Chemistry of Heterocyclic Compounds, Vol. 31, No. 9, 1995

ORIENTATION OF BENZOFURAN BY A MAGNETIC FIELD IN AN ISOTROPIC LIQUID PHASE

A. V. Makarkina, S. S. Golotvin, and V. A. Chertkov

^{1}H NMR spectra of solutions of benzofuran in acetone, registered in NMR spectrometers with low (2.35 T) and high (9.36 T) strength of the magnetic field, have been analyzed with high precision. The orientation parameters of benzofuran have been evaluated. The "two-spectrometer method" gives an adequate accounting for orientation effects in low-symmetry aromatic polycycles in strong magnetic fields.

In high-resolution NMR spectroscopy, one of the areas receiving particular attention is the use of stationary magnetic fields with higher intensities, with the aim of improving the resolution and sensitivity and facilitating interpretation of the spectra. However, when high and superhigh magnetic fields (on the order of 10 T or higher) are used, orientation effects are manifested: molecules with anisotropic magnetic susceptibility are oriented by the stationary magnetic field [1]. In isotropic media, whether liquids or gases, Brownian motion hinders any ordering of the molecules, and the resultant orientation proves to be small. As a consequence of such partial orientation, anisotropic interactions of nuclei such as dipole–dipole or quadrupole coupling are not completely averaged out, so that they can be registered in analyzing high-resolution NMR spectra. On the one hand, these fine effects complicate the spectrum quite significantly and may be the source of significant systematic errors in analyzing spin–spin coupling constants (SSCC); on the other hand, studies of orientation effects may yield data on dipole–dipole [2] or quadrupole [3, 4] coupling of nuclei, on the molecular geometry, and on the anistropy of magnetic susceptibility [5]. At those levels of a stationary magnetic field that are attainable today, dipole–dipole interactions are manifested as a clear relationship between the type of the spectrum and the stationary magnetic field intensity. The only data thus far recorded in the literature are for naphthalene [2], o-dichlorobenzene [5], and benzene [6].

In a program of systematic study of the relationship between orientation effects and structural parameters of molecules, we have investigated in the present work an important model system — the benzofuran molecule. We have analyzed the ^{1}H NMR spectra registered for this compound in spectrometers with magnetic field strength 2.35 and 9.36 T. We have also investigated the applicability of the "two-spectrometer method" in obtaining a precise evaluation of orientation parameters of low-symmetry molecules.

All evaluations of orientation effects that have been reported previously [2, 5, 6] were performed on symmetric molecules, the NMR spectra of which are described by spin systems with chemical equivalence. For these molecules, orientation effects are manifested directly in the NMR spectra. For example, in the case of o-dichlorobenzene (spin system AA'BB') in a spectrum obtained at a high working frequency, significant asymmetry appears. The degree of asymmetry gives a direct indication of the magnitude of the dipole–dipole coupling constant (DDCC).

This method proves to be inapplicable to asymmetric molecules, in particular to benzofuran. The problem is that for spectrometers with a high magnetic field strength, the experimental NMR spectra usually become rather weakly coupled, and they take on attributes of first-order spectra: the principle of equal intensities of transitions (with an precision within the "roof effect") and equivalence of the distances between the corresponding components.

In the general case, NMR spectra are interpreted using the formalism of a spin-Hamiltonian describing all interactions of nuclear spins [2]:

$$H = H_Z + H_\sigma + H_J + H_D + H_Q\,, \tag{1}$$

M. V. Lomonosov Moscow State University, Moscow 119899. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1214-1219, September, 1995. Original article submitted June 5, 1995.

TABLE 1. Results from Analyses of ^{1}H NMR Spectra of Benzofuran (304 K, 2 M Solution in Acetone-d$_6$)

Protons	J^{100}	J^{400}
2-H, 3-H	2,2348 (0,0009)	2,2259 (0,0004)
2-H, 4-H	0,2673 (0,0008)	0,2660 (0,0004)
2-H, 5-H	0,0556 (0,0010)	0,0563 (0,0004)
2-H, 6-H	0,4153 (0,0011)	0,4174 (0,0004)
2-H, 7-H	-0,0213 (0,0008)	-0,0024 (0,0004)
3-H, 4-H	-0,0962 (0,0008)	-0,1060 (0,0004)
3-H, 5-H	0,0186 (0,0010)	0,0027 (0,0004)
3-H, 6-H	-0,1094 (0,0011)	-0,1107 (0,0004)
3-H, 7-H	0,9998 (0,0009)	0,9960 (0,0004)
4-H, 5-H	7,8096 (0,0011)	7,7983 (0,0004)
4-H, 6-H	1,2953 (0,0011)	1,2929 (0,0004)
4-H, 7-H	0,7308 (0,0008)	0,7299 (0,0004)
5-H, 6-H	7,2712 (0,0007)	7,2592 (0,0004)
5-H, 7-H	0,9370 (0,0014)	0,9370 (0,0004)
6-H, 7-H	8,3312 (0,0013)	8,3174 (0,0004)

---

*Data are presented for two different levels of stationary magnetic field strength: low (J^{100}, FX-100, 100 MHz, mean square deviation 0.0046 Hz) and high (J^{400}, VXR-400, 400 MHz, mean square deviation 0.0021 Hz). Values in parentheses denote standard deviations of individual parameters.

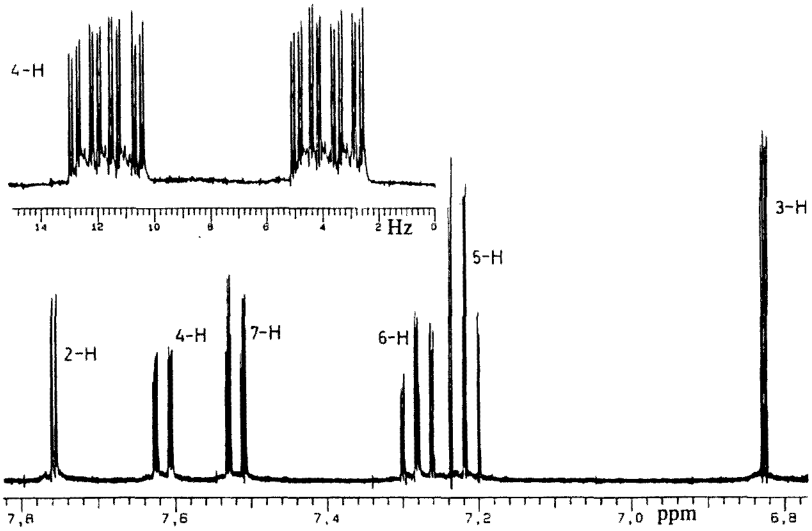

Fig. 1. ^{1}H NMR spectrum of benzofuran (Varian VXR-400, 2 M solution in acetone-d$_6$, 304 K); the insert shows the region of the 4-H proton.

where H_Z describes the Zeeman interaction; H_σ describes the chemical shielding of nuclei; H_J describes indirect interaction; H_D describes direct dipole–dipole interaction; H_Q describes quadrupole interaction (for nuclei with spin $I > 1/2$). Here, the diagonal elements of the Hamiltonian H_{mm} are expressed by means of the relationship

$$H_{mm} = \sum_i \sigma_i I_{zi} + \sum_i \sum_{j>i} (J_{ij}+2D_{ij})\, I_{zi}\, I_{zj}\,, \tag{2}$$

TABLE 2. Spin–Spin J_{ij} and Dipole–Dipole D_{ij} $^1H-^1H$ Coupling Constants in Benzofuran (304 K, 2 M solution in acetone-d_6) (values in parentheses represent standard deviations of individual parameters)

Protons	J_{ij}	D_{ij}
2-H, 3-H	2,2357 (0,0013)	-0,0049 (0,0007)
2-H, 4-H	0,2664 (0,0012)	-0,0002 (0,0006)
2-H, 5-H	0,0551 (0,0016)	0,0006 (0,0008)
2-H, 6-H	0,4163 (0,0016)	0,0006 (0,0008)
2-H, 7-H	-0,0205 (0,0012)	—*
3-H, 4-H	-0,0954 (0,0013)	-0,0053 (0,0006)
3-H, 5-H	0,0173 (0,0017)	—*
3-H, 6-H	-0,1098 (0,0017)	0,0005 (0,0007)
3-H, 7-H	0,9997 (0,0013)	-0,0019 (0,0006)
4-H, 5-H	7,8097 (0,0017)	-0,0053 (0,0009)
4-H, 6-H	1,2960 (0,0017)	-0,0020 (0,0009)
4-H, 7-H	0,7308 (0,0012)	-0,0004 (0,0006)
5-H, 6-H	7,2712 (0,0015)	-0,0060 (0,0007)
5-H, 7-H	0,9371 (0,0022)	-0,0005 (0,0011)
6-H, 7-H	8,3326 (0,0020)	-0,0072 (0,0010)

---

*Not evaluated.

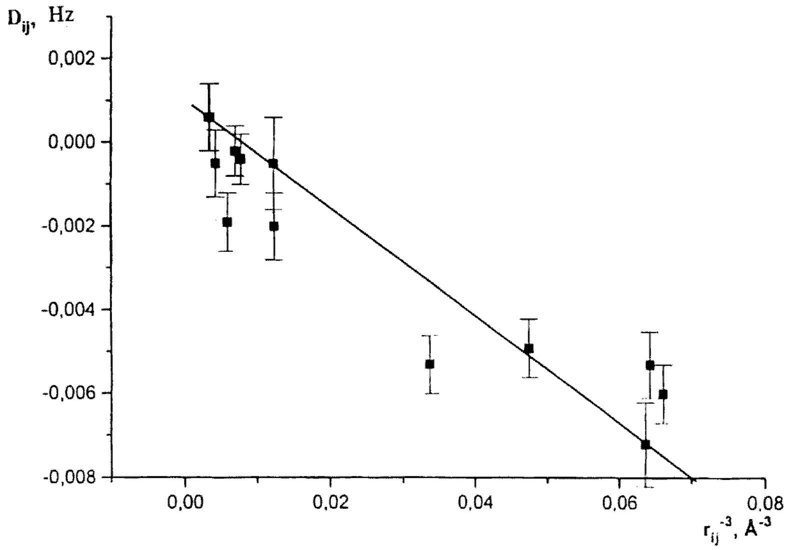

Fig. 2. Dependence of D_{ij} on r_{ij}^{-3} for benzofuran.

where σ_i is the chemical shift of nucleus i; J_{ij} and D_{ij} are the respective SSCC and DDCC for pairs of nuclei i and j; I_{zi} is the projection of the operator of spin moment of nucleus i on the z axis. Thus, in the first-order spectra of oriented molecules, the observed splittings are the respective algebraic sums of the corresponding spin–spin coupling constants and twice the values of the dipole–dipole coupling constants:

$$\Delta\nu = J_{ij} + 2 D_{ij}. \tag{3}$$

The term "two-spectrometer method" implies that the spectra that used as a basis for the calculations have been obtained in at least two spectrometers with very greatly different working frequencies. It is understood that all other conditions of the experiment remain unchanged (temperature, sample composition, and so on). The data currently available in the literature provide a reliable indication that the DDCC is proportional to the strength of the stationary magnetic field B_0 (see [1], and also the discussion that follows in the present article).

The ^{1}H NMR spectrum of benzofuran obtained at a frequency of 100 MHz is a typical strongly coupled spectrum, in which 162 lines are observed. We carried out the preliminary analysis of this spectrum by means of the LAOCON5 program [8, 9]. This iteration procedure carries out a search for spectral parameters (chemical shifts and spin–spin coupling constants), using a Hamiltonian that describes only isotropic interactions of nuclear spins. In the course of this calculation, we obtained all ^{1}H–^{1}H SSCCs for this molecule (J^{100}; see data in Table 1).

Preliminary analysis of the upfield spectrum (the working frequency of the spectrometer for protons was 400 MHz), in which 191 lines were observed, with a relatively simple multiplet structure, close to first-order (Fig. 1), was also performed by means of the LAOCON5 procedure. In Table 1 we have listed values of the spin–spin coupling constant (J^{400}) obtained by analysis of this spectrum.

Analysis of the data presented in Table 1 revealed the following relationships: For most of the ^{1}H–^{1}H SSCC data, we observe extremely close agreement (within the limits of experimental error) between J^{100} and J^{400}, with the exception of $J_{2\text{-H},7\text{-H}}$ and $J_{3\text{-H},5\text{-H}}$, the magnitudes of which in the upfield spectra are less than the experimental width of the line. At the same time, for the four vicinal constants $J_{2\text{-H},3\text{-H}}$, $J_{4\text{-H},5\text{-H}}$, $J_{5\text{-H},6\text{-H}}$, $J_{6\text{-H},7\text{-H}}$, when the sign of the constant is taken into account, the values calculated for J^{400} are systematically lower than those for J^{100} by an amount ranging from 0.009 to 0.013 Hz. This is due to the contribution of the DDCC D_{ij}. Here we must note that in the downfield spectrum, orientation effects were found to be considerably smaller than in the upfield spectrum. In such a case, the difference between J^{100} and J^{400} provides a means for evaluating D_{ij}. Using Eq. (3), we can write an expression for evaluating the DDCC:

$$D_{ij} \cong 0.5\,(J_{ij}^{400} - J_{ij}^{100}). \tag{4}$$

The magnitude of the anisotropic interactions observed in the spectrum depends on the molecular geometry and the degree of orientation of the molecules, which for axisymmetric molecules is characterized by the parameter S, averaged with respect to molecular motion [1]:

$$S = \left\langle \frac{3}{2}\cos^2\theta - \frac{1}{2} \right\rangle_B , \tag{5}$$

where θ is the angle between the axis of symmetry of the molecule and the direction of the external magnetic field vector. The subscript B signifies that the averaging is performed in the presence of an orienting magnetic field. For completely oriented molecules, the orientation parameter is equal to $-1/2$ or 1, depending on how the axis of symmetry of the molecule is directed relative to the external magnetic field. For partially oriented diamagnetic molecules, this parameter may range from 10^{-6} to 10^{-5}. Using Boltzmann statistics, we established that the degree of orientation S is proportional to the anisotropy of magnetic susceptibility $\Delta\chi$, which characterizes the magnetic properties of the molecules, and is also proportional to the square of the stationary magnetic field strength B_0 [3]:

$$S = \frac{\Delta\chi B_0^2}{15kT}, \tag{6}$$

where k is the Boltzmann constant; T is the temperature. The expression for the dipole–dipole coupling constant D_{ij} for two dipolar-coupled spins i and j can be written as follows [7]:

$$D_{ij} = -\frac{\gamma_i \gamma_j h}{2\pi^2 r_{ij}^3}\left\{(1.5\cos^2\varphi - 0.5)S\right\}, \tag{7}$$

where γ_i and γ_j are the gyromagnetic ratios of nuclei i and j; φ is the angle between the vector r_{ij} connecting these nuclei and the axis of symmetry of the molecule.

For a precise evaluation of the orientation parameters of benzofuran, we performed a second series of calculations of NMR spectra by means of the UEA iteration procedure [10]. This program uses the complete Hamiltonian of the spin system, with possible anisotropic interactions taken into account. An analysis of the downfield spectrum gives definitive evaluations of the spin-spin coupling constants J_{ij} (see Table 2) when fixed values are assigned to the DDCC. We used zero values of D_{ij} for all of the DDCC data with the exception of $^4D_{3\text{-H},4\text{-H}}$, $^3D_{2\text{-H},3\text{-H}}$, $^3D_{4\text{-H},5\text{-H}}$, $^3D_{5\text{-H},6\text{-H}}$, $^3D_{6\text{-H},7\text{-H}}$, which were assumed to be equal to -0.0004 Hz. The values obtained for J_{ij} were used in analyzing the upfield spectra. Values of D_{ij} found by this method are listed in Table 2.

For aromatic molecules, two types of orientation of the principal axis of the magnetic susceptibility tensor are possible in principle – in the direction of the orienting field vector and in the opposite direction. Here, the molecular reference system must be related to the principal axes of the magnetic susceptibility tensor [2, 7]. In the first case, the plane of the molecule is orthogonal to the direction of the external magnetic field, in the second case parallel to the field. The second type of orientation is energetically more favorable. According to this model of orientation, the dipole–dipole coupling constants D_{ij} are inversely proportional to the cube of the corresponding internuclear distances r_{ij} (Fig. 2). The values of r_{ij} were taken from [11-13]. Starting with the indicated orientation model and data on the DDCC D_{ij} for benzofuran, we obtained values of $\Delta\chi$ for this molecule, which proved to be $(-0.59 \pm 0.06)\cdot 10^{-28}$ cm^3/molecule. The value of the modulus $\Delta\chi$ for benzofuran is considerably lower than for benzene ($-1.0\cdot 10^{-28}$ cm^3/molecule) [5, 7] or naphthalene ($-2.0\cdot 10^{-28}$ cm^3/molecule) [2]. The lower value for benzofuran is probably explained by the presence of the heteroatom with an unshared electron pair.

EXPERIMENTAL

The ^{1}H NMR spectra of benzofuran were registered in JEOL FX-100 and Varian VXR-400 spectrometers, on 2 M solutions in acetone-d_6 at 304 K (Fig. 1). The data sampling time was 30 sec. In order to improve the resolution, we used a Lorentz transformation of the line shape to Gaussian. The line width in the transformed spectra was 0.03-0.04 Hz with a digital resolution of 1-2 mHz. The spectra were analyzed by means of the iteration programs LAOCON5 [8, 9] and UEA [10], modified for performing calculations in an IBM PC. The accuracy of agreement between the experimental peaks and the theoretical transition frequencies (mean square deviation) was 0.0046 and 0.0021 Hz for the spectra taken at 100 and 400 MHz, respectively.

This work was performed with financial support from the Russian Fund of Fundamental Research (Project Code 95-03-09639).

REFERENCES

1. E. W. Bastiaan and C. MacLean, "Molecular orientation in high-field high-resolution NMR," NMR Basic Princ. Prog., **25**, 17 (1991).
2. E. W. Bastiaan, J. Bulthuis, and C. MacLean, Magn. Reson. Chem., **24**, 723 (1986).
3. C. Gayathri and A. A. Bothner-By, J. Magn. Reson., **56**, 456 (1984).
4. P. R. Luyten, J. Bulthuis, and C. MacLean, Chem. Phys. Lett., **89**, 287 (1982).
5. F. A. L. Anet, J. Am. Chem. Soc., **108**, 1354 (1986).
6. R. Laatikainen, H. Santa, Y. Hiltunen, and J. Lounila, J. Magn. Reson. A, **104**, 238 (1993).
7. C. Gayathri, A. A. Bothner-By, P. C. M. VanZijl, and C. MacLean, Chem. Phys. Lett., **87**, 192 (1982).
8. S. Castellano and A. A. Bothner-By, J. Chem. Phys., **41**, 3863 (1964).
9. M. Attimonelli and O. Sciacovelli, Org. Magn. Reson., **13**, 277 (1980).
10. R. B. Johannesen, J. A. Ferretti, and R. K. Harris, J. Magn. Reson., **3**, 84 (1970).
11. N. G. Zakharova, V. A. Tikhomirov, and I. O. Shapiro, Khim. Geterotsikl. Soedin., No. 8, 1050 (1989).
12. I. V. Edneral, Teor. Éksp. Khim., **19**, 430 (1983).
13. W. E. Bechtold and J. H. Goldstein, Org. Magn. Reson., **16**, 30 (1981).