Research paper

Guanine synthesis from 4-aminoimidazole-5-carbonitrile: A computational mechanistic study

Joong Chul Choe

Department of Chemistry, Dongguk University-Seoul, Seoul 04620, Republic of Korea

HIGHLIGHTS

- Theoretical (CBS-QB3) reaction pathways for the guanine (G) synthesis.
- Pathway for 4-aminoimidazole-5-carbonitrile + H_2O + NCCN → G + HCN.
- Pathway for 4-aminoimidazole-5-carbonitrile + H_3O^+ + NCCN → GH^+ + HNC.
- Addition of a catalytic H_2O greatly enhanced steps occurring by H rearrangement.

ABSTRACT

The potential energy surface (PES) for guanine formation from 4-aminoimidazole-5-carbonitrile (AICN) after adding H_2O and cyanogen (NCCN) was determined from quantum chemical calculations using the CBS-QB3 method. Its activation energy was too high for the reaction to occur in the interstellar medium. The PES for the formation of a protonated guanine from AICN by adding H_3O^+ and NCCN was also determined. Although its overall activation energy was zero, its occurrence in the interstellar gas phase is not likely due to unstable intermediates. When H_2O was added to some reaction steps as a catalyst, their activation barriers were significantly reduced.

1. Introduction

Whether life developed on Earth or from extraterrestrial sources is one of the most attractive subjects for researchers in fields of astrobiology, astrochemistry, and astrophysics. Amino acids and nucleobases (guanine (G), adenine, cytosine, thymine, and uracil) as building blocks of proteins and RNA or DNA, respectively, have not been detected in the interstellar medium (ISM). However, this does not rule out the possibility of their prebiotic syntheses in the ISM because they have been observed in meteorites. Three (guanine, adenine, and uracil) of five nucleobases, have been discovered in several type meteorites [1–4].

It is generally believed that guanine has been formed by the oligomerization of hydrogen cyanide (HCN). To investigate its probiotic synthesis, different reactants have been used under different conditions. In early days of probiotic study, guanine has been synthesized from 4-aminoimidazole-5-carboxamide (AICA), a hydrolysis product of 4-aminoimidazole-5-carbonitrile (AICN), by adding cyanogen (N≡C−C≡N, NCCN) or potassium cyanate to aqueous solution [5]. Heating gas mixtures of CO, H_2, and NH_3 in the presence of catalyst such as Ni-Fe ally, Al_2O_3, or SiO_2 has generated guanine [6–8]. It is

expected that HCN has been formed in the gas mixture and oligomerized for the formation of guanine. In a high-temperature plasma of gas mixture of Co, N_2, and H_2O, the formation of guanine has been reported [9]. In frozen ammonium cyanide solutions prepared from gaseous HCN and NH_3 and held at −20 °C for 25 years [10] or at −78 °C for 27 years [11], guanine has been identified.

Theoretical studies on prebiotic synthesis mechanism of guanine [12,13] have been limited compared to those on adenine [12,14–19] or glycine [20–26]. Jeilani et al. [12] have reported theoretical potential energy surface (PES) for the formation of guanine starting from formamide ($CONH_2$). Four more reactants including radicals, ˙CN, ˙H, NH_3, and $NHCHNH_2$, are involved in eight bimolecular reaction steps of their PES. Da Silva and de Araujo [13] have reported the theoretical mechanism for the formation of guanine from HCN, CCO, HNCNH, and H_2NCN, showing that the six-membered ring is first created, followed by the five-membered ring in their mechanism.
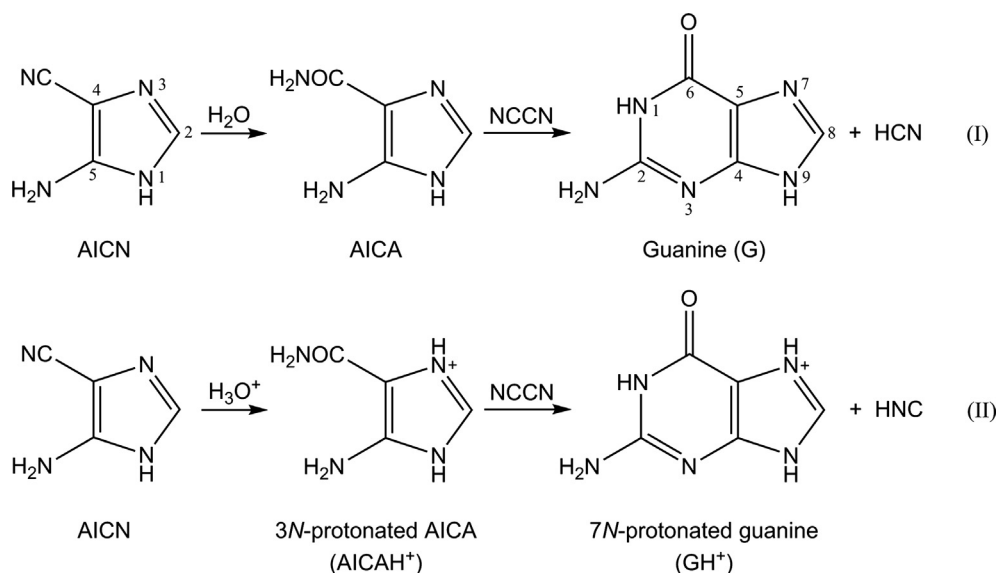
Surprisingly, no attempt has been made to investigate synthetic mechanisms of guanine based on the abovementioned experiments. In this work, we examined the theoretical mechanism for the formation of guanine from AICA and NCCN according to the experimental study by

Scheme 1.

Sanchez et al. [5]. AICA can be formed from AICN by adding H_2O, of which mechanism has not been reported. Therefore, we started from AICN to finally form guanine (reaction I in Scheme 1). AICN, a HCN tetramer, is known to a plausible intermediate in the formation of guanine or adenine by oligomerization of HCN. AICN has been identified as an intermediate in the formation of adenine from HCN in H_2O-NH_3 systems in early days of prebiotic study [27–29]. However, the tetramerization mechanism has not been well understood. In our previous study on the synthetic mechanism of adenine [17], the PES for the formation of AICN from four HCN molecules has been obtained, suggesting that the formation of AICN could hardly occur in the interstellar gas phase by thermal reactions. Ion-molecule reactions generally occur faster than reactions between neutral molecules by several orders of magnitude. Therefore, we also examined ion-molecule reactions starting from hydronium (H_3O^+) instead of H_2O to finally form 7 *N*-protonated guanine (GH^+) (reaction II in Scheme 1). Although AICN has not been observed in the ISM, its presumable precursor, HCN, has been detected in interstellar clouds [30], comets [31,32], and in the atmosphere of Titan [33,34]. H_2O [35] and H_3O^+ [36] among other reactants have been identified in interstellar regions. The presence of NCCN in interstellar and circumstellar clouds has not been proved yet. NCCN cannot be detected through rotational spectrum due to the lack of a permanent dipole moment. However, the identification of ·CN [37,38] and $NCCNH^+$ [39] in the ISM strongly suggests the presence of NCCN in the ISM. NCCN has been observed in the atmosphere of Titan using infrared spectroscopy [40]. Therefore, investigating mechanisms for reactions I and II can provide a clue to the synthesis of guanine in the ISM.

2. Computational methods

Molecular orbital calculations were performed with the Gaussian 09 program package [41]. Geometries of reactants, products, and intermediates were optimized at the Becke, three-parameter, Lee-Yang-Parr (B3LYP) level [42] of the density functional theory using the 6-311G(2d,d,p) basis set. Transition state (TS) geometries connecting the minima were examined and checked by calculating intrinsic reaction coordinates at the same level of theory. For better accuracy of energies, complete basis set (CBS-QB3) model calculations [43] were performed. In addition, CBS-QB3 calculations were performed using the polarized continuum model (PCM) [44] to account for the solvation effects of water.

3. Results and discussion

Several reaction mechanisms were possible for reactions I and II. We presented only the lowest-energy reaction pathways. All energies presented here are results from CBS-QB3 calculations with vibrational zero-point energy correction at absolute zero. Energies of species relative to the sum of the energy of AICN + H_2O + NCCN or AICN + H_3O^+ + NCCN are presented in the potential energy diagram for reaction I or II, respectively.

3.1. Formation of guanine from AICN (reaction I)

Reaction I occurs through three stages: (1) the addition of H_2O to AICN to form AICA, (2) the reaction between AICA and NCCN to form intermediate 4 (abbreviated as INT4) and HCN, and (3) the isomerization of INT4 to guanine. These stages will be called stage I-1, I-2, and I-3, respectively. Stage I-1 starts from the insertion of H_2O to the CN moiety of AICN to form INT1 through TS1 having a relatively unstable four-membered ring structure (Fig. 1). This insertion is the rate-limiting step of stage I-1, with activation energy of 224 kJ mol^{-1}. After two rotation steps, AICA is formed by an H shift from O to N through another four-membered ring TS, TS4.

Stage I-2 occurs by one step through TS5 (see Figs. 1 and 2). As NCCN approaches the amine group (NH_2) attached to 5C of AICA (See Scheme 1 for numbering of the imidazole ring), its C − C bond is cleaved, and then a CN moiety moves toward N of NH_2 while an H of NH_2 moves toward the other CN moiety to form INT4 and HCN, respectively. Its energy barrier (250 kJ mol^{-1}) is larger than the overall activation energy of stage I-1 (224 kJ mol^{-1}). Stage I-3 proceeds through two steps, a ring formation and a 1,3-H shift, to finally produce guanine. For the six-membered ring formation from INT4 through TS6, the rate-limiting step of stage I-3, an energy of at least 238 kJ mol^{-1} is needed. The overall activation energies for the three stages are summarized in Table 1.

The rate equation for a bimolecular reaction A + B → P is given by $\frac{d[P]}{dt} = k[A][B]$ where k is the rate constant and [i] is the molar concentration of a species i, only considering the forward reaction. Therefore, for efficient occurrence of a bimolecular reaction in the gas phase, k should be large under the condition of high densities of reactants. For a thermal reaction occurring at temperature T, k is usually estimated using the Arrhenius equation $k(T) = A\exp(-\frac{E^{\ddagger}}{RT})$ where A is the pre-exponential factor, $E^{\ddagger}$ is the activation energy, and R is the gas