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Gas contaminants capturing by gamma-carbonic anhydrase catalyst: A quantum chemical approach

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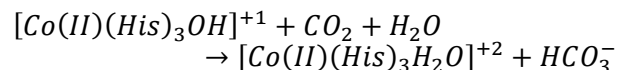[c]*3rd floor, Gas 6th Building, 15988-66515, Amani Ave., Gharani St., Tehran, Iran.*

ABSTRACT

In this paper, we used quantum chemical approach to shed light on the catalytic mechanism of γ-carbonic anhydrase (γ-CA) to convert carbon dioxide to bicarbonate ion. Density functional theory (DFT) using B_3LYP and UB_3LYP functional and three split-valance including 6-31G*, 6-311G** and 6-311++G** basis sets were used to calculate the details of electronic structure and electronic energy of active and inactive forms of γ-CA enzyme active center, and complex between γ-CA and carbon dioxide. The catalytic mechanism involved the nucleophilic attack of cobalt bound hydroxide ion to CO_2. In the following, the five coordinate cobalt complex as a transition state is formed and then the produced bicarbonate is displaced by a water molecule and give cobalt bound hydroxide for the next turn of catalysis. The activation energy barrier for this mechanism is about 7.9 kcal/mol.

Keywords: Carbon dioxide, γ-Carbonic anhydrase, Density functional theory, Catalyst, Co^{2+}.

1. Introduction

The carbonic anhydrases (CAs) comprise a family of ubiquitous metalloenzymes widespread in the bacterial, plants, animals and men [1-3]. These enzymes catalyze interconversion between carbon dioxide and the bicarbonate ion. Carbon dioxide is one of the main greenhouse gases, which is considered as a gas contaminant and has wrecking environmental effects. The Gamma carbonic anhydrase is a dedicated metalloenzyme to this study that role of Cobalt as a central atom has led to the naming of carbonic anhydrase prefixed with gamma. CAs which are currently available in five independently alpha, beta, gamma, delta and zeta classes are widely distributed in nature and play important roles in human health, the global carbon cycle and industrial applications [4]. The α-CAs present in vertebrates, bacteria, algae and plants; the β-CAs predominantly in bacteria, algae and plants; the γ-CAs mainly present in archaea and some bacteria; the δ-CAs and ζ-CAs only found in some marine diatoms [5]. In mammals, at least 16 different CA isoforms were isolated and several novel isozymes

have been identified in non-mammalian vertebrates [6]. Carbonic anhydrase enzyme, which plays an important role as a biological catalyst, is able to convert carbon dioxide to bicarbonate ion in presence of water by some covalent reactions according to Fig. 1. In the mentioned enzymatic catalyst, the cobalt cation is complexed by three histidine amino acid residues and a water or hydroxide ligand depending on the activity of enzyme. The properties of the highly purified enzyme with a molecular weight of about 30000 have been investigated in a number of laboratories [7-17] through studies, which have shown the existence of several isozymes of the enzyme, the dependence of catalytic activity of all isozymes in the presence of the metal ion. By this process we have overcome to remove CO_2 from natural gas and replace it with bicarbonate ion which is safe enough for environment and living organisms. In the present research, the efficacy of central metal on the enzymatic activity of CA is studied using mechanical quantum calculations according to this reaction.

$$[Co(II)(His)_3OH]^{+1} + CO_2 + H_2O \rightarrow [Co(II)(His)_3H_2O]^{+2} + HCO_3^-$$

In this study, we used the quantum mechanical calculations for studying the catalytic mechanism used

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by γ-CA. We study the free energy profile to formation of transition state and intermediate through the catalytic mechanism in order to design most effective model to design efficient catalyst to eliminate carbon dioxide.

2. Computational details

All calculations were carried out with the Gaussian program series 1998 [18]. The geometries of active and inactive forms of carbonic anhydrase enzyme active site (CA), carbon dioxide and the complex between them were fully optimized using DFT method [19] with B3LYP functional and Hartree-Fock (HF) with four standard basis sets including 3-21G, 6-31G*, 6-311G** and 6-311++G**. It is noticeable that restricted formalism was applied to all close-shell systems. For the active and inactive forms of CA and the CA-CO_2 complex, calculations were performed with the unrestricted formalism (UB3LYP and UHF). Full optimizations were performed without any symmetry constrains. We computed the harmonic vibrational frequencies to confirm that an optimized geometry correctly corresponds to a local minimum that has only real frequencies.

The QST2 procedure was used to search for transition states. All TS geometries were double-checked by using IRC and FREQ calculations. In addition, the thermodynamic properties of all compounds were obtained from frequency calculations at 298.15 K and

1.0 atmosphere pressure. All reported enthalpies were zero-point (ZPE) corrected with unscaled frequencies.

3. Results and Discussion

3.1. Geometry optimization of carbonic anhydrase active center in active and inactive forms, $[Co(II)(His)_3OH]^{+1}$ and $[Co(II)(His)_3H_2O]^{+2}$

Structure of carbonic anhydrase active center in active (Cobalt -bond hydroxide) and inactive form (Cobalt-bound water) was fully optimized at UB3LYP and UHF methods using 3-21G, 6-31G*, 6-311G** and 6-311++G** basis sets with no initial symmetry restrictions and assuming C_1 point group. Two different spin states of cobalt, including high spin (S=3/2) and low spin (S=1/2) are possible [20].

Some geometrical details of carbonic anhydrase in both forms are presented in Table 1 and 2. As Table 1 and 2 indicate, the average N(His)-Co-O(OH) and N(His)-Co-O(OH_2) and [N(His)-Co-N(His)]$_{active}$ and [N(His)-Co-N(His)]$_{inactive}$ bond angles are equal to 109.0°, 106.0° and 110.1° and 112.3° respectively, thus both active and inactive forms of CA have tetrahedral geometry.

3.2. Searching for reaction path

According to Fig. 1, the cobalt bound hydroxide ion initiates the hydrolysis by the nucleophilic attack on CO_2.

Table 1. Presentation of some chemical structural details of optimized $[Co(II)(His)_3OH]^{+1}$ complex in high spin state.

Connected atoms	B3LYP		
	6-31G*	6-311G**	6-311++G**
	Bond distance (Å)		
Co1-O2	1.841	1.855	1.841
Co1-Nave	2.033	2.041	2.033
	Bond angle (°)		
Co1-O2-H26	121.24	125.78	121.24
Co1-N3-C6	136.66	137.27	136.66
Co1-N4-C8	116.85	116.28	116.85
Co1-N5-C10	125.99	126.61	125.99
O2-Co1-N(ave$_{3,4,5}$)	109.11	108.47	109.11
N3-Co1-N4	104.46	106.03	104.46
N3-Co1-N5	105.40	107.81	105.40
N4-Co1-N5	121.16	114.42	121.16
	Dihedral angle (°)		
N3-Co1-O2-H26	-85.00	-77.22	-85.00
N4-Co1-O2-H26	150.05	165.81	150.05
N5-Co1-O2-H26	36.63	50.38	36.63

Table 2. Presentation of some chemical structural details of optimized $[Co(II)(His)_3H_2O]^{+2}$ complex in high spin state.

Connected atoms	B3LYP		
	6-31G*	6-311G**	6-311++G**
	Bond distance (Å)		
Co1-O2	2.058	2.073	2.058
Co1-Nave	1.992	2.004	1.992
	Bond angle (°)		
Co1-O2-H26	123.16	126.03	123.16
Co1-O2-H27	126.87	126.39	126.87
Co1-N3-C6	124.51	124.60	124.51
Co1-N4-C8	127.33	128.26	127.33
Co1-N5-C10	125.81	128.08	125.81
O2-Co1-N(ave$_{3,4,5}$)	106.98	105.58	106.98
H26-O2-H27	107.11	107.26	107.11
N3-Co1-N4	107.81	110.07	107.81
N3-Co1-N5	121.16	115.03	112.16
N4-Co1-N5	115.80	114.16	115.80
	Dihedral angle (°)		
N3-Co1-O2-H26	-131.56	-149.48	-131.56
N3-Co1-O2-H27	26.78	23.25	26.78
N4-Co1-O2-H26	109.62	91.62	109.62
N4-Co1-O2-H27	-92.03	-95.64	-92.03
N5-Co1-O2-H26	-11.69	-29.89	-11.69
N5-Co1-O2-H27	-72.18	142.84	-72.18
Co1-O2-H26-H27	-161.14	173.88	-161.14
N3-Co1-N4-N5	-126.54	130.66	-126.54

In the following step, the five coordinate cobalt complex as a transition state is formed and then the produced bicarbonate is displaced by a water molecule and give cobalt bound hydroxide for the next turn of catalysis. The step between the nucleophilic attack and the replacement of bicarbonate was the topic of several studies when the central atom in carbonic anhydrase is zinc ion [21-26].

Fig. 2 depicted the optimized geometry of the catalysis at the high level of calculation. Our calculated results revealed that, as CO_2 approaches the catalytic center, an initial complex as an intermediate is formed in which a lone pair of electrons on the cobalt-bound hydroxide group interacts with the carbon of CO_2.

A bicarbonate transition structure leads to the formation of bicarbonate complex. In order to find the activation energy and optimized compound C as a transition state, (TS), the QST2 procedure has been 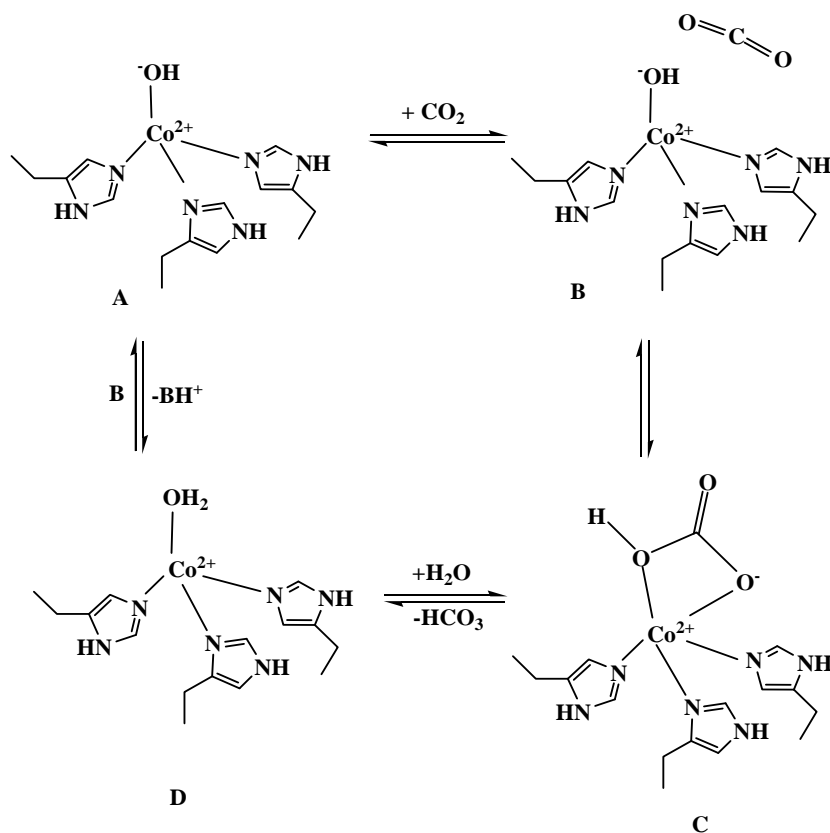used. The frequency calculation with one imaginary frequency confirms the transition state geometry. The loosely bound bicarbonate can then either dissociate from the active site or undergo an ion-return process before dissociating.

The variation energy of this reaction path is presented in Fig. 3. The energy barrier between compound B (R_1) and compound C (TS) is about 7.9 kcal/mol.

Fig. 4 presents the optimized geometry of transition state with some structural details for key atoms and Table 3 showed more structural details of optimized transition state.

The relative energy for the total reaction is presented in Table 4. According to Table 4, high spin state is about 6.2 kcal/mol more stable than low spin state by using different methods.

To calculate the reaction energy, carbon dioxide, water and bicarbonate molecules have been optimized at the same level and used for active and inactive forms of carbonic anhydrase (Fig. 5).

Fig. 1. Proposed reaction mechanism for converting of CO_2 to bicarbonate by γ-CA.

Table 3. Presentation of some chemical structural details of optimized $[Co(II)(His)_3OH]^{+1}$ complex in high spin state.

B3LYP (6-31G*)					
Connected atoms	Bond distance (Å)	Connected atoms	Bond angle (°)	Connected atoms	Dihedral angle (°)
Co1-O2	1.900	Co1-O3-H26	175.31	N6-Co1-O3-H26	-160.22
Co1-O3	2.959	Co1-O3-C5	72.91	N7-Co1-O3-H26	86.66
Co1-C5	2.878	Co1-O2-C5	127.13	N8-Co1-O3-H26	-45.97
Co1-N(ave$_{6,7,8}$)	2.023	O2-Co1-N(ave$_{6,7,8}$)	107.00	Co1-O2-C5-O3	3.70
O2-C5	1.299	O3-Co1-N(ave$_{6,7,8}$)	106.34	O4-C5-O3-H26	1.95
O3-C5	1.404	O2-C5-O3	111.01	O2-C5-O3-H26	-177.59

Table 4. Reaction energies calculated via four different methods.

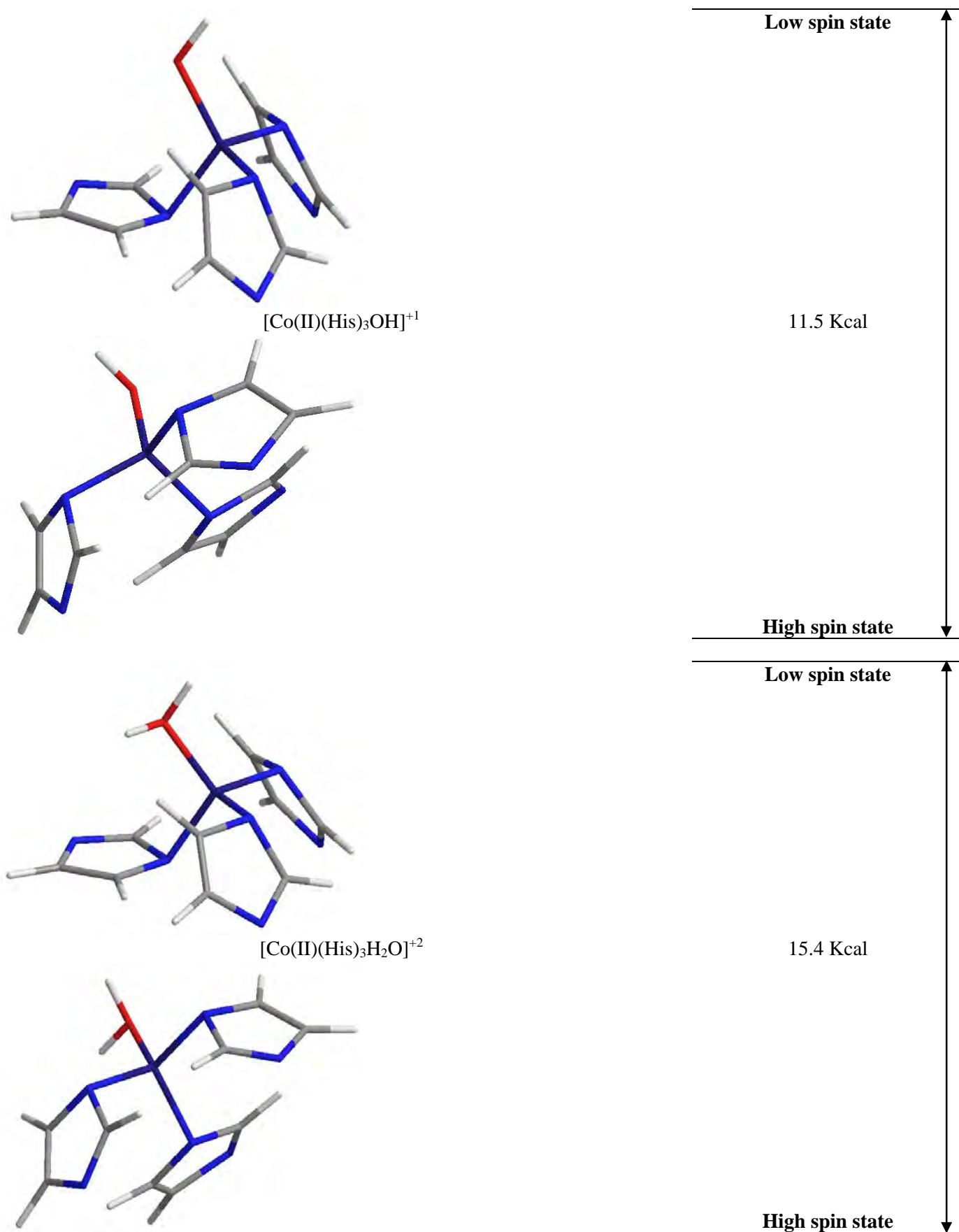| Method	HF		B3LYP					
Basis set	3-21G		6-31G*		6-311G**		6-311++G**	
Spin	L.S.	H.S.	L.S.	H.S.	L.S.	H.S.	L.S.	H.S.
ΔE_{rxn} (Kcal/mol)	167.18	150.84	174.56	170.61	166.39	165.28	170.99	167.50

Fig 2. Optimized structure of $[Co(II)(His)_3OH]^{+1}$ and $[Co(II)(His)_3H_2O]^{+2}$ complexes in the different spin states.
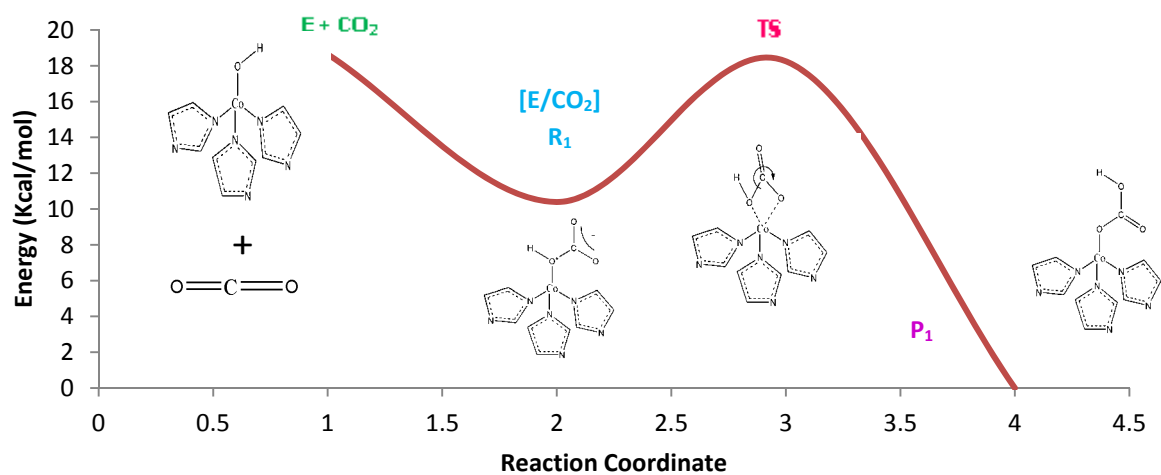
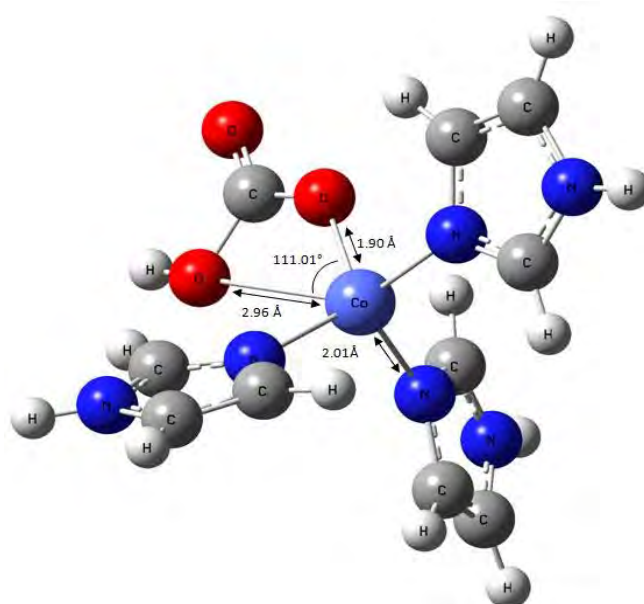**Fig. 3.** Energy profile obtained for γ-carbonic anhydrase.

Fig. 4. Presentation of optimized structure of transition state with some geometrical details.
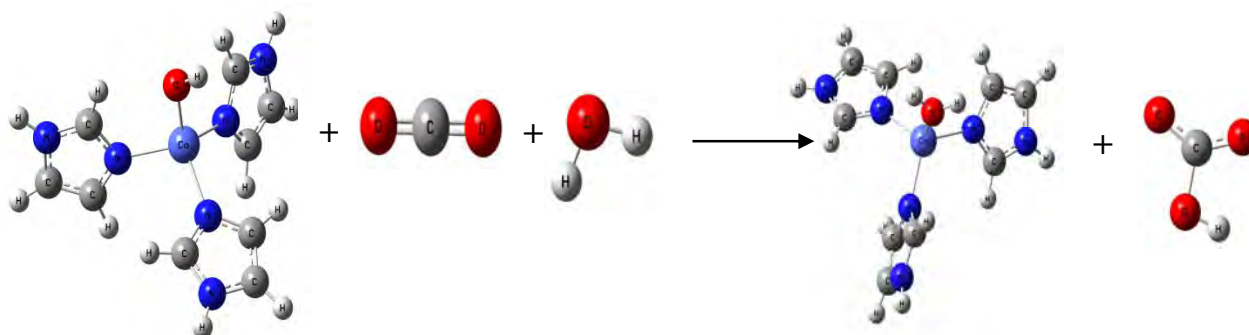

Fig. 5. Presentation of optimized geometry of reactants and products through the reaction path.

4. Conclusions

The quantum mechanical calculations have been applied to study the catalytic mechanism used by γ-carbonic anhydrase to convert the carbon dioxide to bicarbonate. Two different spin states of cobalt, including high spin (S=3/2) and low spin (S=1/2) are possible. According to our calculated results, high spin state is about 6.2 kcal/mol more stable than low spin state by using different methods. In the catalytic mechanism, cobalt bound hydroxide ion has a nucleophilic attack on CO_2 molecule. In the following step, the first intermediate compound B (R_1) is constructed and then the five coordinate cobalt complex as a transition state has been formed and then the produced bicarbonate is displaced by a water molecule and give cobalt bound hydroxide for the next turn of catalysis. The barrier energy for the nucleophilic attack is about 7.9 kcal/mol. Thus our results suggest that the nucleophilic attack could be the rate determining step of the catalytic cycle.

Acknowledgment

References

[1] C.T. Supuran, A. Scozzafava, Expert Opin. Ther. Pat. 12 (2002) 217-242.

[2] C.T. Supuran, A. Scozzafava, Curr. Med. Chem. Imm. Endoc. Metab. Agents 1 (2001) 61-97.

[3] C.T. Supuran, A. Scozzafava, Expert Opin. Ther. Pat. 10 (2000) 575-600.

[4] S.A. Zimmerman, J.G. Ferry, Curr. Pharm. Des. 14 (2008) 716-721.

[5] C.T. Supuran, Bioorg. Med. Chem. Lett. 20 (2010) 3467-3474.

[6] A.J. Esbaugh, B.L. Tufts, Respir. Physiol. Neurobiol. 154 (2006) 185-198.

[7] S. Lindskog, Biochim. Biophys. Acta 39 (1960) 218-226.

[8] P.O. Nyman, Biochim. Biophys. Acta 52 (1961) 1-12.

[9] S. Lindskog, B.G. Malmstrom, J. Biol. Chem. 237 (1962) 1129-1124.

[10] G. Laurent, M. Charrel, F. Luccioni, M.F. Autran, Y. Derrien, Bull. Soc. Chim. Biol. 47 (1965) 1101-1124.

[11] G. Laurent, C. Marrioq, D. Nahon, M. Charrel, Y. Derrien, Compt. Rend. Soc. Biol. 156 (1962) 1456-1461.

[12] E.E. Rickli, S.A.S. Ghazanfar, B.H. Gibbons, J.T. Edsall, J. Biol. Chem. 239 (1964) 1065-1078.

[13] J.C. Kernohan, Biochim. Biophys. Acta 81 (1964) 346-356.

[14] J.C. Kernohan, Biochim. Biophys. Acta 96 (1965) 304-317.

[15] B. Tilander, B. Strandberg, K. Fridborg, J. Mol. Biol. 12 (1965) 740-760.

[16] J.E. Coleman, Biochemistry 4 (1965) 2644-2655.

[17] T.A. Duff, J.E. Coleman, Biochemistry 5 (1966) 2009-2019.

[18] J.B. Foresman, A. Frisch, Exploring chemistry with electronic structure methods, Gaussian Inc. Pittsburg, PA., 1996, pp. 3-9.

[19] R.G. Parr, W. Yang, Density-functional theory of atoms and molecules, Oxford Univ. Press, 1989.

[20] S.A. Zimmerman, J.G. Ferry, C. T. Supuran, Curr. Top. Med. Chem. 7 (2007) 901-908.

[21] S. Lindskog, L.E. Henderson, K.K. Kannan, A. Liljas, P.O. Nyman, B. Trandberg, Carbonic anhydrase in the enzymes. Academic press, New York, 1971, pp. 587-665.

[22] Y. Pocker, S. Sarkanen, Adv. Enzymol. Relat. Areas Mol. Biol. 47 (1978) 149-274.

[23] W.S. Sly, P.Y. Hu, Annu. Rev. Biochem. 64 (1995) 375-401.

[24] C.T. Supuran, A. Scozzafava, A. Cassini, Med. Res. Rev. 23 (2003) 146-189.

[25] S. Pastorekova, S. Parkkila, J. Pastorek, C.T. Supuran, J. Enzyme Inhib. Med. Chem. 19 (2004) 199-229.

[26] C.T. Supuran, Rev. Roum. Chim. 37 (1992) 411-421.