PCCP

Conformational studies of polymorphic *N*-octyl-D-gluconamide with ^{15}N (labeled) ^{13}C (natural abundance) REDOR spectroscopy

I. Sack,† S. Macholl, J. H. Fuhrhop and G. Buntkowsky*

Freie Universität Berlin, Institut für Chemie, Takustrasse 3, D-14195 Berlin, Germany. E-mail: bunt@chemie.fu-berlin.de

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Magnetic dipolar couplings between the ^{15}N atom (labeled) and neighboring ^{13}C atoms (natural abundance) in three solid modifications of *N*-octyl-D-gluconamide are measured with rotational echo double resonance (REDOR). A unique spectral assignment of ^{13}C resonances is possible by means of their dipolar dephasing. While in the monolayer crystal and in the fiber modification the assignment is amenable to the solution spectra, in the bilayer crystallites a different assignment is found. The dipolar couplings in the range 45 to 1220 Hz are converted into CN distances. These distances are employed in conjunction with the ^{13}C chemical shieldings of the CP-MAS spectra to determine sets of possible torsion angles, which define the molecular conformation in the neighborhood of the amide group. In contrast to the monolayer crystal, for the fiber and bilayer crystallite modifications a *gauche* bend at the C2–C3 bond is found, giving the molecules the shape of a $_2$G sickle.

Introduction

Open chain carbohydrate derivatives containing secondary amide groups form a large variety of fibrous assemblies in water due to hydration of chiral centers and strong linear amide hydrogen chains.[1–4] In order to understand the mechanism of the creation of micelles in this group of compounds, it is important to know their individual molecular conformation, which is related to the supermolecular arrangement. Therefore, the correlation of (chemical) molecular structure and supermolecular structure has been studied systematically on *N*-octyl-D-hexonamides.[3,4]

While it was feasible to directly determine the conformations of the carbohydrate chain of the class of well crystallizing compounds by X-ray diffraction, the non- or poorly crystallizing solids were analyzed by an indirect approach employing isotropic ^{13}C chemical shielding (CS) data obtained from ^{13}C CPMAS solid state NMR spectra. Structural information was obtained comparing these data to ^{13}C CS of similar hexonamides with known conformation. The latter approach is based on the availability of a large number of crystal structures of different conformers within the closely related classes of compounds, namely of open-chain glyconamides, glycosylesters and -acetals. The spectral assignment of their ^{13}C atoms was performed by virtue of the ^{13}C CS in solution.

However, as will be shown in detail below, the sensitivity of ^{13}C CS to conformational features[5] or hydrogen bonding may cause an interchange of signal positions in CP-MAS spectra due to different secondary structures. Thus, solution CS values by no means guarantee safe assignments of the resonance frequencies in the solid modifications and the correlation of the liquid-state assigned ^{13}C NMR signals with related crystal data can only in fortunate cases yield the real conformation of the molecule.

In contrast, dipolar solid state NMR spectroscopy can give direct insight into the conformation of a molecule in the solid state and does not depend on the availability of suitable single crystals.[6,7] Two prerequisites are needed for a successful conformational analysis by dipolar solid state NMR: (i) a high spectral resolution to assign individual signal lines to particular atomic positions in the molecule by virtue of their isotropic CS and (ii) a network of adjacency, which contains the information about the interatomic distances.

High resolution is achieved by application of the magic angle spinning (MAS)[8] technique, often in combination with cross polarization (CP-MAS)[9] from protons to enhance the signal of the X-nuclei. CP-MAS spectra obtained in this way do not contain direct geometrical information. Therefore, in recent years an impressive number of experiments has been invented to achieve dipolar recoupling under MAS. These experiments allow the measurement of dipolar couplings under high resolution. A review of some of these techniques can be found in Bennett *et al.*[10] The basic idea of these recoupling experiments is to periodically disturb the evolution of the spin system by rotor-synchronized RF pulses. For heteronuclear systems of two X-nuclei, the rotational echo double resonance (REDOR) experiment[11–17] is of particular importance. This method allows the recoupling of dipolar interactions between different X-nuclei (for example ^{15}N and ^{13}C) by periodically inverting the sign of the heteronuclear dipolar interaction.

Most REDOR studies have been performed by investigating either doubly labeled systems or systems of abundant spins. However, REDOR spectroscopy allows also the combination of a single spin label, for example a ^{15}N nucleus inserted in a molecule, with low abundance spins of another species, for example ^{13}C in natural abundance.[18] These ^{15}N (labeled) ^{13}C (natural abundance) REDOR experiments have several important advantages: (i) expensive and often unfeasible selective ^{13}C isotope labeling is avoided; (ii) a single REDOR experiment gives several dipolar couplings, *i.e.* distances, (iii) distortions of the evolution of the REDOR decay due to ^{13}C–^{13}C homonuclear interactions in a multi-^{13}C labeled system are avoided. The problem with this ^{13}C REDOR approach is the low signal to noise ratio of ^{13}C (natural abundance) spectra of large molecules, in particular

† Present address: Chemical Physics Department, Weizmann-Institute of Science, 76100 Rehovot, Israel.