# Full *ab Initio* Conformational Spectrum of α,α′-Diaminoacetone

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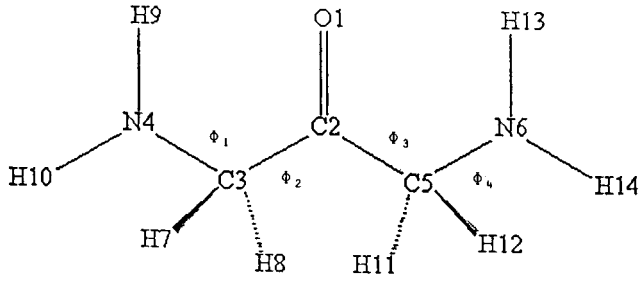
The *ab initio* conformational spectrum of α,α′-diaminoacetone, $(NH_2CH_2)_2CO$, is obtained by systematic conformational space search at the HF/6-31+G* level. The 15 conformers are discussed in terms of near-neighbor interactions such as hydrogen bonding. Conformer **1** with a planar heavy-atom structure and two acceptor-bifurcated $NH_2$:::O:::$H_2N$ hydrogen bonds is the global minimum at all levels of theory: AM1, HF/STO-3G, HF/6-31G, HF/6-31G*, HF/6-31+G*, HF6-311++G**//HF/6-31+G*, HF/6-311++G(3df, 3pd)//HF/6-31+G*, MP2/6-31+G*//HF/6-31+G*, and MP2/6-311++G**//HF/6-31+G*. The double bifurcation appears to be a novelty in hydrogen bonding. The relative energies of higher conformational states show a distinct basis set dependence. Significantly, HF/6-31G calculations do not reproduce the full HF/6-31+G* conformational spectrum, since the pyramidality of amino nitrogens is clearly underestimated at the former level. The AM1 method predicts far too few minima and does not seem to properly describe the NH···O bond.

## Introduction

Diamino ketones and diamino alcohols are important intermediates in chemical and biomimetic syntheses of compounds of diverse biological functions such as enzymes, alkaloids, pteridines, and receptor agonists.[1−7] The α,α′-diaminoacetone (daa) molecule (Chart 1) is an interesting precursor in the formation of peptides and thus may be regarded as a model compound for the elucidation of the conformational stability of "primitive" proteins. The daa is a rather reactive molecule and has so far been studied either in solutions or as salts.[8−13] To the best of our knowledge no structure determination nor theoretical study of daa has been reported in the literature. However, some allied molecules, viz, α-aminoacetone,[14] α-aminoacetaldehyde,[14−17] α-glycolaldehyde,[18] glycine,[15,19−21] and alanine,[22,23] etc., have been investigated by semiempirical and *ab initio* calculations. Although the role of the symmetric intramolecular hydrogen bond in *β*-dicarbonyl compounds has been well-established by theoretical and experimental studies,[24,25] this is still controversial in amino acid systems. In bioactive peptides, proteins, and other biologically important molecular systems, however, intramolecular hydrogen bonds between strands and helices are frequently invoked to explain conformational stability and protein folding and also molecular flexibility as an index of bioactive function.[26−31]

Hoffmann et al.[14] considered H-bonding itself to be insignificant in α-aminocarbonyl compounds and interpreted their extended Hückel and STO-3G calculations on the basis of through-bond and through-space interactions. Vishveswara and Pople,[15] on the other hand, have explained the stability of lowest energy conformers of glycine and α-aminoacetaldehyde determined by Hartree−Fock calculations (HF/4-31G) in terms of distorted intramolecular bifurcated hydrogen bonds from the amino group to the carbonyl oxygen. The change in electron densities on aldehyde protons and on the electronegative atom attached to the α-carbon can be attributed either to dipolar interactions between the nitrogen lone pair and aldehyde hydrogen or to the formation of a distorted NH···OCH hydrogen bond depending on the choice of the reference structure.

**CHART 1**




Conformationally labile α-amino acids have been subjects of conformational studies over the years.[19−21,28−36] But the full ensemble of possible conformations has rarely been considered.[19,20,23,37] The daa not only is labile in the conformational sense but also contains a variety of intramolecular interactions and is of a tractable size for high-level *ab initio* calculations. The objectives of the present study are (i) to investigate the potential of the title compound to form different H bonds and undergo near-neighbor interactions, with special attention to the effect of a second amino group on the conformational profile; (ii) to examine the role of hydrogen bonding in determining geometry, charge distribution, and stability of conformers; (iii) to ascertain the optimal level of quantum mechanical approximation for obtaining reliable results; (iv) to gain more information about the principles governing the intramolecular arrangement of small units of proteins that can possibly impact upon the overall structure of protein assemblies.

## Methods

The conformational space of daa is spanned by four rotations around the C−N and C−C single bonds (Chart 1). A rotation around a C−N bond is expected to give three minimum-energy structures corresponding to the staggered orientations of two adjacent $sp^3$-hybridized groups, with the equilibrium values of the torsional angle C−C−N−H being roughly −60°, 60°, and 180°.[38] A rotation around a C−C bond forms three conformers in which one of three covalent bonds of the $sp^3$-carbon

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eclipses the carbonyl group, so that the expected N−C−C−O torsional angles are −120°, 0°, and 120°.[39] The molecule would have $3^4$, i.e. 81, rotamers, provided the overlap between distant groups would not restrict the conformational space. Accordingly, the full conformational spectrum of the molecule can be obtained by complete energy refinements from these 81 rotamers. As some of the structures are physically equivalent due to symmetry, while others may not exist due to strong van der Waals or electrostatic repulsions, the full conformational spectrum of the molecule consists of a smaller number of different structures.

To avoid physically equivalent minimum-energy structures, only two of three initial values of dihedral angle $\phi_2$ are utilized, namely, 0° and 120°, since all the structures with negative $\phi_2$ could be obtained from those with positive $\phi_2$ by mirror imaging. Thus the number of initial conformations to be considered are reduced to a mere 54.

Full energy refinements from all possible rotamers of daa are performed at the Hartree−Fock HF/6-31+G* level to obtain the conformational spectrum. The energy minimization option of Gaussian-90 has been used. This approach could result in a saddle point structure only if symmetry constraints are used during minimization. However, no symmetry constraints are introduced *a priori*, and the elements of symmetry of conformers, if any, appear as a consequence of energy refinement only.

The equilibrium structures found are reoptimized at lower *ab initio* levels, HF/STO-3G, HF/6-31G, and HF/6-31G* and by the semiempirical AM1 method.[40] The aim is to check whether it is possible to reproduce the conformational spectrum by a smaller computational effort. In addition, the single-point energies of all the equilibrium structures obtained at HF/6-31+G* are calculated at higher *ab initio* levels, e.g. HF/6-311++G**, HF/6-311++G(3df,3pd), and full second-order many-body pertubation Moeller−Plesset MP2(full)6-31+G* and MP2(full)6-311++G**.

The calculations are done by the Gaussian-90 program[41] on the C3440 convex minisupercomputer of the University of the West Indies at Mona, Jamaica. However, the 6-31G* geometries of the seven lowest conformers were optimized by the TX-90 program (P. Pulay, University of Arkansas, 1990) using natural internal coordinates.[42]

A comprehensive conformational analysis of sulfur mustard [$S(CH_2CH_2Cl)_2$] has recently been performed using a Monte Carlo Conformational space search with an empirical force field description of the intramolecular interactions.[43] Such an approach is unlikely to be acceptable for the molecule under consideration; because of the potentially large number of hydrogen bonds, the results of any empirical force field or even semiempirical calculations may give rise to artifacts.

## Results

Table 1 summarizes the relative energies of the conformers obtained by full energy minimization using different methods (AM1 and HF) and various levels of theory. The choice was made in order to illustrate the extent of variation in the conformational spectrum across a range of methods and basis sets.

Table 2 specifies the conformations at the HF/6-31+G* level (HF/B3 in column 5, Table 1) by the equilibrium values of the torsional angles $\phi_1-\phi_4$ introduced in Chart 1. The 15 equilibrium structures obtained at our reference level HF/B3 are displayed in Figure 1. The conformations are also characterized by the hydrogen bond lengths (near-neighbor interactions) in Table 3. A cutoff above 2.85 Å was used for the hydrogen bonds, some of which are angularly distorted. The **Z**-matrices of the fully optimized HF/B3 geometries are given as Supporting Information.

**TABLE 1: Conformational Energies (in kJ/mol) of Different Forms of α,α′-Diaminoacetone**

| | level of theory[a,b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | full energy refinement | | | single-point calculations | | | |
| no. | AM1 | HF/B1 | HF/B2 | HF/B3 | HF/B4 | HF/B5 | MP2/B3 | MP2/B4 |
| **1** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **2** | 0.00[c] | 6.29 | 3.52[d] | 3.99 | 3.48 | 3.23 | 2.69 | 1.98 |
| **3** | 0.00[c] | 4.43 | 1.23[e] | 5.61 | 6.48 | 7.50 | 5.28 | 5.76 |
| **4** | 24.99 | 6.66 | 3.14 | 7.48 | 9.85 | 12.00 | 4.62 | 6.34 |
| **5** | 0.00[c] | 12.16 | 7.55 | 8.05 | 6.92 | 6.25 | 5.74 | 4.39 |
| **6** | 0.00[c] | 10.95 | 4.17 | 9.53 | 9.95 | 10.52 | 8.13 | 8.13 |
| **7** | 16.11 | 7.84 | 5.60 | 11.43 | 13.06 | 14.36 | 8.59 | 9.56 |
| **8** | 0.00[c] | 10.97 | 1.23[e] | 11.44 | 11.76 | 12.26 | 9.33 | 9.47 |
| **9** | 0.00[c] | 9.63 | 5.42[f] | 11.67 | 13.22 | 14.76 | 10.89 | 12.21 |
| **10** | 9.17 | 9.40 | 1.23[e] | 11.96 | 12.19 | 12.25 | 11.05 | 10.54 |
| **11** | 0.00[c] | 15.38 | 3.52[d] | 12.78 | 11.42 | 10.09 | 10.82 | 9.36 |
| **12** | 16.11 | 5.31 | 11.22 | 14.77 | 16.44 | 17.46 | 11.93 | 12.97 |
| **13** | 0.00[c] | 14.08 | 4.17 | 15.66 | 15.26 | 14.38 | 12.61 | 11.67 |
| **14** | 9.17 | 18.11 | 1.23[d] | 16.59 | 16.10 | 15.52 | 14.53 | 13.24 |
| **15** | 18.37 | 16.29 | 5.42[f] | 25.28 | 25.55 | 25.33 | 23.46 | 22.30 |

[a] Basis sets B1, B2, B3, B4, and B5 are STO-3G, 6-31G, 6-31+G*, 6-311++G**, and 6-311++G(3df,3pd), respectively. Total *ab initio* energies of the most stable form **1** at the HF/STO-3G, HF/6-31G, HF/6-31+G*, HF/6-311++G**//HF/6-31+G*, HF/6-311++G(3df,3pd)//HF/6-31+G*, MP2(full)6-31+G*//HF/6-31+G*, and MP2(full)/6-311++G**//HF/6-31+G* levels are −298.155 283, −301.867 154, −302.013 746, −302.100 252, −302.125 517, −302.934 687, and −303.209 494 $E_h$, respectively; the Hartree unit of energy, $E_h$, is equivalent to 2625.5 kJ/mol. [b] TX90 calculations at the HF/6-31G* level yield a total *ab initio* energy −302.002 722 $E_h$ for **1** and 5.46, 6.12, 9.79, 44.62, 11.40, and 11.43 kJ/mol relative energies for structures **2**−**7**. [c] Same geometry as **1**. [d] Same geometry as **2**. [e] Same geometry as **3**. [f] Same geometry as **9**.

**TABLE 2: HF/6-31+G* Equilibrium Values of Torsional Angles (in deg) in the Conformational Spectrum of α,α′-Diaminoacetone**

| | conformational parameter[a] | | | | |
|---|---|---|---|---|---|
| structure no. | $\phi_1$ | $\phi_2$ | $\phi_3$ | $\phi_4$ | symmetry |
| **1** | −58.7 | 0.0 | 0.0 | −58.7 | $C_{2v}$ |
| **2** | −164.5 | +8.0 | +26.8 | −56.3 | |
| **3** | 161.2 | 149.5 | 5.7 | −58.5 | |
| **4** | 164.2 | 126.0 | 154.1 | 77.2 | |
| **5** | 41.8 | −24.0 | −24.0 | 41.8 | $C_2$ |
| **6** | −162.8 | 23.1 | 143.1 | 160.5 | |
| **7** | −60.9 | 137.0 | 142.3 | 167.5 | |
| **8** | 162.0 | 158.5 | −13.5 | 39.3 | |
| **9** | 163.7 | 106.9 | 106.9 | 163.7 | $C_2$ |
| **10** | −58.8 | 4.2 | 150.3 | −60.9 | |
| **11** | −41.3 | 23.5 | −12.4 | 34.4 | $C_s$ |
| **12** | −57.0 | 83.6 | −129.0 | 81.7 | |
| **13** | −58.3 | 88.4 | −20.8 | 38.5 | |
| **14** | −59.9 | 142.7 | 20.9 | −159.2 | |
| **15** | −59.3 | 126.2 | 126.2 | −59.3 | $C_2$ |

[a] Dihedrals: $\phi_1$, H−N−C−C; $\phi_2$, N−C−C−O; $\phi_3$, O−C−C−N; $\phi_4$, C−C−N−H.

**A. Effect of Level of Theory on Geometry Optimizations of Conformers.** At our reference level, HF/6-31+G*, the conformational spectrum consists of 15 different energy minima, into which the 54 possible rotamers have been optimized. Fully refined AM1 calculations yield a very different spectrum comprising five energy levels only. The structures **2**, **3**, **5**, **6**, **8**, **9**, **11**, and **13** of Figure 1 all optimize to **1** on the AM1 potential energy hypersurface. In addition, **14** converges to the equilibrium structure **10**, and **12** to the structure **7**; **4** and **15** complete the spectrum. A lowering of the *ab initio* level by omitting polarization and/or diffuse functions can also produce significant changes in the conformational spectrum. At the HF/

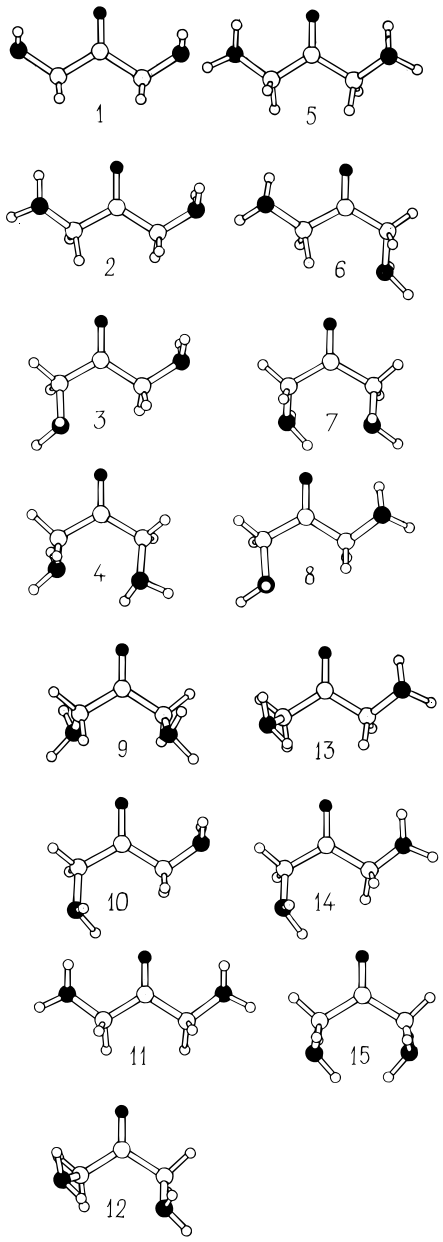


**Figure 1.** Conformers of α,α′-diaminoacetone optimized at the HF/6-31+G* level.

6-31G* level structure **5** changes to a rather flat structure of $C_2$ symmetry, showing the typical convergence characteristics of a saddle point at 44.62 kJ/mol above the reference energy of **1** (see Table 1).

At the HF/6-31G (HF/$B_2$) level, a full refinement of the 15 structures depicted in Figure 1 locates nine rotamers only. Structures **3**, **8**, **10**, and **14** are optimized into a single structure with quasiplanar amino groups. Three pairs of rotamers, viz., (**2**, **11**), (**6**, **13**), and (**9**, **15**), become 2-fold degenerate at the HF/B2 level. The role of the reduced ability to form hydrogen bonds with quasiplanar amino groups is discussed in the next section. The said reduction to just nine rotamers appears to be a particular artifact of the 6-31G basis set, as all 15 structures reappear using the minimal basis set STO-3G in HF/B1.

**B. Effect of Basis Set and Electron Correlation on Relative Energies of Conformers.** Although the number of conformers varies with the level of theory, conformer **1** of $C_{2v}$ symmetry and planar heavy-atom structure is the global energy minimum at all of the levels. The comparison is thus facilitated. At the reference level HF/B3, the conformers **1**−**15** are arranged

**TABLE 3: Hydrogen Bond Lengths (in Å) in the Conformations of α,α′-Diaminoacetone from the HF/6-31+G* Calculations**

| conformer | $NH_2$:::O | HNH···O | HNH···$NH_2$ | HCH···$NH_2$ |
|---|---|---|---|---|
| **1** | 2.752 | | | |
| **2** | 2.692 | 2.382 | | |
| | 2.838 | | | |
| **3** | 2.700 | | | 2.694 |
| | 2.765 | | | |
| **4** | | | 2.525 | 2.697 |
| **5** | | 2.375 | | |
| **6** | | 2.355 | | 2.789 |
| **7** | | | 2.539 | |
| **8** | | 2.354 | | 2.553 |
| **9** | | | | 2.767 |
| **10** | 2.710 | | | |
| | 2.751 | | | |
| **11** | | 2.343 | | |
| **12** | | | 2.724 | |
| **13** | | 2.350 | | |
| **14** | | 2.316 | | |
| **15** | | | | |

in increasing order of energy in column 5, Table 1. At the HF/6-31G* level the dissappearance of **5** is most notable as mentioned above; in addition the relative energies are somewhat raised without further changing the sequence **1**−**4** and **6**−**7**. At the HF/B2 (column 4, Table 1) the energy sequence is considerably altered. Conformer **12** has the highest energy among the nine rotamers, while the lowest energy conformer, **1**, is closely followed by **3**, to which the structures **8**, **10**, and **14** converge. At the minimal basis set (column 3, Table 1) the relative stabilities of **3**, **7**, and **12** are overestimated; thus the energy sequence is changed, with **12** stabilized by 9.5 kJ/mol.

The extension of the basis set by single-point 6-311++G** (B4) and 6-311++G(3df,3dp) (B5) calculations changes the conformational spectrum by subtle increments of less than ±2 kJ/mol. Changing from B3 to B4 places **5** below **4** and stabilizes **11** so that the closely spaced energies of **7** ≈ **8** < **9** < 10 < **11** < **12** < **13** are changed to **11** < **8** < **10** < **7** < **9** < **13** < **12**. As the total *ab initio* energy of conformer **1** is lowered by 227 kJ/mol, or 86.5 × $10^{-3}$ hartrees (Table 1), the above mentioned relative changes by less than ±2 kJ/mol represent 1% of the total effect of basis set extension.

The inclusion of additional polarization functions in basis set B5 lowers the total energy of **1** by another 66 kJ/mol (Table 1) and places **5** lower than **3** and **11** below **6** < **4** < **8** < **10** < **7** < **13** < **9** < **12**. Most conformers are, in fact, destabilized relative to **1**, with **2**, **5**, **11**, **13**, and **14** being important exceptions (Table 1, columns 6 and 7).

The effects of electron correlation are probed by single-point second-order many-body perturbation calculations, Moeller−Plesset MP2(full). The conformers **2**−**15** are almost uniformly stabilized relative to **1** by about 1−3 kJ/mol, an amount almost negligible in view of the total correlation energy of 2418 kJ/mol for **1** at the MP2(full)6-31+G*//HF/6-31+G* level. Only **3** and **4** exchange their places at this level (Table 1, columns 5 and 8). Using the B4 set, the total correlation energy of **1** at the MP2 level increases to 2912 kJ/mol; the differential correlation energy for the 15 rotamers, however, does not exceed 3.5 kJ/mol. The relative stabilizations are at this upper level for **4**, **7**, **12**, and **13** (Table 1, columns 6 and 9). Some of the changes in the conformational energy affected by HF/B4//HF/B3 are reversed toward the HF/B3 spectrum at the MP2/B4/HF/B3 level.

**C. Charge Distribution.** Complementing the energy and geometry considerations, a charge distribution study has been done for the assessment of intramolecular interactions. Table

**TABLE 4: Atomic Charges from the HF/6-311++G** Mulliken Population Analysis at the HF/6-31+G* Optimized Conformations of α,α′-Diaminoacetone[a]**

| | conformers | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| atom | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** |
| O1 | −.0357 | −0.370 | −0.353 | −0.333 | −0.382 | −0.366 | −0.337 | −0.356 | −0.296 | −0.346 | −0.374 | −0.333 | −0.362 | −0.361 | −0.328 |
| C2 | 0.752 | 0.669 | 0.534 | 0.420 | 0.595 | 0.554 | 0.467 | 0.511 | 0.231 | 0.585 | 0.575 | 0.441 | 0.602 | 0.634 | 0.534 |
| C3 | −0.694 | −0.693 | −0.492 | −0.417 | −0.519 | −0.523 | −0.544 | −0.530 | −0.430 | −0.670 | −0.504 | −0.454 | −0.497 | −0.623 | −0.613 |
| N4 | −0.374 | −0.376 | −0.420 | −0.439 | −0.418 | −0.405 | −0.385 | −0.405 | 0.382 | −0.377 | −0.419 | −0.413 | −0.409 | −0.396 | −0.379 |
| C5 | −0.694 | −0.515 | −0.618 | −0.584 | −0.519 | −0.523 | −0.550 | −0.492 | −0.430 | −0.581 | −0.504 | −0.506 | −0.610 | −0.574 | −0.613 |
| N6 | −0.374 | −0.419 | −0.369 | −0.414 | −0.418 | −0.414 | −0.421 | 0.419 | −0.382 | −0.402 | −0.419 | 0.430 | −0.391 | −0.402 | −0.379 |
| H7(C3) | 0.175 | 0.174 | 0.182 | 0.176 | 0.143 | 0.202 | 0.189 | 0.184 | 0.197 | 0.181 | 0.176 | 0.179 | 0.136 | 0.185 | 0.194 |
| H8(C3) | 0.175 | 0.181 | 0.166 | 0.209 | 0.180 | 0.150 | 0.182 | 0.172 | 0.156 | 0.184 | 0.134 | 0.178 | 0.178 | 0.205 | 0.203 |
| H9(N4) | 0.260 | 0.273 | 0.249 | 0.238 | 0.274 | 0.227 | 0.279 | 0.250 | 0.246 | 0.254 | 0.233 | 0.255 | 0.256 | 0.251 | 0.253 |
| H10(N4) | 0.260 | 0.234 | 0.236 | 0.251 | 0.233 | 0.273 | 0.241 | 0.236 | 0.246 | 0.244 | 0.278 | 0.258ϵ | 0.234 | 0.244 | 0.239 |
| H11(C5) | 0.175 | 0.184 | 0.184 | 0.187 | 0.143 | 0.175 | 0.190 | 0.148 | 0.197 | 0.194 | 0.134 | 0.165 | 0.158 | 0.185 | 0.194 |
| H12(C5) | 0.175 | 0.140 | 0.192 | 0.170 | 0.180 | 0.169 | 0.202 | 0.202 | 0.156 | 0.201 | 0.176 | 0.166 | 0.196 | 0.152 | 0.203 |
| H13(N6) | 0.260 | 0.255 | 0.256 | 0.259 | 0.274 | 0.247 | 0.252 | 0.229 | 0.246 | 0.259 | 0.278 | 0.243 | 0.276 | 0.225 | 0.253 |
| H14(N6) | 0.260 | 0.263 | 0.252 | 0.276 | 0.233 | 0.235 | 0.236 | 0.272 | 0.246 | 0.256 | 0.233 | 0.251 | 0.234 | 0.276 | 0.239 |

[a] Values corresponding to the hydrogen-bonded atoms are underlined.

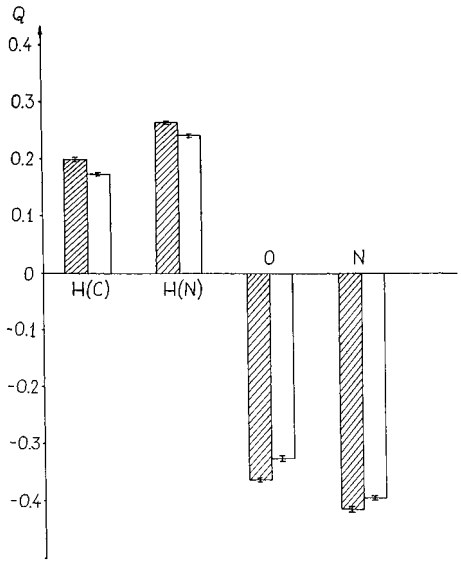


**Figure 2.** Mean values of the net atomic charges (*Q*) at the hydrogen-bonded (shaded bars) and non-hydrogen-bonded (empty bars) atoms. Standard deviations of the mean values are presented.

4 contains the results of a Mulliken population analysis at the HF/B4//HF/B3 level. In Figure 2 a comparison is made between the averaged net charges (*Q*) at the H, N, and O atoms with or without their involvement in hydrogen bonds. As expected, the acceptor atoms become more negative and hydrogen more positive. The increments of charge on H(C) and H(N) are comparable in magnitude, implying the formation of HCH···$NH_2$ to be feasible. Hence, the geometries and the charge shifts concur in assigning hydrogen bonds.

## Discussion

The conformational analysis of the title compound in the gas phase is of great interest, since it displays different types of intramolecular hydrogen bonds, dipole−dipole interactions, e.g. involving the C═O bond dipole, nonbonded through-space and through-bond interactions, and the eclipsing of different bonds. The presence of a second amino group leads to a level of complexity in hydrogen bonding not found in α-aminoacetone, α-aminoacetaldehyde, and simple amino acids like glycine or even alanine. Both amino groups can act as hydrogen bond donors or acceptors.

It is tempting to analyze the conformational spectrum in terms of H bonds alone, and some challenging pictures may evolve from such a discussion. Thus, without losing sight of other possible interactions, we rationalize the spectrum in terms of hydrogen bonding and point out the shortcomings of this approach whenever pertinent. The discussion is based on the HF/B3 results, augmented, if indicated, by those of the single-point calculations, and some HF/6-31G* results.

The symmetry of conformer **1**, also evidenced in the Mulliken population analysis (Table 4), implies equivalent interactions between the C═O and both $NH_2$ groups. According to Vishveswara and Pople,[15] α-aminoacetaldehyde and α-aminoacetic acid (glycine) both display one set of acceptor-bifurcated hydrogen bonds, i.e. $NH_2$:::O, in their most stable conformations. A reasoning along the same lines calls for a novelty in hydrogen bonding: two sets of acceptor-bifurcated H bonds on the same carbonyl oxygen, i.e. $NH_2$:::O:::$H_2N$. The population analysis caters to such an interpretation, as all four amino hydrogens have the same enhanced positive charge (Table 4). This picture postulates two H bonds per lone pair of oxygen. Similarly, structure **2** implies more than two H bonds per oxygen, in this case $NH_2$:::O···HNH. The structures **2**, **3**, and **10**, however, contain distorted bifurcations, conceivable as a consequence of other interactions. The consideration of the two most stable conformers of daa raises the question whether a *single lone pair* is able to sustain a bifurcated hydrogen bond. The answer seems to be yes.

Near-neighbor stabilization between the amino and the carbonyl groups is found in conformers **2**, **5**, **6**, **8**, **11**, **13**, and **14** and is readily described by the NH···O bonds. Two such bonds are encountered in each of the higher energy conformers **5** and **11**. The average over seven NH···O bond lengths is 2.354 Å, whereas the bifurcated $NH_2$:::O bond length is on average 2.744 Å. The fact that **5** is unstable at the HF/6-31G* level adds to the recently published evidence that the basis set has to include both polarization and diffuse functions to be capable of predicting reasonable geometries for amino acids and peptide models.[44]

In **4**, **7**, and **12** the two amino groups interact, one of them being the hydrogen donor and the other acting as the acceptor. At the HF/B3 level, the strength of the $NH_2$···$NH_2$ bond appears to resemble closely that of the HNH···O bond. This seems to be at variance with the established ordering of *intermolecular* H bond strengths, viz. HN···O > NH···N.[45] Our single-point calculations with additional polarization functions, HF/B4 and HF/B5 (Table 1), show a selective stabilization for **2**, **5**, **11**, **13**, and **14**, which can be attributed to a more effective description of the NH···O bond at the higher levels. Note that the stabilization is higher by a factor 2 for **5** and **11** with their two NH···O bonds. Thus the *intramolecular* H bond strengths

are not really at variance with their *intermolecular* counterparts. In general, however, it is hardly possible to compare *intramolecular* H bonds quantitatively because of the difficulty in choosing proper reference points.[15,18]

Relatively weak hydrogen bonds between nitrogen lone pair and methylene hydrogens have been described for intermolecular systems from high-resolution spectroscopic studies[46] and theoretical calculations.[47−49] A systematic survey of crystallographic data has revealed the importance of CH···N and CH···O bonds in determining the stable structures of organic crystals including amino acids and nucleosides.[26,50−52]

In daa the geometry allows for distorted $HCH\cdots NH_2$ bonds to be formed in **3**, **4**, **6**, **8**, and **9**, with the C−H−N angles being around 90° only. The range in hydrogen bond lengths (0.23 Å) is comparable to the variation in bond lengths for $C_{sp}-H\cdots NH_3$ and $C_{sp3}-H\cdots NH_3$ interactions.[50−52] In contrast to the other H bonds, these interactions show very little dependence on the extension of the basis set beyond B3.

Alternatively, the dipole−dipole interaction between the $CH_2$ group moment and the $C-NH_2$ bond moment may have a stabilizing influence upon **3**, **6**, **8**, **10**, and **14**. It is an indication of the complexity of the near-neighbor interactions present that in all conformers with the exception of **1** and **15** at least one dihedral angle deviates strongly from the standard values.

The increased positive net charge on H(C) and H(N) by an average of 0.03 is in excellent agreement with the corresponding increase on H(O) upon intramolecular hydrogen bonding in glycolic acid and glycolaldehyde (0.024)[18] and α-aminoacetaldehyde (0.032) on aldehyde hydrogen.[15] It is interesting to note that the immediate environment of hydrogen does not seem to exert a strong influence in all these diverse intramolecular interactions, as assessed by Mulliken population analysis.

The AM1, STO-3G, 6-31G, and 6-31G* results indicate that it is not safe to survey the full conformational space by a reduced computational effort. The approach recently used by Gronert and O'Hair,[23] i.e. the search for the full conformational spectrum using AM1 optimizations and a subsequent refinement at the HF/6-31G* level, is prohibitive for our system (Table 1, column 2) and cannot be recommended as a general procedure. The AM1 parametrization appears to be deficient for intramolecular NH···O bonds, c.f. conformational energies for **2**, **5**, **6**, **8**, **11**, and **14**. Similarly a comprehensive scanning at the HF/6-31G level is bound to overlook several conformers. At this level the pyramidality of the amino group is significantly underestimated. In consequence the nitrogen atom loses the ability to form hydrogen bonds. The conformers differing by a $HCH\cdots NH_2$ bond at the HF/B3 level, viz., **3** and **10**, **6** and **13**, **8** and **14**, **9** and **15**, cannot be differentiated after a refinement at the HF/B2 level. The importance of diffuse functions is highlighted by the failure to stabilize **5** at the HF/6-31G* level. This is further evidence for the conclusion that polarization and diffuse functions have to be included in the basis set in order to do a successful *ab initio* conformational survey of daa and amino acids.

While diamides are favored mimics for peptide and protein modeling, they are not yet amenable to full conformtional survey nor can the problems of backbone conformation and nearest-neighbor interactions be completely understood. The present case study offers a simpler scenario while retaining the essential structural motifs. It is evident from this full *ab initio* conformation study of α,α′-diaminoacetone that hydrogen bonds and dipole−dipole interactions are responsible for the conformational profile. In the larger molecular assemblies, the dihedral angle deviations would provide clues to the manner in which the spatial orientation of the components is formatted by networks of such noncovalent interactions.

To sum up, the conformational space of α,α′-diaminoacetone consists of 15 structures. The conformer at the global energy minimum possesses high symmetry ($C_{2v}$) at all levels of theory. The systematic conformational space search of the molecule requires relatively high *ab initio* level to calculate the conformational energy sequence.

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**Supporting Information Available:** **Z**-matrices of the fully optimized HF/B3 geometries (16 pages). Ordering information is given on any current masthead page.

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