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Orientation of molecules by magnetic field as a new source of information on their structures

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A complex procedure for quantitative allowance for small but significant effects of molecular orientation by strong static magnetic fields was elaborated. A series of high-resolution ^{1}H NMR spectra of 1,2,3-trichloronaphthalene recorded at magnetic field strength varied over a wide range was analyzed in the framework of a unified approach with high accuracy. The spin-spin coupling constants and the dipole-dipole coupling constants for all pairs of ^{1}H nuclei and the anisotropy and rhombicity parameters of the magnetic susceptibility tensor of the molecule were determined. *Ab initio* CSGT/RHF quantum chemical calculations of this property using a wide range of conventional diffuse and polarization basis set functions were carried out. Augmentation of the basis set with polarization functions affects the values of the calculated parameters to a lesser extent compared to augmentation with diffuse functions. The results of calculations using the 6-311G(df) and 6-311++G(df) basis sets are in good agreement with the experimental values of the magnetic susceptibility anisotropy for 1,2,3-trichloronaphthalene. The advantages of the method proposed and specific features of the effects of orientation by magnetic field as a new source of information on the structure of molecules in solution are discussed.

Key words: NMR spectroscopy, orientation effects in magnetic field, *ab initio* quantum chemical calculatinos, structure of molecules in solution, anisotropy of magnetic susceptibility, spin-spin coupling constants, dipole-dipole coupling constants.

NMR spectroscopy belongs to key methods of investigation of the structures and properties of compounds in solution. Recently, strong and very strong magnetic fields (10—20 T and greater) have been more and more often used. On the one hand, this improves the sensitivity of the method and facilitates interpretation of NMR spectra. On the other hand, this creates pre-requisites for manifestation of the effects of orientation of molecules in strong magnetic fields. This phenomenon was disclosed quite recently;[1] it is due to the interaction of permanent magnetic field with the induced magnetic moment of a molecule.[2] The energy of this interaction is low compared to the energy of thermal motion, which prevents molecules from being ordered, and the resulting extent of orientation of small molecules by magnetic field in isotropic media is low. In liquids and gases the orientation effects can manifest themselves in NMR spectra owing to anisotropic interactions of nuclear spins, namely, a non-vanishing direct interaction between nuclear dipoles and the interaction of the nuclear quadrupole moment with the local electric field gradient produced by the environment. Detailed analysis of the manifestation of this new physical phenomenon can provide important information on the conformational state of molecules containing specifically oriented aromatic residues including such complex objects, as natural proteins, DNA, and their complexes in solution.[3,4] The aim of this study was to elaborate a method of extracting full spectral and structural information on aromatic polycyclic compounds that exhibit the orientation effects in strong magnetic fields.

Until recently, information on the orientation effects was mainly obtained by measuring quadrupole splittings in ^{2}H NMR spectra of selectively deuterated derivatives.[5—7] But this requires the synthesis of these compounds; additionally, deuterium signals are broadened due to fast relaxation and measured with low accuracy and the calculation procedure[8] is rather complicated. Taken altogether, this significantly restricts the field of application of the method. Information on the orientation effects can also be extracted from ^{1}H NMR spectra of symmetrical molecules containing groups of chemically equivalent protons, namely, *o*-dichlorobenzene,[9] naphthalene,[10] and

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^{13}C-enriched benzene.[11] In the corresponding spin systems, the dipole-dipole coupling constants explicitly manifest themselves in NMR spectra (for more detailed treatment of the issue, see Ref. 9), which allows the values of the orientation parameters to be determined in the course of accurate analysis.[9—11]

The NMR spectra of less symmetrical molecules containing no groups of equivalent nuclei recorded on spectrometers operating at high frequencies are, as a rule, similar to first-order spectra. Analysis of the multiplet structure of such spectra permits the determination of the equidistant distances corresponding to, *e.g.*, the interaction of a pair of nuclei A and X ($\Delta\nu_{AX}$), which in the first-order approximation are equal to the algebraic sum of the spin-spin coupling constants J_{AX} and the dipole-dipole coupling constants D_{AX} [12,13]:

$$\Delta\nu_{AX} = |J_{AX} + 2D_{AX}|, \tag{1}$$

Clearly, in this situation it is impossible to estimate the J_{AX} and D_{AX} constants separately without using additional information. At the same time from the theory of orientation effects it follows that the dipole-dipole coupling constant should be proportional to the squared magnetic field strength (for details, see the text below) and this dependence can be used for separation of the constants. Earlier, in studies of benzofuran[14] and benzothiophene[15] this was done using a method based on joint processing of NMR spectra recorded on spectrometers with both low and high magnetic field strength. In this work we will demonstrate the possibilities of the ALIGN (abbreviation of ALIGnment—orientatioN) procedure we have developed, which makes it possible to process an arbitrary number of spectra of arbitrary complexity, recorded on different spectrometers operating at different frequencies in the framework of a unified approach.

1,2,3-Trichloronaphthalene (**1**) was chosen as the object of investigation. The molecule of this compound has a well-developed π-electron system, which is sufficient for providing a necessary degree of orientation. Molecule **1** contains five nonequivalent protons and has no substituents responsible for undesired line broadening effects. The ^{1}H NMR spectra of compound **1** are described by a compact and relatively weakly coupled five-spin system (see Ref. 16). After careful tuning of the magnetic field homogeneity we recorded well-resolved ^{1}H NMR spectra of solutions of compound **1** in acetone-d$_6$ on four different-class spectrometers, which made it possible to study the orientation effects over a wide range of changes in magnetic field strength.

Experimental

^{1}H NMR spectra of compound **1** were recorded on spectrometers with a magnetic field of 4.70 T (Bruker AC-200), 9.39 T (Varian VXR-400), 11.74 T (Bruker DRX-500), and 14.09 T (Bruker AV-600), operating at frequencies of 200, 400, 500, and 600 MHz, respectively. In all cases measurements were carried out using an increased flow rate of heat carrier gas (15 to 19 L min^{-1}) after setting the temperature during a long time (minimum 30 min). The temprature was preliminarily calibrated using conventional MeOH reference (see Ref. 17). According to our estimates, under these conditions the temperature (303.5 K for the experiments with all spectrometers used) was set with an accuracy of ±0.2 K and the uncertainty of temperature setting in bulk samples was at most ±0.1 K. This allowed us to perform fine tuning of the magnetic field homogeneity. The data acquisition time was 30 to 50 s. The Lorentzian lineshape was transformed into Gaussian one with a resolution enhancement factor of 2.0—2.5 and the free induction decay data array was complemented with zeros in order to provide a digital resolution of about 0.001 Hz after the Fourier transformation. The sample of compound **1** (2 *M* solution (0.67 mL) in acetone-d$_6$) was synthesized following a known procedure,[16] degassed, and sealed in a 5-mm NMR tube.

The structures of compound **1** and of the model compounds (benzene, chlorobenzene, and naphthalene) were optimized by the RHF method with the 6-311++G(dp) basis set using the GAUSSIAN-98 program;[18] integrals were calculated with increased accuracy (Grid = UltraFine).

Ab initio calculations of parameters of the magnetic susceptibility tensor were carried out by the CSGT method[19,20] in the RHF approximation with various basis sets (for details, see text below) using the GAUSSIAN-98 program; integrals were also calculated with increased accuracy.

Results and Discussion

Generally, high-resolution NMR spectra with allowance for the orientation effects can be described using the five-term spin Hamiltonian formalism[12]:

$$H = H_Z + H_\sigma + H_J + H_D + H_Q, \tag{2}$$

where H_Z, H_σ, H_J, H_D, and H_Q respectively describe the Zeeman interaction, the nuclear shielding by the system of electrons, the indirect spin-spin interaction, the direct dipole-dipole interaction, and the quadrupole interaction (for the nuclei with the spins $I > 1/2$). In conventional isotropic liquids and gases, Brownian motion of particles causes rapid fluctuations of nuclear spin interactions with time and averaging of parameters of the Hamiltonian (2). In the absence of the orientation effect all positions of a molecule relative to the external field direction are equiprobable and the direct dipole-dipole interaction and anisotropic quadrupole interaction vanish upon averaging. Therefore, one deals with a conventional "isotropic" high-resolution Hamiltonian including the first three terms in Eq. (2). However, if the orientation effects impose certain restrictions on the molecular motion, the tensor nature of the interactions H_D and H_Q explicitly manifests itself in the NMR spectrum. This can be accompanied by the appearance of additional splitting of

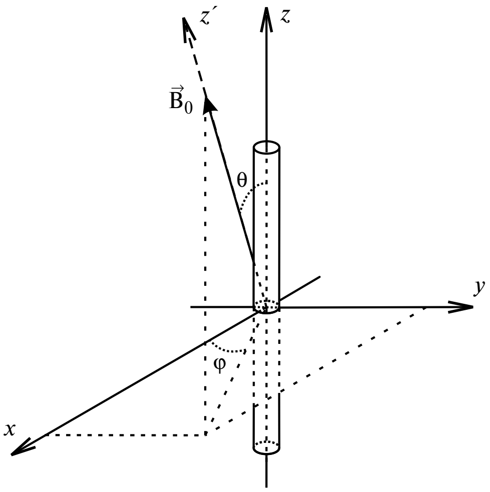

Fig. 1. System of coordinates for axially symmetrical molecule represented by a cylinder; the principal axis z makes an angle θ with the direction of constant magnetic field (vector $\vec{B}_0$).

spectral lines or by deviation of the spin-spin coupling constants observed from their conventional values.[9,12–15]

Model for orientation effects. It is appropriate to express the parameters of the Hamiltonian (2) in the laboratory system of coordinates (x', y', z') in which the measurements are carried out and the z' axis is directed along the vector of external magnetic field $\vec{B}_0$ (Fig. 1). The properties of the molecule under study can be more conveniently represented in the molecular system of coordinates (x, y, z). The orientation of the molecule in a magnetic field is characterized by the magnetic susceptibility χ (second-rank tensor). By choosing a local system of coordinates (x'', y'', z'') in such a manner that the tensor χ be diagonal ($\chi_{x''y''} = \chi_{x''z''} = \chi_{y''z''} = 0$), it is sufficient to use two independent orientation parameters, namely, anisotropy (Δχ) and rhombicity (δχ) of the tensor χ, which are determined by the eigenvalues of this tensor:

$$\Delta\chi = \chi_{z''z''} - 0.5(\chi_{x''x''} - \chi_{y''y''}), \qquad (3)$$

$$\delta\chi = \chi_{x''x''} - \chi_{y''y''}.$$

Establishment of exact correspondence between the directions of the principal axes of the tensor χ and the axes of the molecular system of coordinates requires specification of three angles. In the case of orientation of planar diamagnetic aromatic molecules the situation is significantly simplified. The available published data unambiguously indicate that in these compounds the principal axis of the magnetic susceptibility tensor χ_{zz} is directed normal to the molecular plane.[12] Therefore, unambiguous specification of the axes requires the knowledge of one angle. The second and third axes of the tensor χ are usually directed in such a manner that |Δχ| > |δχ| (Fig. 2).

When an aromatic molecule is placed in a constant magnetic field, the induced magnetic moment Δμ is directed along the z axis of the molecular system of coordinates. The negative sign of the parameter Δχ indicates that the vector Δμ is directed antiparallel to the external magnetic field. The preferred orientation of the molecule in magnetic field is such that the z axis of the molecular system of coordinates be orthogonal to the direction of the vector of the magnetic field $\vec{B}_0$.[21]

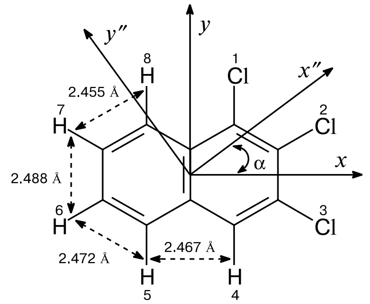

Fig. 2. Geometric parameters of 1,2,3-trichloronaphthalene molecule and orientations of the axes of the molecular system of coordinates (x, y) and of the principal axes of the magnetic susceptibility tensor (x'', y'').

The Hamiltonian of the dipole-dipole interaction can be written as follows:

$$H_D = \sum_{i<j} \mathbf{I}_i \mathbf{D}_{ij} \mathbf{I}_j. \qquad (4)$$

The tensor parameter $\mathbf{D}_{ij}$ characterizes the energy of the interaction between the magnetic moments of the spins i and j and is determined by the magnetic properties of the interacting nuclei and their mutual position in space:

$$\mathbf{D}_{ij} = \frac{\mu_0 h \gamma_i \gamma_j}{16\pi^3 r^3}\left(1 - 3\frac{\mathbf{rr}}{r^2}\right), \qquad (5)$$

where μ_0 is the magnetic permeability of vacuum, γ_i and γ_j are the magnetogyric ratios for the nuclei i and j, respectively, and $\mathbf{r}$ is the vector connecting the interacting nuclei i and j. The uniaxial tensor $\mathbf{D}_{ij}$ has a zero spur and its principal axis is parallel to the vector $\mathbf{r}$. The energy of the dipole-dipole interaction is determined by the projection of $\mathbf{D}_{ij}$ on the direction of the magnetic field $\vec{B}_0$. The full Hamiltonian of the system of oriented nuclei ($I = 1/2$) written with allowance for the dipole-dipole interaction has the form:

$$H = \sum_i \nu_i \hat{I}_{z'i} + \sum_{i<j}(J_{ij} + 2D_{ij})\hat{I}_{z'i}\hat{I}_{z'j} + $$

$$+ 0.5\sum_{i<j}(J_{ij} - D_{ij})(\hat{I}_i^+\hat{I}_j^- + \hat{I}_i^-\hat{I}_j^+). \qquad (6)$$

This expression includes the projection operators of the spin moment on the quantization axis z' ($\hat{I}_{z'i}$) and the raising and lowering operators ($\hat{I}_i^+$, $\hat{I}_j^-$, $\hat{I}_i^-$, and $\hat{I}_j^+$), which act on the spin states of the nuclei i and j. In the first-order approximation one can restrict himself to the first two terms of the Hamiltonian (6). This unequivocally leads to expression (1) for the corresponding equidistant distances in NMR spectra.

Strictly speaking, the parameters ν_i, J_{ij}, and D_{ij} in Eq. (6) should be considered as projections of the corresponding tensors on the z' axis. According to theoretical estimates and scarce experimental data,[22] the tensors of the spin-spin coupling constants (especially, $J_{\mathrm{H,H}}$ constants) are characterized by relatively weak anisotropy, which can be ignored when describing weak orientation effects in isotropic liquids. The tensor character of the shielding parameters can cause orientation-induced shifts of spectral multiplets, but this effect is also weak. Quantitative characterization of the effect requires elaboration of an approach based on the results of *ab initio* calculations of the components of the shielding tensor. The orientation effects influence the NMR spectral shape mainly through the dipole-dipole interaction.

Transformations using the properties of symmetry and the zero spur of the tensor **D** give the following expression for the constant of the dipole-dipole coupling between the nuclei *i* and *j*:

$$D_{ij} = D_{ij\,z'z'} = \frac{h\gamma_i\gamma_j}{16\pi^3 r^3}\Big[S_{zz}(1 - 3\cos^2\theta_{z''r}) + (3/4)(S_{xx} - S_{yy})(\cos^2\theta_{y''r} - \cos^2\theta_{x''r})\Big], \qquad (7)$$

where $\theta_{x''r}$, $\theta_{y''r}$, and $\theta_{z''r}$ are the angles between the vector $\mathbf{r}_{ij}$ and the axes of the local system of coordinates x'', y'', and z'', respectively. The ordering parameters S_{xx}, S_{yy}, and S_{zz} determine the orientation of the whole molecule relative to the magnetic field. They are unambiguously related to the values of the ordering parameters:

$$S_{zz} = \Delta\chi B_0^2/(15\mu_0 kT),$$

$$0.5(S_{xx} - S_{yy}) = \delta\chi B_0^2/(15\mu_0 kT), \qquad (8)$$

where *k* is the Boltzmann constant and *T* is absolute temperature. Substituting the parameters (8) into expression (7) gives the desired relationship for the dipole-dipole coupling constant using the parameters of the magnetic susceptibility tensor:

$$D_{ij} = \frac{h\gamma_i\gamma_j}{480\pi^3}\frac{B_0^2}{kTr^3}\Big[\Delta\chi(1 - 3\cos^2\theta_{z''r}) + (3/2)\delta\chi(\cos^2\theta_{y''r} - \cos^2\theta_{x''r})\Big]. \qquad (9)$$

Relationship (9) establishes the correspondence between the observed dipole-dipole coupling constants D_{ij}, the parameters of the magnetic susceptibility tensor, the internuclear distances, and the angles.

Analysis of NMR spectra. We began our study with qualitative analysis of the orientation effects for 1,2,3-trichloronaphthalene. Using an iterative procedure UEAITR,[12] we analyzed a series of ^{1}H NMR spectra recorded on spectrometers operating at different frequencies and determined the chemical shifts and the spin-spin coupling constants using the Hamiltonian (6) with zero dipole-dipole coupling constants. We thus obtained the preliminary (ignoring the orientation effects) estimates of the spin-spin coupling constant J_{ij}^{200}, J_{ij}^{400}, J_{ij}^{500}, and J_{ij}^{600}, each of them being linearly dependent on the squared magnetic induction B_0^2 (Fig. 3). All the plots have negative slopes (the shorter the distances between the spin-coupled nuclei the larger the slope). The largest slopes were obtained for three vicinal spin-spin coupling constants characterizing the interaction between *ortho*-protons ($^3J_{\mathrm{H(5),H(6)}}$, $^3J_{\mathrm{H(6),H(7)}}$ and $^3J_{\mathrm{H(7),H(8)}}$, see Fig. 3, *a*) and for the spin-spin coupling constants through four bonds for *peri*-protons ($^4J_{\mathrm{H(4),H(5)}}$, see Fig. 3, *b*). The slopes of the dependences of all these constants on B_0^2 are

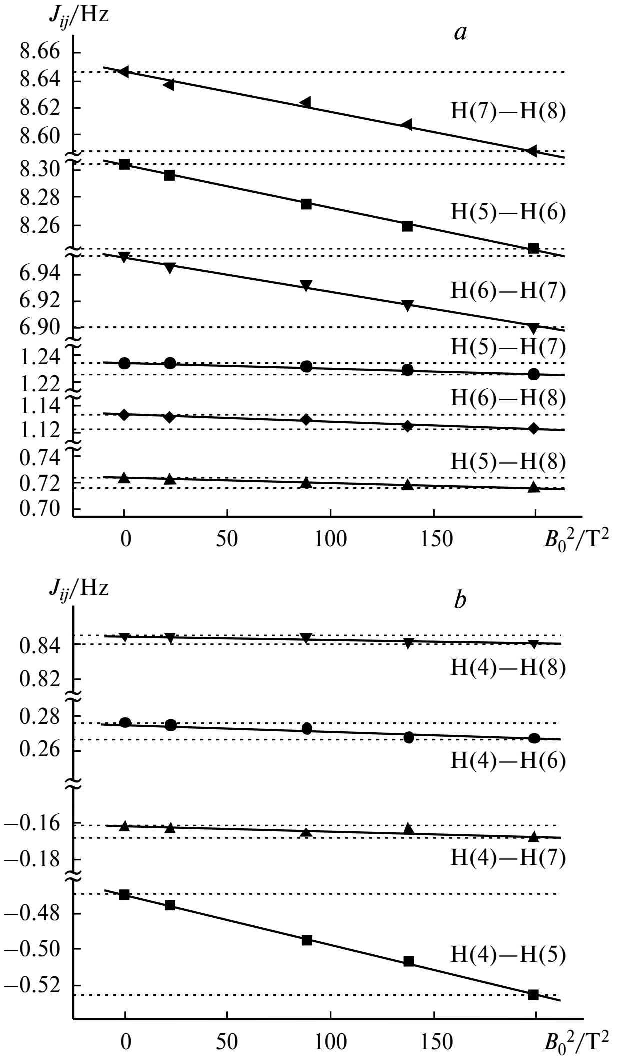

Fig. 3. Intra-ring (*a*) and inter-ring (*b*) spin-spin coupling constants J_{ij} estimated ignoring the orientation effects for 1,2,3-trichloronaphthalene plotted *vs.* squared magnetic induction B_0^2.

nearly equal to one another and all pairs of protons are separated by similar interatomic distances lying in the narrow range from 2.457 to 2.488 Å (see Fig. 2). The results obtained are in qualitative agreement with the simplest orientation model using an uniaxial magnetic susceptibility tensor, which includes only the anisotropy $\Delta\chi$ normal to the molecular plane (rhombicity parameter $\delta\chi$ is negligible). For the protons in *meta*- ($^4J_{\mathrm{H(5),H(7)}}$ and $^4J_{\mathrm{H(6),H(8)}}$, see Fig. 3, *a*) and *para*-positions ($^5J_{\mathrm{H(5),H(8)}}$, see Fig. 3, *a*) relative to one another the absolute value of the slope is about 6 and 9 times smaller, respectively, which is also in good agreement with the data on the interatomic distances in the framework of the model of uniaxial tensor, namely, 4.295 Å ($r_{\mathrm{H(5)-H(7)}}$) and 4.292 Å ($r_{\mathrm{H(6)-H(8)}}$) for *meta*-protons and 4.971 Å for *para*-protons. Long distances between pairs of the inter-ring protons H(4) and H(6) (4.772 Å), H(4) and H(7) (5.928 Å) and *ansa*-protons H(4) and H(8) (5.567 Å) in the framework of the same model determine the small slope of the dependences of the corresponding long-range spin-spin coupling constants through five and six bonds on the magnetic field strength.

Interestingly, the character of the slope of the linear dependences on the squared magnetic induction B_0^2 (see Fig. 3) can be used for the determination of absolute signs of the spin-spin coupling constants without performing complex additional experiments.[17] For planar aromatic molecules in the framework of the model for uniaxial magnetic susceptibility tensor one should expect negative values of the dipole-dipole coupling constants and the observed splittings in the spectra should decrease for positive spin-spin coupling constants or increase for negative ones on going to the spectra recorded at higher magnetic field strength (see expression (1)). The absolute values of all six intra-ring spin-spin coupling constants for compound **1** decrease on going to stronger fields (see Fig. 3). A similar situation occurs in the case of positive inter-ring coupling constants through five bonds, $^5J_{\mathrm{H(4),H(6)}}$ and $^5J_{\mathrm{H(4),H(8)}}$, whereas for the negative inter-ring coupling constants through an even number of bonds ($^4J_{\mathrm{H(4),H(5)}}$ and $^6J_{\mathrm{H(4),H(7)}}$) transition to higher fields is accompanied by an increase in the absolute value of the corresponding splitting in the high-resolution NMR spectra (see Fig. 3, *b*). These observations can be considered as independent substantiation of the conclusions about the signs of the inter-ring spin-spin coupling constants $J_{\mathrm{H,H}}$ for naphthalene derivatives.[10,16]

To obtain the best-fit estimates of the orientation parameters that describe the totality of spectral data in the framework of the orientation model mentioned above, we propose a procedure for simultaneous processing of all available spectra. The parameters to be estimated include the spin-spin coupling constants J_{ij}^0 (one set of parameters for all the spectra studied) and the dipole-dipole coupling constants that characterize individual spectra. In our case one should determine four groups of constants (D_{ij}^{200}, D_{ij}^{400}, D_{ij}^{500}, and D_{ij}^{600}) characterizing the spectra recorded on the spectrometers operating at 200, 400, 500, and 600 MHz, respectively. The spectra were processed using the ALIGN program developed in this study. The first stage of the computational scheme includes a series of iterative calculations of each spectrum ignoring the orientation effects and analysis of the dependences of the apparent spin-spin coupling constants on B_0^2 as described above. In the next stage these dependences are analyzed to estimate the dipole-dipole coupling constants in the first-order approximation and to classify the NMR spectral parameters into the field-dependent dipole-dipole coupling constants (D_{ij}) and field-independent spin-spin coupling constants (J_{ij}^0). The parameters J_{ij}^0 are determined by extrapolating the solution of the equations of the type

$$J_{ij}^0 = J_{ij} - \Lambda_{ij}B_0^2, \tag{10}$$

to zero B_0 value. Equation (10) implies that the parameters Λ_{ij} (doubled first partial derivatives of the dipole-dipole coupling constants with respect to B_0^2) are independent of B_0^2. Then, the dipole-dipole coupling constants for any spectrum studied are estimated in the first-order approximation using the expression

$$D_{ij} = 0.5(J_{ij} - J_{ij}^0). \tag{11}$$

The estimates of the J_{ij}^0 and D_{ij} constants and the chemical shifts are then used as parameters of the intial approximation for the next series of calculations of the spectra using the Hamiltonian of oriented spin system (6). The best correspondence between the frequencies of the experimental lines and transitions for all theoretical spectra is found by varying the values of the chemical shifts (separately for each spectrum) and the dipole-dipole coupling constants. Taking into account the mutual correlation between the spin-spin coupling constants and the dipole-dipole coupling constants for nearly-first-order strong-field spectra, the J_{ij}^0 constants are not varied.

The computational scheme is an iterative one. Subsequent iterations are required to refine the estimates of the D_{ij} and J_{ij}^0 parameters in order to obtain the best-fit description of all experimental data provided the minimum possible deviation from the following relationship

$$D_{ij} = 0.5\Lambda_{ij}B_0^2. \tag{12}$$

The course of the iterative procedure is monitored by calculating the total root-mean-square deviation (RMSD) of the frequencies of the experimental components from the frequencies of theoretical transitions. A set including 305 frequencies from the four NMR spectra of 1,2,3-trichloronaphthalene meets the convergence criteria after four iterations; here, the RMSD is 0.0018 Hz (it decreases by less than 0.01% in the last iteration). The number of the assigned transitions (N) and the RMSD values are listed below.

Operating frequency/MHz	200	400	500	600
N	70	80	77	78
RMSD/Hz	0.0027	0.0020	0.0019	0.0005

The final spin-spin coupling constants and field-dependent dipole-dipole coupling constants are listed in Table 1.

Clearly, the accuracy of experiments is critical to reliable detection of weak orientation effects. For the multi-spectrometer method we propose here it is important to have well-resolved NMR spectra recorded on both low-field and high-field spectrometers. It is believed that high-resolution NMR spectra can be recorded more easily on spectrometers operating at frequencies of 200, 250, or 300 MHz for ^{1}H nuclei (relatively weak magnetic field induction). Attainment of a necessary resolution of ~0.1 Hz on, *e.g.*, a 200-MHz spectrometer requires that the magnetic field inhomogeneity be equal to $\sim 5 \cdot 10^{-10}$ of the nominal B_0 value. The same resolution on a 600-MHz spectrometer formally requires that the magnetic field inhomogeneity be three times lower, *i.e.*, about $1.5 \cdot 10^{-10}$ of the nominal B_0 value. However, analysis of the data listed in Table 1 indicates that the accuracy of determination of spectral parameters using the spectra recorded on high-field spectrometers is usually higher compared to the results obtained with low-field instruments. This seems to be due to the fact that the last-generation high-field spectrometers are equipped with improved frequency synthesizers and data processing system.

Table 1. True spin-spin coupling constants J_{ij}^{0} and dipole-dipole coupling constants D_{ij}^{200}, D_{ij}^{400}, D_{ij}^{500}, and D_{ij}^{600} determined using simultaneous analysis of a series of NMR spectra of 1,2,3-trichloronaphthalene recorded on spectrometers operating at frequencies of 200, 400, 500, and 600 MHz, respectively*

Nuclei	J_{ij}	$-D_{ij}^{200}$	$-D_{ij}^{400}$	$-D_{ij}^{500}$	$-D_{ij}^{600}$
H(4),H(5)	−0.4682	0.0030	0.0125	0.0189	0.0276
	(0.0004)	(0.0006)	(0.0004)	(0.0004)	(0.0001)
H(4),H(6)	0.2771	0.0005	0.0019	0.0036	0.0045
	(0.0004)	(0.0006)	(0.0004)	(0.0004)	(0.0001)
H(4),H(7)	−0.1622	0.0003	0.0013	0.0010	0.0025
	(0.0005)	(0.0008)	(0.0004)	(0.0004)	(0.0001)
H(4),H(8)	0.8444	0.0003	0.0006	0.0016	0.0020
	(0.0004)	(0.0006)	(0.0004)	(0.0004)	(0.0001)
H(5),H(6)	8.3046	0.0034	0.0136	0.0214	0.0304
	(0.0004)	(0.0005)	(0.0004)	(0.0004)	(0.0001)
H(5),H(7)	1.2346	0.0004	0.0020	0.0032	0.0047
	(0.0005)	(0.0007)	(0.0004)	(0.0004)	(0.0001)
H(5),H(8)	0.7229	0.0004	0.0014	0.0022	0.0032
	(0.0004)	(0.0006)	(0.0004)	(0.0004)	(0.0001)
H(6),H(7)	6.9544	0.0035	0.0110	0.0179	0.0266
	(0.0004)	(0.0005)	(0.0004)	(0.0004)	(0.0001)
H(6),H(8)	1.1337	0.0004	0.0022	0.0039	0.0050
	(0.0004)	(0.0006)	(0.0004)	(0.0004)	(0.0001)
H(7),H(8)	8.6470	0.0037	0.0113	0.0189	0.0279
	(0.0004)	(0.0007)	(0.0004)	(0.0004)	(0.0001)

* All constants (in Hz) were measured for 2 *M* solution in acetone-d$_6$ at 303 K; figures in parentheses denote the standard deviations.

The computational scheme includes an iterative procedure. In each step, all variables are separated into field-independent spin-spin coupling constants and field-dependent dipole-dipole coupling constants using the least squares method. The next iteration steps allow for possible deviations from the model used owing to strong nuclear coupling effects in the non-first-order NMR spectra.

The next stage of analysis of the orientation effects in compound **1** consists in determination of the orientation parameters of molecules. A robust system of equations of the type (9) for all dipole-dipole coupling constants (see Table 1) was solved by the nonlinear least squares method (Levenberg—Marquardt version) using the ALIGNSHP program. In symmetrical molecules, *e.g.*, naphthalene the axes of the molecular system of coordinates (x, y, z) coincide with the principal axes of the magnetic susceptibility tensor χ (x'', y'', z''). For less symmetrical molecules (*e.g.*, benzofuran or **1**) the x and x'' axes make an angle α (see Fig. 2).[14,15] Clearly, the parameter $\delta\chi$ depends on the angle α. In this study the y axis of the molecular system of coordinates was directed from the C(9) to the C(10) atom (the midpoint of the C(9)—C(10) bond was specified as the origin) and the x and y axes were directed in such a manner that the x and y coordinates of the atoms of the ring containing substituents be positive (see Fig. 1). The final values of the three desired parameters of the magnetic susceptibility tensor $\Delta\chi$ and $\delta\chi$ and the angle α for compound **1** are listed in Table 2. The solution obtained for all the forty dipole-dipole coupling constants studied in this work is characterized by a RMSD of 0.0006 Hz, which is only slightly larger than the average error of experimental data. A correlation between the experimental and theoretical values (Fig. 4) exhibits no missing points. Apparently, it is possible to calculate the constants with an accuracy as high as the experimental error by allowing variation of particular geometric parameters of molecule **1**. However, we believe that the structure of the rigid naphthalene moiety obtained by optimization using a rather wide basis set should not further be refined.

It is interesting to estimate the maximum possible accuracy of the determination of geometric parameters based on the orientation effects. A specific feature of this procedure is such that the highest accuracy can possibly be obtained for those atoms in the molecule that are separated by the shortest distances, namely, the *ortho-* or *peri*-protons in the naphthalene molecule ($r \approx 2.5$ Å), pairs of diastereotopic geminal protons of CH$_2$ groups ($r \approx 1.8$ Å), *etc.* From the data listed in Table 1 it follows

Table 2. Comparison of experimental and calculated (CSGT method, see text) anisotropy ($\Delta\chi$/m^3 mol^{-1}) and rhombicity ($\delta\chi$/m^3 mol^{-1}) parameters and the angle of rotation of the principal axes (α/deg) of the magnetic susceptibility tensor for 1,2,3-trichloronaphthalene and a series of model compounds[a]

Method	N^b	$-\Delta\chi \cdot 10^{34}$	$-\delta\chi \cdot 10^{34}$	α
		1,2,3-Trichloronaphthalene		
Experiment	—	27.8 (2)[c]	1.4 (2)[c]	54
RHF/6-311G	208	23.3	0.7	17
RHF/6-311+G	260	24.3	0.8	7
RHF/6-311++G	265	24.3	0.8	9
RHF/6-311G(d)	273	26.0	0.6	7
RHF/6-311+G(d)	325	26.9	0.7	−1
RHF/6-311++G(d)	330	26.8	0.8	−1
RHF/6-311G(df)	416	26.9	0.8	−2
RHF/6-311+G(df)	416	26.9	0.8	−2
RHF/6-311++G(df)	421	26.9	0.8	−2
		Benzene		
Experiment[d]		12.6 (2)[c]	0	—[e]
RHF/6-311++G(df)	198	14.8	0	—[e]
		Chlorobenzene		
Experiment[13]		12.8	0.6	0
RHF/6-311++G(df)	231	13.5	0.1	0
		Naphthalene		
Experiment[13]		25.0	0.6	0
RHF/6-311G	154	24.5	0.5	0
RHF/6-311+G	194	25.0	0.7	0
RHF/6-311++G	202	25.0	0.7	0
RHF/6-311G(d)	204	27.6	0.4	0
RHF/6-311+G(d)	244	28.0	0.6	0
RHF/6-311++G(d)	252	28.0	0.6	0
RHF/6-311G(df)	274	27.6	0.5	0
RHF/6-311+G(df)	314	28.0	0.6	0
RHF/6-311++G(df)	322	28.0	0.6	0
RHF/6-311G(3df,3pd)	486	27.2	0.8	0
RHF/6-311++G(3df,3pd)	534	27.4	0.9	0

[a] The directions of the axes of coordinates are given in the text.

[b] Number of wave functions in the basis set.

[c] Figures in parentheses denote the standard deviation.

[d] Parameters of the magnetic susceptibility tensor were estimated in this work using the dipole-dipole coupling constants for benzene taken from Ref. 11.

[e] Not determinable for molecules belonging to this symmetry class.

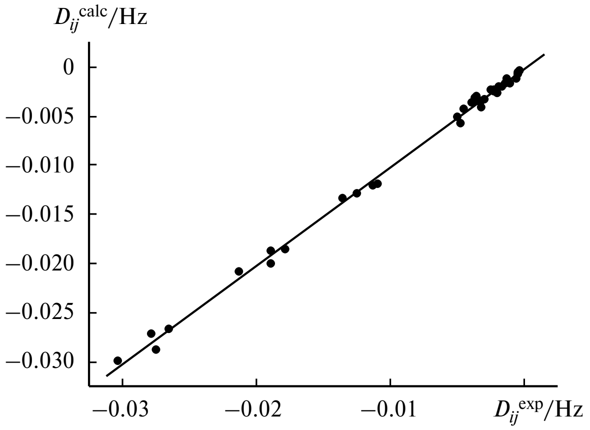

Fig. 4. Correlation between the experimental and theoretical dipole-dipole coupling constants D_{ij}.

that the relative error of measurement of the coupling constants D_0 can lie within 0.3—0.4% or be even smaller. Geminal protons are separated by even shorter distances; therefore, here one can expect a higher accuracy for D_{gem} (about 0.1—0.2%). Since the internuclear distances are cubed in expression (9), the relative accuracy of determination of these parameters should be three times higher than the accuracy of determination of the coupling constants. Therefore, one can expect that the method allows highly acurate estimates of the internuclear distances (relative error ~0.05%), which is of interest for structural studies. The orientation effects provide unique information and make it possible to determine the relative positions of protons (this is a severe problem in X-ray diffraction and gas-phase electron diffraction studies). A natural limitation of this method is that it explicitly treats positions of only those atoms that have magnetic isotopes in the molecule. Useful information on the structure of the molecular skeleton can be obtained by studying the ^{13}C- and ^{15}N-enriched compounds.

***Ab initio* quantum chemical calculations of the magnetic susceptibility.** Valuable information on the molecular structure can be obtained by comparing experimental data with independent thoretical estimates of parameters of the magnetic susceptibility tensor of the molecule. Modern quantitative theory of the magnetic properties of molecules is based on the results of *ab initio* quantum chemical calculations. Recently, it was proposed to calculate the magnetic susceptibility using the CSGT (Continuous Set of Gauge Transformations) method,[23] which proved itself in thoretical prediction of the magnetic properties of hydrocarbons[24] and some nucleotides.[3] Using this method, we calculated the parameters of the magnetic susceptibility tensor for compound **1** and naphthalene (**2**) in the RHF approximation for a wide range of basis sets including the 6-311G, 6-311+G, 6-311++G, 6-311G(d), 6-311+G(d), 6-311++G(d), 6-311G(df), 6-311+G(df), and 6-311++G(df) ones.[25] Calculations for compound **2** were also carried out using the 6-311G(3df,3pd) and 6-311++G(3df,3pd) basis sets. We believe that comparison of the results obtained with a wide range of conventional diffuse and polarization functions can provide information for more substantiated choice of the mode of calculations of the χ tensor parameters for compounds **1** and **2** that are typical medium-size molecules. The theoretical $\Delta\chi$ and $\delta\chi$ values and the angle α are listed in Table 2. By and large, the results of calculations of the parameters $\Delta\chi$ for compounds **1** and **2** are in reasonable agreement with the experimental data. It should be noted that augmentation of the basis set with diffuse func-

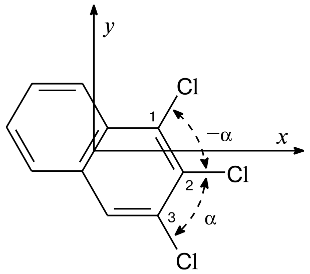

Fig. 5. Orientation of the *x* and *y* axes of the local magnetic susceptibility tensors.

tions afects the results of calculations to a lesser extent compared to augmentation with polarization functions. For compound **1**, the results of calculations using the 6-311G(df) and 6-311++G(df) basis sets are in good agreement with the experimental $\Delta\chi$ value we have obtained. For compound **2**, calculations with so wide basis sets, as 6-311G(3df,3pd) and 6-311++G(3df,3pd), lead to somewhat overestimated (in absolute value) $\Delta\chi$ value. However, this discrepancy can also be a consequence of insufficient accuracy of the available experimental data.[13] The relatively small value of the rhombicity parameter of the magnetic susceptibility tensor $\delta\chi$ for compound **1** is in agreement with experimental data, whereas modern theory predicts the angle α with a low accuracy (see Table 2).

Elaboration of methods for description of parameters of the tensor χ based on simulation using the additive schemes is of undoubtful interest. This is important for estimating the anisotropy of the magnetic susceptibility of complex systems (*e.g.*, biopolymers) since straignhforward quantum chemical calculations are impossible because of too high computational cost. We estimated the parameters of the tensor χ for compound **1** using the additive scheme based on the data for compound **2** and increments that describe substitution of chlorine for hydrogen. The increments used were the changes in the magnetic susceptibility anisotropy ($\Delta\Delta\chi$) and the rhombicity parameter ($\Delta\delta\chi$) of the C—Cl bond, which can be calculated based on comparison of the experimental and/or theoretical parameters of the tensor χ for benzene and chlorobenzene (see Table 2). The parameter $\Delta\Delta\chi$ describes the change in the χ_{zz} tensor component normal to the molecular plane on going from benzene to chlorobenzene. Therefore, the parameter $\Delta\delta\chi$ describes the differences between the transverse components of the tensor χ (see expression (3)). If the axes of the molecular system of coordinates are directed as shown in Fig. 5, one gets a diagonal local magnetic susceptibility tensor for the C(2)—Cl(2) bond, which can simply be expressed using the parameters $\Delta\Delta\chi$ and $\Delta\delta\chi$:

$$\Delta\hat{\chi}_{\mathrm{C(2)-Cl(2)}} = \begin{vmatrix} 0.5\Delta\delta\chi & 0 & 0 \\ 0 & -0.5\Delta\delta\chi & 0 \\ 0 & 0 & \Delta\Delta\chi \end{vmatrix}.$$

The local tensors of the C(1)—Cl(1) and C(3)—Cl(3) bonds have a similar simple form in the local coordinates if the *x* axis is directed along the corresponding bond. They also can be transformed into a system of coordinates that is common to the three bonds C(1)—Cl(1), C(2)—Cl(2), and C(3)—Cl(3), in which the *x* axis is parallel to the C(2)—Cl(2) bond, using the transformations of rotation in the *xy* plane by an angle α of about −60°.

$$\Delta\hat{\chi}_{\mathrm{C(1)-Cl(1)}} = \hat{R}^{-1}(\alpha)\begin{vmatrix} 0.5\Delta\delta\chi & 0 & 0 \\ 0 & -0.5\Delta\delta\chi & 0 \\ 0 & 0 & \Delta\Delta\chi \end{vmatrix}\hat{R}(\alpha) =$$

$$= \begin{vmatrix} -0.25\Delta\delta\chi & (\sqrt{3}/4)\Delta\delta\chi & 0 \\ (\sqrt{3}/4)\Delta\delta\chi & 0.25\Delta\delta\chi & 0 \\ 0 & 0 & \Delta\Delta\chi \end{vmatrix},$$

$$\Delta\hat{\chi}_{\mathrm{C(3)-Cl(3)}} = \hat{R}(\alpha)\begin{vmatrix} 0.5\Delta\delta\chi & 0 & 0 \\ 0 & -0.5\Delta\delta\chi & 0 \\ 0 & 0 & \Delta\Delta\chi \end{vmatrix}\hat{R}^{-1}(\alpha) =$$

$$= \begin{vmatrix} -0.25\Delta\delta\chi & -(\sqrt{3}/4)\Delta\delta\chi & 0 \\ -(\sqrt{3}/4)\Delta\delta\chi & 0.25\Delta\delta\chi & 0 \\ 0 & 0 & \Delta\Delta\chi \end{vmatrix}.$$

Summing the three local tensors, we get the expression for the overall effect of the three chlorine atoms in molecule **1**, $\Delta\hat{\chi}_{\mathrm{add}}$:

$$\Delta\hat{\chi}_{\mathrm{add}} = \Delta\hat{\chi}_{\mathrm{C(1)-Cl(1)}} + \Delta\hat{\chi}_{\mathrm{C(2)-Cl(2)}} + \Delta\hat{\chi}_{\mathrm{C(3)-Cl(3)}} =$$

$$= \begin{vmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 3\Delta\Delta\chi \end{vmatrix}.$$

It follows that the effects of three substituents bonded to the neighboring carbon atoms on the transverse component of the tensor χ are mutually cancelled, which gives a zero rhombicity parameter of the tensor χ in the framework of the additive scheme. On the contrary, all the three substituents contribute to the axial component of the tensor, $\Delta\chi\hat{}_{\mathrm{add}}$. Experimental data for chlorobenzene show no marked changes in the component ($\Delta\Delta\chi^{\mathrm{exp}} = -0.2 \cdot 10^{-34}$ m^3 mol.$^{-1}$, see Table 2). CSGT calculations at the RHF/6-311++G(df) level of theory predict a decrease in absolute value of the magnetic susceptibility anisotropy ($\Delta\Delta\chi^{\mathrm{calc}} = 1.3 \cdot 10^{-34}$ m^3 mol.$^{-1}$, see Table 2) on going from benzene to chlorobenzene, which is in reasonable agreement with the observed trend for the experimental $\Delta\chi$ values (see Table 2) on going from naphthalene to 1,2,3-trichloronaphthalene.

The results obtained suggest that *ab initio* calculations of the magnetic susceptibility anisotropy in the framework of semiempirical additive schemes seem to be quite promising for studying conformations of complex molecules containing several magnetic anisotropic groups with arbitrary spatial orientations.

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References

1. J. A. B. Lohman and C. MacLean, *Chem. Phys.*, 1979, **43**, 144.
2. E. W. Bastiaan, J. Bulthuis, and C. MacLean, *Magn. Reson. Chem.*, 1986, **24**, 723.
3. D. Bryce, J. Boisbouvier, and A. Bax, *J. Am. Chem. Soc.*, 2004, **126**, 10820.
4. B. N. M. Van Buuren, J. Schleucher, V. Wittman, C. Griesinger, H. Schwalbe, and S. S. Wijmenga, *Angew. Chem., Int. Ed.*, 2004, **43**, 187.
5. A. A. Bothner-By and G. Gayathri, *J. Magn. Reson.*, 1984, **56**, 456.
6. A. A. Bothner-By, G. Gayathri, and P. C. M. VanZijl, *Magn. Reson. Chem.*, 1985, **23**, 935.
7. G. Gayathri, A. A. Bothner-By, P. C. M. VanZijl, and C. MacLean, *Chem. Phys. Lett.*, 1982, **87**, 192.
8. P. Pulay, E. M. Scherer, P. C. A. van der Wel, and R. E. Koeppe, *J. Am. Chem. Soc.*, 2005, **127**, 17488.
9. F. A. L. Anet, *J. Am. Chem. Soc.*, 1986, **108**, 1354.
10. R. Laatikainen, *J. Magn. Reson.*, 1988, **78**, 127.
11. R. Laatikainen, J. Ratilainen, R. Sebastian, and H. Santa, *J. Am. Chem. Soc.*, 1995, **117**, 11006.
12. R. B. Johannesen, J. A. Feretti, and R. K. Harris, *J. Magn. Reson.*, 1970, **3**, 84.
13. E. W. Bastiaan and C. MacLean, in *NMR Basic Principles and Progress*, Eds P. Diehl, E. Fluck, H. Guenther, R. Kosfeld, and J. Seelig, Springer, Berlin—Paris—New York, 1991, **25**, 17.
14. A. V. Makarkina, S. S. Golotvin, and V. A. Chertkov, *Khim. Geterotsikl. Soedin.*, 1995, 1214 [*Chem. Heterocycl. Compd.*, 1995 (Engl. Transl.)].
15. A. V. Makarkina, S. V. Zubkov, and V. A. Chertkov, *Khim. Geterotsikl. Soedin.*, 1997, 318 [*Chem. Heterocycl. Compd.*, 1997 (Engl. Transl.)].
16. S. S. Golotvin and V. A. Chertkov, *Izv. Akad. Nauk*, *Ser. Khim.*, 1997, 444 [*Russ. Chem. Bull.*, 1997, **46**, 423 (Engl. Transl.)].
17. T. D. W. Claridge, *High-Resolution NMR Techniques in Organic Chemistry*, Pergamon, Amsterdam, 1999, 104.
18. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, *GAUSSIAN 98W, Revision A.11*, Gaussian, Inc., Pittsburgh (PA), 2001.
19. T. A. Keith and R. F. W. Bader, *Chem. Phys. Lett.*, 1993, **210**, 223.
20. J. R. Cheeseman, M. J. Frisch, G. W. Trucks, and T. A. Keith, *J. Chem. Phys.*, 1996, **104**, 5497.
21. D. L. VanderHart, in *Encyclopedia of NMR*, Wiley, New York—London, 1996, **5**, 2938.
22. J. Vaara, J. Jokisaari, R. E. Wasylishen, and D. L. Bryce, *Progr. Nucl. Magn. Reson.*, 2002, **41**, 233.
23. T. A. Keith and R. F. W. Bader, *Chem. Phys. Lett.*, 1993, **210**, 223.
24. K. Ruud, H. Skaane, T. Helgaker, K. L. Bak, and P. Jørgensen, *J. Am. Chem. Soc.*, 1994, **116**, 10135.
25. J. B. Foresman and A. Frisch, *Exploring Chemistry with Electronic Structure Methods*, Gaussian, Inc., Pittsburgh (PA), 1996, 354.

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