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Formation of Amino Acid Precursors in the Interstellar Medium. A DFT Study of Some Gas-Phase Reactions Starting with Methylenimine

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To evaluate feasibility of the formation of amino acid precursors in dense interstellar clouds from methylenimine, HCN, ·CN radical, water, and ·OH radical, stationary points for four gas-phase reactions have been computed at the B3LYP/6-311++G(d,p) level of theory. All the reactions are exothermic. For the reaction $HN{=}CH_2 + H{-}C{\equiv}N \rightarrow H_2N{-}CH_2{-}C{\equiv}N$, three high-energy transition states have been found (energies of ca. 23−33 kcal mol^{-1} relative to the reactant level) which do not allow this reaction to occur as a purely gas-phase process. The same conclusion has been done for the further glycine amide formation according to the pathway $H_2N{-}CH_2{-}C{\equiv}N + H_2O \rightarrow H_2N{-}CH_2{-}C({=}O){-}NH_2$, where three transitions states have been obtained as well, one of them having relative energy of ca. 52 kcal mol^{-1}. Reaction $HN{=}CH_2 + {\cdot}C{\equiv}N \rightarrow H_2N{-}C({\cdot})H{-}C{\equiv}N$ (>70 kcal mol^{-1} exothermic) exhibits no positive barriers at the theoretical level employed; it is the only one unconditionally feasible in the gas-phase. Despite the fact that for reaction $H_2N{-}CH_2{-}C{\equiv}N + {\cdot}OH \rightarrow H_2N{-}C({\cdot})H{-}C({=}O){-}NH_2$ (ca. 60 kcal mol^{-1} exothermic) four transition states have been found, it might also appear plausible under the interstellar conditions for the following reasons: all the barriers are associated with exclusively proton-transfer processes; only one of them is positive, and three lay below the level of reactants; for the only positive barrier, proton tunneling might facilitate the reaction. Radical products $H_2NC({\cdot})HCN$ and $H_2NC({\cdot})HC({=}O)NH_2$ forming in the latter two cases have a free valence at the carbon atom corresponding to α-C atom in the molecules of biological amino acids. Combining them with a vast variety of open-shell interstellar species is suggested as a possible route to diverse amino acid derivatives in dense molecular clouds.

Introduction

Search for amino acids and their precursors in the interstellar medium is one of the most challenging and exciting topics for modern radio astronomy, astrobiology, extraterrestrial organic chemistry, and the origins of life. Nevertheless, even after more than two decades of systematic search in the interstellar medium, no convincing detection of the simplest amino acid, glycine, has been reported[1−7] (and there is some question as to whether it will ever be detectable even if present, given the background of other spectral features in molecular clouds[6]). At the same time, a rich organic chemistry of molecular clouds gives hope to expect even more complex species of prebiotic interest to be present in the interstellar medium. Among ca. 120 interstellar species identified in the interstellar clouds and circumstellar envelopes (for a review of the known interstellar organic species, see for example[6,7]), methylenimine ($HN{=}CH_2$) merits a special attention. It has been suggested as a possible precursor for glycine and its nitrile,[8,9] and recently definitively detected in several Galactic objects.[10] One can envision different reaction pathways for the formation of glycine and its precursors starting from methylenimine. Its molecule already contains an N−C bond, and the missing part of the amino acid backbone should be constructed with the participation of relatively abundant, commonly found interstellar organic species. One of the earliest suggestions[8] is the reaction

$$HN{=}CH_2 + HCOOH \rightarrow NH_2CH_2COOH \qquad (1)$$

in interstellar dust grains. But besides requiring large concentration of methylenimine and formic acid (which is no common in the molecular clouds), this pathway is not the best choice also from purely chemical point of view: the formation of methylenimine formate seems much more likely to occur than the formic acid addition to the double bond.

A more promising option is hydrogen cyanide (HCN) and its radical ·CN. They are among the most abundant interstellar species.[6,7] Furthermore, in the objects where methylenimine has been detected, the abundance of the cyanide species is often comparable with that of $HN{=}CH_2$.[10] From common considerations, their reaction might produce glycine nitrile (H_2NCH_2-CN, also called aminoacetonitrile):

$$HN{=}CH_2 + H{-}C{\equiv}N \rightarrow H_2N{-}CH_2{-}C{\equiv}N \qquad (2)$$

or the corresponding radical

$$HN{=}CH_2 + {\cdot}C{\equiv}N \rightarrow H_2N{-}C({\cdot})H{-}C{\equiv}N \qquad (3)$$

Although aminoacetonitrile and its radical contain the necessary backbone, further chemical transformations are needed to generate amino acids, namely, a two-step hydrolysis of the nitrile group: first into amino acid amide and finally into amino acid itself. Water is ubiquitous, and it is natural to expect that its interactions with the nitriles (if they really form in the molecular clouds) easily take place. Like HCN and ·CN, water molecules exist in the interstellar medium along with ·OH radicals, and the latter can be equally considered as possible reactants for the nitrile hydrolysis. So, an alternative for the water hydrolysis

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$$\mathrm{H_2N{-}CH_2{-}C{\equiv}N + H_2O \rightarrow H_2N{-}CH_2{-}C({=}O){-}NH_2} \tag{4}$$

might be the following reaction:

$$\mathrm{H_2N{-}CH_2{-}C{\equiv}N + {\cdot}OH \rightarrow H_2N{-}C({\cdot})H{-}C({=}O){-}NH_2} \tag{5}$$

All the above are hypothetical considerations: to the best of our knowledge, no data confirming or disproving possibility of the above pathways under the gas-phase (as well as condensed-phase) conditions of the interstellar medium are available so far.

Laboratory simulation of the formation and reactions of organic molecules in the interstellar medium is a difficult task. On the other hand, during the last three years there is a rapidly growing interest for the use of the quantum chemical ab initio and density functional theory (DFT) methods to study chemical mechanisms and energetics of interstellar organic reactions, mainly in the gas phase.[11−27] While many researches in the field try to employ the true electron correlation models (for example[11−14a,15−18,23−26]), the use of the B3LYP hybrid functional becomes more and more frequently reported.[14,17,18,23,27] Besides the interstellar chemistry, this method was used in the studies of many other organic reactions[28−59] (some of them involving gaseous amino acids and related compounds[51,55,58]). The reason for this growing popularity can be understood from the reported comparison of B3LYP to much more expensive methods: in many cases the DFT results (geometries and energies) were noted to be in a remarkably good agreement with those obtained by the higher-level theories CISD, CCSD, CASSCF[14a,17,28−31,58] and G2[23,30,59] or demonstrated even the top performance approaching, as the ideal case, to experimental data.[14b−e,30,34,36,39,50,54−56] All this, along with a high cost efficiency, makes B3LYP a promising choice for studying diverse organic reactions, including those possible or taking place in the interstellar medium.

The goal of the present work was to study feasibility of the gas-phase reactions (2−5), that might lead from methylenimine to glycine amide and its radical in the interstellar medium, at the B3LYP/6-311++G(d,p) level of theory.

Computational Methods

The Gaussian 98W suite of programs[60] was used. All the computations were performed with Becke's three-parameter hybrid method[61] and the exchange functional of Lee, Yang, and Parr[62] (B3LYP) included in the program package, using the 6-311++G(d,p) basis set.[63−65] Search for transition states was carried out using the QST2 procedure. The stationary point geometries were fully optimized and characterized as minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency) by calculations of vibration frequencies. Intrinsic reaction coordinate (IRC) calculations were performed with the step size of 6 (in units of 0.01 amu$^{-1/2}$ Bohr). Zero-point energies (ZPEs) were retrieved from the vibration frequency calculations. The features of the potential energy surfaces obtained were not affected by the ZPE-corrections. All the optimizations met the default convergence criteria set in Gaussian 98W; however, in some cases (the IRC calculations and optimization of the products of hydrogen elimination from intermediates and products in reactions 3 and 5) it was necessary to set "tight" or "very tight" optimization to reach a real local minimum, and the frequency calculations to give positive wavenumbers only.

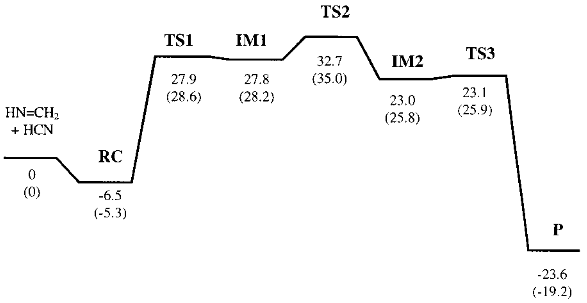

Figure 1. Relative energy profile (kcal mol^{-1}; in parentheses, ZPE-corrected values) for the gas-phase reaction $\mathrm{HN{=}CH_2 + H{-}C{\equiv}N \rightarrow H_2N{-}CH_2{-}C{\equiv}N}$ (2) computed at the B3LYP/6-311++G(d,p) level of theory. For optimized structures for the stationary points, see Figure 2.

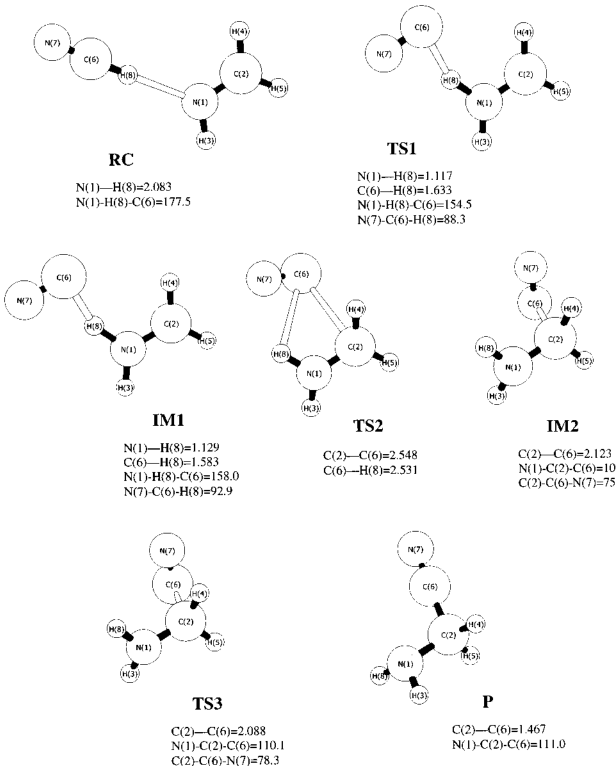

Figure 2. Optimized structures for the stationary points for the gas-phase reaction $\mathrm{HN{=}CH_2 + H{-}C{\equiv}N \rightarrow H_2N{-}CH_2{-}C{\equiv}N}$ (2) computed at the B3LYP/6-311++G(d,p) level of theory, with selected interatomic distances (in angstroms) and angles (in degrees).

Results and Discussion

Reaction $\mathrm{HN{=}CH_2 + H{-}C{\equiv}N \rightarrow H_2N{-}CH_2{-}C{\equiv}N}$ (2). Figures 1 and 2 show, respectively, the potential energy surface and stationary point structures for reaction 2 (detailed geometric parameters for the structures are available as Supporting Information). The initial step is the formation of a van der Waals complex (or reaction complex, **RC**). Its energy is below than that of the reactants by 6.5 kcal mol^{-1} (by 5.3 kcal mol^{-1} with ZPE-correction found from vibration frequency calculations). During its formation, the atom H(8) of HCN is attracted to the N atom of the methylenimine molecule, acting as a proton-acceptor. In the optimized structure, the distance N(1)−H(8) is 2.083 Å, and the angle N(1)−H(8)−C(6) is close to 180° (177.5°).

The resulting spatial orientation of the nitrile group is very remote in respect to the carbon atom C(2) and thus unfavorable for the formation of aminoacetonitrile (**P**). The reaction path is very complicated, with three transition structures found. A QST2 search between **RC** and **P** found transition state **TS2**. Then the same procedure was repeated twice. First, **RC** and **TS2** were taken as the starting structure and product, respectively; this gave one more transition state, **TS1**. Then **TS2** and **P** were input as the starting structure and product, respectively, that gave the third transition state **TS3**.

The first transition structure **TS1** forms due to proton transfer from HCN molecule to the N atom of methylenimine. The distance N(1)−H(8) shortens to 1.117 Å, C(6)−H(8) elongates to 1.633 Å, and the angle N(1)−H(8)−C(6) reduces to 154.5°. The **TS1** energy is +27.9 (+28.6 ZPE-corrected) kcal mol^{-1}. Thus, already the first transition structure makes the overall reaction hardly feasible energetically. For the next **TS2**, even higher activation barrier of +32.7 (+35.0 ZPE-corrected) kcal mol^{-1} was obtained, relative to the level of reactants. This structure corresponds to an intermediate transfer of CN^- anion formed from the protonated imino group of $HN{=}CH_2$ to its carbon atom C(2). In **TS2**, the atom C(6) is about equally distant from H(8) and C(2): the bond lengths C(6)−H(8) and C(2)−C(6) are 2.531 and 2.548 Å, respectively. In **TS3**, corresponding to a complete CN^- transfer to the C-terminus of methylenimine, the C(2)−C(6) distance is 2.088 Å, and the angle N(1)−C(2)−C(6) is 110.1°. For comparison, the corresponding values for the final product aminoacetonitrile are 1.467 Å and 111.0°, respectively. The energy of **TS3** is +23.1 (+25.9 ZPE-corrected) kcal mol^{-1}.

To find intermediates between **TS1** and **TS2**, **TS2** and **TS3**, the intrinsic reaction coordinate (IRC) procedure was employed, which found two species (**IM1** and **IM2**) with geometries insignificantly differing from those for **TS1** and **TS3**, respectively (Figure 2). Correspondingly, both minima connecting the transition states are very shallow (Figure 1), with the energies of 27.8 (28.2 ZPE-corrected) and 23.0 (25.8 ZPE-corrected) kcal mol^{-1}, respectively, above the reactant level.

Although the overall reaction exothermicity computed is 23.6 (19.2 ZPE-corrected) kcal mol^{-1}, the presence of three high-energy transition states makes this reaction hardly feasible in the gas phase.

Reaction $HN{=}CH_2 + {\cdot}C{\equiv}N \rightarrow H_2N{-}C(\cdot)H{-}C{\equiv}N$ (3). At first glance, chemical mechanism for this reaction seems as simple as that described for the reaction of ·CN with acetylene.[12,13] It begins with the radical addition to the methylenimine molecule by disrupting the π system double bond of the latter. The CN bond of $HN{=}CH_2$ loses its π character and elongates up to 1.446 Å (vs 1.267 Å in the reactant). The relative energy of the reaction complex formed (**RC1**, Figure 3) is −52.2 (−50.2 ZPE-corrected) kcal mol^{-1}.

In the transition state **TS1**, one of the methylene hydrogen atoms moves to the N-terminus (Figure 4), thus forming a three-membered ring involving N(1), C(2) and H(5) atoms, with the angle N(1)−H(5)−C(2) of 68.8°. The migrating H atom remains slightly closer to C(2) than to N(1), namely, 1.257 vs 1.302 Å. The relative energy of **TS1** is −19.2 (−19.0 ZPE-corrected) kcal mol^{-1}, i.e., by more than 30 kcal mol^{-1} higher than that for **RC1**. The overall reaction exothermicity calculated is very high, 74.4 (71.2 ZPE-corrected) kcal mol^{-1}. The potential energy surface obtained, which does not exhibit a positive activation barrier (relative to the reactants), is similar to the ones for most cases of ion−molecular reactions. In those cases, exothermicity and the absence of a positive activation barrier is due to strong attractive interaction between ion and neutral species caused by dielectric polarization. The high reactivity found in the present case is similar to that for the reaction of CN radical with acetylene,[12,13] and is apparently a result of the unpaired electron of ·CN attacking the π orbital of methylenimine.

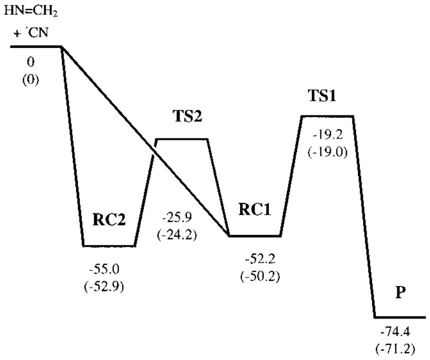

Figure 3. Relative energy profile (kcal mol^{-1}; in parentheses, ZPE-corrected values) for the gas-phase reaction $HN{=}CH_2 + {\cdot}C{\equiv}N \rightarrow H_2N{-}C(\cdot)H{-}C{\equiv}N$ (3) computed at the B3LYP/6-311++G(d,p) level of theory. For optimized structures for the stationary points, see Figure 4.

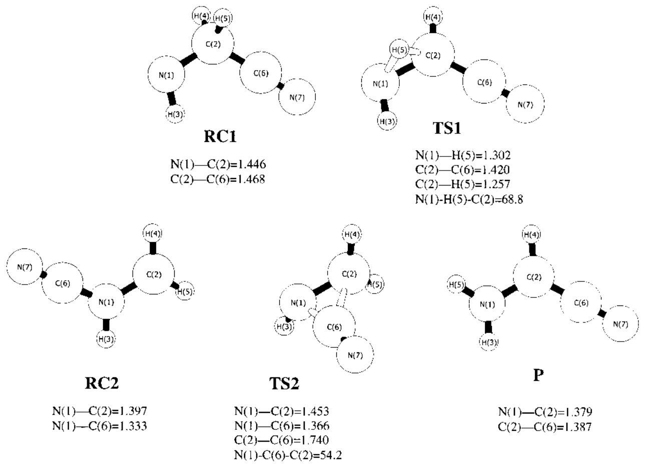

Figure 4. Optimized structures for the stationary points for the gas-phase reaction $HN{=}CH_2 + {\cdot}C{\equiv}N \rightarrow H_2N{-}C(\cdot)H{-}C{\equiv}N$ (3) computed at the B3LYP/6-311++G(d,p) level of theory, with selected interatomic distances (in angstroms) and angles (in degrees).

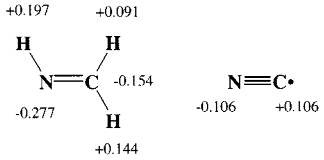

Figure 5. Total atomic charges in methylenimine molecule and CN radical, obtained by Mulliken population analysis.

Mulliken population analysis of the charge distribution in $HN{=}CH_2$ reveals, however, that it is not the C(2) atom that bears the highest negative charge. The latter equals −0.154 only (Figure 5), whereas the charge on N(1) is −0.277, almost twice as much. Therefore, it would be more natural to expect that the ·CN attack should be directed to N(1) rather than to C(2). Indeed, the simplicity of the pathway described in the previous paragraph turned to be a result of input orientation used initially for the reactants, in which ·CN has been placed closer to the C-terminus of methylenimine. If ·CN is pulled to N(1) in the input structure, the interaction results in another reaction complex (**RC2**), where N(1)−C(6) bond forms instead of C(2)−C(6). The relative energy for **RC2** is by ca. 3 kcal mol^{-1} lower

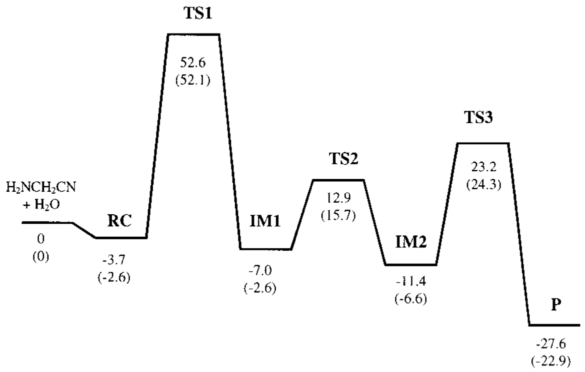

Figure 6. Relative energy profile (kcal mol^{-1}; in parentheses, ZPE-corrected values) for the gas-phase reaction $H_2N{-}CH_2{-}C{\equiv}N + H_2O \rightarrow H_2N{-}CH_2{-}C({=}O){-}NH_2$ (4) computed at the B3LYP/6-311++G(d,p) level of theory. For optimized structures for the stationary points, see Figure 7.

as compared to that for **RC1**: −55.0 (−52.9 ZPE-corrected) kcal mol^{-1}.

To what extent the **RC2** formation can inhibit the shortest pathway to aminonitrile radical **P**? Similarly to reaction 2, a key step is the CN transfer from the N to C-terminus (transition state **TS2**; Figure 4), which is likely to require a similar amount of energy to proceed. Indeed, the energy of **TS2** relative to **RC2** is ca. 30 kcal mol^{-1} [vs 30−40 kcal mol^{-1} for **TS1**−**3** relative to **RC** for reaction 2, Figure 1]. However, if to attribute it to the level of reactants, the energy turns out to be as low as −25.9 (−24.2 ZPE-corrected) kcal mol^{-1}, then **RC2** is easily transformed into **RC1**. Thus, reaction 3, as computed at the B3LYP/6-311++G(d,p) level of theory, is possible in the interstellar medium as a purely gas-phase process, due to the absence of a positive activation barrier and to a high exothermicity.

Reaction $H_2N{-}CH_2{-}C{\equiv}N + H_2O \rightarrow H_2N{-}CH_2{-}C({=}O){-}NH_2$ (4). Amide formation is the most critical of the two hydrolytic stages leading from aminoacetonitrile to glycine itself, since by forming a C=O bond the carbon atom acquires the same oxidation state as in a carboxylic group.

Impossibility of the gas-phase reaction 2 is no obstacle for the formation of glycine nitrile molecule, necessary to proceed to the present transformation (reaction 4). There is an alternative way of supplying this species: combining the glycine nitrile radical, formed through the reaction 3, with hydrogen atoms, i.e., $H_2NC(\cdot)HCN + H\cdot$. We calculated exothermicity of this process at the B3LYP/6-311++G(d,p) level of theory, and it turned to be as high as 83.2 (74.7 ZPE-corrected) kcal mol^{-1}.

As the initial step of reaction 4, a complex forms (**RC**; Figures 6 and 7) in which one of the water H atoms coordinates to the nitrile N atom. It is below the level of the reactants by −3.7 (−2.6 ZPE-corrected) kcal mol^{-1} only. The distance N(4)−H(10) is 2.500 Å (Figure 7), and the angle C(3)−N(4)−H(10) 81.5°, so that O(9) has a favorable spatial orientation for the subsequent interaction with C(3) of the nitrile group [the distance C(3)−O(9) of 3.014 Å]. Nevertheless, the barrier height corresponding to the first transition state **TS1** is as much as 52.6 (52.1 ZPE-corrected) kcal mol^{-1} relative to the reactant level. In **TS1**, the distances N(4)−H(10) and C(3)−O(9) reduce to 1.319 and 1.785 Å, respectively, whereas O(9)−H(10) and C(3)−N(4) increase from 0.965 and 1.153 to 1.292 and 1.204 Å, respectively. Although the latter bond elongates insignificantly, the angle C(2)−C(3)−N(4) bends from 177.6° (in **RC**) to 150.7°. The angle H(10)−O(9)−H(11) distorts less significantly, from 105.7° to 118.5°.

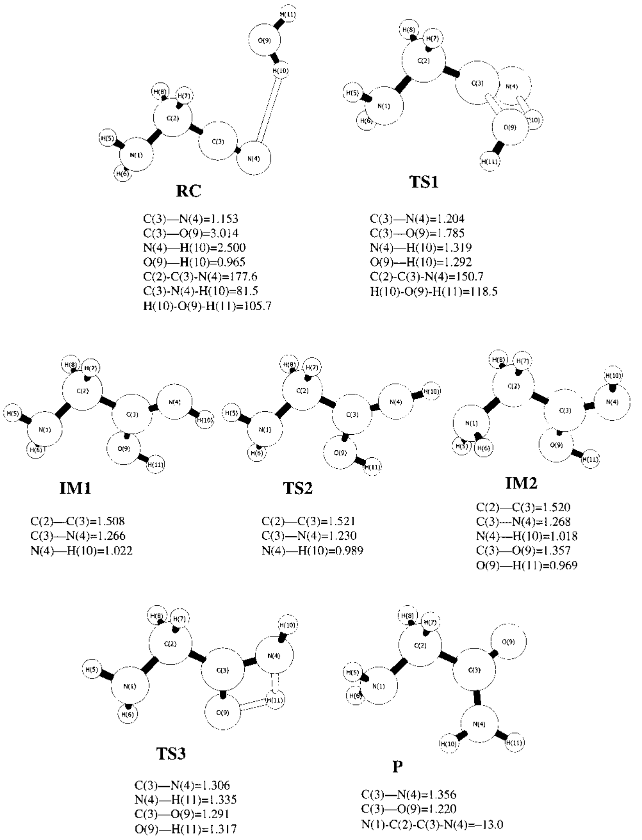

Figure 7. Optimized structures for the stationary points for the gas-phase reaction $H_2N{-}CH_2{-}C{\equiv}N + H_2O \rightarrow H_2N{-}CH_2{-}C({=}O){-}NH_2$ (4) computed at the B3LYP/6-311++G(d,p) level of theory, with selected interatomic distances (in angstroms) and angles (in degrees).

The intermediate **IM1** appearing after the first energetic barrier is an imine species [C(3)−N(4) length of 1.266 Å; the relative energy of −7.0 (−2.6 ZPE-corrected) kcal mol^{-1}] having *cis*-orientation of the newly formed C(3)−O(9) and N(4)−H(10) bonds. This does not allow a direct transfer of the hydrogen atom H(11) to N(4), which is necessary to form the final amide product **P**, so that first *cis-trans*-isomerization of **IM1** should occur. Despite it does not require that high energy as **TS1** formation does, still the **TS2** energy, +12.9 (+15.7 ZPE-corrected) kcal mol^{-1}, is too high for this transformation to be feasible under the cold (ca. 10 K) interstellar conditions. Variation in the C(3)−N(4) bond length during the *cis-trans*-isomerization is 1.266 Å in **IM1**, 1.230 Å in **TS2**, and 1.268 Å in **IM2**. Accordingly, N(4)−H(10) changes on the order of 1.022, 0.989, and 1.018 Å; that is, both bonds are shortened in the transition state as compared to the intermediates.

After the isomerization, even though the transfer of H(11) from the oxygen atom to N(4) becomes sterically unhindered, this final step is again characterized by a high activation barrier, of +23.2 (+24.3 ZPE-corrected) kcal mol^{-1} relative to the reactant level. During the formation of the last **TS3**, H(11) approaches N(4) to a distance of 1.335 Å, with the O(9)−H(11) bond elongating to 1.317 Å (from 0.969 Å in **IM2**). The C(3)−N(4) bond changes less significantly, from 1.268 to 1.306 Å, and only after the complete transfer of the second hydrogen atom adopts in glycine amide **P** a length of 1.356 Å. On the other hand, C(3)−O(9) acquiring a typical double character reduces its length from 1.357 Å in **IM2**, to 1.291 Å in **TS3** and finally to 1.220 Å in **P**. Preferable conformation of the glycine amide molecule is that with *cis*-orientation of the groups NH_2

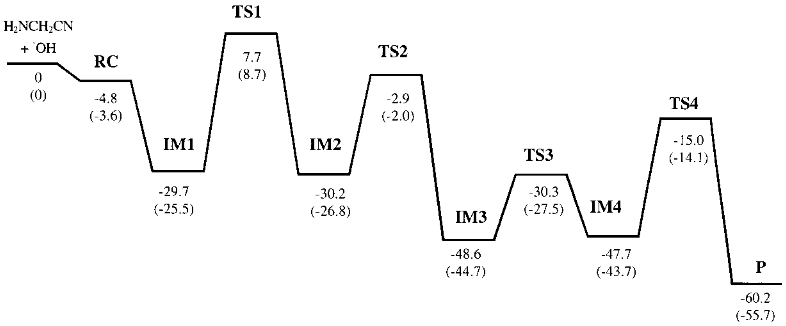

Figure 8. Relative energy profile (kcal mol^{-1}; in parentheses, ZPE-corrected values) for the gas-phase reaction $H_2N{-}CH_2{-}C{\equiv}N + {}^{\bullet}OH \rightarrow H_2N{-}C({}^{\bullet})H{-}C({=}O){-}NH_2$ (5) computed at the B3LYP/6-311++G(d,p) level of theory. For optimized structures for the stationary points, see Figure 9.

(Figure 7), where the dihedral angle N(1)−C(2)−C(3)−N(4) is −13.0°.

Thus, reaction 4 in some respect is similar to reaction 2: three transition states with high positive activation barriers are consecutively formed.

$H_2N{-}CH_2{-}C{\equiv}N + {}^{\cdot}OH \rightarrow H_2N{-}C(\cdot)H{-}C({=}O){-}NH_2$ (5). Among the studied neutral−neutral interstellar reactions with the participation of π-electronic systems, on one hand, and radical species, on the other hand, there are examples when the reactions can proceed without forming transition states of a positive relative energy.[12−14,26] First of all, CN radical can act as the species adding on the π-systems,[12−14] and reaction 3 is one more such case. Can the formation of glycine amide be facilitated in a similar way by changing the hydrolytic reagent from water to hydroxyl radical, also extremely abundant in the interstellar medium?

The potential energy surface for reaction 5 is shown in Figure 8. According to our calculations, the ·OH addition on the triple bond of aminoacetonitrile indeed proceeds smoothly, with exothermic effect of 29.7 (25.5 ZPE-corrected) kcal mol^{-1} relative to the reactant level. Before that, a reaction complex **RC** forms where the nitrile N atom acts as proton acceptor for H(10) of the hydroxyl group. The distance N(4)−H(10) is 2.368 Å (Figure 9), somewhat closer than in **RC** for the previous reaction, and the atom O(9) is about equally distant from C(3) and N(1): by 3.192 and 3.275 Å, respectively.

In the intermediate **IM1**, the bond C(3)−N(4) is 1.254 Å (vs 1.153 Å in **RC**) and C(3)−O(9) is 1.369 Å. The former-nitrile atom N(4) bears no hydrogen atoms, as it should be in glycine amide. So the first necessary step is to transfer H(10) from the hydroxyl group, that corresponds to the first transition structure **TS1**. The atom H(10) is situated here almost exactly between the two heteroatoms, with the interatomic distances O(9)−H(10) and N(4)−H(10) of 1.307 and 1.324 Å, respectively. The bonds C(3)−N(4) (1.277 Å) and C(3)−O(9) (1.343 Å) change insignificantly in respect to those in **IM1**. If to compare the barrier height for **TS1** relative to the preceding **IM1** to the energy for analogous transition in reaction 4 (that is for **IM2**−**TS3** transition; Figure 6), we find very similar values of about 35 kcal mol^{-1}. Nevertheless, relative to the reactants, the activation energy in the present case turns to be much lower (though remaining positive), of +7.7 (+8.7 ZPE-corrected) kcal mol^{-1}. In addition to that, as it will be shown below, this barrier is the highest one on the whole reaction path, and the only positive one relative to the reactant level.

The lowest energy conformation of the intermediate **IM2**, following **TS1**, is that with *cis*-orientation of the C−N bonds, likewise in glycine amide (**P** in Figure 7) as well as in its radical (**P** in Figure 9). This makes a further H-transfer from the α-carbon atom C(2) to O(9) more sterically preferable than to N(4), and the next transition state found, **TS2**, lays below the energy level of reactants by 2.9 (2.0 ZPE-corrected) kcal mol^{-1}. As in the previous **TS1**, the H atom migrating is found approximately in the middle between the two heteroatoms, with the distances C(2)−H(7) of 1.350 Å and O(9)−H(7) of 1.379 Å. The hydroxy-imine intermediate **IM3** formed next is a nearly plain species, with the dihedral angles N(1)−C(2)−C(3)−N(4) and N(1)−C(2)−C(3)−O(9) being −4.2° and 175.9°, respectively. Its relative energy is −48.6 (−44.7 ZPE-corrected) kcal mol^{-1}, by almost 20 kcal mol^{-1} lower as compared to those of the two previous intermediates.

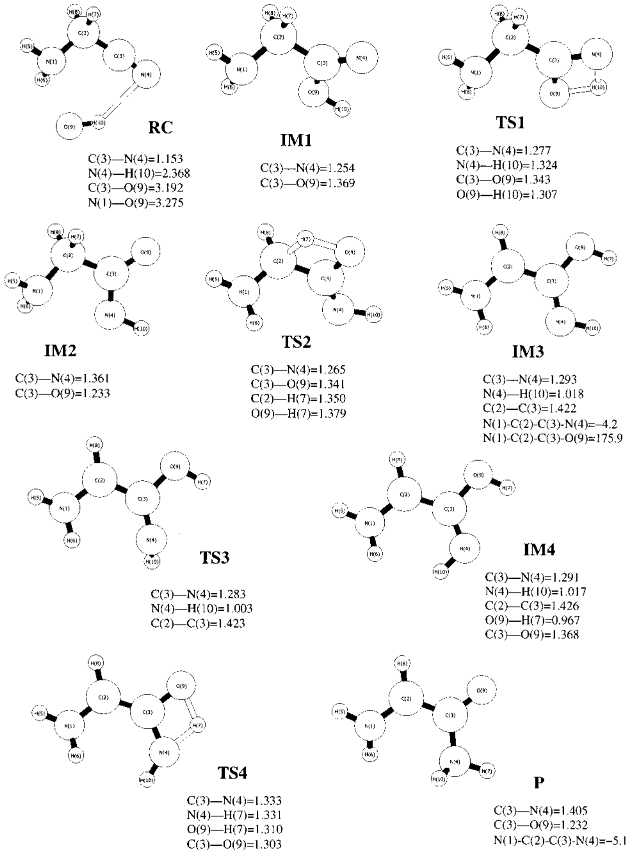

Figure 9. Optimized structures for the stationary points for the gas-phase reaction $H_2N{-}CH_2{-}C{\equiv}N + {}^{\bullet}OH \rightarrow H_2N{-}C({}^{\bullet})H{-}C({=}O){-}NH_2$ (5) computed at the B3LYP/6-311++G(d,p) level of theory, with selected interatomic distances (in Å) and angles (in degrees).

The following series of transformations leading from **IM3** to the final radical product **P** (Figures 8 and 9) are much alike the sequence **IM1-TS2-IM2-TS3-P** for the previous hydrolytic reaction (Figures 6 and 7), from both mechanistic and energetic points of view. To make transfer of the second hydrogen atom from O(9) to N(4) possible, the *cis*-orientation of C(3)—O(9) and N(4)—H(10) is inappropriate and should be changed to the opposite one through the formation of **TS3**. It requires the energy of almost +20 kcal mol^{-1} relative to **IM3**, very similarly to the transition **IM1-TS2** for reaction 4, but in respect to the reactants it is as low as −30.3 (−27.5 ZPE-corrected) kcal mol^{-1}. Besides that, variations in the bond lengths C(3)—N(4) and N(4)—H(10) are very small in the present case: 1.293, 1.283, 1.291 and 1.018, 1.003, 1.017 Å, respectively, in **IM3**, **TS3** and **IM4**. All this can be apparently explained by facilitating delocalization of the π-electronic density by the unpaired electron at C(2): an argument on its favor is a reduced C(2)—C(3) bond length in any of the three radical species (1.422, 1.423, and 1.426 Å, respectively) as compared to their closed-shell counterparts **IM1**, **TS2** and **IM2** (1.508, 1.521, and 1.520 Å, respectively) in reaction 4.

After the *cis-trans*-isomerization, the only remaining barrier is the one corresponding to the H(7)-transfer itself to form a common amide bond in **P**. This barrier is below the reactant level, at −15.0 (−14.1 ZPE-corrected) kcal mol^{-1}, although is higher than the **IM4** energy by roughly 30 kcal mol^{-1} (the difference between **IM2** and **TS3** in the previous reaction was approximately the same). In **TS4**, the atom H(7) approaches N(4) to a distance of 1.331 Å, and the bond O(9)—H(7) elongates to 1.310 Å (from 0.967 Å in **IM4**). The C(3)—N(4) bond length slightly increases from 1.291 to 1.333 Å, and after the complete transfer of H(7) reaches 1.405 Å in the glycine amide radical **P**. Simultaneously the C(3)—O(9) bond length shortens from 1.368 Å in **IM4** to 1.303 Å in **TS4** and finally to 1.232 Å in **P**. As in glycine amide, the lowest-energy conformation of the related radical is that with *cis*-orientation of the groups NH$_2$ (Figure 9), with the dihedral angle N(1)−C(2)−C(3)−N(4) of −5.1°, i.e., plainer than the glycine amide molecule. The overall reaction exothermicity is more than twice as higher as compared to reaction 4: −60.2 (−55.7 ZPE-corrected) kcal mol^{-1}.

Feasibility of the Reactions in the Interstellar Medium. Since the interstellar medium is extremely cold and the gas phase has very low density, chemical reactions can proceed under the following two conditions: (1) the reactions should be exothermic and (2) there should be no positive activation barriers during the reaction course, unless proton tunneling processes are involved.[13]

The first condition is met for any of the reactions, where exothermicity calculated at the B3LYP/6-311++G(d,p) level of theory increases in the order of reactions (3)>(5)>(4)>(2). Higher exothermicity of the reactions involving radicals seems quite natural.

Regarding the problem of positive activation barriers, the only reaction which does not exhibit them (at least at the given theoretical level) is the ·CN radical addition to methylenimine, i.e., reaction 3, including both possible pathways. Its analogue (2) involving closed-shell species, is unconditionally impossible as a purely gas-phase process. The same can be concluded regarding energetic feasibility of the hydrolytic reaction 4, where three positive energy barriers were found as well, and one of them exceeds 50 kcal mol^{-1}. At the same time, these conclusions by no means imply an *absolute* impossibility of reactions 2 and 4: they are very likely to proceed according to totally different mechanisms and energetics in the interstellar grains[3,66−68] and ices.[69] However, even without appealing to a complicated models simulating silicate grain surface chemistry, it was clearly demonstrated that introducing a very small number of water molecules can greatly enhance some reactions of formaldehyde, HCN and other simple species.[24]

Despite the fact that reaction 5 reminds in many respects reaction 4, and moreover, as many as four energy barriers have been found here, it might appear plausible under the interstellar conditions. The reasons for such expectations are (1) that all the barriers are associated with exclusively proton-transfer processes; (2) only one of them is positive, and three lay below the level of reactants; (3) for the only positive barrier (which by the way is not high, ca. 8 kcal mol^{-1}), the possibility of proton tunneling cannot be neglected, which has been suggested to be very common under the cold conditions of dense molecular clouds significantly increasing the number of possible low-temperature chemical reactions.[70,71]

One should mention one more aspect of reactions 3 and 5, which is especially important from the point of view of possible biomolecule formation in the interstellar medium. The final reaction products in both cases are radicals with a free valence at the carbon atom C(2) corresponding to α-C atom in the molecules of biological amino acids. In the present paper these products are referred to as “glycine nitrile radical” and “glycine amide radical”, respectively. Terminologically such names reflect a simple fact that the radicals can originate from H_2NCH_2CN and $H_2NCH_2C({=}O)NH_2$, respectively, as well as are able to combine with a hydrogen atom regenerating the closed-shell glycine precursors, as it was exemplified above for the case of $H_2NC(\cdot)HCN + H\cdot$. Nevertheless, if any of the above radicals combines with a hydrocarbon radical, the resulting product will be nitrile (or amide) of a different amino acid: the combination with methyl radical would produce alanine derivatives; with isopropyl radical, valine derivatives; and so on. For example, exothermicity of the $H_2NC(\cdot)HCN + CH_3\cdot$ combination calculated at the same B3LYP/6-311++G(d,p) level of theory is as high as 67.3 (60.0 ZPE-corrected) kcal mol^{-1}. Thus, such a way of combining radical products $H_2NC(\cdot)HCN$ and $H_2NC(\cdot)HC({=}O)NH_2$ with a vast variety of open-shell interstellar species can be considered as a possible route to diverse amino acid derivatives in dense molecular clouds.

Finally, one should comment on the question whether there is a possibility of some competitive reactions, which, in principle, might reduce formation of the amino acid precursors through the suggested reaction channels. In particular, such a possibility has to be taken into account for the reactions where radical species participate: in our case, for reactions 3 and 5. The most likely competitive reactions are those with hydrogen elimination,[13,14,17] for example, from **RC1**, **RC2**, and **P** (Figure 4) for reaction 3, giving rise to the compounds $HN{=}CH{-}C{\equiv}N$ and $H_2C{=}N{-}C{\equiv}N$. Nevertheless, according to our computations at the B3LYP/6-311++G(d,p) level, an overall exothermicity of these reaction channels turned to be incomparably lower than that for the main reaction 3 (i.e., 74.4 (71.2 ZPE-corrected) kcal mol^{-1}): energy of the system $HN{=}CH{-}C{\equiv}N + H\cdot$ formed is −15.7 (−18.9 ZPE-corrected) kcal mol^{-1} only below the reactant level; for $H_2C{=}N{-}C{\equiv}N + H\cdot$, it is −10.5 (−14.0 ZPE-corrected) kcal mol^{-1}. Furthermore, the latter two systems lay considerably above the *whole* energy profile for reaction 3, where even the highest-energy **TS1** is at ca. −19 kcal mol^{-1}. In the case of reaction 5, the products $HN{=}CH{-}C({=}O)NH_2 + H\cdot$ of a similar hydrogen elimination from glycine amide radical **P** (Figure 9) are even closer to the reactants, with a relative energy of −6.9 (−9.3 ZPE-corrected) kcal mol^{-1}. This is above most stationary points (with the exception of **RC**, **TS1**, and **TS2**): in particular, by ca. 50 kcal mol^{-1} higher than **P**.

Taking into account the above values, as well as the fact that reactions of this nature pass, as a rule, through a transition state,[13,14,17] our conclusion is that the hydrogen elimination cannot be considered as a major reaction pathway, and should not cause a noticeable loss of the main radical products under the cold interstellar conditions.

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Supporting Information Available: Table of interatomic distances (in angstroms) and angles (in degrees) for reaction complexes (**RC**), transition states (**TS**), intermediates (**IM**), and products (**P**) in the reactions 2−5. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Lovas, F. J.; Kawashima, Y.; Grabow, J. U.; Suenram, R. D.; Fraser, G. T.; Hirota, E. *Astrophys. J.* **1995**, *455*, L201.

(2) Combes, F.; Q-Rieu, N.; Wlodarczak, G. *Astron. Astrophys.* **1996**, *308*, 618.

(3) Sorrell, W. H. *Astrophys. Space Sci.* **1997**, *253*, 27.

(4) Snyder, L. E. *Origins Life Evol. Biosphere* **1997**, *27*, 115.

(5) Winnewisser, G. *J. Mol. Struct.* **1997**, *408*, 1.

(6) Irvine, W. M. *Origins Life Evol. Biosphere* **1998**, *28*, 365.

(7) Winnewisser, G.; Kramer, C. *Space Sci. Rev.* **1999**, *90*, 181.

(8) Hoyle, F.; Wickramasinghe, N. C. *Nature* **1976**, *264*, 45.

(9) Dickerson, R. E. *Sci. Am.* **1978**, *239*, 70.

(10) Dickens, J. E.; Irvine, W. M.; DeVries, C. H.; Ohishi, M. *Astrophys. J.* **1997**, *497*, 307.

(11) Herbst, E.; Woon, D. E. *Astrophys. J.* **1996**, *463*, L113.

(12) Woon, D. E.; Herbst, E. *Astrophys. J.* **1997**, *477*, 204.

(13) Fukuzawa, K.; Osamura, Y. *Astrophys. J.* **1997**, *489*, 113.

(14) (a) Fukuzawa, K.; Osamura, Y.; Schaefer, III, H. F. *Astrophys. J.* **1998**, *505*, 278. (b) Balucani, N.; Asvany, O.; Huang, L. C. L.; Lee, Y. T.; Kaiser, R. I.; Osamura, Y.; Bettinger, H. F. *Astrophys. J.* **2000**, *545*, 892. (c) Huang, L. C. L.; Balucani, N.; Lee, Y. T.; Kaiser, R. I.; Osamura, Y. *J. Chem. Phys.* **1999**, *111*, 2857. (d) Balucani, N.; Asvany, O.; Chang, A. H. H.; Lin, S. H.; Lee, Y. T.; Kaiser, R. I.; Bettinger, H. F.; Schleyer, P. v. R.; Schaefer, H. F., III *J. Chem. Phys.* **1999**, *111*, 7457. (e) Balucani, N.; Asvany, O.; Chang, A. H. H.; Lin, S. H.; Lee, Y. T.; Kaiser, R. I.; Bettinger, H. F.; Schleyer, P. v. R.; Schaefer, III, H. F. *J. Chem. Phys.* **1999**, *111*, 7472. (f) Balucani, N.; Asvany, O.; Chang, A. H. H.; Lin, S. H.; Lee, Y. T.; Kaiser, R. I.; Osamura, Y. *J. Chem. Phys.* **2000**, *113*, 8643. (g) Huang, L. C. L.; Asvany, O.; Chang, A. H. H.; Balucani, N.; Lin, S. H.; Lee, Y. T.; Kaiser, R. I.; Osamura, Y. *J. Chem. Phys.* **2000**, *113*, 8656.

(15) Petrie, S.; Herbst, E. *Astrophys. J.* **1997**, *491*, 210.

(16) Kaiser, R. I.; Ochsenfeld, C.; Head-Gordon, M.; Lee, Y. T. *Astrophys. J.* **1999**, *510*, 784.

(17) Osamura, Y.; Fukuzawa, K.; Terzieva, R.; Herbst, E. *Astrophys. J.* **1999**, *519*, 697.

(18) Peppe, S.; Blanksby, S. J.; Dua, S.; Bowie, J. H. *J. Phys. Chem. A* **2000**, *104*, 5817.

(19) Petrie, S.; Dunbar, R. C. *J. Phys. Chem. A* **2000**, *104*, 4480.

(20) Redondo, P.; Calleja, E.; Barrientos, C.; Largo, A. *J. Phys. Chem. A* **1999**, *103*, 9125.

(21) Barrientos, C.; Redondo, P.; Largo, A. *Chem. Phys. Lett.* **1999**, *306*, 168.

(22) Redondo, P.; Saguillo, A.; Barrientos, C.; Largo, A. *J. Phys. Chem. A* **1999**, *103*, 3310.

(23) Redondo, P.; Ruiz, M. J.; Boronat, R.; Barrientos, C.; Largo, A. *Theor. Chem. Acc.* **2000**, *104*, 199.

(24) (a) Woon, D. E. *Icarus* **1999**, *142*, 550. (b) (a) Woon, D. E. *Icarus* **2001**, *149*, 277.

(25) Ding, Y.-H.; Li, Z.-S.; Huang, X.-R.; Sun, C.-C. *J. Chem. Phys.* **2000**, *113*, 1745.

(26) Kaiser, R. I.; Ochsenfeld, C.; Stranges, D.; Head-Gordon, M.; Lee, Y. T. *Faraday Discuss.* **1998**, *109*, 183.

(27) Milburn, R. K.; Hopkinson, A. C.; Sun, J.; Bohme, D. K. *J. Phys. Chem. A* **1999**, *103*, 7528.

(28) Bettinger, H. F.; Schreiner, P. R.; Schleyer, P. v. R.; Schaefer, H. F., III *J. Phys. Chem.* **1996**, *100*, 16147.

(29) Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C.; Marquez, M.; Estévez, C. M.; Baboul, A. G.; Schlegel, H. B. *J. Phys. Chem. A* **1997**, *101*, 6092.

(30) Basch, H.; Hoz, S. *J. Phys. Chem. A* **1997**, *101*, 4416.

(31) Rice, B. M.; Pai, S. V.; Chabalowski, C. F. *J. Phys. Chem. A* **1998**, *102*, 6950.

(32) Irle, S.; Morokuma, K. *J. Chem. Phys.* **1999**, *111*, 3978.

(33) Goldstein, E.; Beno, B. R.; Houk, K. N. *Theor. Chem. Acc.* **1999**, *103*, 81.

(34) Balucani, N.; Asvany, O.; Chang, A. H. H.; Lin, S. H.; Lee, Y. T.; Kaiser, R. I.; Bettinger, H. F.; Schleyer, P. v. R.; Schaefer, H. F., III *J. Chem. Phys.* **1999**, *111*, 7457.

(35) Stevens, P. S.; Seymour, E.; Li, Z. *J. Phys. Chem. A* **2000**, *104*, 5989.

(36) Pérez-Casany, M. P.; Nebot-Gil, I.; Sánchez-Marín, J. *J. Phys. Chem. A* **2000**, *104*, 6277.

(37) Su, H.; Kong, F.; Chen, B.; Huang, M.-B.; Liu, Y. *J. Chem. Phys.* **2000**, *113*, 1885.

(38) Lei, W.; Zhang, R. *J. Chem. Phys.* **2000**, *113*, 153.

(39) Domingo, L. R. *Theor. Chem. Acc.* **2000**, *104*, 240.

(40) Won, D. S.; Choe, J. C.; Kim, M. S. *Rapid Commun. Mass Spectrom.* **2000**, *14*, 1110.

(41) Fadden, M. J.; Hadad, C. M. *J. Phys. Chem. A* **2000**, *104*, 6088.

(42) Fadden, M. J.; Hadad, C. M. *J. Phys. Chem. A* **2000**, *104*, 6324.

(43) Cases, M.; Duran, M.; Sola, M. *J. Mol. Model.* **2000**, *6*, 205.

(44) Castillo, R.; Moliner, V.; Andres, J. *Chem. Phys. Lett.* **2000**, *318*, 270.

(45) Traulsen, T.; Friedrichsen, W. *J. Chem Soc. Perkin Trans. 1* **2000**, 1387.

(46) Yoshizawa, K.; Suzuki, A.; Shiota, Y.; Yamabe, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 815.

(47) Di Valentin, C.; Gisdakis, P.; Yudanov, I. V.; Rosch, N. *J. Org. Chem.* **2000**, *65*, 2996.

(48) Fokin, A. A.; Kushko, A. O.; Kirij, A. V.; Yurchenko, A. G.; Schleyer, P. V. *J. Org. Chem.* **2000**, *65*, 2984.

(49) Nendel, M.; Sperling, D.; Wiest, O.; Houk, K. N. *J. Org. Chem.* **2000**, *65*, 3259.

(50) Strajbl, M.; Florian, J.; Warshel, A. *J. Am. Chem. Soc.* **2000**, *122*, 5354.

(51) Rogalewicz, F.; Hoppilliard, Y. *Int. J. Mass Spectrom.* **2000**, *199*, 235.

(52) Staroverov, V. N.; Davidson, E. R. *J. Am. Chem. Soc.* **2000**, *122*, 7377.

(53) Mori, S.; Nakamura, E.; Morokuma, K. *J. Am. Chem. Soc.* **2000**, *122*, 7294.

(54) Arulmozhiraja, S.; Fujii, S.; Tokiwa, H. *J. Phys. Chem. A* **2000**, *104*, 7068.

(55) Zhu, C. B.; Balta, B.; Aviyente, V.; Lifshitz, C. *J. Phys. Chem. A* **2000**, *104*, 7061.

(56) Choi, Y. M.; Xia, W. S.; Park, J.; Lin, M. C. *J. Phys. Chem. A* **2000**, *104*, 7030.

(57) Fenske, J. D.; Kuwata, K. T.; Houk, K. N.; Paulson, S. E. *J. Phys. Chem. A* **2000**, *104*, 7246.

(58) Balta, B.; Basma, M.; Aviyente, V.; Zhu, C. B.; Lifshitz, C. *J. Phys. Chem. A* **2000**, *104*, 69.

(59) Díaz, N.; Suárez, D.; Sordo, T. L. *J. Am. Chem. Soc.* **2000**, *122*, 6710.

(60) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 98W, Revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(61) Becke, A. D. *J. Phys. Chem.* **1993**, *98*, 5648.

(62) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(63) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1972**, *66*, 217.

(64) Binkley, J. S.; Pople, J. A. *Int. J. Quantum Chem.* **1975**, *9*, 229.

(65) Krishnan, R.; Frisch, M. J.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 4244.

(66) Tielens, A. G. G. M.; Allamandola, L. J. *In Interstellar Processes*; Hollenbach, D. J., Thronson, H. A., Eds.; Reidel: Dordrecht, 1987.

(67) Basiuk, V. A.; Navarro-Gonzalez, R. *Origins Life Evol. Biosphere* **1995**, *25*, 457.

(68) Shalabiea, O. M.; Caselli, P.; Herbst, E. *Astrophys. J.* **1998**, *502*, 652.

(69) Allamandola, L. J.; Bernstein, M. P.; Sandford, S. A.; Walker, R. L. *Space Sci. Rev.* **1999**, *90*, 219.

(70) Goldanskii, V. I.; Frank-Kamenetskii, M. D.; Barkalov, I. M. *Science* **1973**, *182*, 1344.

(71) Goldanskii, V. I. *J. Phys. Chem. A* **1997**, *101*, 3424.