The γ Turn: Ab Initio Calculations on Proline and *N*-Acetylproline Amide

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Abstract: Ab initio calculations were used to obtain geometries and total energies for proline, *N*-formylproline amide, and *N*-acetylproline amide. The most stable conformation of *N*-acetylproline amide contains a hydrogen bond between the acetyl oxygen and one amide hydrogen, as found in γ turns. With few exceptions, the predicted geometrical parameters are in good agreement with the experimental results. These results provide a basis for ab initio calculations on γ and β turns containing proline, which would be useful in the design of unnatural protein structures.

Proline

The important role played by proline (Pro) and its derivatives in enzymes and in proteins and peptide hormones is well-known. Its structural features have been studied by experimental methods (X-ray crystallography, NMR, IR, and CD spectroscopies) and theoretical calculations (molecular mechanics,[3] PCILO[4]).

Proline-containing peptides have been investigated in the solid state and in solution. Some of these studies focused on tight turns, specifically on the β turn with a 1:4 hydrogen bond and the γ turn with a 1:3 hydrogen bond. While β turns are a common occurrence in proteins and peptides, γ turns are less frequent. Nemethy and Printz[5] first proposed the γ turn as a possible feature of polypeptide and protein conformations.

This study describes ab initio calculations on proline (**1**), *N*-formylproline amide (**2**), and *N*-acetylproline amide (**3**). The atomic names for these compounds are shown in Figure 1A. These calculations were motivated by the need for theoretical support for the evidence of γ turns in small peptides as well as by the need to predict feasible β turns in engineered proteins such as betabellin 3,[6] which has six β turns containing proline. These results will facilitate ab initio calculations on larger structures that are reasonable models of β turns containing proline. One such model having proline in the second of the four positions of the β turn is shown in Figure 1B. *N*-Acetylproline amide represents a part of this model.

Two instances of gamma turns found in crystalline proteins are Ser(25)-Thr(26)-Tyr(27) of thermolysin[7] and Ile(79)-Thr(80)-Val(81) of satellite tobacco necrosis virus protein.[8] In both cases a 1:3 hydrogen bond is present between the carboxyl oxygen of the first residue and the amino hydrogen of the third residue. Gamma turns have been observed in several instances in small cyclic peptides containing proline. Among these are the Gly-Pro-Gly turn of *cyclo*-(Pro-Gly-Pro-Gly-Pro-Gly),[9] the D-Ala-Pro-Gly turn of the *cyclo*-(Gly-D-Ala-Pro-Gly-Pro) in solution[10] and in the crystalline state,[11] and the D-Phe-Pro-Gly turn of a *cyclo*-(Gly-D-Phe-Pro-Gly-Pro) pseudopeptide in solution.[12] In each of these cases, the central residue is proline. This tendency for proline to favor the formation of an intramolecular hydrogen bond is even seen for *N*-acetylproline methylamide in carbon tetrachloride.[13] In the crystalline state, however, this compound forms intermolecular hydrogen bonds rather than the intramolecular 1:3 hydrogen bond of the γ turn.[14] Therefore, ab initio calculations were performed in order to see if the most stable conformations for *N*-formylproline amide and *N*-acetylproline amide resemble the γ turn.

The C7 structure which features a seven-atom ring formed via a hydrogen bond between CO and NH which is the 1:3 hydrogen bond of a γ turn has been found experimentally and predicted theoretically for other systems also.[15]

Avignon et al.[16] considers the general formula $CH_3CO_3NR_1CHR_2(ON(R_3)_2$, which can feature a C_5 or a C_7 structure depending on the nature of R_1, R_2, or R_3. Their infrared studies prove the stability of the hydrogen-bonded structures. Pullman et al.[17,18] use the PCILO procedure to predict a C_7 structure for glycyl-L-alanine dipeptide. Their PCILO studies of *N*-acetyl-*N'*-methylproline amide, which is the system studied in this paper, suggest the existence of a C_7 structure but not as a global minimum on the energy curve.

Cabrol et al.[4] attribute this to the planarity of the proline ring. Their PCILO calculations of Ac-Pro-Pro-GlyMe_2A show C_7 to be the most stable structure for an endo proline ring. Since the geometries are not optimized, but kept rigid in both studies, the influence of the ring puckering on the stability of C_7 is not clear. Indeed, other systems such as Ac-Ala-NHMe, where the proline ring is totally absent, are found experimentally and theoretically to exhibit the 1:3 hydrogen bond,[15] but this might be due to the freedom of movement of Ac-Ala-NHMe which allows it to adopt the C_7 conformation. However, the endo conformation of the proline ring studied by Cabrol[4] as well as the ORD studies of Schellman and Neilson [19] indicate C_7 to be the most stable structure for *N*-acetyl-*N'*-methylproline amide.

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(2) The Rockefeller University.
(3) DeTar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1977**, *99*, 1232.
(4) Cabrol, D.; Brock, H.; Vasilescu, D. *Int. J. Quantum Chem.* **1979**, *6*, 365.
(5) Nemethy, G.; Printz, M. P. *Macromolecules* **1972**, *6*, 755.
(6) Erickson, B. W.; Daniels, S. B.; Reddy, P. A.; Unson, C. G.; Richardson, J. S.; Richardson, D. C. In *Computer Graphics and Molecular Modeling*; Zoller, M., Fletterick, R., Eds.; Cold Spring Harbor Laboratory: Cold Spring Harbor, New York, 1986; pp 53-57.
(7) Matthews, B. W. *Macromolecules* **1972**, *6*, 818.
(8) Jones, T. A.; Liljas, L. *J. Mol. Biol.* **1984**, *177*, 735.
(9) Madison, V.; Atreyi, M.; Deber, C. M.; Blout, E. R. *J. Am. Chem. Soc.* **1974**, *96*, 6725.
(10) Pease, L. G.; Watson, C. *J. Am. Chem. Soc.* **1978**, *100*, 1279.
(11) Karle, I. L. *J. Am. Chem. Soc.* **1978**, *100*, 1286.
(12) Spatola, A. F.; Anwer, M. K.; Rockwell, A. L.; Gierasch, L. M. *J. Am. Chem. Soc.* **1986**, *108*, 825.
(13) Mizushima, S.; Shimanoucki, T.; Tsuboi, M.; Sugita, T.f Kurosaki, K.; Matagu, M.; Souda, S. *J. Am. Chem. Soc.* **1952**, *74*, 4639.
(14) Matsuzaki, T.; Itaka, Y. *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen Crystallogr.* **1971**, *27*, 5007.
(15) Beveridge, D. L.; Ravishankar, G.; Mezei, M.; Gedulin, B. Sarma, M. H., Eds.; Adenine: 1986 and references within.
(16) Avignon, M.; Huong, P. V.; Lascombe, J.; Lascombe, M.; Marraud, M. Neel, J. *Biopolymers* **1969**, *8*, 69.
(17) Pullman, B.; Maigret, B.; Perahia, D. *Theor. Chim. Acta* **1970**, *18*, 44.
(18) Maigret, B.; Perahia, D.; Pullman, B. *J. Theor. Biol.* **1970**, *29*, 275.
(19) Schellman, J. A.; Neilson, E. B. In *Conformation of Biopolymers*, Ramachandrau, G. N., Ed.; Academic: London, 1967; Vol. 1, p 109.
(20) Bandekar, J.; Krimm, S. *Int. J. Pept. Protein Res.* **1985**, *26*, 407.

0002-7863/87/1509-3526$01.50/0

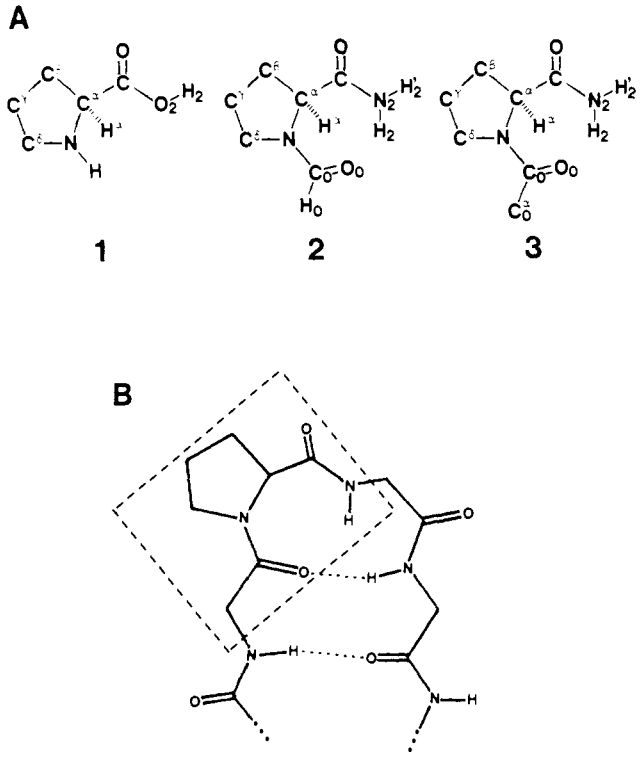

Figure 1. (A) Atomic names for proline (**1**), *N*-formylproline amide (**2**), and *N*-acetylproline amide (**3**). (B) Structure of a β turn. The boxed atoms are present in **3**.

Table I. Optimized Geometries of Proline Structure **1**

parameter	STO-3G	6-31G	exp (ref 25)
	Lengths, Å		
$NC^{\alpha} = NC^{\delta}$	1.488	1.480	1.480
$C^{\alpha}C^{\beta} = C^{\gamma}C^{\delta}$	1.557	1.540	1.530
$C^{\beta}C^{\gamma}$	1.560	1.546	1.530
$C^{\alpha}C$	1.574	1.554	
CO	1.217	1.212	1.240
CO_2	1.388	1.353	
O_2H_2	0.990	0.956	
NH	1.033	.996	
	Angles, deg		
$C^{\alpha}NC^{\delta}$	108.0	108.0	107.1
$NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$	110.0	110.0	106.2
HNC	107.3	115.8	
$NC^{\alpha}C$	112.0	105.8	
CO_2H	104.8	114.0	
$NC^{\alpha}CO_2(\psi_1)$	173.0	177.0	170.0
$NC^{\alpha}CO$	−7.0	−0.3	−6.9

Methods and Results

The Gaussian 80 computer program[21] was used to solve the Roothaan equations for the Hartree–Fock approximation with Gaussian basis sets. The basis sets used are the minimal set STO-3G[22] and the split-valence basis set 6-31G,[23] both with standard scaling factors. The geometries were optimized with the Berny gradient optimization method,[24] except that the angles $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ and the angle $C^{\alpha}NC^{\delta}$ were subjected to point-by-point optimization.

Proline. The proline molecule was investigated with both the STO-3G and 6-31G basis sets. The geometry was optimized with the carboxyl group set on the same side of the ring (cis) as the N–H bond. The angles $C^{\alpha}NC^{\delta}$ and $NC^{\alpha}C^{\delta} = NC^{\delta}C^{\gamma}$ were optimized point-by-point by using a grid search with 0.5° increments and the STO-3G basis set. The search was performed by setting these three angles at fixed values and relaxing all other parameters of the molecule with the constraints that $NC^{\alpha} = NC^{\delta}$ and $C^{\alpha}C^{\beta} = C^{\delta}C^{\gamma}$. The values thus obtained for the three angles were used to optimize the rest of the molecule with the 6-31G basis set. The optimized geometries of the resulting structure **1a** (Figure 2) are compared with experimental values[25] for proline in Table I.

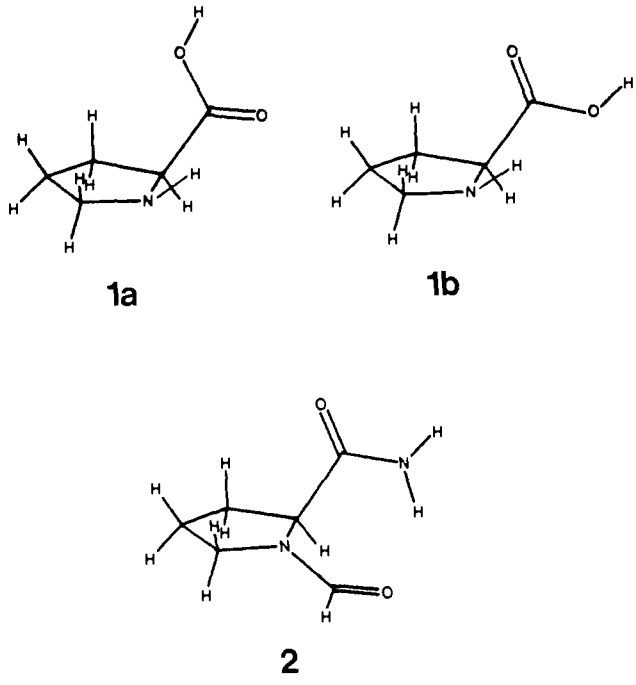

Figure 2. Optimized geometries of proline (**1**) and *N*-formylproline amide (**2**).

Table II. Optimized Geometries of *N*-Formylproline Amide (**2**) and *N*-Acetylproline Amide (**3**)

parameter	2	3a	3b	exp (ref 14)	exp (ref 11)
		Lengths, Å			
NC^{α}	1.465	1.464	1.465	1.471	1.494
NC^{δ}	1.464	1.463	1.462	1.476	1.473
$C^{\alpha}C^{\beta} = C^{\gamma}C^{\delta}$	1.555	1.555	1.559	1.530	1.533
$C^{\beta}C^{\gamma}$	1.573	1.572	1.569	1.503	1.512
C_0N	1.408	1.419	1.430	1.338	
C_0O_0	1.223	1.227	1.220	1.244	
$C_0{}^{\alpha}C_0$	1.542	1.542	1.490		
C^{α}	1.573	1.573	1.568	1.530	
CO	1.221	1.221	1.220	1.231	1.223
CN_2	1.397	1.396	1.403	1.317	1.365
N_2H_2	1.016	1.016	1.013		
		Angles, deg			
$C^{\alpha}NC^{\delta}$	114.0	114.0	114.0	112.2	112.2
$NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$	106.5	106.5	106.5	103.4	103.1
C_0NC^{δ}	120.5	122.4	122.8	125.5	127.6
O_0C_0N	124.4	121.	120.9	120.1	
$C_0{}^{\alpha}C_0N$		116.0	115.6	117.0	
$C^{\alpha}CO$	123.6	123.4	122.7	117.7	123.3
$C^{\alpha}CN_2$	112.4	112.5	114.3	117.9	113.5
$C_0NC^{\alpha}C^{\delta}$	−155.5	−156.2	−153.0	176.3	
$C_0NC^{\alpha}C(\phi_1)$	−83.5	−84.0	−85.1	−76.3	−86.0
$NC^{\alpha}CN_2(\psi_1)$	62.7	65.0	−24.0	−15.9	70.0
$O_0C_0NC(\omega_0)$	16.8	12.0	7.6	4.3	
$C_0{}^{\alpha}C_0NC^{\alpha}$	−164.8	−170.0	−174.8	−177.0	
$NC^{\alpha}CO$	−118.7	−117.0	157.9		
$CC^{\alpha}N$	112.0	112.3	112.8	114.3	

(21) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seegar, R.; DeFrees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. Gaussian 80; Carnegie Mellon University: Pittsburg, PA, 1981.
(22) Hehre, W. J.; Stewart, R. F.; Pople, J. A. *J. Chem. Phys.* **1969**, *51*, 2657.
(23) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2256.
(24) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214.
(25) Kayushina, R. L.; Vainshtein, B. K. *Sov. Phys.—Crystallogr.* (*Engl. Transl.*) **1966**, *10*, 698.

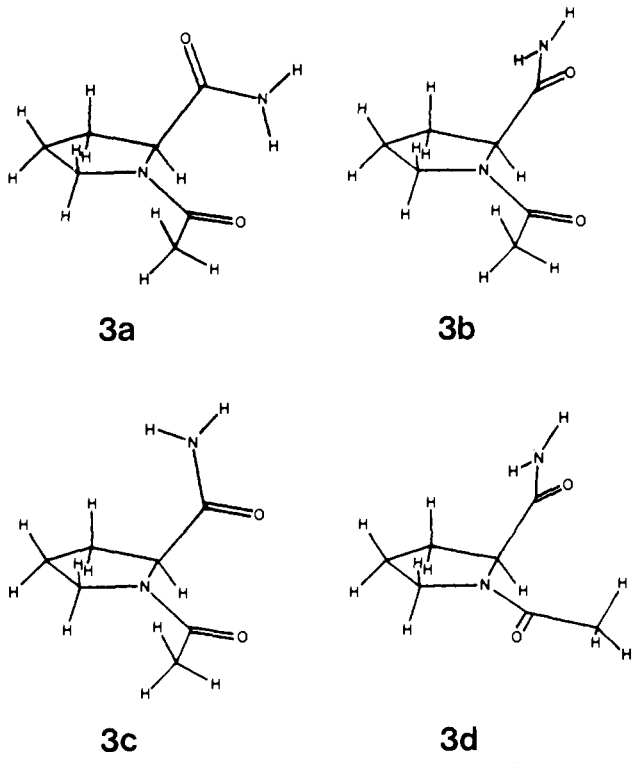

Figure 3. Optimized geometries of *N*-acetylproline amide (**3**).

Table III. Total Energies (Hartrees) and Relative Energies (kcal/mol)

structure	STO-3G	6-31G	STO-3G	6-31G
1a	−393.7066	−398.5713	0	0
1b	−393.7016	−398.5642	3.1	4.5
2	−485.4196			
3a	−524.0072		0	
3b	−524.0013		3.7	
3c	−523.9886		11.7	
3d	−524.0007		4.1	

Ring puckering, which was investigated by optimizing $C^{\beta}C^{\alpha}NC^{\delta}$ and $C^{\gamma}C^{\delta}NC^{\alpha}$ dihedral angles, differs from the experimental values for both the STO-3G and 6-31G results. In addition, the $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ angles assume a larger value than the experimental one. Thus an additional set of calculations was performed by fixing the latter angles at their experimental values and allowing the ring to pucker by starting with a larger value for the dihedral angles $C^{\gamma}C^{\delta}NC^{\alpha}$ and $C^{\beta}C^{\alpha}NC^{\delta}$. During energy optimization, these dihedral angles became quite small, which made the ring nearly planar. The resulting total energy was higher than the one reported in Table III for structure **1a**.

Calculations were also performed with the carboxyl group trans to the N–H bond. The optimized parameters for this case were the $C^{\gamma}C^{\delta}NC^{\alpha}$, the $C^{\beta}C^{\alpha}NC^{\delta}$, and the ψ_1 angles. The rest of the molecular parameters were assigned the values obtained for structure **1a** through optimization. In all of the above calculations, the CH bond lengths for ring carbons were set equal, the $HC^{\beta}C^{\alpha}$ and $HC^{\gamma}C^{\delta}$ angles were set equal, and the ring HCCN dihedral angles were set equal.

In order to determine the strength of the electrostatic stabilization provided by the proximity of atoms H and O, calculations were performed on structure **1b** having the $NC^{\alpha}CO_2$ angle (ψ_1) fixed at 90° and the $NC^{\alpha}CO$ angle fixed at −90°, by optimizing the rest of the molecular geometry as described above.

***N*-Formylproline Amide.** This proline derivative was investigated by only the STO-3G basis set because no major differences were seen between the optimal geometries calculated for proline with the STO-3G or 6-31G basis set. Structure **2** of Figure 2 having an intramolecular hydrogen bond between O_0 and H_2 was studied. Since the formyl group was presumed to be coplanar with the ring due to π overlap, the ring N was expected to assume sp^2 character. Thus the $C^{\alpha}NC^{\delta}$ and the $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ angles were reoptimized by using a grid search with a 1° increment for $C^{\alpha}NC^{\delta}$ and an 0.5° increment for the $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ angles. During this search the $NC^{\alpha} = NC^{\delta}$ bond constraint was removed.

In order to test the reliability of the $C_0NC^{\alpha}C^{\delta}$ angle predicted by the STO-3G basis set, a calculation was performed for *N*-formylpyrrolidine. As expected, the formyl group was found to be coplanar with the ring. Table II shows the final parameters for structure **2**. A calculation in which $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ were kept at the experimental value[14] was also performed for *N*-formylproline amide. For both STO-3G and 6-31G basis sets, the ring became planar and the final energy was higher than in the absence of this constraint.

***N*-Acetylproline Amide.** The $C^{\alpha}NC^{\delta}$ and $NC^{\alpha}C^{\beta} = NC^{\delta}C^{\gamma}$ angles were kept fixed at the values found for *N*-formylproline amide, and the rest of the parameters of the molecule were optimized under the same constraints applied to the *N*-formylproline amide. Three *trans*-peptide conformations of *N*-acetylproline amide were investigated. Structure **3a** has a 1:3 hydrogen bond between O_0 and H_2. Structure **3b**, which is similar to the experimental structure seen for *N*-acetylproline methylamide,[14] lacks a hydrogen bond between O_0 and H_2 and has N_2 above the plane of the ring. Structure **3c** has oxygens O_0 and O set cis to one another in close proximity (2.8 Å). Finally, one *cis*-peptide conformation of *N*-acetylproline amide (**3d**), which differs from **3b** by the reversal of the positions of O_0 and C_0^{α}, was studied. Optimized geometries for **3a** and **3b** are shown in Table II. Also listed are crystallographic parameters for *N*-acetylproline methylamide[14] and for the D-Ala-Pro-Gly γ turn of *cyclo*-(Gly-D-Ala-Pro-Gly-Pro).[11]

Discussion

As seen from Tables I and II, most of the predicted geometrical parameters are in good agreement with the experimental results. The parameters of structure **3a** are close to the experimental values found by Karle[11] for crystalline *cyclo*-(Gly-D-Ala-Pro-Gly-Pro), specifically those of the proline residue Pro in the γ turn. Structure **3b** is close to the crystal structure of *N*-acetylproline methylamide investigated by Matsuzaki and Iitaka,[14] which contains intermolecular rather than intramolecular hydrogen bonds. Particularly good agreement is obtained for the ψ_1 angle, for the $C^{\alpha}NC^{\delta}$ angles of proline and the other structures, and for most of the bond lengths. As observed before,[26] the lengths of the NC peptidic bonds are somehwat overestimated at the STO-3G level.

The puckering of the pyrrolidine ring is poorly predicted by both the STO-3G and 6-31G basis sets. As found experimentally, C^{β} and C^{γ} are found on the same side of the average plane of the ring. But the dihedral angles which they form with the $C^{\alpha}NC^{\delta}$ plane are only 0.3° and 0.2°, respectively, for STO-3G and only 0.6° and 0.2°, respectively, for 6-31G. The ring in proline is thus calculated to be almost planar, as is also the case for *N*-formyl- and *N*-acetylproline amide. These results are not surprising, because the inability to predict ring pucking is a known flow of Hartree–Fock calculations using minimal or split-valence Gaussian basis sets.[27] Although this inadequacy can be removed by the addition of polarization functions, this modification is not feasible for systems of the present size.

If the ψ_1 angle of proline is frozen at 90° to give **1b**, which removes the electrostatic stabilization due to the proximity of O and H, the energy increases by 3.11 (STO-3G) or by 4.5 kcal/mol (6-31G). The geometry of the rest of the molecule does not change significantly. A structure having H on the opposite side of the ring from the carboxyl group is less stable than **1a**.

For both **2** and **3a**, C_0 is found below the plane of the ring, so that the $C_0NC^{\alpha}C^{\delta}$ angle is 155° instead of the expected 180°. Since this effect is absent in *N*-formylpyrrolidine, we conclude that the STO-3G calculations overestimate the repulsion between

(26) Sapse, A. M.; Fugler, L.; Cowburn, D. *Int. J. Quantum Chem.*, in press.
(27) Pople, J. A. In *Applications of Electronic Structural Theory*; Schaefer, H. F., Ed.; Plenum: New York, 1977.

O_0 and the carboxamide group on C^α. The peptide dihedral angle ω_0 is twisted slightly out of plane, which agrees with the X-ray results of Karle.[11] Structure **3b** ($\omega_0 = 7.6°$) exhibits less twist than **3a** ($\omega_0 = 12°$), which suggests that the twisting is partially due to 1:3 hydrogen bond formation. the ϕ_1 and ψ_1 angles are in good agreement with the respective experimental results and with the results of Cabrol et al.[4] The angle ϕ_1 is related to the $C_0N_1C_1^\alpha C_1^\beta$ angle which describes the puckering of the ring. As such, it might be expected to differ from the experimental values. However, this difference is very small, as seen in Table II.

Table III shows that **3a** is the most stable conformation for *N*-acetylproline amide. Since the calculations did not take into account solvent effects and can not reproduce the solid-state environment, the calculated results should more closely resemble experimental results in the gas phase or a nonpolar solvent. Indeed, they best reproduce the results obtained for *N*-acetylproline methylamide in carbon tetrachloride.[13] In this solution the intramolecular 1:3 hydrogen bond is present, while in the crystalline state[14] intermolecular hydrogen bonding is observed. Since in the gas-phase intermolecular hydrogen bonding is not considered, structure **3b** is higher in energy than **3a** by 3.7 kcal/mol. This energy difference is an estimation of the strength of the 1:3 hydrogen bond and is typical of a strained hydrogen bond. This bond is strained because the $O_0H_2N_2$ angle is 149° instead of the more favorable 180°. This angle and the 1.80-Å distance between O_0 and H_2 agree well with the values of 138° and 1.78 Å predicted for the 1:3 hydrogen bond of the γ turn.[5] The estimated hydrogen bond energy of 3.7 kcal/mol is close to the value of 4.5 kcal/mol found by Nemethy and Printz[5] (a molecular mechanics calculation). Their ψ_1 and ω_0 angles are also in good agreement with our results and in good agreement with the experimental data of ref 11.

As shown by Bandekar and Krimm,[20] for $CH_3CO(L\text{-}Ala)_3NHCH_3$, in a γ turn the $H_i + 2 - O_i$ distance is in the range 1.86–2.13 Å, close to the 1.8-Å value found in this work. Their ϕ_2 and ψ_2 angles, called in this work ϕ_1 and ψ_1 agree with our result for the structures they call γ_m and γ_1, where γ_m contains an equatorial C_7.

Structure **3c** is much higher in energy than **3a** because of the repulsion between the negatively charged oxygens O_0 and O_2. This structure does not represent a local minimum but only a point on the energy surface.

The cis structure **3d** is higher in energy than **3a** by 4.1 kcal/mol. This energy difference, which is due to the loss of the hydrogen bond, is very close to the value of 3.7 kcal/mol between **3a** and **3b**. Replacing the acetyl and amide groups by amino acid residues may permit formation of the 1:4 hydrogen bond present in the *cis*-proline turn. The energy thus obtained may compensate for the loss of the 1:3 hydrogen bond.

In conclusion, ab initio calculations have shown that *N*-acetylproline amide forms the 1:3 hydrogen bond found in the γ turn. The energy of the hydrogen bond is estimated to be 3.7 kcal/mol. The cis conformation **3d** of *N*-acetylproline amide is higher in energy than the 1:3 hydrogen-bonded trans conformation **3a** by 4.1 kcal/mol and higher than the trans conformation **3b** with no hydrogen bond by only 0.4 kcal/mol. This last result agrees well with the results of the molecular mechanics calculations of DeTar and Luthra[3] for the cis and trans conformations of *N*-acetylproline methyl ester, which cannot form a hydrogen bond. It also agrees with the result of Pullman et al., who find a 0.5 kcal/mol stability of the trans non-hydrogen-bonded isomer over the cis isomer.

It is clear that the ab initio calculations at the STO-3G level are able to identify the structure C_7 as the most stable, being a global minimum on the energy hypersurface even though the puckering of the proline ring is underestimated.

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Electrostatic Potentials and Relative Bond Strengths of Some Nitro- and Nitrosoacetylene Derivatives

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Abstract: A computational analysis of the structures and properties of a group of substituted acetylenes has been carried out by means of an ab initio self-consistent-field molecular orbital procedure (GAUSSIAN 82). The molecules studied were acetylene, its singly and doubly substituted nitro and nitroso derivatives, methylnitroacetylene, and aminonitroacetylene. The properties computed were the molecular electrostatic potentials and the bond orders, used as measures of relative bond strengths. Among the interesting structural features found for these molecules are a slight nonlinearity of the C≡C—N portions of mono- and dinitrosoacetylene and the fact that the two substituents in dinitro- and dinitrosoacetylene are not coplanar but rather lie in perpendicular planes. The presence of NO_2 is observed to strengthen the C≡C bond, whereas NO substitution weakens it. The combination of NO_2 and NH_2 (a strong electron donor) has an overall weakening effect, relative to acetylene. The C–NO_2 bonds are found to be stronger than the C–NO bonds. The electrostatic potential analyses show that the introduction of NO_2 completely eliminates the negative regions associated with the triple bond, thus rendering it less susceptible to electrophilic attack. There are found to be buildups of positive potential above the C–NO_2 bonds, indicating that these can serve as initial sites for nucleophilic attack.

Substituted acetylenes, R—C≡C—R′, are of considerable interest as potential precursors in a variety of useful syntheses; e.g., cycloadditions with carbenes, olefins, and other acetylene derivatives yield small ring systems, while Diels–Alder reactions with cyclic dienes can lead to aromatic and cage-type molecules.[1,2] Depending upon the choice of substituents R and R′, a wide range of products can, in principle, be obtained. It is important, therefore, to understand how the reactive properties of R—C≡C—R′ are affected by the natures of R and R′.

(1) March, J. *Advanced Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1977; Chapter 15.

(2) Bastide, J.; Henri-Rousseau, O. *The Chemistry of the Carbon-Carbon Triple Bond*, Part 1; Patai, S., Ed.; John Wiley & Sons: New York, 1978; Chapter 11.

0002-7863/87/1509-3529$01.50/0