data presented that resolution of the angle of scatter of kilovolt energy ions after collision with neutral gas molecules provides access to this range of lifetimes. This information had previously only been available via more complex methods. Much in the same way that the "phenomenological" rate constant determined by FIK can be ascribed to the internal energy content of a given molecular ion, we have demonstrated that angle-resolved mass spectrometry has a similar capability of specifying the lifetime[16] of an ion after collisional activation. Most significantly, a wide range of ion lifetimes is available, including those corresponding to the shortest accessible in field ionization kinetics. These findings should facilitate fundamental studies of ion chemistry.

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(16) These ions would not fragment without collisional activation; the total lifetime of the molecular ion is of the order of microseconds, but the lifetime after collisional activation is variable in the range 10^{-11}–10^{-6} s. If isomerization occurs prior to collisional activation, the two techniques would sample the same time interval but do so for ions of different structure.

Observation of Conformationally Distinct Proline Residues in Two Cyclic Peptides by Solid-State Nuclear Magnetic Resonance

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High-resolution ^{13}C NMR spectroscopy of crystalline cyclic peptides allows the comparison of their conformations in the solid state to those assumed in solution. The solid-state NMR spectra have individual ^{13}C resonances at their isotropic chemical shift positions.[1,2] Both intramolecular (conformational) and intermolecular (crystal packing) effects can play important roles in determining the actual magnetic environment of nuclei in solid samples which is reflected in the isotropic chemical shift.[3] In contrast, solution samples have chemical shifts dominated by intramolecular factors, since most intermolecular interactions are averaged out by rapid molecular motions. It is of interest to find examples of molecules where the solid-state NMR chemical shift data can be interpreted in terms of conformational and packing effects separately. Cyclic peptides with solved crystal structures and well-analyzed solution NMR spectra showing defined conformational features are attractive choices for study.

We have obtained ^{13}C NMR spectra of two crystalline peptides with chemical shifts that can be uniquely attributed to molecular conformation, and these are the same effects manifested in the solution spectra. Both of the peptides studied contain two proline residues, and the ^{13}C chemical shifts of proline resonances are indicative of particular conformational states of the peptide.

The cyclic pentapeptide *cyclo*-(D-Phe-Pro-Gly-D-Ala-Pro) has essenitally the same conformation in solution (in a variety of solvents)[4] and crystals.[5] This conformation is stabilized by the two intramolecular hydrogen bonds shown in Figure 1A. The two prolines in the molecule have very different ring geometries; the one involved in the 4 → 1 hydrogen bond (β turn)[6] has a ring conformation similar to that found in many linear peptides with rotational angles $\phi = -64°$ and $\psi = 128°$,[7] while the other has a more unusual conformation with $\phi = -82°$ and $\psi = 59°$, probably because it is residue 2 of the 3 → 1 hydrogen bond (γ turn).[6] This latter local conformation has the carbonyl oxygen of the proline eclipsed with its β-methylene group, resulting in an unusually high-field chemical shift position for the β-carbon resonance.[8,9] This is shown in the solution spectrum of Figure 2B where the arrows point out the 5-ppm difference between the C_β resonances of the two prolines; the upfield shifted β signal is near those from the proline γ carbons.

Figure 2A contains the ^{13}C NMR spectrum of the crystalline cyclic pentapeptide. It is a well-resolved spectrum with aliphatic

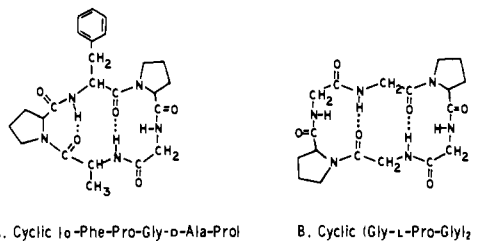

Figure 1. Structures of the two cyclic peptides whose solid-state NMR spectra are discussed. (A) *cyclo*-(D-Phe-L-Pro-Gly-D-Ala-L-Pro), showing 3→1 (γ turn) and 4→1 (β-turn) hydrogen bonding, present in both solution and crystal conformations of this peptide. (B) *cyclo*-(Gly-L-Pro-Gly)$_2$, showing 4→1 (β turn) hydrogen bonding present in the proposed (ref 12) solution conformation. Only one hydrogen bond exists in the conformation observed in crystals.

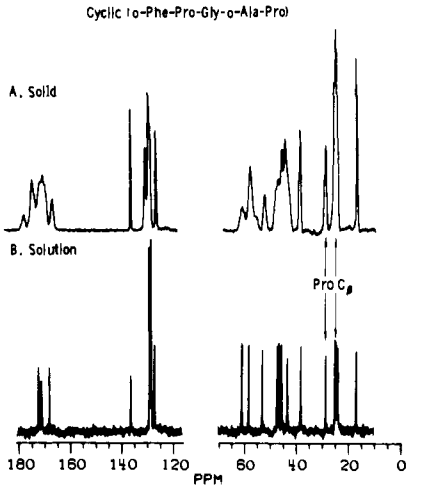

Figure 2. ^{13}C NMR spectra of *cyclo*-(D-Phe-Pro-Gly-D-Ala-Pro) at 38 MHz with chemical shifts relative to external Me_4Si. (A) Polycrystalline peptide sample. This spectrum was obtained on a home-built double-resonance spectrometer from ca. 300 mg of material in an Andrews-Beams rotor spinning at the magic angle. The spectrum is the result of 15 000 single 1-ms cross-polarizations from the protons, recycled every 5 s with 2.5-mT proton decoupling during the 0.1-s acquisition time. To avoid interference from spinning sidebands the spectral region 120–180 ppm is from the sample in a Kel-F rotor spinning at 2.4 kHz while the 0–70-ppm region is from the sample in a Delrin rotor spinning at 3.2 kHz. (B) Peptide in $CDCl_3$ solution. This spectrum was obtained on a Nicolet NT-150 spectrometer with 300 mg of sample in 10-mL volume in a 20-mm tube. It is the result of 9000 accumulations after 90° pulses recycled every 7 s. Square-wave modulated proton decoupling was applied continuously.

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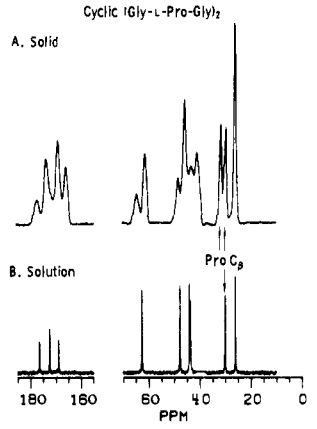

Figure 3. ^{13}C NMR spectra of *cyclo*-(Gly-L-Pro-Gly) at 38 MHz with chemical shifts relative to external Me_4Si. (A) Polycrystalline peptide sample. Same spectrometer and conditions as for Figure 2A using a Kel-F rotor spinning at 2.5 kHz. (B) Peptide in Me_2SO/H_2O solution. Same spectrometer and conditions as for Figure 2B using a recycle time of 5 s. The zeroed points near 40 ppm mark the position of the Me_2SO-d_6 solvent resonances.

resonances in the 10–40-ppm region, essentially superimposable with those from the solution spectrum. The differentiation of the two proline C_β's is clear in the solid-state spectrum, with one resonance at the normal isotropic chemical shift position of 29 ppm and the other shifted upfield about 5 ppm where it overlaps with the two Pro C_γ's in the three-carbon resonance at 25 ppm. All carbonyl, C_α, and Pro C_γ resonances are split into broadened asymmetric doublets because ^{13}C–^{14}N dipolar couplings of the peptide bonds are not removed by magic-angle sample spinning.[10] The difference in appearance for the 45–65- and 165–175-ppm regions between the solid-state and solution spectra is a consequence of the spin interactions and not of alterations of peptide structure. The chemical shift correlation for the solution and solid-state spectra indicates that the predominant factors leading to the isotropic chemical shifts of the crystalline cyclic pentapeptide are conformational and packing effects play a secondary role; this is in contrast to the situation for amino acids or linear peptides.[3] Inspection of the arrangement of the peptide molecules in the crystal lattice[5] suggests that packing constraints do not contribute strongly to the molecular environment in the solid. There are no solvent molecules in the crystal, and the only intermolecular hydrogen bonding occurs between the Pro-Gly units of two molecules. The highly magnetically anisotropic phenyl rings lie over the molecules to which they belong but do not come into close range of other molecules. The direct correspondence between chemical shifts of the cyclic pentapeptide in the solid and solution seems to derive from the well-defined and highly conserved conformation and the absence of strong packing effects.

The cyclic hexapeptide *cyclo*-(Gly-L-Pro-Gly)$_2$ has an asymmetric structure in the solid state with one intramolecular hydrogen bond.[11] Both Pro-Gly units are in β turns, although one has a proline ψ angle of 126° (type II) and the other, without a hydrogen bond, has $\psi = 36°$ (type I). Their ϕ angles are similar at −53 and −66°, respectively. The ^1H and ^{13}C NMR spectra of the cyclic hexapeptide in solution[12] are very simple with the minimum number of lines and are consistent with the C_2 symmetric conformation, having the two intramolecular hydrogen bonds drawn in Figure 1B or with rapid averaging of asymmetric conformations.

The ^{13}C NMR spectrum of *cyclo*-(Gly-L-Pro-Gly)$_2$ in the solid state in Figure 3A has well-resolved Pro C_β resonances, indicative of molecular asymmetry. In contrast, the solution ^{13}C NMR spectrum in Figure 3B has a single resonance for the two proline residues. Solution NMR studies on a series of *cyclo*-(X-L-Pro-Y)$_2$ hexapeptides suggest that different Pro C_β resonance positions may be associated with the $\psi = -30°$ (type I) and $\psi = 120°$ (type II) β turns.[13] However, conclusive interpretation of the observed resonance positions in terms of conformation and change in conformation between the two phases must await the results from additional model compounds, because the relationship between Pro C_β chemical shifts and β-turn conformational states is not rigorously established[14] and because of the competition between inter- and intramolecular factors on chemical shifts in the solid state. Nonetheless, on the basis of the solid-state spectrum of Figure 3B, it can be anticipated that prolines in type I and type II β turns will have different NMR parameters, notably C_β chemical shifts.

NMR spectroscopy can bridge the gap between solid-state and solution studies of peptide conformation. When intramolecular effects determine chemical shifts, then the multiplicities and positions of resonances can be correlated with structural features present in solution and in the solid state. In particular, in the two cyclic peptides studied, the carbon chemical shifts of proline resonances were found to reflect the participation of this residue in local hydrogen-bonded conformations with consequent differences in ring geometries and backbone dihedral angles.

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1-Azetine: Thermal Ring Opening to 2-Azabutadiene

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The thermal decomposition of cyclopropyl azides leads usually to ring-expanded 1-azetine derivatives with minor amounts of nitriles and olefins. However, no azetine was observed when the carbon substituent α to the azido group is a hydrogen atom.[1] Similarly, 2-phenyl-1-azetine was obtained from the base-promoted 1,2-elimination of HCl from 2-phenyl-*N*-chloroazetidine,[2] whereas the unknown parent compound was too unstable to be isolated under the same conditions. We now wish to report the preparation, spectroscopic data, and some chemical properties of 1-azetine (**2**).

We have recently shown[3] that highly strained olefins could be easily obtained by vacuum gas-phase elimination of the halogenated precursor over silica supported *KO-t-Bu*. By use of the same apparatus,[4] dehydrohalogenation of *N*-chloroazetidine (**1**)[2]

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