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Solid-State NMR Characterization of ^{13}C- and ^{15}N-Labeled Phthalimides as Model Compounds for Studying Polyimides

WILLIAM L. JARRETT, C. GREG JOHNSON, AND LON J. MATHIAS*

University of Southern Mississippi, Department of Polymer Science, Hattiesburg, Mississippi 39406-0076

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^{15}N CSA spectra were acquired for four isotopically labeled bisphthalimide compounds. The ^{15}N CSA tensor elements (δ_{11}, δ_{22}, and δ_{33}) for the labeled derivatives were determined from CSA lineshape analysis. In addition, the CSA spectrum for the ^{15}N, ^{13}C-labeled *N*-methylphthalimide was obtained. From CSA lineshape analysis, it was determined that δ_{33} lies approximately along the N–C bond axis, with δ_{22} assumed to be approximately perpendicular to the imide plane. The angles α and β were found to be 90° and 7°, respectively. The dipolar coupling constant for the ^{13}C–^{15}N bond was 883 Hz, corresponding to a bond length of 1.51 Å.

INTRODUCTION

High-resolution solution and solid-state NMR techniques have been used for a number of years to characterize biological and polymeric systems. Until the past 10–15 years, however, techniques which only observe the isotropic chemical-shift (δ_{iso}) value were utilized, thereby ignoring the valuable information that may be obtained from the δ tensor, which is sensitive to the structural and chemical environment of the observed site. Recently, with the advent of isotopic labeling techniques, researchers have been able to determine the principal components of the δ tensor (δ_{11}, δ_{22}, and δ_{33}) for a variety of ^{13}C- and ^{15}N-labeled organic compounds (*1*). In addition, the use of dipole-coupled solid-state NMR spectroscopy to determine the orientation of the δ_{33} tensor element with respect to the dipole coupling axis has been used on peptides and polypeptides (*2–6*), nitrosobenzenes (*7*), oximes (*8*), and acetanilides (*9*). A two-dimensional variation of this technique utilizing the ^{15}N–^{1}H dipolar interaction has been used to study the chain conformation and dynamics for oriented proteins (*10*). Although this particular technique has been used for biological systems, its application to synthetic polymers has been rare. In addition, little has appeared regarding the magnitude and orientation of the δ tensor for imides, a key component in the polyimide family of semicrystalline, heterocyclic polymers possessing excellent physical properties and thermal stability.

Tensor evaluations of biological polymers are usually based on labeled-model-compound studies; thus, a series of labeled model imide compounds based on the phthalimide moiety ($C_6H_4(CO)_2N^*{-}R$ with R = $-H$, $-CH_3$, $-C_{16}H_{33}$, $-CH_2C_6H_5$) have been synthesized and analyzed by solid-state ^{15}N NMR spectroscopy. In addition, *N*-[^{13}C]methyl-[^{15}N]phthalimide was synthesized and its solid-state ^{15}N NMR spectrum acquired in order to obtain information on the orientation of the δ tensor with respect to the local molecular geometry, with the eventual purpose of this study to apply this information to ^{15}N-labeled polyimides.

EXPERIMENTAL

NMR Measurements

CP/MAS spectra. Solid-state CP/MAS NMR spectra were obtained on a Bruker MSL-200 equipped with a Bruker MAS probe operating at 50.32 and 20.287 MHz for ^{13}C and ^{15}N, respectively. Powdered samples were placed in fused zirconia rotors fitted with Kel-F caps and spun with dry air, with rotation rates of 4 to 5 kHz for carbon MAS and 2 to 3 kHz for nitrogen MAS. The ^{13}C spectra were referenced to external adamantane (29.5 ppm), while ^{15}N spectra were referenced downfield from external glycine (0 ppm). The ^{1}H 90° pulse was 4.5 μs for ^{13}C acquisition and 6.0 μs for ^{15}N acquisition, while a mixing pulse of 2 ms and a acquisition period of 50 ms were used in acquiring spectra for each nuclei. A recycle delay of 210 s, corresponding to ~3–4 ^{1}H T_1 values was used for observation of both nuclei.

Powder spectra. Solid-state ^{15}N chemical-shift anisotropy (CSA) spectra were acquired with the same probe used for CP/MAS work except that the spinning rate was set to zero. For ^{15}N powder spectra, a spin-echo sequence with a tau delay of 200 μs was used to minimize artifacts due to pulse bleedthrough. In addition, a 90° flip-back pulse was implemented at the end of acquisition in order to circumvent the long ^{1}H T_1 values. The ^{1}H 90° pulse width was ~3.98–4.05 μs, the acquisition time was 50 ms, and the recycle delay was 30 s. The cross-polarization contact time was 5 ms. The number of scans acquired varied from 2560 to 3200.

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* To whom correspondence should be addressed.

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All chemical-shift values are referenced to crystalline glycine (0 ppm).

CSA simulations. CSA spectra were simulated using the POWFIT program developed by Dr. T. G. Oas (*11*). Fits were done by performing analyses on either the zeroth or first derivative of selected regions of the experimental spectrum. In addition, the theoretical spectrum was convoluted with Lorentzian and Gaussian line broadening to reproduce the natural line broadening present. All simulations were done on a MicroVax 3100.

Synthesis

All reagents were obtained from Aldrich Chemical Co. and used without purification. *N*,*N*-dimethylformamide (DMF) was reagent grade and used as received.

A typical procedure for the preparation of an *N*-substituted phthalimide is as follows: A clean, dry flask was charged with equimolar amounts of [^{15}N] potassium phthalimide and methyl iodide (for the *N*-methylphthalimide) followed by enough DMF to give a mixture that was 15–20% solids by weight. The flask was submerged in a preheated oil bath at approximately 60°C for 2 to 3 h. The cooled reaction mixture was poured into rapidly stirring water (10 times reaction volume). The precipitate was collected and recrystallized from aqueous ethanol (70 to 85% yield). For the doubly labeled *N*-[^{13}C]-methyl-[^{15}N]-phthalimide compound, the above procedure was followed except that ^{13}C-labeled methyl iodide was used.

THEORETICAL BACKGROUND

The theory of NMR powder spectra has been given elsewhere (*12*) and will be only outlined here. The powder spectrum for a nucleus undergoing a particular transition is given by (*11*)

$$S_i(\omega) = \int_{\theta=0}^{\pi} \int_{\phi=0}^{2\pi} P_i\, g_{i,\theta,\phi}(\omega, \omega_i(\theta, \phi)) \sin\theta\, \partial\theta\partial\phi,$$

where P_i is the probability of the transition, g_i is the lineshape function, and θ and ϕ are the polar and azimuthal angles describing the orientation of the magnetic field with respect to some molecular frame of reference. P_i and g_i are usually assumed to be orientation independent. For the chemical-shift interaction, $\omega(\theta, \phi)$ can be expressed explicitly:

$$\omega(\theta, \phi) = \sigma_{11}\sin^2\theta\cos^2\phi + \sigma_{22}\sin^2\theta\sin^2\phi + \sigma_{33}\cos^2\theta.$$

Here σ_{11}, σ_{22}, and σ_{33} are the principal components of the chemical-shielding tensor ($\sigma_{33} \geqslant \sigma_{22} \geqslant \sigma_{11}$). Experimentally, the chemical-shift-tensor elements δ_{11}, δ_{22}, and δ_{33} are measured, and in this paper the convention $\delta_{11} \geqslant \delta_{22} \geqslant \delta_{33}$, where δ_{33} corresponds to the most shielded component of the chemical-shift tensor, will be used. If the nucleus being studied is dipolar-coupled to another spin-$\frac{1}{2}$ system, $\omega(\theta, \phi)$ is given by

$$\omega_{\pm}(\theta, \phi) = \omega(\theta, \phi) \pm \frac{\Delta\omega(\theta, \phi)}{2},$$

where the splitting due to the dipole coupling interaction $\Delta\omega(\theta, \phi)$ is

$$\Delta\omega(\theta, \phi) = D\{1 - 3[\sin\beta\sin\theta\cos(\phi - \alpha) + \cos\beta\cos\theta]^2\}.$$

Here D is the dipolar coupling constant ($\gamma_1\gamma_2 h/r_{12}$) and β and α are the polar and azimuthal angles describing the orientation of the dipolar vector with respect to the principal-axis system of the chemical-shielding tensor. In making initial guesses for the values of α and β, the procedure outlined by Teng and Cross was utilized (*6a*).

RESULTS AND DISCUSSION

^{15}N-Labeled Model Imides CSA Spectra

Figure 1 shows the CSA spectra for the four model imides along with the spectral simulations used to determine the values of δ_{11}, δ_{22}, and δ_{33}; these values are summarized in Table 1. The calculated spectra fit well to the experimental data, with some variation probably due to anisotropic T_2 and cross-polarization effects (*11*). All the *N*-substituted phthalimides have approximately the same width ($\delta_{11} - \delta_{33}$) of ~120 ppm. However, there are substantial changes in the isotropic shift δ_{iso}, mainly due to the δ_{22} tensor element. This is also reflected in the rather large differences in η for these systems.

Doubly Labeled N-methylphthalimide

Figure 2 shows the experimental and simulated CSA spectra for ^{15}N–^{13}C labeled *N*-methylphthalimide. The CSA spectrum is modulated by both the magnitude of the ^{15}N–^{13}C dipolar coupling and its orientation with respect to the δ axis system. In the simulation, the values of δ_{11}, δ_{22}, and δ_{33} were initially held fixed and D, α, and β were allowed to vary. After these parameters were optimized, the chemical-shift-tensor elements were then permitted to vary in order to get the best fit to the spectrum. Table 2 gives the best fit values used in Fig. 2. From the values of α and β, the orientation of the N–CH$_3$ bond vector with respect to the δ axis system was determined; this is shown in Fig. 3. Although the orientation of δ_{33} with respect to the molecular structure cannot be determined strictly from the data presented here, from previous work performed on sp^2 ring nitro-

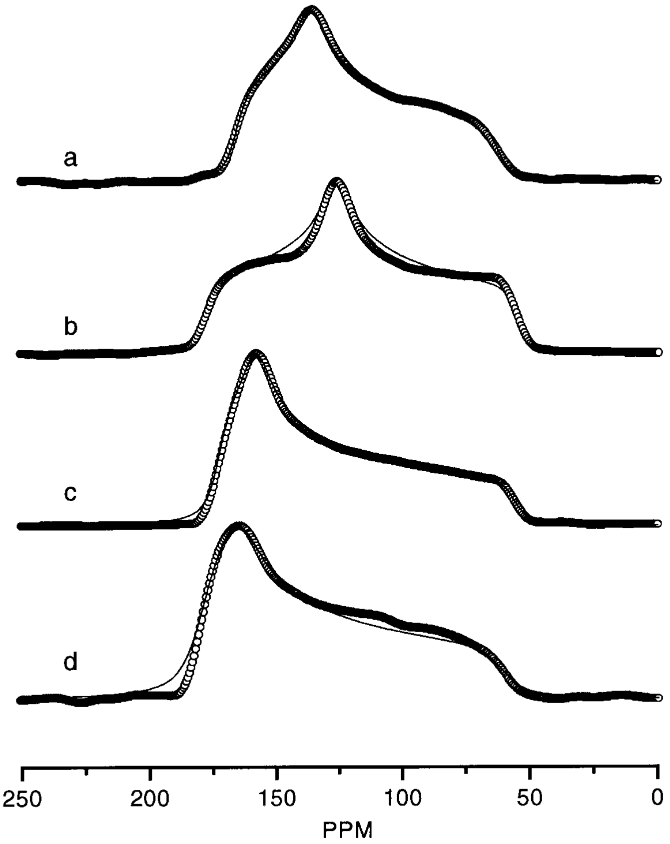

FIG. 1. ^{15}N CSA spectra of (a) phthalimide, (b) *N*-methylphthalimide, (c) *N*-stearylimide, and (d) *N*-benzylphthalimide. All spectra were apodized using a Kaiser digital filter ($\alpha = 4$, $N = 3$–5 ms) and zero-filled to 8092 data points before Fourier transformation. Experimental data are represented by open circles, spectral simulation by a solid line.

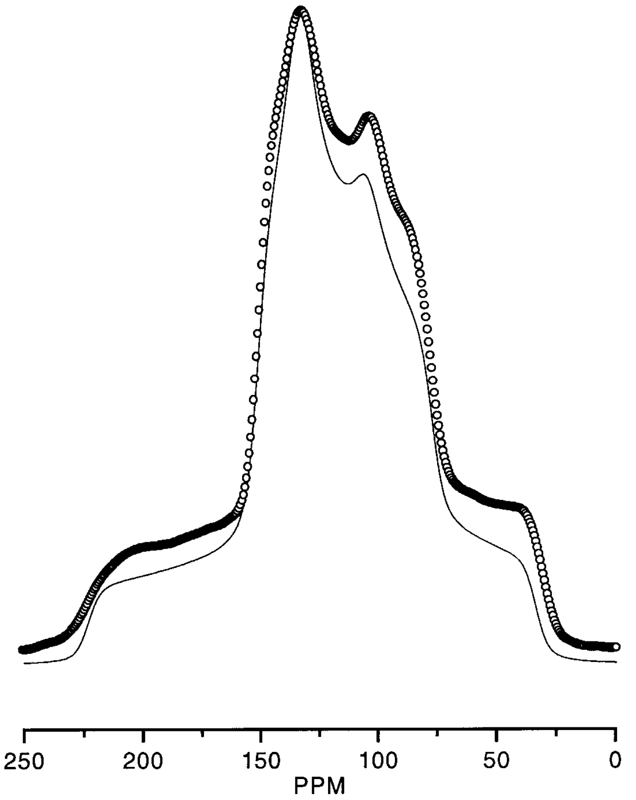

FIG. 2. Experimental and simulation ^{15}N CSA spectra of doubly labeled *N*-methylphthalimide. The experimental data are represented by open circles, the spectral simulation by a solid line. The raw data were processed in the same manner as the spectra in Fig. 1.

gens, the δ_{33} tensor was found to be perpendicular to the ring (*13, 14*). Accordingly, we are tentatively placing δ_{33} perpendicular to the imide plane. Figure 4 shows the orientation of the principal components of the chemical-shift tensor.

From the magnitude of the ^{15}N–^{13}C dipolar coupling constant, the length of the ^{15}N–^{13}C bond is calculated to be 1.51 Å. The X-ray structure for *N*-methylphthalimide is not known, although the calculated bond length at the AM1 level is 1.45 Å (*15*). The N–C bond distance for a related compound, bis(*N*-hexylphthalimide) was determined via single-crystal X-ray methods to be 1.44 ± 0.01 Å (*16*). Since NMR spectroscopy and X-ray diffraction measure different vibrational averages ($(\langle r^{-3}\rangle^{-1/3}$ versus $\langle r\rangle$), the experimental result is in good agreement with what is expected for this system.

TABLE 1

^{15}N Chemical-Shift Data for ^{15}N-Labeled Model Imides[a]

Compound[a]	$\delta_{\mathrm{iso}}^{(\mathrm{exptal})b}$	$\delta_{\mathrm{iso}}^{(\mathrm{calc})c}$	$\delta_{11}{}^{d}$	$\delta_{22}{}^{d}$	$\delta_{33}{}^{d}$	η^{e}
Phthalimide	121.5	121	165	136	62	0.492
N-methylphthalimide	119.8	119	177	125	55	0.813
N-stearylphthalimide	128.9	128	172	157	55	0.274
N-benzylphthalimide	134.2	135	179	165	60	0.189

[a] All data reported in parts per million and referenced to glycine ($\delta_{\mathrm{iso}} = 0.0$ ppm).

[b] Based on ^{15}N CP/MAS spectral analysis.

[c] Determined by $\frac{1}{3}$ ($\delta_{11} + \delta_{22} + \delta_{33}$).

[d] Uncertainty in δ is ±3.0 ppm.

[e] $\eta = (\delta_{22} - \delta_{11})/(\delta_{33} - \delta_{\mathrm{iso}})$.

TABLE 2

^{15}N Chemical-Shift Parameters for *N*-[^{13}C]-methyl[^{15}N]-phthalimide[a]

δ_{11}	δ_{22}	δ_{33}	α	β	D
179	125	55	7	90	883

[a] All values for the chemical-shift tensor are parts per million. The values of α and β are referenced with respect to the N—CH$_3$ bond axis. The value of the dipolar coupling constant D is in hertz. Uncertainties are ±3.0 ppm for δ, ±5° for α, and ±2° for β, respectively.

Discussion

The invariance of the δ_{33} tensor indicates that the aromaticity of the imide ring is fairly consistent for the substituents given here. Instead, the largest changes appear in the δ_{11} and δ_{22} tensor elements. For δ_{11}, the changes in substituent would correspond to differences in the N–R σ bond (δ_{11} varies 14 ppm from phthalimide to *N*-benzylphthalimide). However, it is not clear how the different substituents effect the δ_{22} tensor element. Shoji and co-workers have shown that, in the case of polypeptides, δ_{22} was quite sensitive to molecular composition and conformation, due to changes in the hydrogen bonding (*17*). Hiyama *et al.* have observed different ^{15}N CSA spectra for two distinct crystal forms of Boc-glycylglycylglycine benzyl ester, an effect attributed to a nonplanar peptide bond for one of the crystal forms (*5*).

The orientation of the nitrogen chemical-shift-tensor elements with respect to the nitrogen–carbonyl plane for *N*-methylphthalimide is quite different compared to their orientation for the amide linkage in polypeptides (*2–6*), including the proline ring in Boc-l-alanyl-l-proline (*4*). In particular, it is interesting to note how the δ_{22} changes orientation from being perpendicular to the amide plane for peptides to being in the imide plane for the compound studied here as well as for l-histidine (*13*). This change in tensor orientation probably reflects the difference between the partial double-bond character for amides and the more delocalized bonding nature for imides. Currently, computational and synthetic efforts are in progress in order to further investigate the nature of the bonding about the ^{15}N site for imide systems.

SUMMARY

A procedure has been developed for incorporating ^{15}N and ^{13}C isotopic labeling into *N*-substituted phthalimides, for use as model compounds for studying polyimides. From solid-state ^{15}N NMR spectroscopic and computational methods, the values of the δ shift tensor for the model imides were determined. In addition, for *N*-[^{13}C]-methyl-[^{15}N]-phthalimide, the δ_{11} tensor was found to lie approximately along the N–CH$_3$ bond axis, with the δ_{33} tensor element perpendicular to the imide plane. From the magnitude of the ^{15}N–^{13}C dipolar coupling, the N–CH$_3$ bond length was determined to be 1.51 Å. Future work concerning the determination of the δ tensor orientation with respect to the molecular frame is in progress.

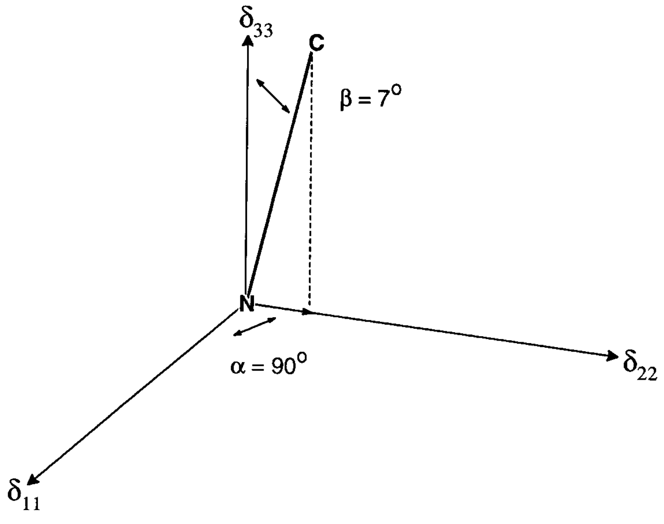

FIG. 3. Orientation of the N–CH$_3$ bond with respect to the δ axis system.

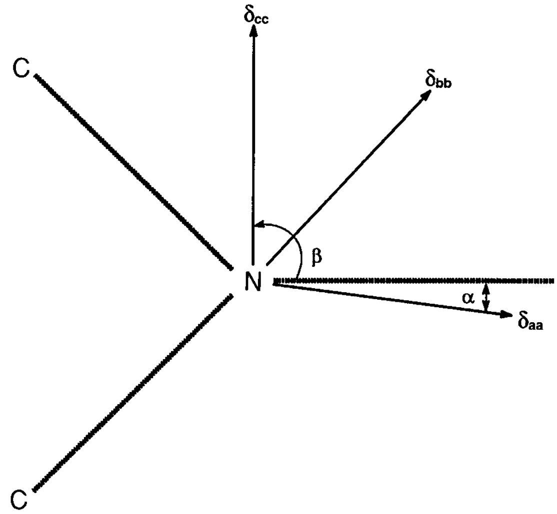

FIG. 4. Orientation for the chemical-shift tensor with respect to the imide plane. Here the terminology of Teng *et al.* (*6a*) has been used. However, for imides, the tensor element perpendicular to the plane δ_{cc} corresponds to δ_{33}, while the tensor element along the N–C bond δ_{aa} corresponds to δ_{11}.

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