

MOLEKUL
www.jmolekul.com

Articles

https://doi.org/10.20884/1.jm.2021.16.2.723

Ab-Initio Computational Study : The Activation Energy and Steric Effects in Peptide Synthesis of Ac-AA-NH_2 and Ac-AP-NH_2

Indah Pratiwi[1], Bambang Cahyono[1], Parsaoran Siahaan[1]*

[1]Department of Chemistry, Faculty of Sciences and Mathematics, Diponegoro University, Semarang, Indonesia

*Corresponding author email: siahaan.parsaoran@live.undip.ac.id

Received November 05, 2020; **Accepted** April 21, 2021; **Available online** July 20, 2021

ABSTRACT. Ab-Initio computational method can be used for simulating reaction mechanisms, such as concerted reaction mechanism on peptide synthesis. The concerted reaction is one of many possible pathways on how peptide can be synthesized. The purpose of this study are probing the concerted reaction mechanism and comparing the steric effect to the reaction, given by different side-chain of alanine (A) and proline (P). Two dipeptides formed from alanine and proline were computed at HF-SCF/6-31G** theory level: Ac-AA-NH_2 and Ac-AP-NH_2. The res.lts show the activation energy of Ac-AA-NH_2 and Ac-AP-NH_2 forming via concerted pathway are 167.541 kJ/mol and 161.044 kJ/mol, respectively. The steric difference in side-chain affects the dihedral angle of the structure, and also gives difference to the entropy value of reaction.

Keywords: ab-initio; activation energy; peptides; reaction mechanism

INTRODUCTION

Condensation of amino acids is a crucial reaction in protein chemistry as it represents a key reaction for all life processes. An essential structural element of all proteins is a peptide bond (C–N), which is formed because of the conjugation between the α-amino group of one amino acid and the α-carboxylic group of another amino acid (Santos et al., 2014). The detailed knowledge of the peptide bond formation mechanism is vital for understanding of various biological processes, and it is a subject of intensive investigations as such.

Non-catalyzed reaction of peptide bond formation has been studied by Bhunia et al. (2016) and Monajemi et al. (2012). Concerted reaction mechanism is one of possible mechanism propose. It also has been studied using molecular dynamics approach by Trobro and Aqvist (2005) and further by Wallin and Aqvist (2010), as a process of peptides synthesis occurring at cell level. Ribosome transforms genetic information, expressing genes into proteins (Ramkumar & Ramakrishnan, 2010; Yonath, 2010). Briefly, a peptide formation reaction is a reaction between two active groups: the amine (-NH_2) group and the carboxylic group (-COOH) from two different amino acids. The reaction mechanism involves the nucleophilic attack of the nitrogen atom from amine group to the carbon of the carboxylic group. Furthermore, a hydrogen atom of the amine group will be attracted to the oxygen atom (hydroxyl group of carboxylic), out in the molecular form of H_2O and the dipeptide will be produced (Anslyn & Dougherty, 2006a; Konwar et al., 2016; Solomons et al., 2014). The peptide bond forming reaction according to concerted mechanism shown in **Figure 1**.

The kind of mechanism in term of the topology of the potential energy surface, the nature of the transition states, the presence or absence of intermediates. Reactants progress over transition states on to intermediates, perhaps through multiple intermediates and ending at products. This type of scenario analysis has a long successful story for studying organic reactions (Dai et al., 2018; Gale et al., 2020; Singh et al., 2020; Trinchillo et al., 2016).

Besides of only studying the pathway from thermodynamics and kinetics, the steric effect also studied as well in some previous studies. It can be seen from the bulky steric structure, bond torsions, or the size of atom attached to the particular chain of organic compound (Elias et al., 2020; Ghosh et al., 2007; Mukherjee et al., 2019). Steric effect relates on how electron are occupied in space and reaction mechanism itself tells how electron go through particular reaction pathway which we desired. However, steric can affect the electron, and finally, can affect on how reaction occurs.

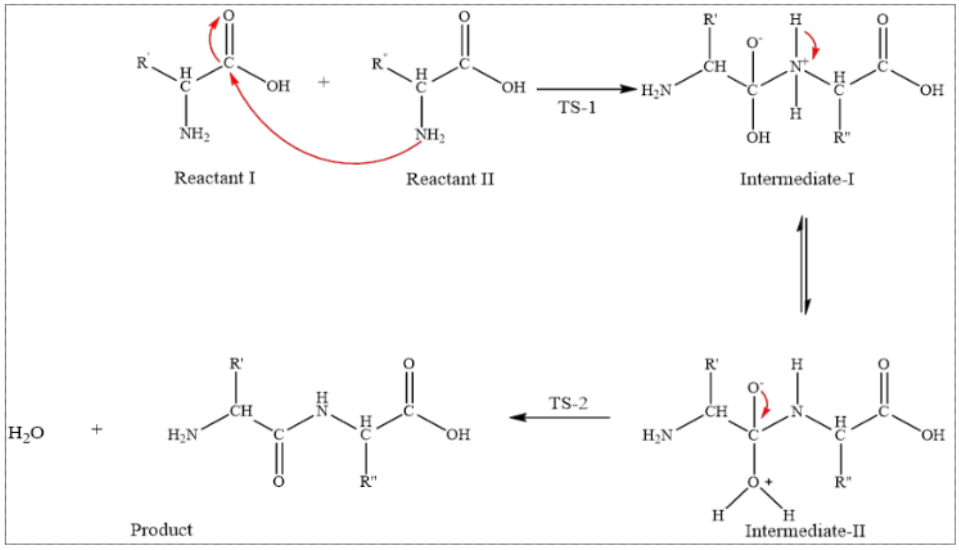


Figure 1. Concerted reaction pathway

In our previous studies, it has compared the steric effect on some dipeptides products of two amino acids with simple side structures, valine (isopropyl side chains) and glycine (hydrogen atom side chains) by Maftukhah (2019) and between alanine amino acids (methyl side chains) and glycine (hydrogen atom side chains) by Dzikrullah et al. (2019). It has been studied the steric effect by concerning some parameters i.e. charge distribution on each atoms, bond lengths, bond angles, torsions (Dzikrullah et al., 2019; Maftukhah, 2019; Siahaan et al., 2017; Siahaan et al., 2019). It also showed there were significant changes in dihedral.

This study will probe the mechanisms of dipeptides formation reactions through concerted reaction pathways between the amino acids alanine and proline. Both amino acids were chosen because in previous studies have been modeled against simpler amino acids namely glycine and valine. In addition, proline has a side chain in the form of a pyrrolidine ring that connects with its amine group. The structure tends to be rigid and less flexible, this may be interesting to study and observe the effect on the geometric changes of its dipeptides products (Das & Mandal, 2014; El Guerdaoui et al., 2014; Ramaniah et al., 2011; Santos et al., 2014).

The aim of this study is modelling the reaction mechanism of peptide formation on two kinds of dipeptide from alanine (A) series : Ac-AA-NH_2 and Ac-AP-NH_2 concerted pathway, As well as comparing how different R-groups tends to influence reaction and structural parameters on products formed. This study conducted using ab-initio computational method, employing HF/SCF theory level and 6-31G** basis set as the suitable basis set used for C, H, O, and N atoms (Cramer, 2013).

EXPERIMENTAL SECTION

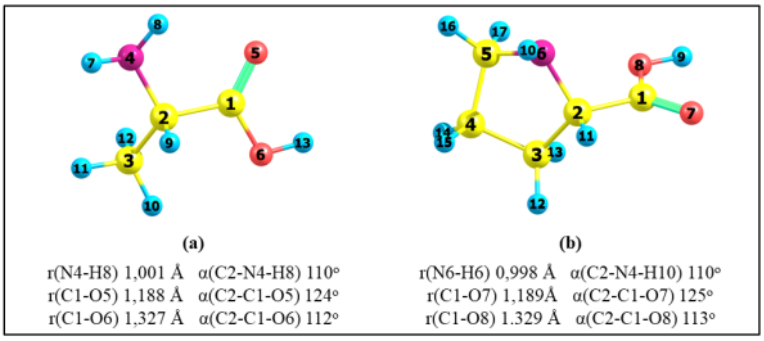
In this study, we started the calculation by proposing reasonable structures for each species involved : reactants, intermediates, transition states, and products (as may be seen in **Figure 1**). Basis set 6-31G** was used according the character of the atoms. This kind of small basis set can be employed in order to give sufficient insight into the energy of the molecules. Going along with the low theory level used, the calculation time can also be shorter (Valiev et al., 2010). We also computed the vibrational frequencies analysis at the same level of theory to verify whether each structure is in a stable or transition state (James. et al., 2013).

All calculations were performed using NWChem 6.8 program package, modelled in gas phase. The calculation was done with "task scf optimize" to optimize the molecular structure and "task scf freq" to analyze the vibrational motion. Furthermore, "task scf saddle" was used to search the transition state molecules. (Dykstra et al., 2011; Freza, 2019) .

RESULTS AND DISCUSSION

As stated in the introduction, two different kinds of products produced through concerted reaction mechanisms: Ac-AA-NH_2 mechanism pathway (denoted as mechanism I) and Ac-AP-NH_2 mechanism pathway (denoted as mechanism II). In each case, the energy values, the geometry, and parameters of the stationary points are successively discussed.

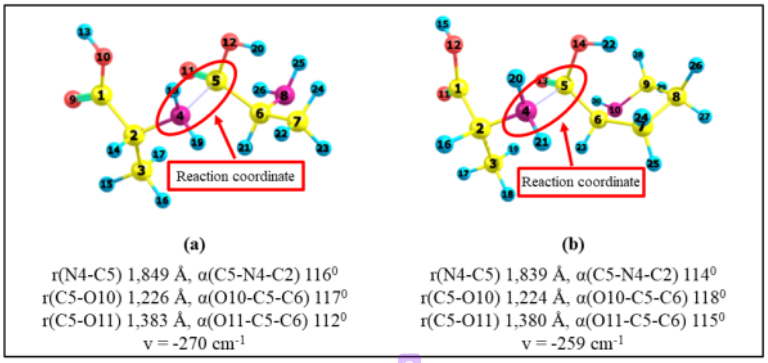
The amino acids structures were calculated to obtain stable molecule structures and minimum energy. The optimized structure of results of alanine (A) and proline (P) can be seen in **Figure 2** below. Symbols r and α are used for bond length and bond angle parameters. Optimization of alanine and proline molecules produces molecular energy of -8,448,105 kJ/mol and -10,473,105 kJ/mol. Reaction begins with the presence of separated two amino acid molecules as the reactants (R). Reactants in mechanism I consist of two alanine molecules and mechanism II consist of alanine and proline. Those two molecules are attracted by intermolecular forces and become closer, forming into first transition state molecule (TS^1). In this stage, the amine group from one alanine ($-NH_2$) attacks the carbon atom of the carbonyl group (-COOH) in other alanine, since $-NH_2$ is a good nucleophile. This attack leads to C5-N4 bond forming.



(a)
r(N4-H8) 1,001 Å α(C2-N4-H8) 110°
r(C1-O5) 1,188 Å α(C2-C1-O5) 124°
r(C1-O6) 1,327 Å α(C2-C1-O6) 112°

(b)
r(N6-H6) 0,998 Å α(C2-N4-H10) 110°
r(C1-O7) 1,189Å α(C2-C1-O7) 125°
r(C1-O8) 1.329 Å α(C2-C1-O8) 113°

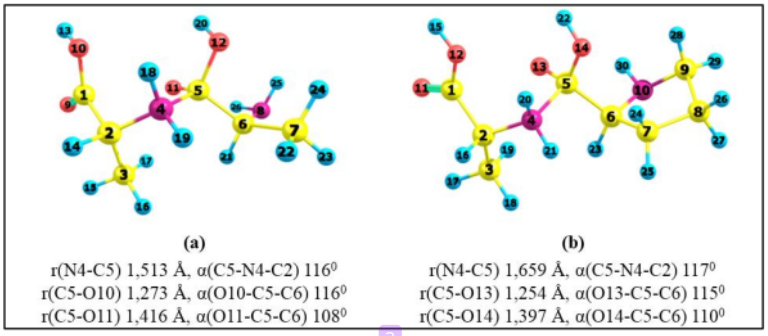
Figure 2. Optimized structures of alanine (a) and proline (b)



(a)
r(N4-C5) 1,849 Å, α(C5-N4-C2) 116^0
r(C5-O10) 1,226 Å, α(O10-C5-C6) 117^0
r(C5-O11) 1,383 Å, α(O11-C5-C6) 112^0
v = -270 cm^{-1}

(b)
r(N4-C5) 1,839 Å, α(C5-N4-C2) 114^0
r(C5-O10) 1,224 Å, α(O10-C5-C6) 118^0
r(C5-O11) 1,380 Å, α(O11-C5-C6) 115^0
v = -259 cm^{-1}

Figure 3. First transition state (TS^1) structures for mechanism I (a) and mechanism II (b)



(a)
r(N4-C5) 1,513 Å, α(C5-N4-C2) 116^0
r(C5-O10) 1,273 Å, α(O10-C5-C6) 116^0
r(C5-O11) 1,416 Å, α(O11-C5-C6) 108^0

(b)
r(N4-C5) 1,659 Å, α(C5-N4-C2) 117^0
r(C5-O13) 1,254 Å, α(O13-C5-C6) 115^0
r(C5-O14) 1,397 Å, α(O14-C5-C6) 110^0

Figure 4. First intermediate (I^1) structures for mechanism I (a) and mechanism II (b)

The structures of TS^1 and I^1 for each mechanism are shown above, on **Figure 3** and **Figure 4**. TS^1 has a negative frequency along its reaction coordinate, while I^1 only has positive frequencies. It implies there is no electron transferring from N4 to C5 anymore because the N4-C5 bond is already formed. Negative frequency implies the structure is in the saddle point (Bachrach, 2014). The negative frequency vibration mode refers to the part where the bond is formed. C5-N4 bond keep shortening, increase its peptide bond character during the reaction. H18-O12 length in mechanism I and H20-O14 in mechanism II also get closer. Therefore, the proton (H^+) is transferred to the O atom. As a result, H_2O molecule is formed inside the second intermediate (I^2) structure. Furthermore, H_2O also act as the side product released together with the main dipeptide product of the mechanisms. The releasing H_2O process illustrated as the second transition state (TS^2) as elimination of H_2O. This occurs by breaking of O-C bond from I^2 structure.

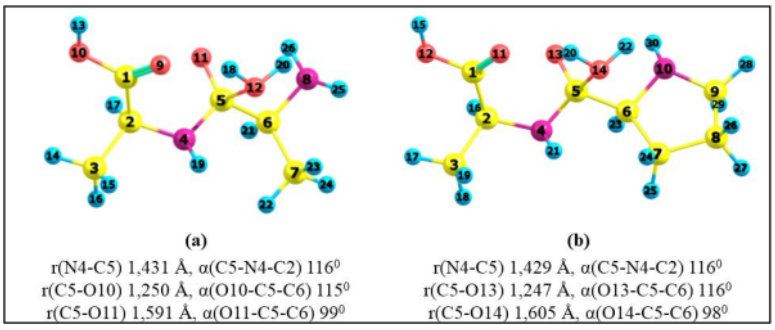


Figure 5. Second intermediate (I^2) structures for mechanism I (a) and mechanism II (b)

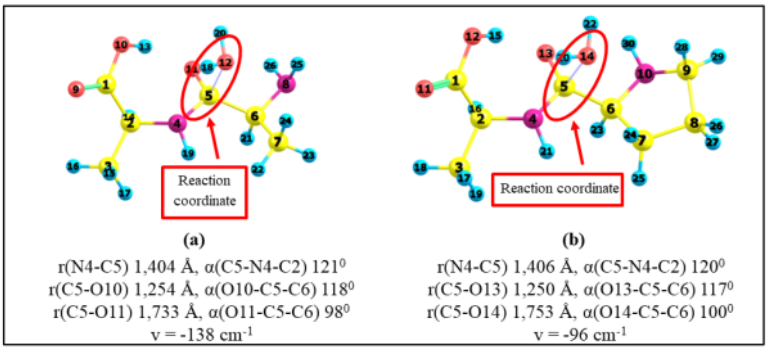


Figure 6. Second transition state (TS^2) structures for mechanism I (a) and mechanism II (b)

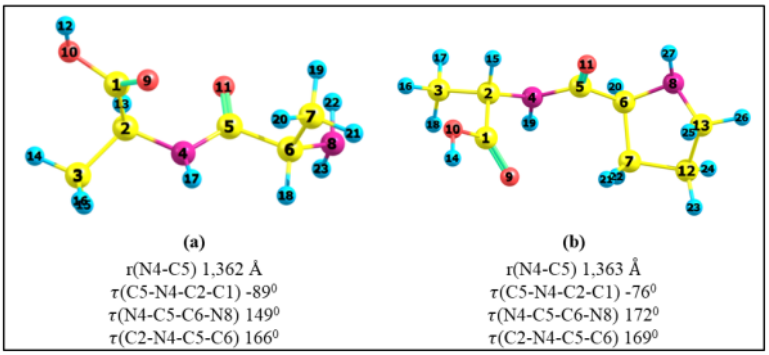


Figure 7. Structure of Ac-AA-NH_2(a) from mechanism I and Ac-AP-NH_2 (b) from mechanism II

The main dipeptide products Ac-AA-NH_2 and Ac-AP-NH_2 are shown in **Figure 7**. The molecular energy formation of Ac-AA-NH_2 is -14,901.10^5 kJ/mol, while for Ac-AP-NH_2 is -16,919.10^5 kJ/mol, lower than Ac-AA-NH_2 energy. We plotted the potential energy surface from each reaction as shown below in **Figure 8**. X axis resembles to reaction coordinate, Y axis resembles to relative potential energy of each molecule from reactant. Both mechanisms have TS^1 as their global maximum coordinate. As the matter of fact, we assumed TS^1 is the step determining the rate of the overall reaction.

Table 1 shows the potential energy corresponding to the TS^1, I^1, I^2, TS^2, and product for both mechanisms with respect those of reactant. It can be observed in all cases TS^1 lies higher than TS^2. In mechanism I, the activation energy is slightly higher than mechanism II. We can imply that mechanism I is not favorable compared to mechanism II. This trend has also been studied previously by Keresedzile et al. (2014). In the study, a concerted reaction mechanism with the H_2O molecular catalyst for dipeptides from alanine series (dipeptide in order Ac-AX-NH_2, with X is another amino acid) showed Ac-AP-NH_2 mechanism has lower activation energy compared to Ac-AA-NH_2.

Furthermore, the other energy profiles such as enthalpy, entropy, Gibbs free energy, HOMO-LUMO gap energy, and reaction rate constant are shown in **Table 2**. The activation energy of both mechanisms is around 40 kJ/mol. The same activation energy range value was predicted by Bhunia et al. (2016) for the same mechanism under non-catalyzed reaction condition.

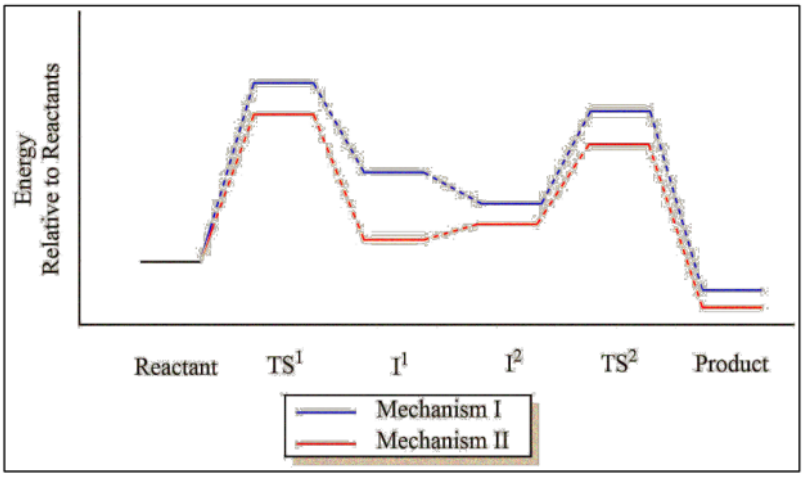


Figure 8. Potential energy surface (PES) plot from mechanism I (blue) and mechanism II (red)

Table 1. Summary of energies (kJ/mol) at the HF/6-31G** level of calculation for concerted mechanism

Mechanism	Reactant	TS^1	I^1	I^2	TS^2	Product
I	0.000	167.541	166.677	159.216	161.650	-16.372
II	0.000	161.044	143.046	152.800	153.128	-20.263

Table 2. Summary of energies (kJ/mol) at the HF/6-31G** level of calculation for concerted mechanism

Mechanism	Ea (kJ/mol)	Ea (kKal/mol)	ΔH (kJ/mol)	ΔG (kJ/mol)	ΔS (kJ/mol)	E_{Gap} (kJ/mol)
I	167.541	40.043	-10.277	-8.110	-0.007	2.473
II	161.044	38.490	-15.219	-9.636	-0.022	2.487

Table 3. Dihedral Torsion of mechanism I and mechanism II

Dihedral (τ) C5-N4-C2-C1	Degree (^{0})	
	Mechanism I	Mechanim II
I_1	-62	-60
I_2	-57	-58
Product	-86	-76
$\Delta\tau$	34	20

Table 3. Dihedral Torsion of mechanism I and mechanism II

Dihedral (τ) N8-C6-C5-N4	Degree (^{0})	
	Mechanism I	Mechanim II
I_1	173	174
I_2	-167	-165
Product	149	172
$\Delta\tau$	24	16

In the other hand, we observed that the entropy changes of mechanism I is slightly higher than mechanism II. The differences between these mechanisms can be attributed to the differences in dipeptide (products) conformations. To see how the conformation changes affect the reaction, we observed some of important dihedrals in the structures which gives significant change during the reaction.

During the reaction, dihedral (τ) C5-N4-C2-C1 seems very dynamic and changes significantly. In mechanism I, when I^1 underwent proton transfer to form I^2, it was able to experience a freer rotation compared to the two intermediates in mechanism II, seen from the changes of its intermediates on Ac-AA-NH_2 mechanism the dihedral can rotate freer than mechanism II's intermediates. Effect of the pyrrolidine ring structure also indicated by the torsion angle changes of N8-C6-C5-N4 during the reaction. Bulky ring structure of proline residue inhibits the single bond free-rotation around the N terminal of the Ac-AP-NH_2 peptides. As a result, the angle of dihedral torsion cannot vary that much.

Single bond rotation is a common phenomenon occur in peptide chain. This intramolecular movement does not occur in every bond in the peptide chain, but only a single bond outside the peptide bonds (Bhagavan & Ha, 2015). The C2-C1 is one of those single bonds, its rotation cause changes in peptide chain conformation in the atoms C1-C2-N4-C5. In the course of the reaction through this concerted pathway, rotation plays a role in increasing hydrogen binding in the structure of the first intermediate so that H_2O molecules can be formed in second intermediate and released as a side product.

The limitations of free-rotation are seen from the entropy change (ΔS) on each mechanism. When the ability for free-rotation decreases, the molecular-free path also decreases, resulting in a low entropy (S) value (Peter Atkins, 2010). Ac-AA-NH_2 has a considerable entropy change value compared to other mechanisms. Thus, it can be concluded that the Ac-AA-NH_2 mechanism has a larger free path, which is a result of its more dynamic side chain rotation.

Overall, the dipeptide products have a trans conformation geometry structure, pointed out as the dihedral between 2 Cα, indicated by C2-N4-C5-C6 atoms. These conformations are the most common in dipeptides bonds. With trans geometry, each side chain can have the position as far as possible so that the steric hindrance becomes minimal and provides stable product geometry (Padmanabhan, 2014).

However, this study was only able to provide rough estimates on explaining the differenced in side chains of amino acids can affect the reaction, both in terms of activation energy and other parameters such as enthalpy, entropy, and so on. Further research is needed to provide more exact values using more expensive theory level and basis set, as well as calculating other dipeptide products with the same reaction mechanism employed.

ACKNOWLEDGEMENTS

Thankful to Faculty of Science and Mathematics, Diponegoro University whch has funded the 2020 research and technology funding scheme.

CONCLUSIONS

Different side chain of amino acid can affect the peptide bond formation reaction. The activation energies of Ac-AA-NH_2 and Ac-AP-NH_2 via concerted pathway are 167.541 kJ/mol and 161.044 kJ/mol, respectively. Ac-AA-NH_2 formation has the highest

energy. On the structure, the steric difference in side chains affects the dihedral angle of the structure thus giving slight difference to the entropy value of reaction. Intermediates in mechanism I tend to move freer than mechanism II, the entropy of mechanism I higher than mechanism II.

REFERENCES

Anslyn, E. V., & Dougherty, D. A. (2006). Modern physical organic chemistry. In *Choice Reviews Online*,*43*(06). https://doi.org/10.5860/CHOICE.43-3398

Anslyn, E. V, & Dougherty, D. A. (2006b). *Modern physical organic chemistry*. University science books.

Bachrach, S. M. (2014). *Computational organic chemistry*. John Wiley & Sons.

Bhagavan, N. V, & Ha, C. E. (2015). Chapter 15—Protein and Amino Acid Metabolism. *Essential of Medical Biochemistry, 2nd Ed.; Academic Press: Amsterdam, The Netherlands*, 227–268.

Bhunia, S., Singh, A., & Ojha, A. K. (2016). Uncatalyzed peptide bond formation between two monomers of glycine, alanine, serine, threonine, and aspartic acid in gas phase: a density functional theory study. *The European Physical Journal D*, *70*(5), 106.

Cramer, C. J. (2013). *Essentials of computational chemistry: theories and models*. John Wiley & Sons.

Dai, Y., Hua, Q., Ling, J., Shao, C., Zhong, C., Zhang, X., Hu, Y., Zhang, L., & Liu, Y. (2018). Quantum chemical calculation of free radical substitution reaction mechanism of camptothecin. *Journal of Molecular Graphics and Modelling*, *84*, 174–181.

Das, G., & Mandal, S. (2014). Quantum mechanical investigations on the role of C-terminal residue in influencing the structural features of dipeptides containing N-terminal proline. *Journal of Molecular Graphics and Modelling*, *49*, 1–10.

Dykstra, C., Frenking, G., Kim, K., & Scuseria, G. (2011). *Theory and applications of computational chemistry: the first forty years*. Elsevier.

Dzikrullah, A., Cahyono, B., Laksitorini, M. D., & Siahaan, P. (2019). Ab initio computational study of electronic structure part-1: reaction mechanism of peptide bond formation between amino acid alanine and glycine. *Journal of Physics: Conference Series*, *1217*(1), 12053.

El Guerdaoui, A., El Kahoui, Y., Bourjila, M., Tijar, R., & El Gridani, A. (2014). Potential Energy Surface (PES) scan of gas-phase L-proline. *International Letters of Chemistry, Physics and Astronomy*, *19*(1), 26–34.

Elias, R. S., Saeed, B. A., Kamounah, F. S., Duus, F., & Hansen, P. E. (2020). Strong intramolecular hydrogen bonds and steric effects involving C= S groups: An NMR and computational study. *Magnetic Resonance in Chemistry*, *58*(2), 154–162.

Farikhatul Maftukhah, Mekanisme Reaksi Sintesis Peptida Ac-GV-NH_2 dan Ac-VG-NH_2 : Studi Komputasi Ab-Initio (Ab-Initio Computational Studies), Departemen Kimia, Universitas Diponegoro. 2019

Freza, S. (2019). Water-assisted peptide bond formation between two double amino acid molecules in the gas phase. *Journal of Molecular Modeling*, *25*(7), 184.

Gale, A. G., Odbadrakh, T. T., Ball, B. T., & Shields, G. C. (2020). Water-Mediated Peptide Bond Formation in the Gas Phase: A Model Prebiotic Reaction. *The Journal of Physical Chemistry A*, *124*(20), 4150–4159.

Ghosh, S., Mondal, S., Misra, A., & Dalai, S. (2007). Investigation on the structure of dipeptides: A DFT study. *Journal of Molecular Structure: THEOCHEM*, *805*(1–3), 133–141.
https://doi.org/10.1016/j.theochem.2006.11.004

James., Foresman, J. B., & Frisch, A. (2013). Exploring Chemistry With Electronic Structure Methods.pdf. In *Exploring Chemistry with Electronic Structure Methods* (Vol. 2013, Issue 15). https://doi.org/10.1002/adma.200400767

Kereselidze, J., Kvaraia, M., & Mikuchadze, G. (2014). Quantum-chemical description of influence of the R-groups on formation of peptide bond. *Computational Molecular Bioscience*, *4*(02), 35.

Konwar, M., Ali, A. A., & Sarma, D. (2016). A Green Protocol for Peptide Bond Formation in WEB. *Tetrahedron Letters*, *57*(21), 2283–2285. https://doi.org/10.1016/j.tetlet.2016.04.041

Monajemi, H., Daud, M. N., Mohd. Zain, S., & Wan Abdullah, W. A. T. (2012). ONIOM and ab-initio calculations on the mechanism of uncatalyzed peptide bond formation. *Biochemistry and Cell Biology*, *90*(6), 691–700.

Mukherjee, G., Alili, A., Barman, P., Kumar, D., Sastri, C. V, & de Visser, S. P. (2019). Interplay Between Steric and Electronic Effects: A Joint Spectroscopy and Computational Study of Nonheme Iron (IV)-Oxo Complexes. *Chemistry–A European Journal*, *25*(19), 5086–5098.

Padmanabhan, S. (2014). *Handbook of pharmacogenomics and stratified medicine*. Academic Press.

Peter Atkins, J. D. P. (2010). *Physical Chemistry 9th Edition*.

Ramaniah, L. M., Chakrabarti, A., Kshirsagar, R. J., Kamal, C., & Banerjee, A. (2011). Density

functional study of α-amino acids: structural, energetic and vibrational properties. *Molecular Physics*, *109*(6), 875–892.

Ramkumar, S. G., & Ramakrishnan, S. (2010). Two-Step Folding of Donor− Acceptor Foldamers. *Macromolecules*, *43*(5), 2307–2312.

Santos, A. F. L. O. M., Notario, R., & Ribeiro da Silva, M. A. V. (2014). Thermodynamic and conformational study of proline stereoisomers. *The Journal of Physical Chemistry B*, *118*(34), 10130–10141.

Siahaan, P, Lalita, M. N. T., Cahyono, B., Laksitorini, M. D., & Hildayani, S. Z. (2017). Ab initio computational study of reaction mechanism of peptide bond formation on HF/6-31G (d, p) level. *IOP Conference Series: Materials Science and Engineering*, *172*(1), 12040.

Siahaan, Parsaoran, Sipangkar, M. J., Salimah, S. N. M., Aminin, A. L. N., Asyari, M., & Laksitorini, M. D. (2019). Electronic properties study of reaction mechanism of CN bonding formation in Ac-DT-NH2 and Ac-TD-NH2 peptide by ab initio computational on HF/6-31g** level. *IOP Conference Series: Materials Science and Engineering*, *509*(1), 12107.

Singh, A., Chayawan, Mehta, S. K., & Singh, K. (2020). Catalyst free enantioselective amination via SN2 nucleophilic substitution reaction: a computational study. *Molecular Simulation*, *46*(12), 942–946.

Solomons, T. W. G., Fryhle, C. B., & Snyder, S. A. (2014). *Organic chemistry*.

Trinchillo, M., Belanzoni, P., Belpassi, L., Biasiolo, L., Busico, V., D'Amora, A., D'Amore, L., Del Zotto, A., Tarantelli, F., & Tuzi, A. (2016). Extensive experimental and computational study of counterion effect in the reaction mechanism of NHC-gold (I)-catalyzed alkoxylation of alkynes. *Organometallics*, *35*(5), 641–654.

Trobro, S., & Aqvist, J. (2005). Mechanism of peptide bond synthesis on the ribosome. *Proceedings of the National Academy of Sciences*, *102*(35), 12395–12400. https://doi.org/10.1073/pnas.0504043102

Valiev, M., Bylaska, E. J., Govind, N., Kowalski, K., Straatsma, T. P., Van Dam, H. J. J., Wang, D., Nieplocha, J., Apra, E., & Windus, T. L. (2010). NWChem: A comprehensive and scalable open-source solution for large scale molecular simulations. *Computer Physics Communications*, *181*(9), 1477–1489.

Wallin, G., & Åqvist, J. (2010). The transition state for peptide bond formation reveals the ribosome as a water trap. *Proceedings of the National Academy of Sciences*, *107*(5), 1888 LP – 1893. https://doi.org/10.1073/pnas.0914192107

Yonath, A. (2010). Hibernating bears, antibiotics, and the evolving ribosome (Nobel Lecture). *Angewandte Chemie International Edition*, *49*(26), 4340–4354.

Ab-Initio Computational Study : The Activation Energy Changes and Steric Effects In Peptide Synthesis Of Ac-AA-NH2 and Ac-AP-NH2

ORIGINALITY REPORT

6%	3%	4%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Acosta-Silva, Carles, Joan Bertran, Vicenç Branchadell, and Antoni Oliva. "Quantum Mechanical Study on the Mechanism of Peptide Release in the Ribosome", The Journal of Physical Chemistry B, 2013. Publication	<1%
2	Submitted to Universitas Diponegoro Student Paper	<1%
3	Erdem, S.S.. "Thermal rearrangement of 2-acetoxy-2,6,6-trimethylbicyclo[3.1.0]hexane: Theoretical elucidation of the mechanism", Journal of Molecular Structure: THEOCHEM, 20070715 Publication	<1%
4	Fang Liu, Robert S. Paton, Seonah Kim, Yong Liang, K. N. Houk. "Diels–Alder Reactivities of Strained and Unstrained Cycloalkenes with Normal and Inverse-Electron-Demand Dienes: Activation Barriers and Distortion/Interaction	<1%

Analysis", Journal of the American Chemical Society, 2013
Publication

5	www.freepatentsonline.com Internet Source	<1 %
6	Katta Venkateswarlu. "Ashes from organic waste as reagents in synthetic chemistry: a review", Environmental Chemistry Letters, 2021 Publication	<1 %
7	Submitted to Universitas Jenderal Soedirman Student Paper	<1 %
8	videolectures.net Internet Source	<1 %
9	www.research.manchester.ac.uk Internet Source	<1 %
10	www.science.gov Internet Source	<1 %
11	www.yumpu.com Internet Source	<1 %
12	Masoud Kazemi, Fahmi Himo, Johan Åqvist. "Peptide Release on the Ribosome Involves Substrate-Assisted Base Catalysis", ACS Catalysis, 2016 Publication	<1 %

d-nb.info

13	Internet Source	<1%
14	eprints.undip.ac.id Internet Source	<1%
15	researchspace.ukzn.ac.za Internet Source	<1%
16	Shella V Yuliani, S N M Salimah, Dwi Hudiyanti, Marlyn Dian Laksitorini, Parsaoran Siahaan. "Ab Initio Computational Study of electronic structure of -O-C Bonding Formation on Chitosan Polymer-Part 1: Effects of NaOH", Journal of Physics: Conference Series, 2019 Publication	<1%
17	Pavel Pospíšil, Aditya Kumar, Ankush Prasad. "Reactive oxygen species in photosystem II: relevance for oxidative signaling", Photosynthesis Research, 2022 Publication	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	On		

Ab-Initio Computational Study : The Activation Energy Changes and Steric Effects In Peptide Synthesis Of Ac-AA-NH2 and Ac-AP-NH2

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8