Molecular Dynamics in Ordered Structures: Computer Simulation and Experimental Results for Nylon 66 Crystals

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A detailed comparison between molecular dynamics computer simulations and the experimental characterization of molecular motion through deuterium nuclear magnetic resonance (NMR) spectroscopic methods has been carried out for the crystalline phase of nylon 66 (polyhexamethyleneadipamide) at room temperature and just below the melting point. The computer simulations agree quantitatively with the experimental results at room temperature and qualitatively near the crystalline melting point. Both methods demonstrate that individual methylene groups within the crystals exhibit librational motion, which becomes very large in amplitude near the melting point, rather than undergoing discrete conformational jumps; furthermore, the hydrogen-bonded amides are relatively immobile at all temperatures below 230 degrees Celsius. The simulations are shown to be particularly useful for examining the cooperativity of motion and for providing insight into structural-dynamical correlations. These aspects of the simulations are exemplified by the observation of concerted counterrotation of odd-numbered bonds within the methylene segments and the entropic stabilization of the crystal structure.

MOLECULAR MOTION IN PROTEINS AND SYNTHETIC POLYMERS is of fundamental interest due to the insight that it can provide as to the relationship of structure with properties such as activity, permeability, and mechanical performance. Correlation of static (average) structures with properties can, in some cases, be quite misleading. Knowledge of the dynamic structure has been critical in defining this correlation in a number of examples: establishing the relationship of the dynamic structure of the cytochrome c–cytochrome b_5 complex to its function as an electron transfer complex (*1*), modeling the permeability of gases through dynamic pores in polymeric membranes (*2, 3*), and developing a microscopic model of the mechanical deformation of synthetic polymers to produce ultra-extended, high modulus (stiff), structures (*4, 5*).

The experimental determination of the dynamic structure (at the length scale of a primary chemical bond) of an entire macromolecule has not been feasible; hence, computer simulation of these dynamic structures has been an area of considerable interest (*6, 7*). Furthermore, a detailed quantitative comparison of computer simulation and experiment, for a large fraction of a macromolecule on the appropriate time scale, has not been possible because of the absence of the necessary experimental data. In this article such a direct quantitative comparison is made for a synthetic polyamide, polyhexamethyleneadipamide (nylon 66). Comparison of the motion of each individual methylene group and the amide group within the repeat unit of the crystalline phase of this polymer illustrates the complementary values of the two methods.

For a variety of reasons nylon 66 is an excellent model system with which to compare molecular dynamics computer simulations and experimental results. A room-temperature crystal structure (*8, 9*) as well as the temperature dependence of the unit cell parameters have been determined with x-ray scattering methods (*10*). More importantly, a recent experimental determination (*11, 12*) of the molecular dynamics of individual C–D and N–D bonds using solid-state ^{2}H NMR methods affords the opportunity to make a direct comparison of the computer simulations to experiments on the same time (~10 ps) and length scales (~1 Å). The NMR experiments used allow the determination of both the rate and the amplitude of reorientation of individual bonds within the molecule. These experimental results provide a description of the dynamics of each individual carbon-hydrogen (deuterium) and nitrogen-hydrogen (deuterium) bond at every site within the molecule. The NMR methodology is quite different from that customarily used in the determination of either the molecular structure of small molecules or the connectivity of small peptides in solution. The experiments and the simulations may be compared not only with each other, but also with a number of models (*13–18*) of segmental motion of polymethylene chains that have been proposed for both amorphous and crystalline environments. This comparison illustrates that the methods are complimentary in that the experimental results provide a quantitative determination of the molecular dynamics, whereas the computer simulations are shown to provide semiquantitative results at ambient temperature and are particularly valuable for examining the cooperativity of motion. Finally, these results illustrate the synergism of

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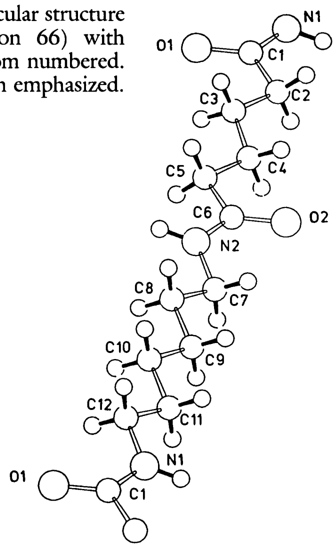
methods from the fields of molecular biology and polymer physics.

Molecular dynamics computer simulations. Molecular dynamics calculations were performed with an all-atom Cray-XMP version of the program AMBER (*19, 20*) modified to accept general unit cell parameters. Although the force field in this algorithm is parameterized for the atom types in proteins, the nylon 66 atom types and geometries are available within the database and were used without re-optimization. Values for the atomic charges were expected to be more environmentally dependent than other parameters, so these were obtained in a fashion similar to those in AMBER from a 3-21 G (*21*) self-consistent field calculation on the monomer units with the program GAMESS (*22*), and were then adjusted to obtain neutral units. Simulations were carried out for three cases: a room-temperature form (RT) at 25°C and two high-temperature (HT) forms that had slightly different unit cells and temperatures: HT-1 (240°C) (*10*) and HT-2 (230°C) (*12*). The unit cell parameters and atomic geometry of the RT form were taken from Colclough (*9*). A detailed structural model for each high-temperature unit cell was developed by starting from the RT unit cell and atomic structure and rescaling it to the HT unit cell in five uniform increments of the unit cell parameters. The resulting high-temperature structures were energy–minimized with 1000 steps of steepest descent minimization for each step in the unit cell rescaling, then minimized for another 2000 steps at the final HT geometry. All of the calculations were done with a residue-based cutoff of 8 Å, a time increment of 2 femtoseconds (fs), and SHAKE applied to the hydrogen atoms (*19, 20*). Sixty-four unit cells were used (four along each axis) with minimum image, triclinic periodic boundary conditions. Initial structures were energy–minimized, and molecular dynamics calculations were then carried out for 10 ps of equilibrium followed by 50 ps of data collection for all forms.

Fig. 1. Schematic drawing of the molecular structure of polyhexamethyleneadipamide (nylon 66) with each carbon, nitrogen, and oxygen atom numbered. The carbon–hydrogen bonds have been emphasized.



Several unit cell–averaged structural parameters are listed in Table 1 (see Fig. 1 for atom labeling). The root-mean-square (rms) difference between the atomic coordinates determined in an x-ray fiber diffraction study (*9*) and the energy-minimized RT structure is 0.08 Å for all non-hydrogen atoms, indicating that the form of the potential energy function used is reasonable. The rms difference between the 50-ps–averaged dynamic structure and the x-ray coordinates is 0.37 Å. The largest differences are found in the amide linkage and the methylene carbons in positions α to it. Similar differences are found in the thermal fluctuations of the dynamic structure, B_i (see Table 1). This similarity suggests that the rms differences between the averaged dynamic structure and the crystal structure reflect the local motions present at room temperature. Visual examination of the trajectory of motion indicates that the hydrogen bonding within the sheets is always maintained, with most of the large amide B_i values arising from local motion perpendicular to the hydrogen-bonded sheets rather than any librational motion. In the RT simulation, the B_i values of both of

Table 1. Average structural parameters. The atom labels are defined in Fig. 1; other definitions are given in the text. The root-mean-square (rms) deviations (Å) of the positions of non-hydrogen atoms in a 50-ps–averaged dynamic structure are referenced to the starting structure based upon the structure determined by fiber x-ray diffraction. The B_i values are calculated as $B_i = (8/3)\pi^2\langle x_i^2\rangle$, where x_i is the rms displacement of the i^{th} atom about its average position. Angle variations are in degrees and are one standard deviation. Angles for each methylene carbon are the average of the angles for the two C–H bonds. Angles for the N–H and C=O bonds are listed with the relevant N and C atoms.

Atom	rms	B_i			Angle variations					
					β			ψ		
	RT	RT	HT-1	HT-2	RT	HT-1	HT-2	RT	HT-1	HT-2
N1	0.46	1.47	5.78	3.49	4.13	7.03	6.56	9.30	10.9	9.60
H1		2.93	8.98	5.69						
C1	0.52	1.82	6.38	3.41	4.14	6.86	6.47	8.87	10.8	9.50
O1	0.31	1.23	7.15	4.00						
C2	0.47	2.82	10.04	5.31	6.70	11.6	10.3	17.2	30.1	23.3
C3	0.24	1.95	8.25	6.71	7.22	12.2	11.6	16.1	31.7	24.9
C4	0.27	1.91	8.16	6.99	7.10	11.5	11.6	15.8	31.5	25.4
C5	0.49	2.81	9.94	5.48	6.64	11.2	10.3	17.1	30.4	24.2
C6	0.51	1.86	6.16	3.40	3.68	6.37	5.93	7.68	10.1	8.64
O2	0.29	1.24	6.95	4.07						
N2	0.49	1.49	5.69	3.44	3.68	6.16	5.79	7.41	10.0	8.32
H2		3.04	8.93	5.59						
C7	0.45	1.24	6.94	4.54	5.33	8.02	8.37	7.65	27.2	23.6
C8	0.18	1.19	6.25	4.26	4.81	8.31	8.02	7.05	28.5	24.6
C9	0.20	1.22	6.77	4.74	4.58	7.85	7.68	6.88	29.8	26.8
C10	0.20	1.22	6.80	4.78	4.58	7.74	7.65	6.88	30.0	26.8
C11	0.18	1.19	6.29	4.27	4.81	8.37	7.94	7.05	28.8	24.9
C12	0.46	1.24	6.83	4.45	5.36	7.91	7.56	8.42	27.6	24.1

the amide linkages are approximately the same, whereas the B_i values for the methylene groups in the adipoyl moiety are approximately twice those found for the methylene groups in the longer diamine moiety. In the HT forms, the methylene groups in the shorter adipoyl moiety still have larger B_i values than those in the longer diamine moiety, but now only one-half again as large.

^{2}H NMR spectroscopic determination of molecular motion. Modern NMR spectroscopic methods (*23*) have been particularly fruitful in the study of molecular motion of deuterium nuclei bonded to carbon, nitrogen, oxygen, and other elements. These methods allow the study of the motion of chemically distinct primary chemical bonds by observation of the characteristic relaxation times and powder line shapes of the deuterium nucleus. Pulsed radio-frequency ^{2}H NMR techniques (*24*) were used to obtain these data for specifically deuterated (*25*) nylon 66 semicrystalline polymers. Data for the crystalline phase alone were obtained by using spin-lattice relaxation time discrimination so as to observe only magnetization from these regions (*12*). The ^{2}H NMR line shapes are illustrated in Fig. 2 for five polymers selectively deuterated at each of the pairs of chemically distinct methylene groups within the repeat unit. In addition, ^{2}H NMR spectra of the N-D–labeled polymer indicate that there is very little rotational motion of these bonds below 230°C, which is near the melting point of 250° to 260°C.

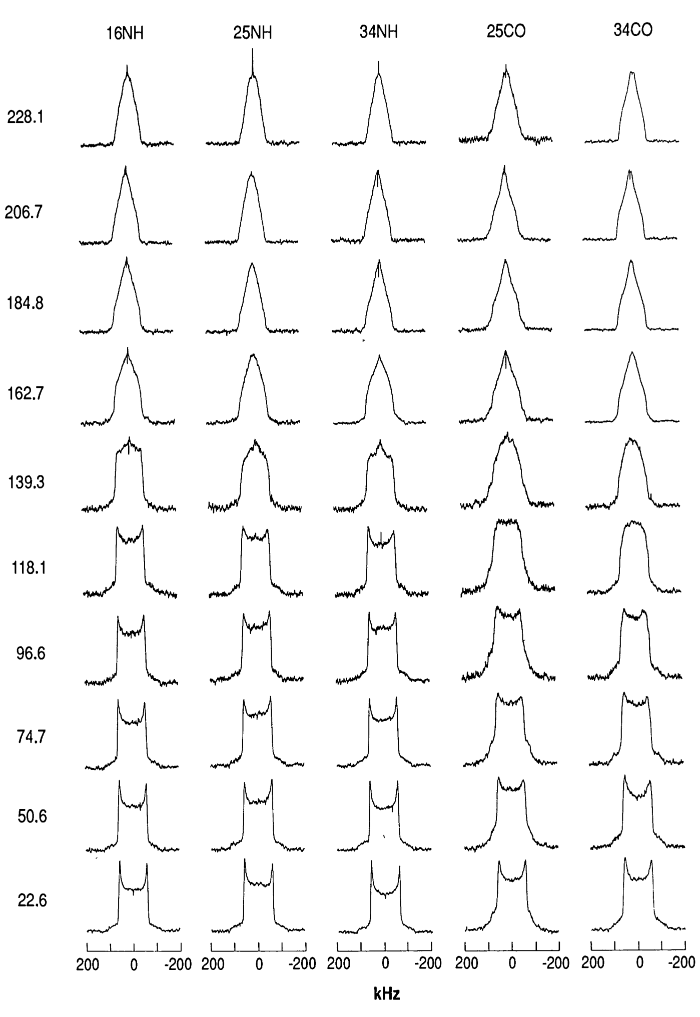


Fig. 2. ^{2}H NMR spectra of specifically deuterated nylon 66 polymers as a function of temperature. The isotopically labeled polymers are designated by the following nomenclature (labeled monomer): 16NH (hexamethylene-1,1,6,6-d_4-diamine), 25NH (hexamethylene-2,2,5,5-d_4-diamine), 34NH (hexamethylene-3,3,4,4-d_4-diamine), 25CO (adipoyl-2,2,5,5-d_4 chloride), and 34CO (adipoyl-3,3,4,4-d_4 chloride).

Table 2. Average dihedral angles in degrees (error is one standard deviation).

Central dihedral bond	RT	HT-1	HT-2
C1–C2	200.950 (13.873)	235.583 (31.310)	260.567 (22.823)
C2–C3	178.497 (6.880)	185.050 (11.087)	187.250 (10.443)
C3–C4	179.550 (11.890)	179.353 (25.897)	178.160 (29.037)
C4–C5	181.367 (6.903)	175.373 (11.057)	173.203 (10.360)
C5–C6	159.667 (13.623)	124.987 (31.120)	100.420 (23.783)
N2–C7	188.480 (7.637)	196.710 (21.130)	196.023 (17.757)
C7–C8	177.190 (6.320)	182.273 (12.427)	179.187 (11.407)
C8–C9	178.727 (5.453)	183.700 (14.130)	184.247 (14.067)
C9–C10	180.077 (5.447)	180.017 (11.327)	180.027 (10.103)
C10–C11	181.257 (5.430)	175.593 (14.063)	174.983 (14.290)
C11–C12	182.833 (6.263)	177.567 (12.517)	180.727 (11.560)
C12–N1	171.443 (7.537)	164.207 (20.240)	164.983 (17.180)

The line shapes of Fig. 2 and associated relaxation data have been the subject of extensive analysis elsewhere (*12*), which has lead to a detailed quantitative description of the motions in this system. However, simple examination of these line shapes leads directly to some qualitative conclusions about the motions extant in this system. The line shapes at each temperature are essentially identical for the deuterated methylene groups within each moiety; additionally, above ~160°C the line shapes of all five types of methylene groups look very similar. Below ~160°C the line shapes of the methylene groups located in the hexamethylenediamine (HMDA) moiety are characteristic of less motional averaging than the line shapes of the methylene groups located in the adipoyl moiety. These observations indicate that the motion of individual methylene groups within each moiety are quite similar and that below ~160°C the motion of methylene groups in the longer moiety (HMDA) are hindered relative to methylene groups in the shorter moiety (adipoyl). Furthermore, the line shapes and spin-lattice relaxation data together indicate that the motion extant in this system is not one that may be described as jumps between discrete sites (such as trans ↔ gauche isomerization) with the rate increasing with temperature in the usual fashion for a thermally activated process, but rather is one in which the rate of the motion ($\approx 10^{11}$ Hz) shows only very weak temperature dependence and the angular amplitude increases substantially with temperature. This latter type of motion is denoted a libration and can be demonstrated to be the proper model in this system from the line shape distortions due to the anisotropy of spin-lattice relaxation (T_{1Q}) (*12, 26*). The conclusion that the temperature dependence of the NMR data mainly reflects a growth in the amplitude of motion, as opposed to simply an increase in the rate of the motion, has been observed previously in other polymeric systems (*27*). This observation once again indicates that many of the models of motion (*13–18*) of polymethylene segments in macromolecular systems are not universally applicable.

Discussion. Selected frames from the molecular dynamics simulation of one sheet of the nylon 66 crystal are shown in the two multiple exposure stereoscopic pictures of Fig. 3. There is more motion in the shorter segment (adipoyl moiety) than in the longer segment (HMDA moiety) at room temperature, whereas at high temperature the amplitude of motion is quite comparable in both moieties. To facilitate a more direct comparison of this motion with the experimental results, the distribution of polar angles (β, ψ) for each methylene group has been calculated. The polar axis is defined by the amide nitrogens in each structure, β is the angle between this axis and the C–H bond, and ψ is the rotational angle about this axis. These results (Table 1) are in excellent qualitative agreement with the experimental data in that: (i) the motion of each C–H bond within an individual moiety is similar at each temperature; (ii) the amplitude of motion of the C–H bonds within the shorter adipoyl moiety is larger than in the HMDA moiety in the low-temperature form; and (iii) the amplitude of motion of all of the C–H bonds is similar at high temperature.

Whereas the (β, ψ) polar angles are the appropriate representation for generating a direct comparison of the molecular dynamics simulations with the NMR data (Fig. 4), examination of backbone-atom dihedral-angle distributions (Table 2) allows one to more easily examine questions of cooperativity of the motion. These data illustrate that in the RT form all of the backbone bonds in the HMDA moiety appear to be fairly similar in their mobility with the C–C bonds on average quite close to an all-trans configuration, whereas in the adipoyl moiety there is substantial variation in the mobility of individual bonds even though the average structure of each C–C bond is also quite close to an all-trans configuration. These data and visual inspection of the simulation indicate that there is substantial concerted motion about the C1–C2 and C5–C6 bond pair in the adipoyl moiety corresponding to a near-rigid restricted rotation of all four carbon atoms; additionally, there is also concerted motion about the C1–C2 and C3–C4 bond pair and about the C5–C6 and C3–C4 bond pair corresponding to a near rigid restricted rotation of each end pair of carbon atoms.

The motion in the RT form may be qualitatively summarized as one in which all of the bonds have standard deviations of at least 5° to 6° with the bonds in the adipoyl group α to the amide linkage and at the center of this four-carbon segment having larger deviations (~12°) due to concerted motion of two and four carbon atoms. In

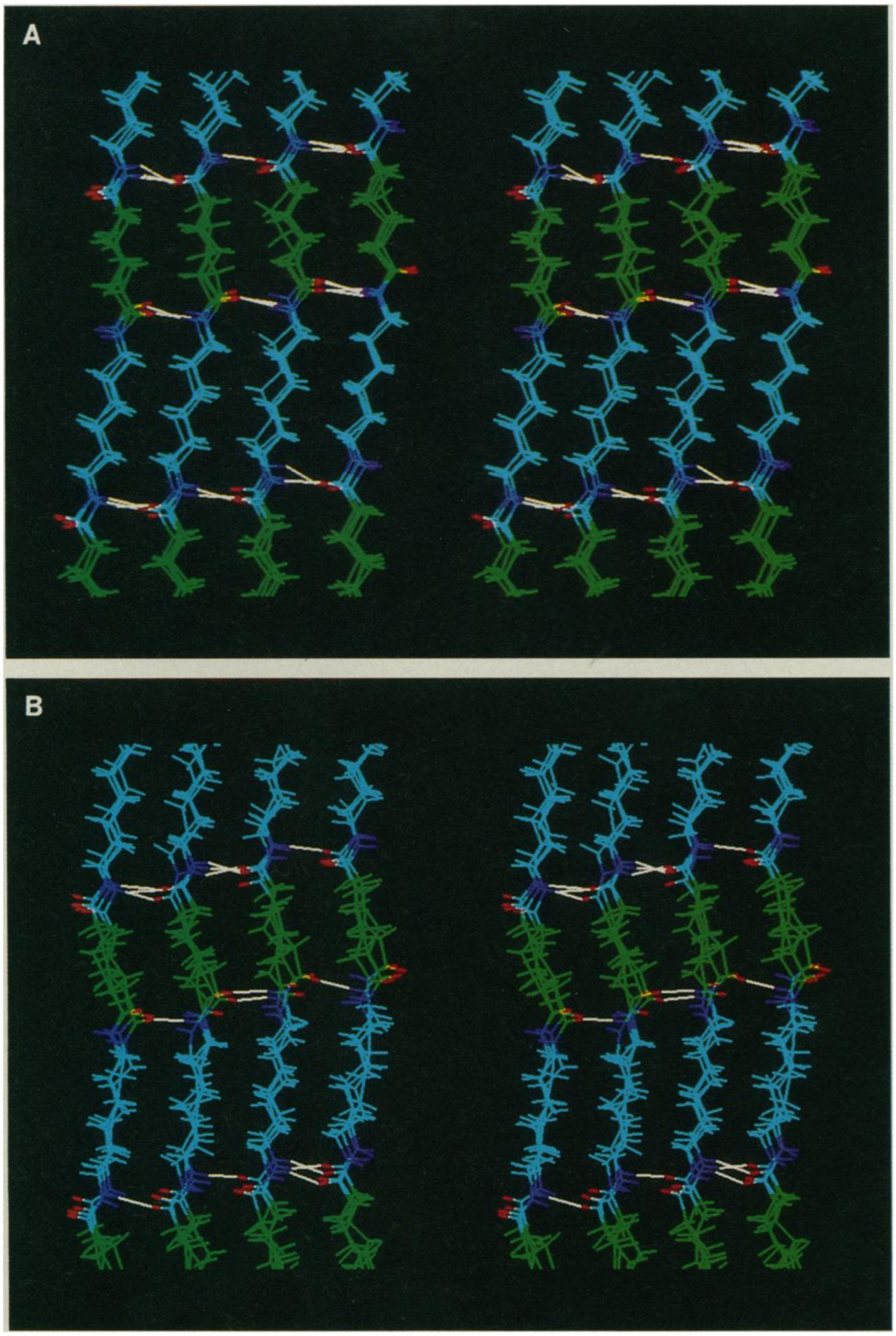


Fig. 3. Steroscopic views of (**A**) the room-temperature simulation and (**B**) the HT-1 simulation of a single sheet of polyhexamethyleneadipamide chains within a crystal (viewed down the crystallographic *b* axis) constructed from selected frames of a molecular dynamics simulation. The carbonyl groups are shown in red, the nitrogens in dark blue, and the hydrogen bonds in white. The methylene groups in the adipoyl moiety (green) are seen to be executing larger amplitude motions than are the methylene groups located in the HMDA moiety (blue) at room temperature, whereas in the HT-1 form all methylene groups are undergoing very large amplitude motions.

the HT-1 form (*10*) all of the bonds have standard deviations of at least 11° to 12° where additionally the HMDA moiety executes a near-rigid restricted rotation of the entire six-carbon segment (N2-C7 and C12-N1), whereas the adipoyl moiety still shows evidence of both four-carbon and two-carbon segmental motions. In the HT-2 form (*12*) all of the bonds have standard deviations of at least 10° to 11° where again the adipoyl moiety still shows evidence of both four-carbon and two-carbon segmental motions, whereas the HMDA segment shows evidence of only a slight preference for six-carbon motion as compared to two-carbon motions. The motion of

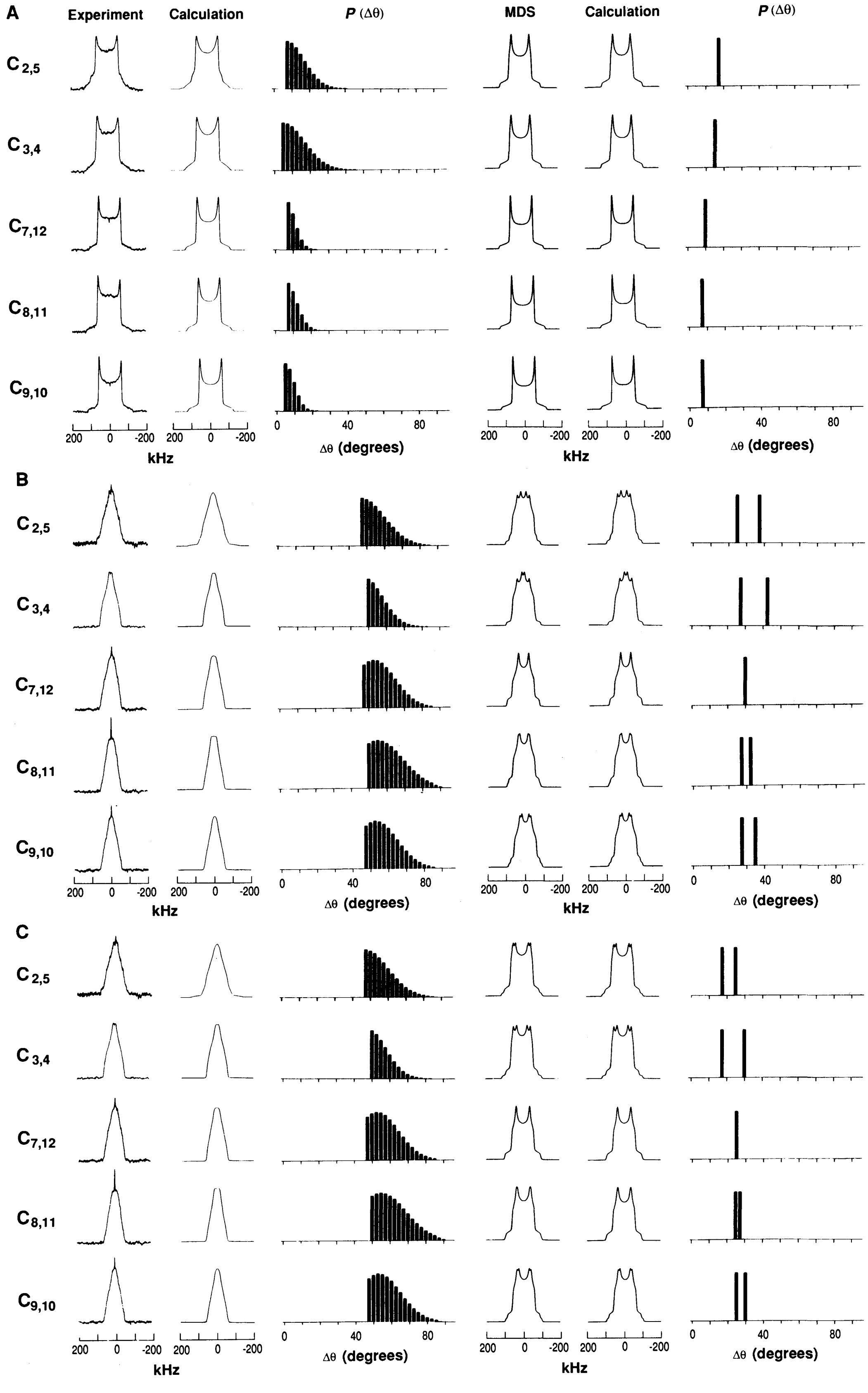


Fig. 4. Comparison of ^2H NMR experimental line shapes, for selectively labeled nylon 66 polymers, with line shapes calculated from the results of the molecular dynamics simulations, and comparison of both of these line shapes to that calculated from a model of a Gaussian distribution [$P(\Delta\theta)$] of predominantly uniaxial librational motion about the C–C tetrahedral bond. $P(\Delta\theta)$ for each calculation is shown in the center and right-hand side of the figure. (**A**) Results at room temperature; the mean value ($\langle\Delta\theta\rangle$) of the librational distributions for each methylene groups are experimental (calculated): $C_{2,5}$ = 14.5° (19.0°); $C_{3,4}$ = 14.0° (16.0°); $C_{7,12}$ = 9.7° (9.0°); $C_{8,11}$ = 10.5° (7.0°); and $C_{9,10}$ = 8.7° (7.0°). (**B**) Results for the HT-1 form; the mean value ($\langle\Delta\theta\rangle$) of the librational distributions for each methylene groups are experimental (calculated): $C_{2,5}$ = 57.7° (31.5°); $C_{3,4}$ = 55.5° (34.5°); $C_{7,12}$ = 58.6° (30.0°); $C_{8,11}$ = 61.5° (30.5°); and $C_{9,10}$ = 58.6° (31.5°). (**C**) Results for the HT-2 form; the mean value ($\langle\Delta\theta\rangle$) of the librational distributions for each methylene groups are experimental (calculated): $C_{2,5}$ = 57.7° (22.0°); $C_{3,4}$ = 55.5° (23.5°); $C_{7,12}$ = 58.6° (25.0°); $C_{8,11}$ = 61.5° (25.5°); and $C_{9,10}$ = 58.6° (27.0°).

the methylene groups observed both experimentally and computationally is limited to librations, with no evidence of discrete rotational isomeric modes, such as trans-gauche jumps, because the amide hydrogen bonds are preserved and show very little motion relative to that observed in the methylene groups at all temperatures. Thus the amide linkages act as "pinning points" and impose nearly rigid structural constraints on the modes of motion available to the methylene chains. Furthermore, the simulations give insight into the origin of the relative inhibition of motion in the longer (HMDA) methylene chain moiety as compared with the adipoyl moiety at room temperature. Rotation of either a two- or four-carbon segment in the adipoyl moiety requires that the methylene group α to the amide linkage must be able to rotate past the adjacent N–H bond, while the methylene group α to the amide linkage in the HMDA moiety must be able to rotate past the adjacent C=O bond in order to execute a two-, four-, or six-carbon group near-rigid rotation. Since the oxygen is expected to have a much larger steric volume than the hydrogen (*19, 20*), rotations of methylene groups in the adipoyl moiety should occur more easily than those in the HMDA moiety.

Direct comparison of the computer simulation with the experimental results is made in Fig. 4. The experimental ^{2}H NMR line shapes are compared both with those calculated directly from the motion indicated by the computer simulations and to those calculated for a model of predominantly uniaxial librational motion about a tetrahedral C–C axis (*12*) to fit either the experimental or computer simulation line shapes; additionally, the distribution of uniaxial librational angles $[P(\Delta\theta)]$ is illustrated for each calculation and the mean value ($\langle\Delta\theta\rangle$) of each distribution is given in the caption (*28*). This comparison illustrates that the motion observed in the computer simulation for the RT form yields line shapes in very good agreement with experiment and the simulations for the HT forms are in qualitative agreement with experiment. The much broader distribution of librational angles observed experimentally is consistent with the finite size of the actual crystallites compared with the effectively infinite crystal (periodic boundary conditions) used in the simulations. The lack of quantitative agreement of the HT simulations with the experiments also suggests that the potential energy function used in the simulations is not sufficiently accurate at these very high temperatures. Nevertheless, the results illustrate that the computer simulations, over a range of temperatures, yield results which are qualitatively correct and provide insight into the cooperativity of motion and the structural-dynamical correlations. This first point has been illustrated by the observation of concerted counterrotation about the odd-numbered bonds in the methylene sequences within the crystal. An example of the latter point is the observation that the low-symmetry unit cells adopted by the RT and HT forms permit the large-amplitude librations, which of themselves provide entropic stabilization of the crystals (*29*).

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28. Note that the predominantly uniaxial librational model not only is capable of generating very good fits of the experimental line shapes, but is able to fit the molecular dynamics simulation results quite well. This result indicates that this model is a good representation of the more complicated motion generated in the computer simulation.
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