isotope effects and suicide inactivation in P450-mediated epoxidations[11] and primary kinetic isotope effects in methyl group hydroxylations.[12]

It is important to note that the simple oxene model's apparently wide applicability suggests only that the active oxygen species of cytochrome P450 oxidations has radical character. It should not be construed as implying that the enzymatic oxygen is a free atomic oxygen. What has been claimed is that, thus far, the *reactions* of triplet oxene with various organic compounds seem to have a great deal in common with P450-mediated oxidations of the same or similar compounds and have provided a qualitative framework within which a consistent set of mechanisms has been built up. The actual relationship of this oxygen with both the heme iron and the substrate during oxidation remains to be elucidated.

Acknowledgment. Computations were performed on the CDC 7600 computer at Lawrence Berkeley Laboratory and the Computer Resources VAX 11/780 at SRI International. We thank Dr. Dale Spangler for helpful comments and advice and Dr. Tetsuro Oie for performing the ab initio calculations. Support from NIH Grant No. GM 27943-02 and NCI Contract No N01-CP-15730 is gratefully acknowledged. B.A.M. is a Pharmacology Research Associate, National Institute of General Medical Sciences.

Registry No. CCl_4, 56-23-5; $CHCl_3$, 67-66-3; cytochrome P450, 9035-51-2.

Ab Initio Studies of Molecular Geometries. 27. Optimized Molecular Structures and Conformational Analysis of N^{α}-Acetyl-N-methylalaninamide and Comparison with Peptide Crystal Data and Empirical Calculations

J. N. Scarsdale,[†] C. Van Alsenoy,[†] V. J. Klimkowski,[†] Lothar Schäfer,*[†] and Frank A. Momany[‡]

Contribution from the Departments of Chemistry, University of Arkansas, Fayetteville, Arkansas 72701, and Memphis State University, Memphis, Tennessee 38152.
Received April 6, 1982

Abstract: The molecular geometries (bond distances and bond angles) of N^{α}-acetyl-N-methylalaninamide were refined in seven characteristic areas of its conformational space by ab initio gradient relaxation at the 4-21G level. The optimized conformations in order of increasing energy are C_7^{eq} (I), C_5 (II), C_7^{ax} (III), β_2 (IV), α_R (V), α_L (VI), and α' (VII). The variations in local geometry found between the conformations investigated are discussed in detail. It is found that comparable bond distances and bond angles in different conformations can vary by 0.025 Å and up to 7.5°, respectively. Small deviations from planarity of the peptide group (up to 8°) are found for some of the conformations. The calculations confirm a previously suggested correlation between the ϕ and ψ angles in the helical forms of the dipeptide, which is in agreement with observed protein structure data and high-resolution crystal structures of small polypeptides. Details in the refined local geometries confirm that it is reasonable to rationalize this correlation in terms of a dipeptide specific intramolecular interaction between atoms N7 and H18 (Figure 1). This interaction, which is directed perpendicularly to the peptide bond, may be an important contribution to the formation and stability of bend type structures in proteins. The significance of the variations in local geometry for empirical conformational analysis of proteins is discussed.

In the last decade it has become common practice to investigate the conformational and structural features of peptides by computational methods. Model dipeptides and other systems have been studied by limited basis set ab initio methods,[1-4] as well as by many different semiempirical and empirical methods.[5-8] These calculations have given us a general understanding of conformational parameters at low-energy minima in the conformational space. However, little detailed information is available for comparing the effects of changes in conformation on the local geometry of the peptide. This is true even when considering high-resolution experimental data found from crystal structures, where a variety of conformations for equivalent molecules are simply not found.

For molecules larger than dipeptides, one must move away from rigorous computational studies into the area of empirical energy calculations, where approximations of forces and geometries are only as good as the data and equations used to define the force field. Empirical methods are necessary if one wishes to study larger molecular systems simply because the rigorous methods are incapable of handling a large number of atoms at a reasonable computational expense. Thus, empirical methods have been used to find low-energy conformations of polypeptides containing up to ~14 amino acids[9,10] and have been used in protein structure refinement studies.[11]

The study described here on the molecule N^{α}-acetyl-N-methylalaninamide (Ala) is an attempt to fill in some important gaps in our understanding of peptide structure. One point of interest, for example, concerns the variations in local geometry

[†] University of Arkansas.
[‡] Memphis State University.

(1) Schäfer, L.; Van Alsenoy, C.; Scarsdale, J. N. *J. Chem. Phys.* **1982**, *76*, 1439–1444.
(2) Peters, D.; Peters, J. *J. Mol. Struct.* **1979**, *53*, 103–119; **1980**, *69*, 249–263; **1980**, *62*, 229–247.
(3) Peters, D.; Peters, J. *J. Mol. Struct.* **1981**, *85*, 107–123.
(4) Shipman, L. L.; Christofferson, R. E. *Theor. Chim. Acta* **1973**, *31*, 75–82.
(5) Pullman, B.; Pullman, A. *Adv. Protein Chem.* **1974**, *28*, 347–526.
(6) Yan, J. F.; Momany, F. A.; Hoffman, R.; Scheraga, H. A. *J. Phys. Chem.* **1970**, *74*, 420–433.
(7) Scheraga, H. A. "Peptides"; Goodman, M., Meinenhofer, J., Eds.; Wiley: New York, 1977; pp 246–256.
(8) Momany, F. A. *Top. Curr. Phys.* **1981**, *26*, 41–79.
(9) Momany, F. A. *J. Am. Chem. Soc.* **1976**, *98*, 2990–2996.
(10) Momany, F. A.; Drake, L. G.; AuBuchon, J. R. *Int. J. Quantum Chem., Quantum Biol. Symp.* **1978**, *5*, 381–391.
(11) Warme, P. K.; Momany, F. A.; Rumball, S. V.; Tuttle, R. W.; Scheraga, H. A. *Biochemistry* **1974**, *13*, 768–782.

0002-7863/83/1505-3438$01.50/0

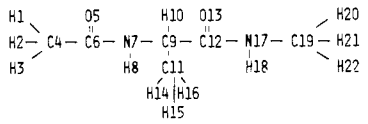

Figure 1. Atom numbering for N^{α}-acetyl-N-methylalaninamide.

that are encountered when bond lengths and angles of the same type are compared in different energy-optimized conformations. Comparing the geometry-refined extended (β) or C_5 region conformer with the refined α-helix (α_R or α_L) conformers or the two hydrogen-bonded ring conformers C_7^{eq} and C_7^{ax} with the other regions will give us consistent structural trends which can be used to characterize any given conformation of minimum energy. Data of this kind are unavailable by any other method of study.

An additional goal of this paper will be to examine the procedures used in empirical energy calculations of peptides by comparing the ab initio structural and conformational results with empirical predictions, so that obvious deficiencies in the empirical studies can be focused upon and ultimately corrected. Modifications for the improvement of empirical potentials and geometry will be presented elsewhere.[12]

Computational Procedures

The ab initio calculations reported here were executed by using Pulay's[13] gradient method, Pulay's[14] program with the 4-21G basis set,[15] and a normal coordinate force relaxation procedure described previously.[16] The initial starting conformations (i.e., torsional angles) were taken from results of empirical energy calculations (ECEPP).[17] Additional details characterizing the computational procedures can be found elsewhere.[18] Estimates for uncertainties, in bond distances and bond angles based on comparisons of calculated with experimental structures, are presented in ref 1 (Table I).

On the basis of the experiences made during this refinement and that of the homologuous glycine compound,[1] one can conclude that computations of this kind, on relatively complex and floppy molecules, cannot be carried out with similar expectations as equivalent calculations for small, rigid molecules. This is so, because the potential energy surfaces of such systems are relatively flat in many areas of conformational space. Thus significant variations in geometry may be accompanied by nearly negligible changes in energy. For example, a change of 3° in the ψ angle of conformer I, from 73° (Tables I and II) to 70°, with simultaneous relaxation of bond distances and bond angles at the new point in conformational space, has been found to correspond to a change in energy of only 0.06 kcal/mol. Similarly, a change of ϕ and ψ in II from −165° and 167°, respectively, to −155° and 157°, was accompanied by an energy change of only 0.5 kcal/mol. When a molecular system is this flexible, the concept of a *local* conformational energy minimum becomes less meaningful for the thermally averaged, real molecule. Rather, one should think in terms of characteristic *areas* of the conformational energy surface, in which the thermally averaged system is characterized by large amplitude motions.

In accordance with these considerations, the geometries presented in Table II are not minimum energy conformations in the traditional (i.e., small molecule) sense. Rather, the geometries given in this paper are structures (bond distances and bond angles) relaxed at specific points of the potential energy surface of Ala defined by their torsional angles. These points represent typical conformationally allowed areas in the ϕ–ψ space of the alanine dipeptide and were arrived at in the following way. In all the conformations refined, (for details see below) the optimized torsional angles obtained by empirical energy calculations[17] were used as starting values. For these structures the bond distances and angles were allowed to relax without any geometrical constraints. Torsional angles were also optimized, but in small steps by applying a large value to the corresponding second-order force constant in the stepping procedure. This made it possible for the torsional angles to move away from their empirical values into the corresponding flat areas of potential energy in 4-21G space, but it did not necessarily allow them to seek the exact positions of relatively shallow minima. This procedure was followed because the shallow energy surfaces, as considered above, did not at present justify the huge computing expenses needed to locate exact minima and because it is the primary purpose of this paper to compare trends in local geometries (differences in bond distances and bond angles) for different characteristic conformations of Ala such as the α-helical, C_7, or C_5 conformers.

This then is the exact import of the geometries reported here. The primary structures are highly relaxed at each point of the potential energy surface considered. That is, estimates for the *largest* deviations of bond distances and bond angles from their true 4-21G minima at a given combination of torsional angles are approximately 4×10^{-4} Å and 0.5°, respectively. (As a rule, most parameters are relaxed much better than that.) The calculated energies are practically the exact 4-21G values for the given combinations of torsional angles. These energies characterize the specific conformations of Ala considered but, for the reasons specified above, not necessarily at their exact shallow bottom of potential energy. These values are, therefore, approximate but, at the same time, they are immensely more accurate than ab initio energies obtained in the most frequently practiced way, i.e., from totally unrelaxed, "standard" geometries. Uncertainties in the torsional angles, at which the refinement was terminated (i.e., their relations to true 4-21G minima), are impossible to estimate with confidence because of the reasons discussed above. A very extensive grid and path search, between the various characteristic areas of potential energy, including complete geometry optimization at each point, would be necessary to determine the exact topography of the Ala potential energy. This may be worthwile to do in the future, but it is not the purpose of this paper. In spite of these uncertainties in the

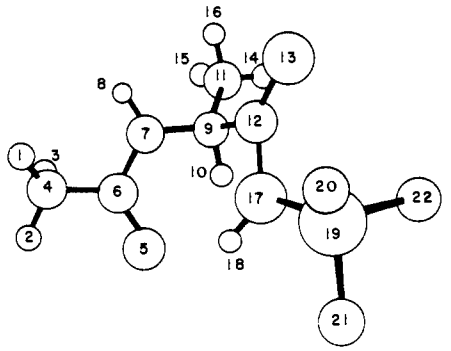

Figure 2. Conformer I of N^{α}-acetyl-N-methylalaninamide.

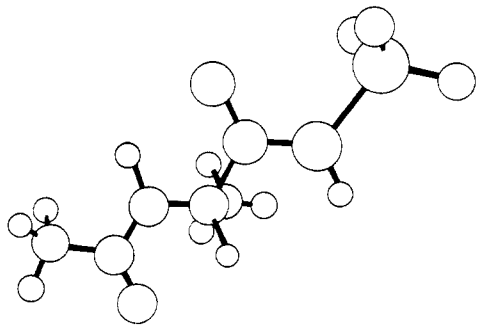

Figure 3. Conformer II of N^{α}-acetyl-N-methylalaninamide.

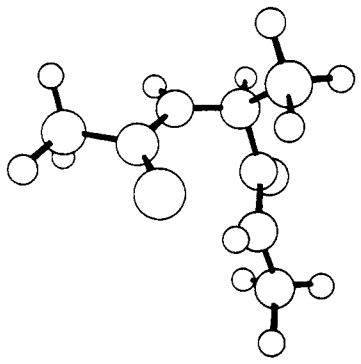

Figure 4. Conformer III of N^{α}-acetyl-N-methylalaninamide.

(12) Chuman, H.; Momany, F. A.; Schäfer, L., in preparation.
(13) Pulay, P. *Mol. Phys.* **1969**, *17*, 197–204.
(14) Pulay, P. *Theor. Chim. Acta* **1979**, *50*, 299–312.
(15) Pulay, P.; Fogarasi, G.; Pang, F.; Boggs, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 2550–2560.
(16) Sellers, H. L.; Klimkowski, V. J.; Schäfer, L. *Chem. Phys. Lett.* **1978**, *58*, 541–544.
(17) Lewis, P. N.; Momany, F. A.; Scheraga, H. A. *Isr. J. Chem.* **1973**, *11*, 121–152.
(18) (a) Van Alsenoy, C.; Scarsdale, J. N.; Schäfer, L. *J. Chem. Phys.* **1981**, *74*, 6278–6284. (b) Schäfer, L.; Sellers, H. L.; Lovas, J. F.; Suenram, R. D. *J. Am. Chem. Soc.* **1980**, *102*, 6566–6568. (c) Schäfer, L.; Van Alsenoy, C.; Scarsdale, J. N. *J. Mol. Struct.* **1982**, *86*, 349–364.

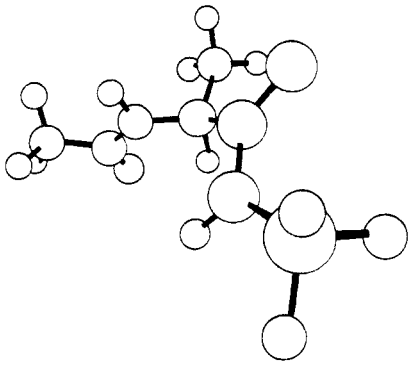

Figure 5. Conformer IV of N^{α}-acetyl-N-methylalaninamide.

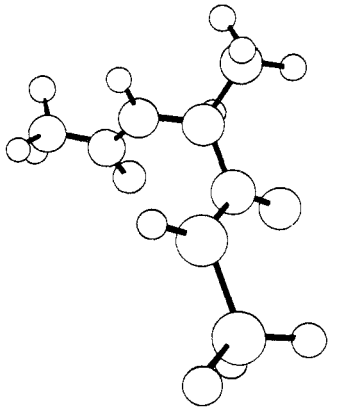

Figure 6. Conformer V of N^{α}-acetyl-N-methylalaninamide.

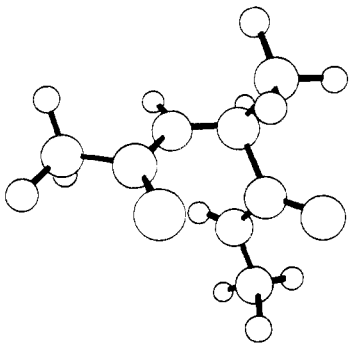

Figure 7. Conformer VI of N^{α}-acetyl-N-methylalaninamide.

torsional angles, the ϕ and ψ values given will nevertheless allow for some interesting and definite conclusions (see below), because of the *directions* in which the 4-21G optimization *moved* away from the ECEPP conformational energy minima used as the starting positions. Finally, uncertainty estimates for out-of-plane bends are given at approximately 0.5°.

Results and Discussion

The results of the calculations are presented in Tables I and II. The atom numbering for N^{α}-acetyl-N-methylalaninamide (Ala) is given in Figure 1. The seven conformations (I–VII), which were geometry optimized for this study, are denoted as C_7^{eq} (I), C_5 (II), C_7^{ax} (III), β_2 (IV), α_R (V), α_L (VI), and α' (VII) and are presented in Figures 2–8, respectively. Optimized Cartesian coordinates of I–VII, total energies, calculated dipole moments, and largest Cartesian residual force components on any atom are listed in Table I. Some selected internal coordinates (bond lengths, bond angles, and dihedral angles) can be found in Table II. In Table III we present a comparison of the ϕ and ψ 4-21G torsional angles reported here and the corresponding ECEPP (empirical conformational energy program for Peptides[19]) minimum energy

(19) Zimmerman, S. S.; Pottle, M. S.; Nemethy, G.; Scheraga, H. A. *Macromolecules* **1977**, *10*, 1–9.

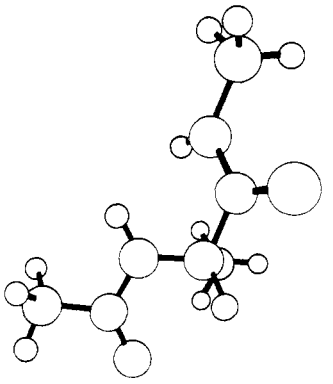

Figure 8. Conformer VII of N^{α}-acetyl-N-methylalaninamide.

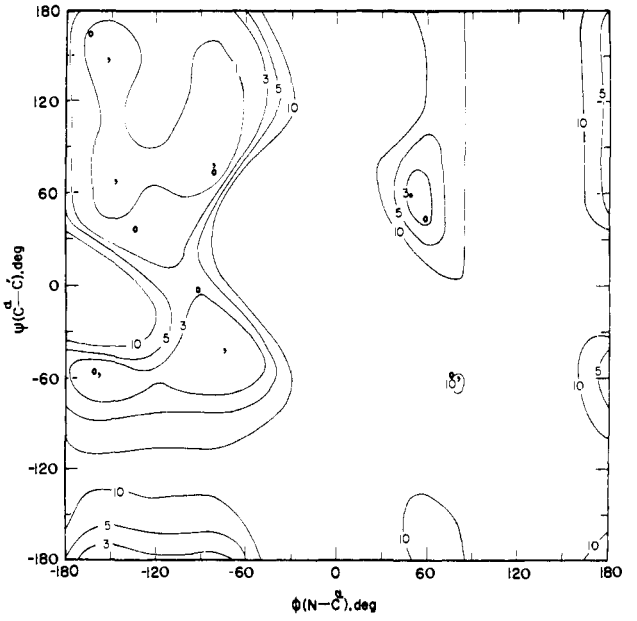

Figure 9. A ϕ (N–C$^{\alpha}$), ψ (C$^{\alpha}$–C') conformational isoenergetic contour diagram for the molecule N^{α}-acetyl-N-methyl-L-alaninamide. The energy is in kilocalories per mole and the solid dots are energy minima found by using ECEPP, while the circles are the local geometry positions corresponding to the torsional angles obtained by the present 4-21G analysis. (See text for details concerning the nature of the torsional angles.)

values for Ala and Gly. The ab initio results for Gly were taken from ref 1, and similar considerations apply to the reported values of its torsional angles as specified for Ala above. To further characterize the displacement of ϕ and ψ during the 4-21G refinement from their starting (ECEPP) values, ϕ and ψ angles of Table III are plotted in Figure 9 on an isoenergetic ϕ–ψ map for Ala obtained by using ECEPP.

The existence of one or more local conformational minima, not included in the seven structures studied here, cannot be excluded on the basis of this study. However, a more rigorous search of the potential energy surface of this compound is not possible at this time due to computational limitations imposed by the large size of the molecule. In the next sections, details of the refined geometries, and their interpretation with respect to allowed minimum energy states, will be discussed.

C_7^{eq} and C_7^{ax} States. The conformation of lowest energy found by the 4-21G calculations is the C_7^{eq} conformer (I). ECEPP calculations also find this conformation to be that of lowest energy.[19] However, compared to C_7^{eq}, C_7^{ax} is much more unstable in the ECEPP calculations (8.8 kcal/mol, see Table III) than in 4-21G space (2.6 kcal/mol). One reason for this difference in the two results may be found in the fact that rigid geometries were used in the ECEPP calculations, whereas significant changes in backbone parameters resulted from the 4-21G geometry optimization. For example (see Table II), the C6–N7–C9 angle is

Table I. 4-21G Optimized Cartesian Coordinates (Å), Total Energies, E (kcal/mol), Dipole Moments, D (debye), and Largest Residual Cartesian Force Component on Any Atom, F (mdyn), for the Conformations I–VII of N^{α}-Acetyl-N-methylalaninamide[a]

		I			II			III		
		x	y	z	x	y	z	x	y	z
1	H	−2.654 57	−2.006 39	−0.061 52	1.282 97	1.696 28	−0.040 56	−2.779 32	−1.920 80	0.137 68
2	H	−2.515 36	−0.470 04	−0.920 66	1.943 15	0.299 26	−0.894 63	−2.643 40	−0.402 60	−0.749 14
3	H	−2.560 75	−0.491 11	0.836 80	1.935 19	0.325 30	0.861 55	−2.517 74	−0.404 94	1.005 08
4	C	−2.214 55	−1.023 61	−0.040 50	1.388 07	0.624 31	−0.023 57	−2.287 75	−0.963 14	0.106 78
5	O	−0.142 77	−2.262 87	0.025 85	−1.028 68	0.659 18	−0.044 56	−0.310 76	−2.324 59	−0.080 73
6	C	−0.705 29	−1.169 32	0.000 83	0.004 48	0.000 07	−0.021 87	−0.790 60	−1.193 45	−0.004 24
7	N	−0.013 93	−0.005 93	0.011 25	−0.006 42	−1.352 44	0.009 25	−0.045 59	−0.064 06	−0.019 59
8	H	−0.495 15	0.863 29	0.060 84	0.823 14	−1.904 19	0.039 30	−0.521 36	0.808 99	−0.042 56
9	C	1.458 49	0.025 08	−0.014 21	−1.254 22	−2.097 02	0.042 97	1.430 53	−0.000 93	−0.035 71
10	H	1.777 56	−0.825 39	−0.595 97	−1.905 36	−1.667 61	0.791 84	1.685 05	1.037 09	0.099 04
11	C	1.946 01	1.331 78	−0.637 29	−1.967 55	−2.073 50	−1.326 78	2.067 16	−0.826 26	1.098 47
12	C	2.000 31	−0.129 23	1.418 34	−0.891 48	−3.528 67	0.432 89	2.026 03	−0.360 30	−1.407 83
13	O	2.486 79	0.810 22	2.035 17	0.267 11	−3.930 91	0.405 02	2.706 59	0.455 47	−2.019 71
14	H	3.024 27	1.327 34	−0.706 10	−2.896 32	−2.628 89	−1.296 03	3.144 83	−0.753 33	1.034 08
15	H	1.529 10	1.450 17	−1.628 11	−2.179 04	−1.046 05	−1.578 71	1.749 34	−0.430 80	2.054 21
16	H	1.663 38	2.168 79	−0.015 07	−1.323 77	−2.505 18	−2.080 97	1.772 73	−1.859 64	1.032 68
17	N	1.881 37	−1.371 52	1.923 37	−1.925 98	−4.319 44	0.780 21	1.779 82	−1.604 03	−1.852 05
18	H	1.398 44	−2.064 50	1.391 67	−2.847 19	−3.951 60	0.821 75	1.169 80	−2.198 72	−1.331 32
19	C	2.334 32	−1.660 21	3.283 04	−1.698 42	−5.724 28	1.131 40	2.325 96	−2.040 73	−3.135 61
20	H	3.382 60	−1.418 83	3.387 79	−1.264 60	−6.255 64	0.296 71	1.949 39	−1.429 19	−3.944 79
21	H	1.779 47	−1.081 21	4.009 37	−1.024 24	−5.797 29	1.972 44	3.404 47	−1.968 23	−3.131 93
22	H	2.188 98	−2.711 77	3.478 68	−2.645 06	−6.173 53	1.389 54	2.037 47	−3.067 82	−3.300 29
			$E = -308\,576.3$			$E = -308\,574.9$			$E = -308\,573.7$	
			$D = 3.6$			$D = 2.8$			$D = 4.2$	
			$F = 0.004_2$			$F = 0.001_9$			$F = 0.005_2$	

		IV			V			VI		
1	H	1.237 66	1.718 86	0.150 38	1.317 65	1.686 62	−0.051 06	−2.777 37	−1.831 87	0.034 49
2	H	1.849 66	0.452 75	−0.913 00	1.974 03	0.282 02	−0.891 22	−2.588 34	−0.292 64	−0.808 03
3	H	1.964 33	0.259 44	0.829 98	1.944 17	0.314 20	0.865 44	−2.534 65	−0.342 87	0.948 31
4	C	1.353 47	0.654 94	0.028 50	1.410 30	0.613 73	−0.027 81	−2.272 78	−0.880 28	0.045 09
5	O	−1.058 28	0.653 99	0.090 40	−1.000 45	0.668 52	−0.126 76	−0.283 68	−2.241 94	−0.049 61
6	C	−0.022 03	0.012 75	0.038 47	0.019 04	0.006 54	−0.046 24	−0.775 88	−1.127 77	−0.007 45
7	N	−0.008 05	−1.355 42	−0.006 28	−0.006 49	−1.361 18	0.038 59	−0.009 95	0.006 16	−0.030 06
8	H	0.856 78	−1.828 86	−0.145 39	0.848 93	−1.868 03	−0.002 36	−0.447 18	0.887 96	0.110 85
9	C	−1.243 72	−2.128 12	−0.169 78	−1.256 02	−2.106 04	−0.116 30	1.457 46	−0.058 82	0.039 38
10	H	−2.043 11	−1.448 20	0.087 73	−1.927 04	−1.509 75	−0.714 37	1.804 25	0.960 32	−0.081 13
11	C	−1.427 98	−2.629 83	−1.605 70	−0.999 41	−3.455 22	−0.810 27	1.975 59	−0.627 99	1.364 95
12	C	−1.284 78	−3.296 72	0.822 53	−1.989 57	−2.373 96	1.204 18	2.033 86	−0.845 27	−1.150 35
13	O	−1.775 17	−4.376 61	0.523 43	−3.077 87	−2.937 43	1.184 19	3.020 34	−1.553 05	−1.031 82
14	H	−2.327 47	−3.221 06	−1.675 81	−1.932 38	−3.992 04	−0.882 88	3.054 47	−0.632 47	1.360 69
15	H	−1.494 40	−1.786 90	−2.279 40	−0.595 47	−3.296 95	−1.801 20	1.619 87	−0.022 80	2.188 65
16	H	−0.593 85	−3.254 08	−1.899 45	−0.301 97	−4.053 54	−0.235 20	1.627 82	−1.641 51	1.481 15
17	N	−0.788 74	−3.035 30	2.049 86	−1.366 29	−2.009 12	2.338 11	1.440 57	−0.604 43	−2.340 42
18	H	−0.383 62	−2.148 84	2.232 36	−0.516 59	−1.503 40	2.279 03	0.599 23	−0.081 32	−2.368 62
19	C	−0.837 99	−4.054 01	3.098 91	−2.012 67	−2.211 90	3.634 51	1.927 73	−1.267 20	−3.550 12
20	H	−1.849 53	−4.411 93	3.223 13	−2.833 15	−1.520 63	3.775 48	2.973 81	−1.042 90	−3.699 31
21	H	−0.207 78	−4.896 48	2.848 05	−2.400 31	−3.217 57	3.689 00	1.816 03	−2.340 01	−3.473 05
22	H	−0.496 31	−3.615 87	4.024 51	−1.282 75	−2.062 97	4.416 32	1.360 23	−0.907 51	−4.395 57
			$E = -308\,572.4$			$E = -308\,571.4$			$E = -308\,569.6$	
			$D = 4.9$			$D = 6.5$			$D = 7.1$	
			$F = 0.005_9$			$F = 0.007_1$			$F = 0.006_7$	

		VII					VII		
		x	y	z			x	y	z
1	H	−2.680 25	−1.958 28	0.018 48	14	H	3.115 83	−0.341 41	−1.327 00
2	H	−2.577 20	−0.385 11	−0.773 83	15	H	1.691 46	−1.326 89	−1.642 94
3	H	−2.499 98	−0.489 55	0.979 79	16	H	1.699 32	0.374 06	−2.092 24
4	C	−2.223 45	−0.983 52	0.056 69	17	N	1.509 40	2.414 51	−0.129 64
5	O	−0.168 96	−2.239 03	−0.129 79	18	H	1.004 82	2.298 69	−0.976 64
6	C	−0.716 61	−1.152 26	−0.021 75	19	C	1.949 10	3.756 83	0.261 99
7	N	−0.008 22	0.009 45	0.029 08	20	H	1.651 07	3.963 07	1.279 59
8	H	−0.472 16	0.873 65	0.189 89	21	H	3.024 97	3.840 97	0.198 91
9	C	1.462 67	−0.016 68	0.037 29	22	H	1.492 50	4.478 52	−0.398 25
10	H	1.791 62	−0.760 36	0.743 12				$E = -308\,568.4$	
11	C	2.033 79	−0.344 87	−1.355 65				$F = 6.0$	
12	C	1.967 01	1.328 90	0.549 51				$G = 0.005_8$	
13	O	2.727 28	1.429 45	1.497 82					

[a] Atom numbering and atom symbols are given in the first two columns on the left.

Table II. Some Selected Internal Coordinates[a] for the 4-21G Optimized Structures I-VII of N^{α}-Acetyl-N-methylalaninamide

	I	II	III	IV	V	VI	VII
C4-H1	1.077	1.077	1.077	1.077	1.077	1.077	1.077
C4-H2	1.082	1.083	1.083	1.083	1.083	1.083	1.083
C4-H3	1.083	1.083	1.082	1.083	1.083	1.083	1.083
C11-H14	1.080	1.083	1.082	1.079	1.079	1.079	1.082
C11-H15	1.081	1.079	1.082	1.081	1.082	1.082	1.079
C11-H16	1.081	1.081	1.077	1.082	1.084	1.078	1.082
N7-H8	0.995	0.997	0.995	0.996	0.995	0.994	0.994
N17-H18	0.998	0.993	0.998	0.992	0.991	0.991	0.993
C6=O5	1.230	1.226	1.231	1.220	1.218	1.219	1.222
C12=O13	1.225	1.227	1.226	1.223	1.226	1.220	1.220
C6-C4	1.517	1.518	1.519	1.518	1.518	1.518	1.518
C6-N7	1.353	1.353	1.353	1.369	1.371	1.369	1.362
C9-N7	1.473	1.453	1.478	1.467	1.463	1.470	1.471
C11-C9	1.528	1.545	1.540	1.532	1.539	1.533	1.541
C12-C9	1.539	1.527	1.538	1.534	1.534	1.538	1.526
C12-N17	1.346	1.348	1.343	1.349	1.344	1.351	1.360
C19-N17	1.462	1.466	1.462	1.463	1.463	1.463	1.466
C9-H10	1.079	1.081	1.077	1.081	1.079	1.083	1.077
N7-C6-C4	115.2	114.7	114.6	114.4	114.5	114.7	114.8
N7-C6-O5	122.0	122.1	123.5	122.4	121.1	122.1	121.9
C9-N7-C6	121.9	121.3	125.9	121.4	122.2	121.4	120.3
C12-C9-N7	109.5	106.4	112.7	110.6	114.0	111.1	108.5
C12-C9-C11	110.7	110.5	111.8	110.7	108.3	110.6	111.6
O13-C12-C9	122.1	121.7	120.3	121.7	119.4	121.6	122.7
H14-C11-C9	109.9	111.3	109.4	109.9	108.8	109.6	110.2
H15-C11-C9	110.1	108.2	109.5	109.6	110.3	109.8	108.5
H16-C11-C9	110.1	109.7	110.9	110.5	110.6	109.5	111.1
N17-C12-C9	114.2	115.7	116.1	115.5	117.2	115.2	115.2
C19-N17-C12	120.2	120.3	119.9	120.3	120.3	120.1	119.8
C9-N7-H8	117.8	115.5	116.1	117.8	118.1	118.1	118.8
C12-C9-H10	108.6	109.8	104.2	107.8	106.0	106.0	106.7
H8-N7-C6-C4	4.6	0.7	−5.5	−6.9	−7.1	8.1	5.3
H8-N7-C6-O5	−175.3	−179.2	174.1	173.5	173.0	−173.1	−175.1
C9-N7-C6-C4	−177.0	178.7	176.0	−172.4	−173.1	174.5	176.6
C9-N7-C6-O5	3.1	−1.2	−4.4	8.1	7.0	−6.7	−3.8
C11-C9-N7-C6	153.5	73.7	−52.9	101.6	145.7	−64.4	74.9
N17-C12-C9-H10	−43.2	49.2	−176.5	−76.7	−124.1	−73.8	−172.4
C12-C9-N7-C6	−84.6	−165.7	74.6	−134.2	−91.9	60.8	−161.7
H14-C11-C9-C12	62.0	61.9	51.4	53.9	52.7	55.6	57.4
H15-C11-C9-C12	−177.8	−178.3	170.4	174.4	172.9	176.0	176.8
H16-C11-C9-C12	−56.3	−58.9	−69.4	−65.2	−66.4	−63.5	−63.4
O13-C12-C9-N7	−106.5	−14.0	119.6	−144.1	176.7	−144.7	124.8
O13-C12-C9-C11	15.0	107.3	−112.5	−19.1	−59.7	−18.0	−111.8
N17-C12-C9-N7	73.0	167.3	−62.0	38.1	−5.5	40.6	−55.4
N17-C12-C9-C11	−165.4	−71.4	65.9	163.1	118.1	167.3	68.1
H18-N17-C12-C9	−5.1	−3.4	5.5	−3.6	6.3	−10.3	−9.2
H18-N17-C12-O13	174.4	177.9	−176.2	178.6	−176.0	175.1	170.7
C19-N17-C12-C9	−179.0	178.1	−178.9	176.9	179.0	178.3	−178.9
C19-N17-C12-O13	0.5	−0.7	−0.6	−0.9	−3.3	3.7	1.0

[a] Bond distances in angstroms and angles in degrees.

Table III. A Comparison of ECEPP Conformational Positions of Minimum Energy for N^{α}-Acetyl-N-methyl-L-alaninamide and N^{α}-Acetyl-N-methylglycinamide with the Corresponding 4-21G Values Obtained As Described in the Text

	dihedral angles, deg				relative energy, kcal/mol			
	Ala		Gly		Ala		Gly	
	4-21G	ECEPP[a]	4-21G[b]	ECEPP[a]	4-21G	ECEPP[a]	4-21G[b]	ECEPP[a]
I	−84.6	−84	−83.4	−83	0.0	0.0	0.0	0.0
	73.0	79	70.7	76				
II	−165.7	−154	−180.0	−180	1.4	0.4	0.8	0.8
	167.3	153	180.0	180				
III	74.6	78			2.6	8.8		
	−62.0	−64						
IV	−134.2	−150	−159.1	−173	3.9	0.7	4.7	1.0
	38.1	72	40.5	62				
V	−91.9	−74	−86.6	−72	4.9	1.1	4.3	1.2
	−5.5	−45	−14.1	−53				
VI	60.8	54			6.7	2.3		
	40.6	57						
VII	−161.7	−158			7.9	1.6		
	−55.4	−58						

[a] Reference 19. [b] Reference 1.

121.9° in the C_7^{eq} form and 125.9° in the C_7^{ax} form, an opening of this angle by ~4°. For the N7–C9–C12 and C9–C12–N17 angles, the differences are ~2–3° in the same direction. The opening is probably related to the fact that the ϕ and ψ values are smaller in magnitude (ϕ = 74.6° vs. ϕ = −84.6° and ψ = −62.0° vs. ψ = 73.0°) in the C_7^{ax} form than in the C_7^{eq} form. This leads to a more favorable interaction between the C6═O5 and N17—H18 bonds and the side-chain methyl group while, at the same time, it retains optimal hydrogen bonding between H18···O5. Clearly, the empirical energy calculations do not allow the bond angles to open in the C_7^{ax} form and the nonbonded contact energy is thus not reduced. The result is an energy which may be abnormally high for the C_7^{ax} conformation when calculated by empirical methods in this manner.

Some interesting bond length variations with conformation can be seen from Table II. For example, in C_7^{eq} and C_7^{ax} the C6═O5 and N17—H18 bonds, which participate in hydrogen bonding are lengthened considerably (1.230 (1) Å and 0.998 Å, respectively) compared to the non-hydrogen bonding C12═O13 and N7—H8 (1.225 (6) Å and 0.995 Å, respectively). This effect is to be expected from a charge polarization effect and is in qualitative agreement with previous calculations.[1,20,21] A second observation that seems to follow the pattern described above is seen for the peptide bond lengths C6–N7 and C12–N17. In this case, the ω_1 (C6–N7) bond is shorter for the low-energy structures (I–III) and longer for the higher energy structures (IV–VII). This is the reverse of the C═O bond distance trends and in accord with the usual resonance effects. The ω_2 (C12–N17) bond shows little variation with change in conformation (except for VII) and is shortest in C_7^{ax}.

C_5 Extended State. The extended form C_5 (II) represents a particularly flat area of the potential energy surface of Ala. The ab initio energy of the C_5 (II) conformation relative to I is higher than that found from ECEPP (see Table III). As pointed out below, this difference may have important implications for the interpretation of the solution data of Ala.

Some additional geometrical properties which are of particular interest can be noted in Table II. For example, the backbone N7–C9–C12 bond angle (around the C^{α} carbon) is smaller (106.4°) in C_5 than in any other of the calculated structures. The relatively small value for this angle may be an indication of the fact that C12═O13 and N7—H8 attract each other in a hydrogen bond type interaction. In this context, it is also interesting to note that the O13–C12–C9 angle in C_5 is not significantly smaller than that found in the other conformations. Thus, the smaller bond angle around the C^{α} may be a result of bond···bond or conjugative effects. The H8···O13 hydrogen bond length in C_5 is 2.13 Å and short enough to stabilize this conformation.

The attractive interaction between N7—H8 and C12═O13 can also be inferred from a weak correlation between ϕ and ψ in the C_5 conformational region which is apparent from the calculations: During the 4-21G refinement the optimization followed a path from the starting values of ϕ = −154° and ψ = 153° to ϕ = −165° and ψ = 167° in which the ϕ and ψ values maintained the N7—H8 and C12═O13 bonds in approximately parallel orientation to one another.

α_R and α_L States. The positions of minimum energy of the right- and left-handed helix regions found from the 4-21G calculations are shifted in the direction of the bridge structures relative to the equivalent positions found from the empirical ECEPP studies (see Figure 9). In particular, α_R is found as an energy trough passing through the bridge ($\psi \sim 0°$) region in both the Gly and Ala geometry-optimized calculations (see Table III). This result is a significant finding, since the ϕ, ψ values obtained here for these model compounds are obviously closer to ϕ, ψ values found in type I (LL or GG)[8] bends in proteins, than are the values found from empirical calculations.[8] Examination of Figure 6 shows that in the α_R conformer the amide hydrogen H18 lies directly in the region of space occupied by the lone-pair orbital associated with the amide nitrogen N7. The H18···N7 contact distance in the Ala compound is 2.30 Å. This contact distance is quite short, indicating a favorable attractive interaction. In the α_L conformer (Figure 7), one also finds the same favorable interaction, but at a distance of 2.42 Å. That is, the orientation of the H18 atom relative to the orbital on N7, perpendicular to the plane of the peptide group, is retained in both structures, even though the ϕ angle in the α_L conformation cannot become as large in magnitude as it is in α_R, probably because of unfavorable interaction between the C5═O6 bond and the side-chain methyl group. Since ϕ in α_L remains at ~60°, the ψ value prefers an angle near ~40°, apparently to optimize the overlap between N7···H18.

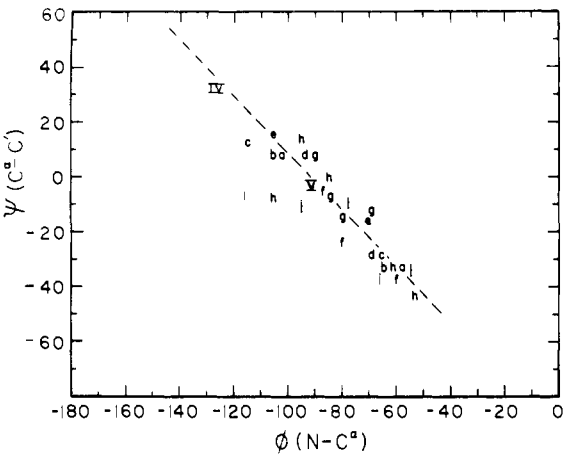

Figure 10. ϕ (N–C^{α}) and ψ (C^{α}–C′) values found from experimental crystal structures of small peptides: (a) ref 25, (b) ref 26, (c) ref 27, (d) ref 28, (e) ref 29, (f) ref 30, (g) ref 31, (h) ref 24, (i) ref 32, (j) ref 33. Structures IV and V are values from Table III.

Evidence for the importance of the H18···N7 interaction is also found from the following observations. First, by draining charge from the N7 atom one would anticipate that the peptide bond (C6–N7) would be long. Indeed, this bond is ~1.37 Å compared to 1.34–1.35 Å for the C12–N17 bond and 1.35 Å for C6–N7 bonds of structures without this interaction. Furthermore, the C6═O5 bond should become shortened, as should N17—H18 and both are found to be short, in agreement with the overlap effect.

The local geometry effects just described can be used to confirm the hypothesis, originally put forward by Gieren et al.[22,23] in connection with a crystallographic study of *N,N′*-di-*tert*-butyl-2-[*N*-(1-phenylethyl)benzamido]malonamide (DTBMA), that a ϕ–ψ correlation exists in crystal data of proteins which can be rationalized in terms of a perpendicular N–H···N hydrogen bond of the type described above. In searching for additional evidence for this important interaction, it can be expected that the concomitant local geometry effects are apparent only with considerable scatter in crystal structures of linear peptides where multiple hydrogen bonding between molecules is found or in larger polymers or proteins, particularly when observed in the helix structure, where hydrogen bonding dominates the conformational energy. However, the trend suggested seems to be found very clearly in structures such as *cyclo*(L-alanyl-L-alanyl-glycyl-glycyl-L-alanyl-glycyl) monohydrate and *cyclo*(L-alanyl-L-alanyl-glycyl-L-alanyl-glycyl-glycyl) dihydrate[24]. In these structures one finds that as ϕ

(20) Williams, J. O.; Van Alsenoy, C.; Schäfer, L. *J. Mol. Struct.* **1981**, *76*, 109–112.
(21) Van Alsenoy, C.; Williams, J. O.; Schäfer, L. *J. Mol. Struct.* **1981**, *76*, 179–185.
(22) Gieren, A.; Dederer, B.; Schanda, F. *Z. Naturforsch., C: Biosci.* **1980**, *35C*, 741–746.
(23) (a) Gieren, A.; Dederer, B. *Tetrahedron Lett.* **1977**, 1503–1506. (b) *Acta Crystallogr., Sect. B* **1978**, *B34*, 533–539.
(24) Hossain, M. B.; Van der Helm, D. *J. Am. Chem. Soc.* **1978**, *100*, 5191–5198.
(25) Ueki, T.; Ashida, T.; Kakudo, M.; Sasada, Y.; Katsube, Y. *Acta Crystallogr., Sect. B* **1969**, *B25*, 1840–1849.
(26) Ueki, T.; Bando, S.; Ashida, T.; Kakudo, M. *Acta Crystallogr., Sect. B.* **1971**, *B27*, 2219–2231.
(27) Rudko, A. D.; Lovell, F. M.; Low, B. W. *Nature (London), New Biol.* **1971**, *232*, 18–19.

goes from ~−50° to ~−100°, ψ goes from ~−40° to ~0°. That is, the values of both angles are correlative, in that one does not find any combination such as $\phi \sim -50°$, $\psi \sim 0°$ or $\phi \approx -100°$, ψ −40°. The dihydrate also contains an Ala in the α_L conformation ($\phi = +53.8°$, $\psi = +37.7°$) indicating the availability of the α_L conformation in these cyclic structures. In Figure 10 are plotted the ϕ and ψ values found from X-ray structures of a variety of small peptides. No protein data are included, since they have been presented elsewhere.[22,23] The correlation is quite good throughout the range of angles shown, and remarkably, the low-energy structure IV which also exhibits the N7···H18 interaction lies on the best fit line shown. The distribution of dihedral angles taking part in protein bends has been presented elsewhere as plots of ϕ and ψ (Figure 1, ref 33), and they also show a similar trend, although with considerably more scatter than the data given here. This is not suprising since one would expect long-range as well as steric effects to produce perturbations on these conformational states.

Clearly, the N–H···N interaction defined in this way (such as between N7 and H18 in this study) is a significant factor in peptide structure. It appears to be an important contribution to the formation and stability of bend conformations. Long-range interactions undoubtedly also play a role in stabilizing bend structures in proteins, as do the constraints imposed by cyclization of medium-sized polypeptides. However, the dominance of this interesting local interaction in dipeptide sequences must have significant implications in the mechanism of folding of proteins and in the overall stability of native protein structures.

The α_R local geometry is somewhat perturbed from the average of the other conformations with the bond angle around the C^α (N7–C9–C12) expanded to 114.0° (111.1° in α_L) in the Ala and 115.2° in the Gly molecule.[1] The side-chain methyl group in the Ala molecule seems also to have moved toward the neighboring carbonyl group in the α_R structure as shown by the small C11–C9–C12 angle (i.e., 108.3°). This angle is smaller in α_R than in any other conformation.

It is also most compelling to note that, in the crystal structure of DTBMA,[22,23] the H···N contact distance is 2.27 Å in excellent agreement with the 2.30 Å found here. The peptide bond length of the nitrogen involved in this interaction is also longer (1.37 Å) than those peptide bonds which are not involved.

Comparison with Solution Studies. Blocked single residue molecules have been the subject of several experimental[36] studies, and several interpretations of the spectra have been given.[36] The spectral analysis has usually been based on the presence of two conformation in solution: the C_5 conformation with $(\phi, \psi) \simeq (-170°, 170°)$ and the C_7^{eq} conformation with $(\phi, \psi) \simeq (-80°, 80°)$. A third conformation, called γ with $(\phi, \psi) \simeq (-60°, 140°)$ has also been proposed.[37] Recently,[38] it was noted that in chloroform solution, no evidence for the strongly hydrogen-bonded C_7^{eq} could be found, even though absorption bands attributable to C_5 were observed.

From the calculated ab initio energies (Table III), one would expect C_7^{eq} and C_5 to predominate in solution. However, the actual populations of the C_7^{eq} and C_5 states in solution are also affected by unknown entropic terms. If the ECEPP potential energy surface (Figure 9) gives a qualitatively reasonable description of the Ala system, then it can be inferred that there is a larger number of low-lying states in the vicinity of C_5 than of C_7^{eq}, whereas very few low-lying energy states should be available in the vicinity of C_7^{ax}, which is also one of the relatively stable forms of this system. The higher ab initio energy of C_5 in Ala as compared to C_5 in Gly relative to C_7^{eq} seems to be reasonable because the C_5/C_7^{eq} ratios inferred from the solution spectra[38] are ~0.4 for Ala and 0.7 for Gly.

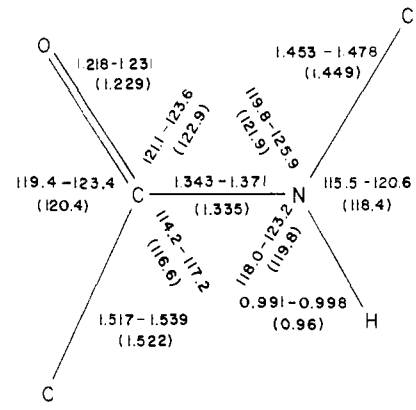

Figure 11. Geometry around the peptide bond. The ab initio values listed are the minimum and maximum values found from seven conformers of Ala optimized. Experimental values are given in parentheses.

Geometry of the Peptide Unit. The variation in geometry found here as a function of conformation leads one to approach cautiously any comparison of calculated bond lengths and angles to those found experimentally. In making such comparisions it must also be reiterated that ab initio calculations do not reproduce experimental structures exactly but that there are characteristic constant differences for parameters of a given type.[1,15,18c] A summary of such differences for 4-21G structures is given in ref 1 and 18c.

For a comparison of calculated and experimental geometric parameters around the peptide bond, we will use here a recent summary of crystal data of some 20 linear peptide derivatives with trans-peptide units.[39] This summary refers to different amino acids in different conformational states which are in addition also affected by differences in the crystal environment. Variations in local geometry with conformational arrangement are, therefore, averaged out in the experimental data.

The calculated peptide geometry shown in Figure 11 is in remarkably good agreement with the experimental average. The ab initio values bracket the experimental results in most cases, the major exception being the C′–N (peptide) bond length where the calculated values are always longer than the crystal average. Interestingly, long C′–N bonds are also found from gas-phase electron diffraction studies of formamide (r_{CN} = 1.368 Å),[40] methylformamide (r_{CN} = 1.366 Å),[41] acetamide (r_{CN} = 1.380 Å),[42] and *N*-methylacetamide (r_{CN} = 1.386 Å).[43] The C=O bonds in the same series are all relatively short (r_{CO} = 1.212 Å,[40] 1.219 Å,[41] 1.220 Å,[42] and 1.225 Å,[43] respectively). It seems to be a general trend that C=O bond distances are always longer in the solid state than in the gas phase, whereas C–N bonds in the crystalline state are shorter than in the vapor phase. Since the gas-phase results are also consistent with the ab initio calculations, one might suggest that these parameters are affected by their environment in the crystal.

Peptide Bond (ω_1 and ω_2). The two peptide groups (see Table II) are nonplanar in all the Ala conformers, but deviations from planarity can be nearly negligible in some structures as, for example, in II. As discussed previously, the backbone conformation

(28) Karle, I. L.; Karle, J. *Acta Crystallogr.* **1963**, *16*, 969–980.
(29) Karle, I. L.; Gibson, J. W.; Karle, J. *J. Am. Chem. Soc.* **1970**, *92*, 3755–3760.
(30) Kostansek, E. C.; Lipscomb, W. N.; Yocum, R. R.; Thiessen, W. E. *Biochemistry* **1978**, *17*, 3790–3795.
(31) Karle, I. L. *J. Am. Chem. Soc.* **1974**, *96*, 4000–4006.
(32) Kostansek, E. C.; Thiessen, W. E.; Schomburg, D.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1979**, *101*, 5811–5815.
(33) Yang, C. H.; Brown, J. N.; Kopple, K. D. *J. Am. Chem. Soc.* **1981**, *103*, 1715–1719.
(34) Burgess, A. W.; Ponnuswamy, P. K.; Scheraga, H. A. *Isr. J. Chem.* **1974**, *12*, 239–286.
(35) Manavalan, P.; Momany, F. *Biopolymers* **1980**, *19*, 1943–1973.
(36) Burgess, A. W.; Scheraga, H. A. *Biopolymers* **1973**, *12*, 2177–2183.
(37) Maxfield, F. R.; Leach, S. J.; Stimson, E. R.; Powers, S. P.; Scheraga, H. A. *Biopolymers* **1979**, *18*, 2507–2521.
(38) Avignon, M.; Huong, P. V. *Biopolymers* **1970**, *9*, 427–432.
(39) Benedetti, E. "Peptides"; Goodman, M., Meinenhofer, J., Eds.; Wiley: New York, 1977; pp 257–273.
(40) Kitano, M.; Kuchitsu, K. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 67–77.
(41) Kitano, M.; Kuchitsu, K. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 631–634.
(42) Kitano, M.; Kuchitsu, K. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3048–3051.
(43) Kitano, M.; Fukuyama, T.; Kuchitsu, K. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 384–387.

plays an important role in the degree of nonplanarity of ω_1. Interestingly, the ECEPP calculations do not show significant deviations from planarity in ω resulting from different low-energy backbone conformations[34] even though upon N-methylation large deviations are found.[35]

Comparison to Other ab Initio Calculations. A comparison of the results presented here with other ab initio calculations of Ala[3] shows one very obvious difference. That is, in the ϕ–ψ map prepared without geometry optimization on the STO-3G level,[3] the C_7^{ax} conformation does not appear as a region of low energy. We believe that this difference is an artifact of refinement related to the special nature of C_7^{ax} as a narrow cavity in the Ala potential energy surface.

As indicated in Figure 9, C_7^{ax} is a narrow potential energy minimum in the ECEPP calculation. Even though our torsional angles are somewhat uncertain for the reasons pointed out above and even though the space around this conformation has not been examined here on the 4-21G level, it is not impossible that this conformer was missed in the 20° grid used to obtain the ϕ–ψ map.[3] In addition, the rather large geometry change (see above) is required for this structure to be optimized. Thus, conformational problems inherent in the use of rigid geometry appear to be present whether empirical methods or the more rigorous ab initio calculations are used. The other conformational regions of low energy found in the STO-3G ϕ–ψ map[3] are relatively close to the characteristic areas considered here.

Conclusion

The geometry-optimized conformations described here clearly show the structural changes that must be considered in future conformational studies of peptides. Some geometry changes are very significant, such as that found for the C_7^{ax} conformer, while others are more subtle. We consider the perpendicular peptide interaction between the nitrogen N7 and second amide hydrogen H18 to be a most significant and important factor for the understanding of dipeptide conformation. The calculated details of local geometry make it very likely that this interaction is responsible for the observed correlation (see Figure 10) between the ϕ and ψ torsional angles in the α-helix conformational region and must play an important role in the formation and stability of protein structure. Its role in bend structures is being examined, and its incorporation into empirical calculations should lead to improved conformational predictions of larger polypeptides.

Acknowledgment. We thank Dr. F. R. Helm, Dr. B. Ashmore, Ron Fowler, C. Stromberg, and J. Swayze of Computing Services for their assistance and the University of Arkansas Computing Center for executing the calculations. This research was supported in part by NSF Grants CHE-7920790 and ISP-8011447. C.V.A. is grateful for a NATO Research Fellowship. L.S. acknowledges helpful discussions with Prof. P. Pulay (Arkansas). The technical assistance of Ms. Monica L. Mabie is gratefully acknowledged.

Registry No. N^{α}-Acetyl-N-methylalaninamide, 19701-83-8.

Gas-Phase Derivatization for Determination of the Structures of $C_3H_5^+$ Ions

J. O. Lay, Jr., and M. L. Gross*

Contribution from the Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68588. *Received August 11, 1982*

Abstract: The structure of the $C_3H_5^+$ ions formed via halide atom loss from ionized allyl, cyclopropyl, and 1- and 2-propenyl halides was investigated by derivatizing the ions with neutral benzene and substituted benzenes to produce gas-phase adduct ions. The structures of pressure stabilized adduct ions were directly determined by obtaining their collision-induced decomposition spectra and comparing them with the CID spectra of model ions. Two $C_3H_5^+$ ion structures were found to be stable, the allyl cation from cyclopropyl and allyl halides and the 2-propenyl cation from 2-propenyl halides. The $C_3H_5^+$ ions from 1-propenyl halides exist as a 2:1 mixture of the two ion structures. The mechanism of reaction was shown to be electrophilic attack on the ring π system to produce a Wheland intermediate or other structure with the proton relocated. The reaction pathway was confirmed by Fourier transform mass spectrometry, and rate constants for the derivatization reaction were determined by using pulsed ICR.

Vinyl and allyl cations have been the subjects of considerable study both in solution[1] and in the gas phase. In solution, the ions are important as reactive intermediates in synthesis[2] and as models for rearrangement reactions.[3] However, direct observation has been limited to studies of appropriately substituted ions or those formed via loss of "super" leaving groups.[4] Moreover, their reactivity in solution may largely reflect the nature of the solvent system rather than the properties of the ions themselves.

The simplest vinyl–allyl system, namely, the $C_3H_5^+$ isomers and in particular the allyl cation, has been the subject of a number of recent studies in the gas phase. The vertical and adiabatic ionization potential (IP) of the allyl radical as well as the appearance potential (AP) of allyl cations were measured.[5] These measurements lead to a heat-of-formation of 226 kcal/mol, which has been independently verified.[6] The heats of formation of numerous $C_3H_5^+$ fragment ions from simple hydrocarbons were determined to be identical with the value for allyl cation.[7]

(1) See for example: (a) Hanack, M. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 331. (b) Deno, N. C. In "Carbonium Ions"; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1970; Vol. II, 783.

(2) See for example: (a) Stang, P. J.; Rappoport, Z.; Hanack, M.; Subramanian, L. R. "Vinyl Cations"; Academic Press: New York, 1979. (b) Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819. (c) Klein, H.; Mayr, H. *Ibid.* **1981**, *20*, 1027.

(3) See for example: Olah, G. A.; Mayr, H. *J. Am. Chem. Soc.* **1976**, *98*, 7333.

(4) (a) Grob, C. A., Cseh, G. *Helv. Chim. Acta* **1964**, *47*, 194. (b) Grob, C. A. *Chimia* **1971**, *25*, 87. (c) Rappoport, Z.; Gal, A. *J. Am. Chem. Soc.* **1969**, *91*, 5246. (d) Rappoport, Z. *Acc. Chem. Res.* **1976**, *9*, 265. (e) Hanack, M. *Ibid.* **1976**, *9*, 364; **1970**, *3*, 209. (f) Stang, P. J.; Summerville, R. H. *J. Am. Chem. Soc.* **1969**, *91*, 4600. (g) Stang, P. J. *Acc. Chem. Res.* **1978**, *11*, 107. (h) Pfeifer, W. D.; Bahn, C. A.; Schleyer, P. v. R.; Bocher, S.; Harding, C. E.; Hummel, K.; Hanack, M.; Stang, P. J. *J. Am. Chem. Soc.* **1971**, *93*, 1513.

(5) (a) Lossing, F. P. *Can. J. Chem.* **1971**, *49*, 357. (b) Beck, D.; Osberghaus, O. *Z. Phys.* **1960**, *160*, 406. (c) Beck, D. *Discuss. Faraday Soc.* **1963**, *36*, 56. (d) Lossing, F. P.; Ingold, K. U.; Henderson, I. H. S. *J. Chem. Phys.* **1954**, *22*, 621. (e) Omura, I. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 1227; **1962**, *35*, 1845.

(6) (a) Golden, D. M.; Benson, S. W. *Chem. Rev.* **1969**, *69*, 125. (b) Golden, D. M.; Rodgers, A. S.; Benson, S. W. *J. Am. Chem. Soc.* **1966**, *88*, 3196. (c) Buff, R. D.; Parr, A. C.; Jason, A. J. *Int. J. Mass Spectrom.* **1981**, *40*, 31.

(7) (a) Lossing, F. P. *Can. J. Chem.* **1972**, *50*, 3973. (b) Meisels, G. G.; Park, J. Y.; Giessner, B. G. *J. Am. Chem. Soc.* **1969**, *91*, 1555, **1970**, *92*, 254.

0002-7863/83/1505-3445$01.50/0