Experimental Section

Isolation of 2,4-Methanoproline. Finely ground mature seed of *Ateleia herbert smithii* (119 g) was extracted six times at room temperature with 75% ethanol (200 mL). After filtration the combined extracts were concentrated to 150 mL under reduced pressure and applied to a column (75 × 3 cm) of cation-exchange resin (Dowex 50 × 8) in the H^+ form. The column was washed with water until the effluent was colorless. The neutral and acidic amino acids were then displaced with 1 N pyridine and the effluent was collected in 10-mL fractions. The ninhydrin-reacting fractions (40–170) were combined and concentrated under reduced pressure and the concentrate (50 mL) was applied to a column (75 × 3 cm) of anion-exchange resin (Amberlite 1R-45) in the OH^- form. The neutral amino acids were displaced from the column with water and those fractions containing the neutral "unknown" were taken to dryness in a rotary evaporator at <40 °C. The residue was triturated with boiling ethanol and water added drop by drop with continued heating until the residue was dissolved. The hot solution was filtered and on cooling crystals separated from the filtrate. These were recrystallized three times from aqueous ethanol; yield 0.3 g. Anal. ($C_6H_{13}NO_4$) C, H, N.

Isolation of 2,4-Methanoglutamic Acid. After the neutral amino acids were removed from the column of anion-exchange resin with water, with the acidic amino acids were displaced with 1 N acetic acid and the fractions containing the "unknown" acidic compound (as determined by electrophoresis) were taken to dryness under reduced pressure. The residue was recrystallized from water, yield 0.3 g. Anal. ($C_6H_{11}NO_5$) C, H, N.

HVPE. Electrophoresis was carried out on paper at pd of 75 V/cm using buffer solutions of pH 1.9 and 3.6.[11]

Two-Dimensional Chromatography. The ascending technique was employed using Whatman no. 1 paper. Solvents were 1-butanol–acetic acid–water (12:3:5 by vol) and phenol–water (4:1 w/v) in the presence of NH_3 (0.88) vapor.

Acknowledgments. This work was supported by the S.R.C., U.K., and the NSF, DEB 77-4889.

Supplementary Material Available: Tables of fractional coordinates (Table 1), bond distances (Table 2), bond angles (Table 3), and observed and calculated structure factors for both the neutral imino acid and the acidic amino acid (10 pages). Ordering information is given on any current masthead page.

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Solution Structure, Dynamics, and Proton Relaxation Mechanisms of Natural Products and Biopolymers. *N*-Acetyl-D-alloisoleucine

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Received February 28, 1979

Abstract: The NT_1 values of the ^{13}C atoms and the proton–proton scalar coupling established the existence of multiple conformations in *N*-acetyl-D-alloisoleucine. The principal (χ^1; $\chi^{2,1}$) conformations in solution are those which exist in the crystal. Selective and nonselective proton spin–lattice relaxation rates of the NH, Hα, Hβ, Hγ11, Hγ12, Hγ2, and Hδ yielded F^i ratios (nonselective/monoselective relaxation rate) and cross-relaxation rates, σ. The proton relaxation rates yielded correlation times and side chain conformational information and removed the ^3J v ϕ degeneracy. The proton relaxation mechanism is, within experimental error, exclusively dipolar. This combined scalar coupling constant, ^{13}C, and proton relaxation study of stereochemistry, motion, and relaxation of the first-order coupled amino acid *N*-acetyl-D-alloisoleucine establishes the potential of proton relaxation spectroscopy as a technique for studying individual amino acid residues in peptides and proteins.

I. Introduction

Here we extend the type of investigation described for the relatively rigid saxitoxin molecule[1c] to *N*-acetyl-D-alloisoleucine, which should exhibit simultaneous rotations, with different correlation times, around its ω, ϕ, χ^1, χ^2, χ^{21}, and χ^3 bonds. Although this amino acid should fulfill the extreme narrowing conditions, the methodology and findings, suitably modified, should be applicable to amino acid residues in larger peptides and proteins. A preliminary communication has appeared[2] in which it was observed that the essentially first-order nature of the isoleucine ^1H NMR spectrum facilitated the accumulation and interpretation of proton relaxation parameters; the latter could be compared with those described from scalar coupling constants; the crystal structure is also known.[3]

Here we present a study of the structure, dynamics, and equilibria of *N*-acetyl-D-alloisoleucine obtained from (1) proton relaxation parameters, (2) ^{13}C relaxation rates, and (3) scalar coupling constants. The proton relaxation parameters

0002-7863/80/1502-1412$01.00/0

Table I. Chemical Shifts, δ, and Relaxation Rates, R, of the Protons, i, of *N*-Acetyl-D-alloisoleucine[a]

H_i	δ_i,[d] ppm	R_1^i(NS),[b] s^{-1}	R_1^i(SE),[b] s^{-1}	$F^i = R_1^i(NS)/R_1^i(SE)$[c]
NH	7.87	1.30	1.10	1.19
H_α	4.28	0.76	0.52	1.46
H_β	1.79	1.19	0.82	1.45
$H_{\gamma 11}$	1.23	1.99	1.39	1.43
$H_{\gamma 12}$	1.10	1.91	1.34	1.42
$H_{\gamma 2}$	0.80	1.22	1.13	1.09
H_δ	0.80	1.61	1.42	1.13

[a] Concentration = 2×10^{-2} and temperature = 26 °C. [b] Initial rates calculated from semilogarithmic plot of $(A_\infty - A_\tau)/2A_\infty$ vs. τ. A least-squares analysis using a minimum of ten data points in the region $\tau < T_1$ indicates 98% confidence of the reported rates. [c] The accuracy of F^i values has to be considered within a ±5% experimental error. [d] Chemical shifts are measured from internal Me_4Si.

used are (a) mono-, bi-, and nonselective relaxation rates, (b) F values and σ values derived from these. The experimental procedures and methods have been previously described.[1c,2,4-6]

II. Results and Discussion

As previously discussed,[1c,4,5] if $\omega_0^2\tau_c^2 \ll 1$ holds, the $F^i = R_1^i(NS)/R_1^i$ is 1.5. This ratio has been used[2,5,6] to evaluate the dipole-dipole contributions to the relaxation of a given proton.

Several explanations for experimental ratios <1.5 exist; these will be described and then their relevance to the D-alloisoleucine relaxation data investigated. (1) Spin-rotation (SR) and chemical shift anisotropy (CSA) lower the F ratio by affecting only the R^i terms; no σ_{CSA} and σ_{SR} contributions arise from these relaxation mechanisms.[7] (2) Scalar coupling relaxation mechanisms (SC) have a negative σ_{SC} term.[7,8] (3) Sets of equivalent nuclei, such as CH_2 or CH_3 groups, even when "selectively" excited, still have a cross-relaxation contribution from the intermethylene or intermethyl proton dipolar interaction.

Although the relaxation behavior of these equivalent sets of protons may be complicated by cross-correlation effects,[9] if initial slopes are taken into account to evaluate both their nonselective and monoselective relaxation rates, the latter can be described by equations only related to additive pairwise proton dipole-dipole interactions.[9-11] Thus, in the selective excitation relaxation rate measurements, for methylene and methyl protons all the $\sigma_{ij} = 0$ except the σ_{gem}, and the following equations hold:

$$R_1^{CH_2}(SE) = R^{CH_2} + \sigma_{gem} \quad (1)$$

$$R_1^{CH_3}(SE) = R^{CH_3} + 2\sigma_{gem} \quad (2)$$

The left-hand side are the experimentally determined monoselective excitation rates, but the true monoselective value is R^{CH_2} or R^{CH_3} on the right. The latter can be calculated if F^{CH_2} and F^{CH_3} are assumed equal to 1.5 in the absence of the cross-relaxation term. Thus, combining experimental and calculated selective relaxation rates, σ_{gem} is estimated and, because the geminal interproton distance is known, τ_{gem} can be evaluated. (4) When correlation times are such that the extreme narrowing approximation is not applicable, e.g., size or aggregation, the ratio can be lowered to a minimum value of 0 at $\omega_0^2\tau_c^2 \gg 1$. (5) When the spectra contain overlapping resonances from different nuclei exhibiting dipolar interaction, the experimental selective values of R still contain σ terms related to this interaction. As in eq 1 and 2, the ratio will be lower than 1.5. (6) The dipolar interaction of protons with other nuclei which possess a nonzero magnetic moment and a high natural abundance can be relevant in the proton spin-lattice relaxation. A small internuclear distance between these two dipoles and a suitable correlation time for such a vector can yield a sizable contribution for the relaxation of protons bound to ^{14}N nuclei as recently shown.[12] The F value for amide protons can, therefore, be shortened drastically by this effect.

Table II. Chemical Shifts, δ, and Relaxation Times, T_1, of the ^{13}C Atoms of *N*-Acetyl-D-alloisoleucine[a]

$^{13}C_i$–H	δ_i, ppm	NT_1^i, s[b]	$\tau_c\, C^i$–H[b]
$^{13}C^\alpha$–H	59.02	0.34	1.3×10^{-10}
$^{13}C^\beta$–H	37.41	0.35	1.3×10^{-10}
$^{13}C^{\gamma 1}$–H_2	25.60	0.71	6.5×10^{-11}
$^{13}C^{\gamma 2}$–H_3	15.75	1.95	2.3×10^{-11}
$^{13}C^\delta$–H_3	11.23	3.57	1.3×10^{-11}

[a] Temperature = 26 °C and concentration = 8×10^{-1} M. Correlation times τ_c were calculated from NT_1 values. [b] The ±5% experimental error on NT_1 is entirely reflected on the calculated τ_c's.

Table III. Scalar Coupling Constants, J, Cross-Relaxation Rates, σ, and Correlation Times, τ_c, for Various Interproton Vectors of *N*-Acetyl-D-alloisoleucine

H_i–H_j	$^3J_{H_i-H_j}$, Hz[a]	σ_{ij}, s^{-1} [b]	τ_c^{ij}, s[c]
NH–H_α	8.6	0.12	6.9×10^{-11}
H_α–H_β	4.7	0.13	6.9×10^{-11}
H_β–$H_{\gamma 11}$	6.6		
H_β–$H_{\gamma 12}$	7.4		
H_β–$H_{\gamma 2}$	6.8		
$H_{\gamma 11}$–H_δ	7.7		
$H_{\gamma 12}$–H_δ	7.7		
$H_{\gamma 11}$–$H_{\gamma 12}$	−13.6	0.29	3.4×10^{-11}
H_α–$H_{\gamma 11}$			
H_α–$H_{\gamma 12}$			
$H_{\gamma 2}$–$H_{\gamma 2}$		0.16	2.1×10^{-11}
H_δ–H_δ		0.17	1.8×10^{-11}

[a] Scalar coupling constants refined by computer simulation. [b] σ_{ij} values are obtained from the two differences $R^i(\tilde{i},\tilde{j}) - R^i(SE)$ and $R^j(\tilde{i},\tilde{j}) - R^j(SE)$; averaged cross-relaxation rates are, therefore, reported with a minimum of 90% of reliability. [c] Correlation times calculated, as discussed in the text, from the relative σ's; the experimental error of the letters affects similarly the τ_c values.

The applicability of this discussion to D-alloisoleucine, a complex amino acid found in several naturally occurring species, will now be explored.

1. Monoselective and Nonselective Relaxation Rates and Mechanisms. The proton relaxation data and calculated ratios $F^i = R_1^i(NS)/R_1^i(SE)$ are shown in Table I. Because $F^i = 1.45$, the dipole-dipole interaction is the only efficient pathway for Hα, Hβ, and Hγ1's relaxation. The lower ratios for the Hγ2 and Hδ methyl protons are accounted for by (3).

The low F^{NH} value can be analyzed in terms of (6) in the previous section. In fact, taking into account the ^{14}N–^1H dipolar intersection,[12] using a $d_{N-H} = 1.02$ Å[13] and $\tau_c^{NH} = 7.5 \times 10^{-11}$ s, a $R^{NH} = 0.550\ s^{-1}$ was calculated. Subtracting this contribution both from $R^{NH}(NS)$ and $R^{NH}(SE)$, the corrected F value is equal to 1.40 and, therefore, also for the amide proton there is no need to invoke relaxation mechanisms other than the dipolar ones if the value of the used τ_c^{NH} is consistent with the other correlation times differently calculated within the molecule.

2. ^{13}C Spin–Lattice Relaxation Rates and Internal Motion. The NT_1 values for each $^{13}C\alpha$, $^{13}C\beta$, $^{13}C\gamma_1$, $^{13}C\gamma_2$, and $^{13}C\delta$ atoms are shown in Table II. As expected, the C–H vectors of both CH_3 groups have similar correlation times, τ_c^{CH} of 1.3×10^{-11} and 2.3×10^{-11} s; the faster τ_c corresponds to the δ CH_3 group farthest from the α carbon atom. The $C\gamma_1$–H vector of the methylene (CH_2) group has a smaller τ_c (=6.5×10^{-11} s) than the corresponding CH_3 group.

Table IV. Observed Vicinal Coupling Constants, ^3J, and Derived Populations for Classical Rotamers of the C^α–C^β and C^β–C^γ Bonds of *N*-Acetyl-D-alloisoleucine at 303 K

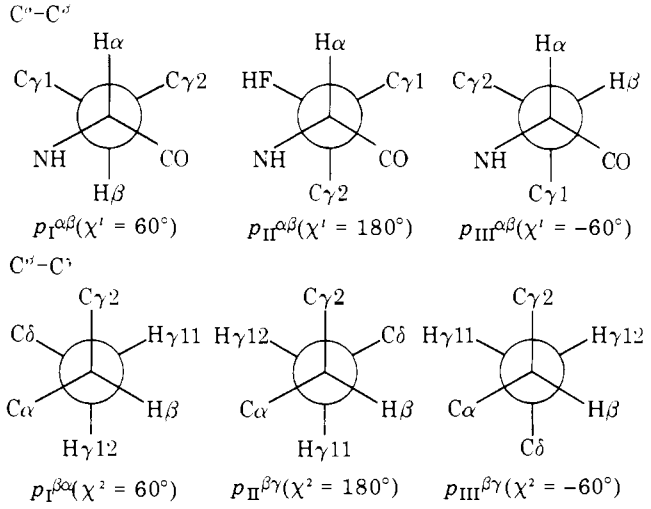
bond	$\langle^3J\rangle$, Hz	rotamer populations p_I	p_{II}	p_{III}
C^α–C^β	4.7	0.30[c]	0.70[c]	
C^β–C^γ	6.6[a]	0.20[d]	0.45[d]	0.35[d]
	7.6[b]			

[a] $^3J_{\beta\gamma 11}$. [b] $^3J_{\beta\gamma 12}$. [c,d] Refer to χ^1 and $\chi^{2,1}$ rotations. I, II and III refer to 60, 180, and −60°, respectively.

The $^{13}C^\beta$–H and $^{13}C^\alpha$–H correlation times are equal and considerably larger (1.3×10^{-10} s) than those of the $^{13}C^{\gamma 1}$–H and $^{13}C^{\gamma 2}$–H and C^δ–H vectors.

Unfortunately, the ^{13}C T_1 data were obtained at solute concentrations 40 times greater than those used for the proton relaxation data or the scalar coupling constant data and direct use of it is difficult. However, it was necessary that it be used to establish the dynamic nature of the isoleucine molecule.

3. Rotamer Analysis from Scalar Coupling Constants. The possible rotamers for C^α–C^β and C^β–C^γ rotation are shown.



$p_I^{\alpha\beta}(\chi^1 = 60°)$ $p_{II}^{\alpha\beta}(\chi^1 = 180°)$ $p_{III}^{\alpha\beta}(\chi^1 = -60°)$

$p_I^{\beta\alpha}(\chi^2 = 60°)$ $p_{II}^{\beta\gamma}(\chi^2 = 180°)$ $p_{III}^{\beta\gamma}(\chi^2 = -60°)$

The observed scalar coupling constants $\langle^3J_{\alpha\beta}\rangle$ = 4.7, $\langle^3J_{\beta\gamma 11}\rangle$ = 6.6, and $\langle^3J_{\beta\gamma 12}\rangle$ = 7.4 Hz deviate from the intrinsic component coupling constants, ^3J_G = 2.6 and ^3J_T = 13.6 Hz, characteristic of the individual rotamers. This confirms the existence of internal rotation around the C^α–C^β and C^β–C^γ bonds; only the latter was detected by the ^{13}C T_1 experiments.

The data in Table III were used to evaluate the rotamer populations for each of the nine classical isoleucine rotamers. It can be concluded from the data in Table IV that all nine rotamers are significantly populated; the range, 20–45%, means that rotation around both bonds is extensive. Only the sum $(p_{II}^{\alpha\beta} + p_{III}^{\alpha\beta})$ = 0.70 was evaluated but it is unlikely that either $p_I^{\alpha\beta}$ or $p_{II}^{\alpha\beta}$ does not exist when $p_{II}^{\beta\gamma}$ and $p_{III}^{\beta\delta}$ are 45 and 35% populated, respectively. The $\chi_{60}^{2,1}$ and χ_{60}^{1} rotamers are least populated. All these conclusions agree with the conformations found in *N*-acetyl-D-alloisoleucine crystals,[3] where the highest statistical weights were found for the χ_{180}^{1} and $\chi_{180}^{2,1}$ rotamers. The crystal structures also revealed that the combinations $(\chi_{-60}^{1}; \chi_{180}^{2,1})$ and $(\chi_{180}^{1}; \chi_{180}^{2,1})$ have the highest statistical weights. Multiplication of the individual rotamers statistical weights (Table V) shows that these combinations are also energetically favored in solution. In the $(\chi_{-60}^{1}; \chi_{180}^{2,1})$ conformation, the Hα, Hβ, Hγ11, and Hγ12 arrangement predicts small cross relaxation between Hα and both Hγ11 and Hγ12.

It was important to use this approach to detecting dynamic equilibria around the χ^1 and χ^2 bonds because it eliminates the interpretation of the similarity of the C^α and C^β spin-lattice relaxation rates in terms of frozen C^α–C^β rotation.

Table V. Statistical Weights for the $(\chi^1, \chi^{2,1})^a$ Combinations of *N*-Acetyl-D-alloisoleucine

$\chi^{2,1}$	$\chi^1 = 60°$	180° [b]	−60° [b]
60°	0.06_0	0.08_0[c]	0.06_0[e]
		(0.06_0)[d]	(0.08_0)[f]
180°	0.13_5	0.18_0[c]	0.13_5[e]
		(0.13_5)[d]	(0.18_0)[f]
−60°	0.10_5	0.14_0[c]	0.10_5[e]
		(0.10_5)[d]	(0.14_0)[f]

[a] χ^1 refers to C^α–C^β rotation and $\chi^{2,1}$ refers to C^β–$C^{\gamma 1}$ rotation. [b] The values in parentheses are what will be expected for the statistical weights of the 180 and −60° (assignments of *R* and *S* protons) were the reverse of that given. In this case *c*, *d*, *e*, and *f* were taken to be 0.40, 0.30, 0.30, and 0.40, respectively.

4. Structural and Vectoral Analysis from σ Parameters. In the presence of internal rotation and multiple conformational equilibria, it is not straightforward to convert the experimental σ_{ij} and σ_{ji} values into either correlation times or interproton distances. In general, the equation $\langle\sigma\rangle$ observed = $\Sigma\sigma_{ij}$. For C^α–C^β rotation of isoleucine we can write

$$\langle\sigma_{\alpha\beta}\rangle = p_I^{\alpha\beta}[\sigma_I] + p_{II}^{\alpha\beta}[\sigma_{II}] + p_{III}^{\alpha\beta}[\sigma_{III}]$$

All the $[\sigma]$ can be regarded as similar to the component coupling constants, ^3J_G and ^3J_T, and are called intrinsic rotamer σ values. Each has the form $[\sigma] = \hbar^2\gamma^4 (1/d^6)(f\tau_c)$.

If we assume that $f(\tau_c)$ is identical for all $[\sigma]$ and equal to that for $\langle\sigma\rangle$, these equations take the form

$$\langle d_{\alpha\beta}^{-6}\rangle = p_I^{\alpha\beta}[d_T^{-6}] + p_{II}^{\alpha\beta}[d_G^{-6}] + p_{III}^{\alpha\beta}[d_G^{-6}]$$

where d gauche = d_G = 2.49 Å and d_{trans} = d_T = 3.07 Å.

In the previous section, $p_I^{\alpha\beta}$ and $(p_{II}^{\alpha\beta} + p_{III}^{\alpha\beta})$ were evaluated, and this leads to an average distance $\langle d_{\alpha\beta}\rangle$ 2.59 Å; this distance and σ yield a $\tau_c(H\alpha\text{–}H\beta) = 6.9 \times 10^{-11}$ s for isoleucine.

A value of $^3J_{HNC^\alpha H}$ = 8.6 Hz, when corrected for electronegativity and assuming no φ motion, corresponds to distances of d_1 = 2.95 Å or d_2 = 2.3 Å. The d_2 value and $\sigma^{NH\text{-}H\alpha} = 0.12$ s give $\tau_c = 4.7 \times 10^{-10}$ or 6.4×10^{-11} while d_1 cannot yield the observed cross relaxation in any motional region.

The correlation times for the geminal vectors of both $C^\delta H_3$ and $C^{\gamma 2}H_3$ groups were evaluated according to eq 2, assuming no (SR) contribution to the relaxation of the methyl protons. This assumption is reasonable, because, according to previous discussion,[7,10] in the temperature dependence of the $C^{\gamma 2}H_3$ and $C^\delta H_3$ proton relaxation rates positive slopes representing activation energies respectively of 1.4 and 1.0 kcal/mol were found. Using an interproton distance of 1.77 Å for the protons of the CH_3 group and $\sigma^{H\gamma 2\text{-}H\gamma 2} = 0.16$ s^{-1} and $\sigma^{H\delta\text{-}H\delta} = 0.17$ s^{-1}, the correlation times for these vectors were found to be $\tau_c^{H\gamma 2\text{-}H\gamma 2} = 2.1 \times 10^{-11}$ s and $\tau_c^{H\delta\text{-}H\delta} = 1.8 \times 10^{-11}$ s, respectively.

Other structural information was obtained from the σ values in Table II. The small $\sigma^{H\alpha\text{-}H\gamma 1}$'s, within the experimental error range, are consistent with a very large population for the $(\chi^1; \chi^{2,1}) = (-60; 180°)$ conformation, in which the Hα does not approach closer than 3.5 Å to the Hγ11 and Hγ12.

The agreement between the correlation times calculated for the CH_3 groups from ^{13}C and ^1H spin-lattice relaxation analysis is encouraging; both sets of values are consistent with extensive, fast reorientation along the C^β–$C^{\gamma 1}$, C^β–$C^{\gamma 2}$, and $C^{\gamma 1}$–C^δ axes. The higher solution viscosity of the proton relaxation experiments produces a corresponding lower τ_c value, but the effect is primarily on the Brownian motion and therefore molecular, as distinct from internal, reorientation.

III. Conclusions

A spin-spin analysis of *N*-acetyl-D-alloisoleucine yielded all its scalar coupling constants including $\langle {}^3J_{\alpha\beta} \rangle$ and $\langle {}^3J_{\beta\alpha} \rangle$ and hence the rotamer populations for χ^1 and $\chi^{2,1}$ rotation. The products of the individual rotamer statistical weights gave the possible statistical weights of the (χ^1; $\chi^{2,1}$) conformations of the whole molecule. The largest of the latter agreed with those discovered by crystallography. The existence of multiple equilibria due to rotation around single bonds was confirmed by evaluation of NT_1 values for ^{13}C nuclei and yielded correlation times for $^{13}C_3$, $^{13}C_2$, and ^{13}CH vectors.

Mono-, bi-, and nonselective proton spin-lattice relaxation rates were measured for the NH, Hα, Hβ, Hγ11, Hγ12, and Hδ protons and the corresponding F ratios ($= R_1^i(\mathrm{NS})/R_1^i(i)$) and cross-relaxation rates, σ, calculated from these.

The distance, $d^{\alpha\beta}$, between the Hα and Hβ protons is averaged by C^α-C^β internal rotation and, by using $d^{\alpha\beta}_{\mathrm{trans}} = 3.07$ Å and $d^{\alpha\beta}_{\mathrm{gauche}} = 2.49$ Å, with the rotamer populations, $\langle d^{\alpha\beta} \rangle$ was found to be 2.59 Å. This in turn yielded $\tau_c{}^{\alpha\beta} = 6.9 \times 10^{-11}$ s.

The cross relaxation parameters, σ, yielded τ_c values for the two CH_3 groups (2.1×10^{-11} and 1.8×10^{-11} s) in satisfactory agreement with the corresponding ^{13}C-derived values (2.3×10^{-11} and 1.3×10^{-11} s).

The $\langle {}^3J_{\mathrm{NHCH}} \rangle$ value gave $\langle d_{\mathrm{NHCH}} \rangle = 3.0$ or 2.3 Å—only the latter, using $\sigma_{\mathrm{NHCH}} = 0.12\ \mathrm{s}^{-1}$, gave the correct $\tau_c{}^{\mathrm{NHCH}} = 6.4 \times 10^{-11}$ s. This therefore represents a method of removing the fourfold ${}^3J\ v\ \phi$ degeneracy in the Karplus curve.

The small value of σ between Hγ11 and Hγ12 with Hα confirmed the above conclusions (based upon scalar coupling constants) that the (χ^1; $X^{2,1}$) combination has a high statistical weight.

The F^i values of Hα, Hβ, and Hγl's confirmed that their relaxation mechanisms are exclusively dipolar while the low F^i value for the methyl group is entirely attributed to efficient cross relaxation among its protons. The low value $F^{\mathrm{NH}} = 1.2$ is attributed to the dipolar contribution relaxation between ^{14}N and its contiguous proton, because the assumed $\tau_c{}^{\mathrm{NH}} = 7.5 \times 10^{-11}$ s is consistent, within experimental errors, with the correlation time of the NH-C$^\alpha$H interproton vector evaluated from ${}^3J_{\mathrm{NHCH}}$ and $\sigma^{\mathrm{NH\text{-}H\alpha}}$.

This type of experiment is important in that it will permit extension of the use of proton relaxation rates to amino acid residues in peptides and proteins.

Acknowledgment. This work was supported by grants from NIH (AM186), NSF (BMS 70.23819 and PCM 77.13976), and the College of Agricultural and Life Sciences. Partial expenses for the Bruker WH270 campus facilities were provided by the Graduate School Research Committee and the University of Wisconsin Biomedical Research Grant RR 07098.

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