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INVESTIGATION ON PROTONATION OF N-ACETYL-L-ALANINE BY QUANTUM CHEMICAL CALCULATIONS

VITHAYA RUANGPORNVISUTI

Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok, Thailand 10330

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ABSTRACT

Protonation potentials of N-acetyl-l-alanine molecule were evaluated by means of ab-initio LCAO-MO-SCF calculations. First and second protonation potentials (in gas phase) are −179.4 and −90.7 kcal/mol, respectively. In aqueous solution, only one protonation can take place.

INTRODUCTION

N-acetyl-l-alanine is an amino acid derivative whose N-terminal group is acetylated.[1] This compound can form complex with many metal ions; N-acetyl-peptide compounds can form complexes with divalent metal ions.[2] Information of the protonation of ligand compounds is very useful for the further study of their complex formations.[2] In general, amino acids could form complex with many metal ions and they have been widely studied by various methods.[3-11]

A study of protonation by ab-initio LCAO-MO-SCF method was, therefore, a relevant topic of interest.

METHOD

The optimized structure of N-acetyl-l-alanine and its protonated species have been carried out by ab-initio calculations with minimal basis functions[12] using the HONDO programme.[13] The geometrical parameters of N-acetyl-l-alanine (listed in Table 1) taken from reference were kept constant throughout the computations. Minimal GLOs were used as basis functions of atoms in N-acetyl-l-alanine molecule. For quantum chemical calculations applied on hydronium ion (protonated water) and water, different basis sets such as GLO, DZP and STO were employed

All calculations were performed on the IBM 3031/08 computer of Computer Service Center, Chulalongkorn University.

RESULTS AND DISCUSSION

Optimized structure of N-acetyl-l-alanine (Figure 1) was obtained from ab-initio LCAO-MO-SCF calculations using minimal GLO basis set. Total energy of N-acetyl-l-alanine (most stable structure) is −402.153602 au. The net charges of donor atoms, obtained from the Mulliken population analysis[15] are N6 = −0.524, O7 = −0.345, O8 = −0.247, and O9 = −0.198

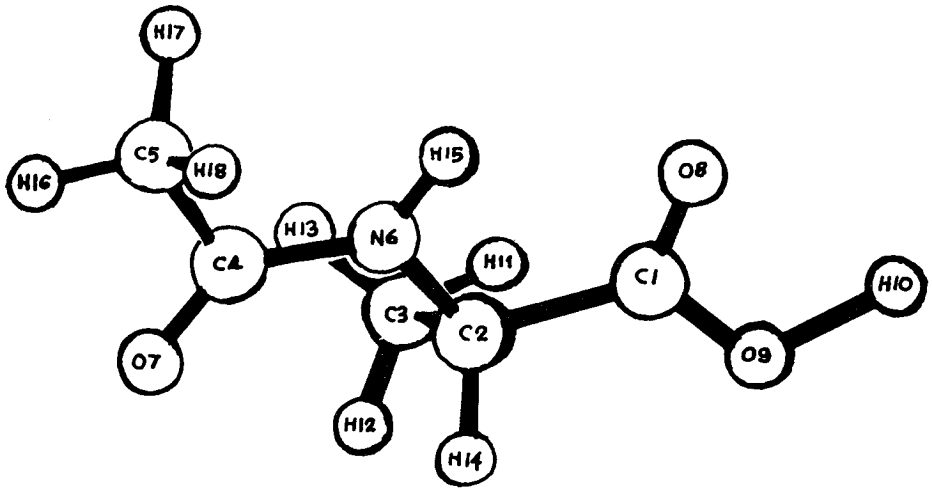

Fig. 1 Optimized structure of N-acetyl-l-alanine

atomic units. All atomic charges and the structure of N-acetyl-l-alanine are represented by the dipole moment of 3.168 D. The protonation on donor atoms of N-acetyl-l-alanine is in the preferable sequence as O9>O8>O7>N6 (see Table 2).

According to the stability of each protonated form, the first protonation energy could correspond to the structure of [O8–NAA–O9...H]; [O8–NAA–O9...H] is an N-acetyl-l-alanine protonated at O9 atom. The second can also be the configuration of [H...O8-NAA-O9...H]; the protonation on O8-atom is taken place after the first (see Table 3). For more understanding, the first and the second protonations can represented as follows :

$$\text{O8-NAA-O9} + \text{H} \xrightarrow{\text{First protonation}} \text{O8-NAA-O9...H}$$

$$\text{O8-NAA-O9...H} + \text{H} \xrightarrow{\text{Second protonation}} \text{H...O8-NAA-O9...H}$$

Table 3 shows two possible steps of the protonations of N-acetyl-l-alanine in gas phase. Ab-initio calculations of hydronium ion using several types of basis functions (Table 4), show that the binding energy of proton on water are within −222.8 to −172.5 kcal/mol. From consideration of the binding energies of proton on N-acetyl-l-alanine with respect to the water, the second protonation (−90.7 kcal/mol) could not be possible. We can conclude that only one protonation of N-acetyl-l-alanine occurs in aqueous solution.

TABLE 1. Geometrical parameters used in the quantum chemical calculations

Bond length	(Å)	Bond	Angle (degree)
C4–C5	1.53	CN̂H	116
C1–C7	1.321	CN̂C	121
C1–C8	1.24	NĈO	125
N–H	1.03	NĈC	114
C–H	1.09	HN̂H	109.47
N–C	1.45	CĈO	117.5
O8–H	1.011		

TABLE 2. Total energy and protonation energies of protonated N-acetyl-l-alanine at various donor atoms (optimized forms).

Atom	Hydrogen bond length (Å)	Total energy (au)	Binding energy (kcal/mol)
N5	1.400	−402.13346	−88.3
O7	1.100	−402.39489	−151.3
O8	1.075	−402.42169	−168.1
O9	1.075	−402.43973	−179.4

TABLE 3. Total energies and stepwise protonation energies of the protonated N-acetyl-l-alanine in gas phase.

Configulation/total energy (au)	Configulation/total energy (au)	Stepwise protonation energy (kcal/mol)
NAA −402.15360	NAA(O9) −402.43973	−179.4
NAA(O9) −402.43973	NAA(O9)(O8) −402.58441	− 90.7
NAA(O9)(O8) −402.58441	NAA(O9)(O8)(O7) −402.49356	+ 57.0 (destabilized)
NAA(O9)(O8)(O7) −402.49356	NAA(O9)(O8)(O7)(O6) −402.01032	+303.1 (destabilized)

TABLE 4. Protonation energy of water, calculated using various minimal basis sets

Basis set	Bond length (au)	Total energy (au)		Binding energy (kcal/mol)
		water	hydronium ion	
GLO	1.10	−64.52117	−64.79656	−172.7
DZP	0.95	−76.04638	−76.32136	−172.5
STO	1.00	−74.96290	−75.31812	−222.8

Deprotonation of N-acetyl-l-alanine based on the dissociation of acid proton was also investigated. The quantum chemical-calculated energy of 464.1 kcal/mol was obtained as the deprotonation energy of the compound.

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บทคัดย่อ

การศึกษาพลังงานรวมตัวของโปรตอนบนสารประกอบ เอ็น-อะเซ็ตทิล-แอล-อะลานีน โดยวิธีการคำนวณทางเคมีควอนตัมที่เรียกว่า ab-initio LCAO-MO-SCF ในสภาวะก๊าซของสารประกอบพบว่า พลังงานการรวมตัวของโปรตอนตัวแรกและตัวที่สองมีค่าเท่ากับ −179.4 และ −90.7 kcal/mol ตามลำดับ สำหรับสารประกอบในสารละลายของน้ำพบว่าเกิดการรวมตัวของโปรตอนได้เพียงตัวเดียว