

New Semi-empirical Approach for the Calculation of ^{13}C Chemical-Shift Tensors

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The semi-empirical bond polarization theory is applied to the calculation of ^{13}C chemical-shift tensors. This method allows prediction of shift tensors with deviations from experiment comparable to the errors of the *ab initio* methods. In contrast to *ab initio* calculations, a set of empirical parameters is needed, which can be estimated from experimental chemical-shift tensors solving a set of linear equations. The coefficients of this overdetermined set of equations are bond polarization energies that must be calculated within the framework of this theory. The parameters for C–C, C–H, and C–O bonds of sp^3 and sp^2 hybridized carbons and C–N bonds of sp^3 carbons were obtained from 606 equations formed from experimental data from 20 substances taken from the literature. The substances include sugars, aromatic compounds, amino acids, and organic acids. The mean deviation of calculated from experimental ^{13}C chemical-shift tensor components is 9 ppm. © 1997 Academic Press

INTRODUCTION

The three principal values of the ^{13}C chemical-shift tensors can be determined in solid-state ^{13}C NMR investigations of crystalline powders, whereas for the determination of the orientation of the tensor with respect to the crystalline axes, single-crystal investigation must be carried out. A comprehensive overview covering the chemical-shift tensors of several nuclei was given by Duncan (1). Using modern experimental techniques [Grant (2)], the tensors can be measured very precisely even in the case of many overlapping lines. With the possibility of measuring a large number of tensors for complicated substances, one must face two closely interconnected problems: assignment and interpretation. The tensors must be assigned to distinct carbon sites within the crystal. This set of six measured figures per carbon atom bids fair to contain detailed information about the spatial geometry and electronic environment of the carbon atom under study.

The problem is that up to now there are no simple rules for the estimation of the tensors as in the case of the isotropic chemical shift. Isotropic chemical shifts can be estimated from empirical increments and correlations, and these estimates are in most cases precise enough to reveal the topology or constitution of a molecule. Until now, *ab initio* quantum

chemical calculations on the IGLO (3), GIAO (4), or LORG (5) level must be performed if chemical-shift tensors are to be understood with respect to the structure of a molecule. This approach is limited to medium-size molecules that do not interact too strongly with their neighbors within the crystal lattice, as for instance naphthalene. If tensorial data is to be used in molecular mechanics calculation, the computational effort of the *ab initio* methods inhibits its application.

The aim of this work is the introduction of a semi-empirical scheme for the calculation of chemical-shift tensors. This method is based on the bond-polarization theory (6–9). It will be demonstrated that ^{13}C chemical-shift tensors can be reproduced with this method with deviations from experiment comparable to the errors of the *ab initio* methods. The calculations can be performed for molecules with hundreds of atoms even on a PC computer. In contrast to the *ab initio* method, a set of empirical parameters is needed for the calculations. By use of the bond-polarization theory, these parameters can be estimated directly from experimental chemical shifts through solving a set of linear equations.

THEORY

A detailed outline of the theory is given in (6), and within this section only the central ideas are summarized. According to the bond polarization theory, most of the observed changes of chemical shifts, as for instance the β , γ , or δ effects, are caused by the polarization of the bonds that are connected to the atom under study by surrounding charge distributions. The best-suited quantum chemical description are in this case localized orbitals. We therefore introduce two center bond orbitals that are linear combinations of two hybrids χ_a and χ_b at the bonded atoms a and b :

$$\psi_i = c_{ai}\chi_a + c_{bi}\chi_b \quad \psi_i^* = c_{bi}\chi_a - c_{ai}\chi_b \quad [1]$$

In addition to the bond orbital ψ , the anti-bond ψ^* is introduced. Orthogonality is forced between different bond orbitals and anti-bond orbitals by neglecting overlap contri-

butions between hybrids at different centers. In this case, only the bond polarity d must be determined for every bond:

$$c_{ai} = \sqrt{\frac{1+d_i}{2}} \quad c_{bi} = \sqrt{\frac{1-d_i}{2}}. \quad [2]$$

The ground-state wave function of the molecular system Ψ_0 is constructed as a Slater determinant of bond orbitals

$$\Psi_0 = \frac{1}{\sqrt{2n!}} \text{Det} |\psi_1^+ \psi_1^- \cdots \psi_i^+ \psi_i^- \cdots \psi_n^+ \psi_n^-|, \quad [3]$$

where + and - designate the possible spin states. Polarizations and delocalizations are introduced by adding to the determinant Ψ_0 excited configurations Ψ_i by substituting one or two bonds by anti-bonds:

$$\Psi_i = \Psi \begin{pmatrix} j^* \\ i \end{pmatrix} = \frac{1}{\sqrt{2n!}} \text{Det} |\cdots \psi_j^{+*} \psi_i^- \cdots|. \quad [4]$$

The wave function including configuration interaction will contain configurations of the type $\Psi(i \rightarrow j^*)$ describing delocalizations and $\Psi(i \rightarrow j^*, k \rightarrow l^*)$ for double excitations.

If influences of charge distributions surrounding a bond are of interest, polarizations will play a dominant role. Polarizations are described by configurations of the type $\Psi(i \rightarrow i^*)$ where an electron from bond i is excited into its own anti-bond i^* . If only those excited configurations are taken into account that describe polarizations, the valence electrons are confined to bonds and shifted only within the bonds by surrounding charges. In this way, it is possible to restrict all consideration to that part of the molecular system that is of dominant interest. This part of the molecule is designated A and we consider only the polarization of the bonds within the molecular part A by the charge distribution of part B. The contribution of excited configurations to the molecular wave function including polarization Ψ_p is now calculated by using perturbation theory:

$$\begin{aligned} \Psi_p = \Psi_0 + \sum_{i \in A}^{N_A} \frac{\langle \Psi_0 | \hat{\mathbf{F}}_B^0 | \Psi \begin{pmatrix} i^* \\ i \end{pmatrix} \rangle}{E_0 - E \begin{pmatrix} i^* \\ i \end{pmatrix}} \\ \times \Psi \begin{pmatrix} i^* \\ i \end{pmatrix} + \sum_{i \in B}^{n_B} \cdots \end{aligned} \quad [5]$$

The first sum in [5] runs only over the N_A bonds of the molecular part A and the perturbation by B is expressed using the Fock operator $\hat{\mathbf{F}}_B^0$.

Next we calculate the expectation value of a one-electron operator $\hat{\mathbf{O}}$ inserting the wave function [5] and neglect all terms that are higher than the first order. The expectation value of a Slater determinant constructed from bond orbitals gives a sum over bond contributions, and we can easily separate the contributions of part A of the molecular system:

$$\begin{aligned} \langle \psi_p | \hat{\mathbf{O}} | \psi_p \rangle_A \\ = 2 \sum_{i \in A}^{N_A} \{ \langle i | \hat{\mathbf{O}} | i \rangle + \frac{2}{\Delta E_i} \langle i | \hat{\mathbf{F}}_B^0 | i^* \rangle \langle i^* | \hat{\mathbf{O}} | i \rangle \} \\ = \sum_{i \in A}^{N_A} \{ C_i + A_i \langle i | \hat{\mathbf{F}}_B^0 | i^* \rangle \}. \end{aligned} \quad [6]$$

This formula is of central interest throughout the paper and will be interpreted in more detail [see Sternberg (6)]. For an expectation value of a one-electron operator, we obtain a sum over the N_A bond contributions of the type $\langle i | \hat{\mathbf{O}} | i \rangle$ that can be regarded as bond increments C_i . To every bond contribution C_i , a term is added that depends linearly on the polarization energy of the bond $\langle i | \hat{\mathbf{F}}_B^0 | i^* \rangle$ multiplied with a slope A_i being proportional to an integral of the type $\langle i^* | \hat{\mathbf{O}} | i \rangle$. Bond polarization can be treated within this scheme in a strictly bond-additive form. Instead of calculating the integrals containing the operator $\hat{\mathbf{O}}$, we introduce at this point for every type of bond an empirical constant C_i for the expectation value of the unpolarized bond (bond increment) and the empirical slope A_i describing the linear change of the bond contribution with polarization. We now must only discuss the matrix elements of the Fock operator.

The matrix elements of the Fock operator in Eq. [6] involve the calculation of complicated coulomb and exchange integrals over Slater atomic orbitals. If we consider the part B of the molecule as a distribution of point charges, we can replace the Fock operator $\hat{\mathbf{F}}_B^0$ by the point potential $\hat{\mathbf{V}}_B$. This approximation is in most cases justified because the interaction is of long range. With this assumption, simple formulas for the matrix elements of $\hat{\mathbf{V}}_B$ can be derived, but they are not a necessary prerequisite of the bond polarization theory. For the polarization energy in Eq. [6], the following expression is obtained using Eqs. [1] and [2] (small overlap contributions are neglected):

$$\begin{aligned} V_{ab} = \langle i | \hat{\mathbf{V}}_B | i^* \rangle \\ = \frac{\sqrt{1-d_i^2}}{2} \sum_{x \in B}^{N_B} q_x \left\{ \left\langle \chi_a \left| \frac{1}{|\vec{\mathbf{R}}_{ax} - \vec{\mathbf{r}}|} \right| \chi_a \right\rangle \right. \\ \left. - \left\langle \chi_b \left| \frac{1}{|\vec{\mathbf{R}}_{bx} - \vec{\mathbf{r}}|} \right| \chi_b \right\rangle \right\}. \end{aligned} \quad [7]$$

According to Eq. [7], the bond polarization energy V_{ab} depends linearly on the bond order of the bond between

a and b and on the charge q_x . Each term of the sum in Eq. [7] is for σ bonds a difference of two integrals depending on the geometry and on atomic parameters. Explicit formulas for common hybrid functions are given in (6–8). With the exception of the bond order and the charges, the formulas can be easily evaluated from the molecular geometry.

BOND POLARIZATION AND CHEMICAL SHIFT

Let us now give an interpretation of the bond polarization formula [6] in terms of the chemical shift. At first, we introduce a one-electron operator $(\hat{O}^{\text{cs}})_a$, producing as expectation value the chemical shift (or nuclear shielding) of the nucleus a . Conventionally, second-order perturbation theory must be applied to calculate the nuclear shielding, but the perturbation can be included into the operator $(\hat{O}^{\text{cs}})_a$ using

$$\hat{H} = \hat{H}^{(2)} - \sum_{k'} \frac{1}{(E_k^{(0)} - E_0^{(0)})} \hat{H}^{(1)}|k\rangle\langle k|\hat{H}^{(1)}. \quad [8]$$

The perturbation of the wave function caused by a magnetic field is calculated from the vector potentials \vec{A} of the external field \vec{H} and the magnetic dipole fields of the nuclei $\vec{\mu}$

$$\hat{H}^{(2)} = \sum_j \left(\frac{e^2}{2m} \right) \vec{A}_j^2 \quad [9]$$

$$\hat{H}^{(1)} = \left(\frac{\hbar e}{2i} \right) \sum_j \{ \vec{A}_j \vec{\nabla}_j + \vec{\nabla}_j \vec{A}_j \} \quad [10]$$

$$\vec{A}_j = \left(\frac{\mu_0}{2} \right) \vec{H} \times \vec{r}_j + \left(\frac{\mu_0}{4\pi} \right) \frac{\vec{\mu} \times \vec{r}_j}{r_{nj}}. \quad [11]$$

From Eq. [8], the perturbation contribution to the ground state energy can be calculated if the solution of the unperturbed Hamiltonian problem is known. Only those terms in $\hat{H}^{(1)}$ and $\hat{H}^{(2)}$ that are bilinear in the magnetic moment of the nucleus a and to the external magnetic field contribute to the nuclear shielding:

$$\sigma_{\alpha\beta} = \left(\frac{\partial^2 E}{\partial H_\alpha \partial \mu_\beta} \right)_{H_\alpha \mu_\beta \rightarrow 0}. \quad [12]$$

Fortunately the explicit form of the operator for the chemical shift $(\hat{O}^{\text{cs}})_a$ is not needed because we introduced empirical parameters for its expectation values. Only two properties of this operator shall be used in our discussion. At first from Eq. [12], it can be seen that we must introduce

the two indices α and β , one for the components of the magnetic field vector H_α and one for μ_β representing components of the nuclear dipole moment. Consequently, we must write $(\hat{O}_a^{\text{cs}})_{\alpha\beta}$.

The operator $(\hat{O}_a^{\text{cs}})_{\alpha\beta}$ contains in its denominator the distance from the nucleus a to the electron j , and therefore, this operator will act mainly on bonds that are directly connected to the nucleus of interest a . In this way, a very simple definition of the molecular part A is introduced, containing only the first bond sphere of atom a . The sum in Eq. [6] over all bonds of part A of the molecular system needs to be extended in most cases only over the first coordination sphere of atom a including its inner shell orbitals. The constants C_i in Eq. [6] represent bond increments of the chemical shielding σ^{ai} , and the sum gives the first sphere chemical shielding σ_a^{fs} . The bond increments of the chemical shielding are defined by the integrals

$$\sigma_{\alpha\beta}^{ai} = \langle i | (\hat{O}_a^{\text{cs}})_{\alpha\beta} | i \rangle \quad [13]$$

and because the bond increments are tensors we must define its three principal values and the orientation.

Let us now suppose that the bond-tensor contributions become diagonal within the bond coordinate system. The z axis of the bond coordinate system is defined by a vector pointing from one bonded nucleus to the other. For π bonds, the plane of the π system contains the x axis and the y axis is perpendicular to it. This definition of the bond tensors excludes bent bonds and only cases of strict σ – π hybridization are possible. The same symmetry constraints can be introduced for the coefficients A in Eq. [6] because they are calculated from similar integrals:

$$A_{\alpha\beta}^{ai} = \left(\frac{2}{\Delta E_i} \right) \langle i^* | (\hat{O}_a^{\text{cs}})_{\alpha\beta} | i \rangle. \quad [14]$$

The tensorial coefficients $A_{\alpha\beta}^{ai}$ will be diagonal within the same bond coordinate system as the $\sigma_{\alpha\beta}^{ai}$. From these considerations, it can be deduced that we need, for every type of bond, the three empirical bond shieldings σ_{11}^{ai} , σ_{22}^{ai} , σ_{33}^{ai} and the three empirical values for the change of the bond shielding with polarization A_{11}^{ai} , A_{22}^{ai} , A_{33}^{ai} . For every bond of the first coordination sphere, we introduce transformation matrices $D_{\alpha\beta}^i$ for the transformation of the bond coordinate system into a common molecular coordinate system.

With these definitions, we can now write Eq. [6] in terms of tensorial contributions to the chemical shift of a nucleus δ^a , replacing the absolute shielding (for the Greek subscripts the Einstein sum convention is introduced):

$$\delta_{\alpha\beta}^a = \delta^{\text{is}a} + \sum_i^{N_a} D_{\alpha\alpha'}^i D_{\beta\beta'}^i [\delta_{\alpha'\beta'}^{ai} + A_{\alpha'\beta'}^{ai} V_{ai}]. \quad [15]$$

Here δ^{is}_a is the chemical shift caused by the inner shell orbitals of the nucleus under study. The actual value depends on the choice of origin of the chemical-shift scale. The sum of Eq. [15] over the N_a (coordination number of atom a) bond contributions adds up to the chemical-shift contribution tensor of the first coordination sphere. The second term represents a correction that is linearly dependent on the bond polarization energy V_{ai} . This scalar energy is multiplied by a tensorial slope $A_{\alpha\alpha}^{ai}$ representing the change of the chemical shielding tensor with bond polarization. Instead of calculating the integrals in Eq. [13] and [14], we calculate only the bond polarization energies V_{ab} and determine the parameters δ^{fs} and A by linear regression, inserting experimental shifts on the left hand side of Eq. [15].

DOUBLE BONDS AND DELOCALIZED π SYSTEMS

For double bonds, the sum in Eq. [15] must run over the σ bonds and π bonds of the nucleus under study, and separate sets of parameters are needed for both types of bonds. Isolated π bonds introduce no problems into the concept of localized bond contributions as long as the strict σ - π separation is not violated.

Delocalized π systems are not adequately described by a Slater determinant of the type [2]. To account for delocalization, the ground state wave function Ψ_0 is constructed as a linear combination of Slater determinants of localized states that contribute to the ground state:

$$\Psi_0 = \sum_I c_I^0 \Psi_I^0 \quad [16]$$

For instance, in the case of benzene, these localized states would be represented by the Slater determinants of the two Kekulé structures and one would obtain $c = 1/\sqrt{2}$ (disregarding contributions from the nonorthogonality of the Slater determinants). Even on the level of simple semi-empirical theories, the calculation of the distribution of the π electrons requires a solution of the π -Hamiltonian problem. With respect to molecular mechanics or dynamics, this procedure is too demanding.

Within this work, a much simpler approach is proposed. A description of the ground state of the electronic system in terms of multiple configurations according to Eq. [16] would lead to natural orbitals with occupation numbers lower than one. Therefore, we introduced into Eq. [15] π -occupation numbers n_i for the localized π orbitals (see Eq. [17]). These occupation numbers are to be estimated from the valence of a bond. We therefore set $n_i(\pi) = 1$ -valence. The valence is estimated from the bond distance using the formulas of O'Keefe and Brese (10). This approach seems promising since the valence formulas take into account bond shortening from ionic contributions and the true π -electron effects can be separated. For π bonds, the first-sphere π term in Eq.

[17] is multiplied by the π valence, and the last term, being the product of two integrals, is multiplied by the square of the π valence. The parameters $A_{\alpha\beta}^{ai}$ and $\sigma_{\alpha\beta}^{ai}$ must be regarded as parameters for localized π bonds with a π valence of one (or a valence of 2).

PARAMETRIZATION

The parameters of the bond polarization were calculated from an overdetermined set of equations by least-squares fit, using experimental ^{13}C shift tensor data taken from literature. The unpolarized first-sphere chemical-shift tensors $\sigma_{\alpha\alpha}^{\sigma i}$ need to be distinguished depending on the hybridization of the carbon since the electronic environments are different, but the same slope $A_{\alpha\alpha}^{\sigma i}$ was used for sp^3 and sp^2 hybridization. Of course, the π -bond parameters only apply to sp^2 carbons.

The usual tensor representation by symmetrical 3×3 matrices in a general Cartesian coordinate system was found to be unsuitable for this calculation because diagonal elements and off-diagonal elements are not equivalent, and hence it is difficult to fit them in the same set of linear equations. A favorable approach lies in the use of the icosahedral representation as given by Alderman *et al.* (11). The tensors are described by the shift values in six different directions which can be considered as the connection of opposite corners of an icosahedron. These values are independent and equivalent for any given chemical-shift tensor. Thus, the transformation matrices $D_{\alpha\alpha}^i$ in Eq. [15] are now replaced by the transformation to the icosahedral representation $T_{\gamma\alpha}^i$ where γ runs over the six icosahedral components. With these considerations, Eq. [15] now becomes

$$\delta_\gamma^a = \delta^{is} + \sum_i^{N_a} T_{\gamma\beta}^{i2} [\delta_{\beta\beta}^{\sigma i} + A_{\beta\beta}^{\sigma i} V_{\sigma i} + n_{\pi i} \delta_{\beta\beta}^{\pi i} + n_{\pi i}^2 A_{\beta\beta}^{\pi i} V_{\pi i}]. \quad [17]$$

For the calculation of the parameters, precise NMR data with the full tensor information are required with no ambiguities in the assignment of the tensors to the different carbon sites in the crystal. Despite the fact that the full tensor information is useful for many purposes, the experimental procedures are somewhat demanding, and thus the available experimental data are limited.

The ^{13}C shift tensors are very sensitive to the bond geometry of the molecules and their neighborhood. It was demonstrated by Grant *et al.* (12) that the ^{13}C chemical-shift tensors are influenced by structural parameters that cannot even be resolved by modern diffraction techniques. Therefore, precise structural information is necessary as well. In particular, the exact positions of the neighboring hydrogen atoms are needed. Hydrogen positions can be determined correctly

TABLE 1
Substances Used for the Parametrization of the Bond Polarization Model

Substances	used	References		Remarks
		C sites	NMR data	
Calculation of C-C, C-H, C(sp ³)-O, and C(sp ³)-N bond polarization parameters				
Sucrose	12	(2,14)	(15)	
Methyl- α -D-glucopyranoside	7	(16)	(17)	
Methyl- α -D-galactopyranoside	7	(18)	(19)	
Methyl- β -D-galactopyranoside	7	(18)	(19)	
Methyl- α -D-mannopyranoside	7	(18)	(17)	
Methyl- β -D-xylopyranoside	6	(18)	(20)	
Naphthalene	5	(12)	(21)	structure of deuterated form
Pyrene	5	(22)	(23)	
Perylene	20	(24)	(25)	
α -glycine	1	(26)	(27)	
L-alanine	2	(28)	(29)	optimized H positions
L-threonine	3	(30)	(13)	
L-serine monohydrate	2	(31)	(32)	
L-asparagine monohydrate	2	(33)	(34)	C(4) not included
Calculation of C(sp ²)-O bond polarization parameters				
α -glycine	1	(26)	(27)	
L-alanine	1	(28)	(29)	optimized H positions
L-threonine	1	(30)	(13)	
L-serine Monohydrate	1	(31)	(32)	
L-asparagine Monohydrate	1	(33)	(34)	
Acetic acid	1	(35)	(36)	optimized H positions
Malonic acid	2	(37)	(38)	optimized H positions
Oxalic acid dihydrate	1	(39)	(40)	optimized H positions
Pyromellitic acid	2	(37)	(41)	optimized H positions
1,4 dimethoxybenzene	1	(42)	(42)	optimized H positions
1,2,3 trimethoxybenzene	3	(42)	(42)	optimized H positions

only from neutron diffraction studies. When the structure determination is carried out with X-ray diffraction, the positions of hydrogen atoms can only be derived indirectly. In most cases, this results in too short C-H bonds, as it was shown in comparing neutron diffraction studies to X-ray studies of the same material (13). Therefore, in most cases where no neutron diffraction data are available, the hydrogen positions need to be corrected. Nevertheless, in these

cases, the structural information may still include considerable errors.

Taking these demands as a starting point, the data for 14 compounds with a total of 92 different carbon sites were found where the ¹³C chemical-shift tensors are known as well as is a reasonable structure (Table 1).

There is only one *sp*² hybridized carbon with a C-N bond in this set of data [C(4) of L-asparagine monohydrate] and

TABLE 2
Bond Polarization Parameters, Bond Components of the Diagonal Tensor in the
Bond Coordinate System (See Text) in the Order xx , yy , zz

bond type	δ^σ in ppm	A^σ in ppm/Hartree	δ^π in ppm	A^π in ppm/Hartree
C-C	sp^3	33.5 ^a 33.5 ^a -13.5 ^b	29.9 81.8	
	sp^2	138.7 6.8 -13.5 ^b	49.3	69.3 5.4 -24.8 1187 -1499 3128
C-H	sp^3	21.6 ^a 21.6 ^a -13.5 ^b	-75.8 -49.0	
	sp^2	117.5 18.0 -13.5 ^b	-14.5	
C-O	sp^3	75.7 ^a 75.7 ^a -13.5 ^b	217.9 470.3	
	sp^2	148.5 ^c 69.9 ^c -13.5 ^b	-386.5	88.6 ^c -3.4 ^c -10.9 ^c -2599 ^c -232 ^c -1366 ^c
C-N	sp^3	31.0 ^a 31.0 ^a -13.5 ^b	-218.0 -306.4 11.2	

Note. An inner shell contribution $\delta^{is} = -21.92$ ppm must be added to obtain the usual ^{13}C chemical shift values relative to TMS.

^a The tensor components perpendicular to the bond direction of an unpolarized σ bond of a sp^3 carbon are equal.

^b The shift tensor component parallel to an unpolarized σ bond was set to a fixed value of -13.5 ppm taken from *ab initio* calculations to overcome ambiguities arising from symmetry (see text).

^c Values from a separate calculation with possibly less accurate experimental data (see text).

thus only six independent equations for the determination of parameters of this type. Since there are nine parameters needed for this particular bond type, this set of equations is not sufficient. Therefore, no parameters could be determined for bonds between sp^2 carbons and nitrogen.

Furthermore, the C–O π bond of sp^2 carbons was represented only by carboxy groups of zwitterionic amino acids. Unfortunately, all these bonds have very similar parameters and surroundings. The π bonds are delocalized with a π -bond valence of approximately 0.5. The low variance of the bond-polarization parameters could cause considerable errors in the results. Therefore, this bond type was excluded from the calculation at first.

In a second step, additional experimental data were included to estimate these parameters. At this time, older and probably less exact data were allowed as well as structural information from X-ray diffraction studies where the hydro-

gen positions were corrected using force field optimization of the molecular structure. By means of the separate calculation, the influence of possible errors on the other parameters through the coupled set of equations could be avoided, although this may result in a lower accuracy of the resulting C–O π -bond parameters of sp^2 carbons, but the negative effect is limited to this particular bond type.

The charges which cause the polarization of the bonds in question (see Eq. [7]) were calculated using the bond-polarization method again. This method was introduced by Sternberg *et al.* (43), and the necessary parameters are given which allow one to reproduce the charges from STO3G level *ab initio* calculations with high precision. From Eq. [15], it can be deduced that only the relative values of these atomic charges influence the results. According to Eq. [7], the polarization energy V_{ai} depends linearly on the polarizing charge, and any change concerning the scale of the charges

is compensated by the empirical slope $A_{\alpha\alpha}^{ai}$. Therefore, the results do not depend very much on the method of population analysis as long as the relations between the charges are not affected too much.

Since the bond-polarization approach is able to describe the influence of the surroundings of the molecular bond system, it was necessary to include the charges of neighbors of the molecule in question. While the charges in the same molecule have the largest effect on the bond polarization because of the short distance to the particular bond, in some cases the contribution of the crystal lattice cannot be neglected. In order to obtain the same conditions for all molecules in the data set, a lattice part of $3 \times 3 \times 3$ unit cells was modeled for each substance and the bond polarization by this rudimentary crystal lattice was calculated. The bond polarization decreases with the square of distance of the point charge. Additionally, the effects of positive and negative charges compensate in larger distances. Thus, a lattice part of 27 unit cells should be able to give sufficient accuracy.

While the charges in the outer molecules were taken as calculated for an isolated molecule, the net atomic charges in the central molecule were refined in a second step under consideration of the bond polarization by the crystal lattice field. A further refinement of this procedure did not change the bond-polarization results significantly.

All calculations including structure optimization, charge calculation, and bond polarization were performed using the bond-polarization routines of the program COSMOS [com-

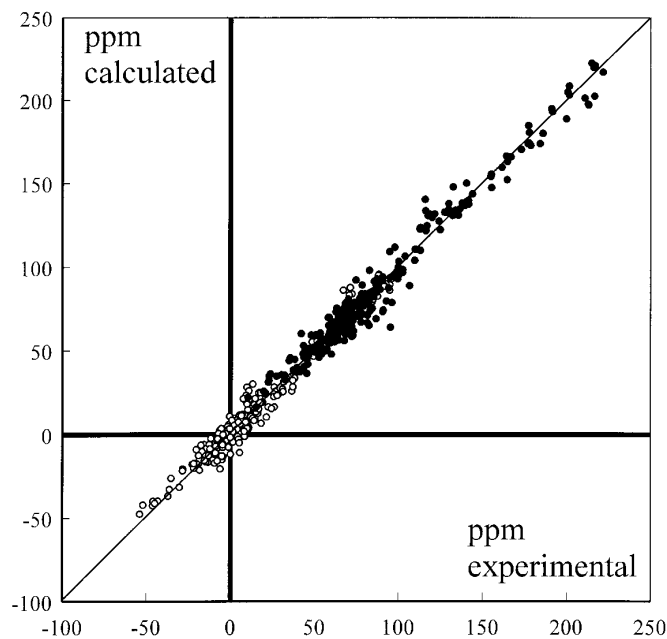


FIG. 1. Comparison of calculated and experimental ^{13}C shift tensor elements in the Cartesian representation (●, diagonal elements; ○, off-diagonal elements).

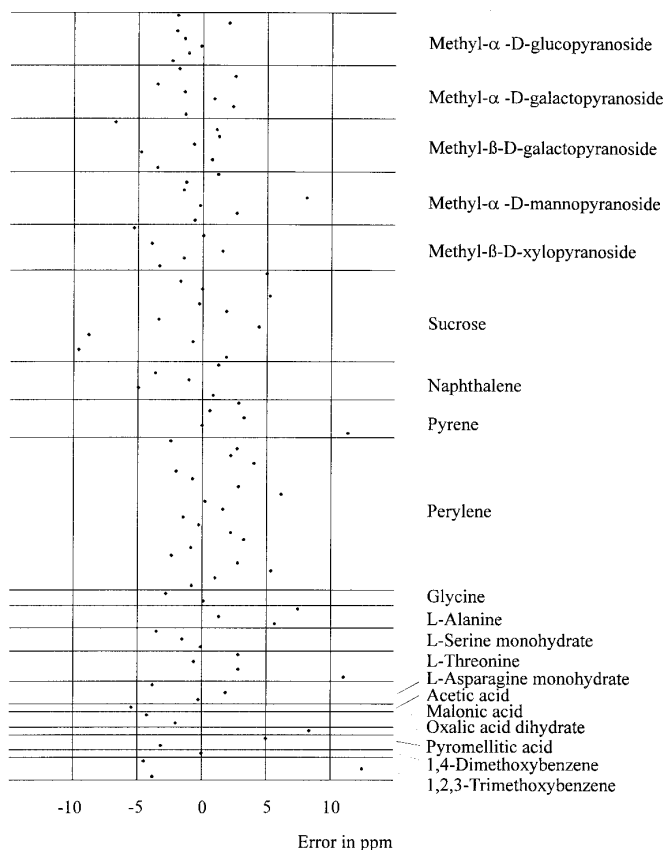


FIG. 2. Deviation of calculated isotropic ^{13}C chemical shifts from experimental values for all substances used in the calculation. The mean deviation is 3.8 ppm. The isotropic shifts were taken as $\frac{1}{3}\delta_{11} + \frac{1}{3}\delta_{22} + \frac{1}{3}\delta_{33}$. The order of carbon sites for each substance was taken as in the corresponding structure determination reference.

puter simulation of molecular structures (44)]. COSMOS¹ is a PC program which unites computer graphics, crystallography, and molecular modeling with calculations of molecular properties.

The magnetic shielding of a unpolarized bond in the direction of the connecting line of the two nuclei, represented by the shift tensor component $\sigma_{33}^{\sigma i}$, is determined only by the inner shell shielding and a diamagnetic contribution which has nearly the same value for all bond partners. The paramagnetic contribution is zero in this particular direction. The fact that $\sigma_{33}^{\sigma i}$ is the same for all bond types in the almost symmetrical arrangement of the bonds around the carbon leads to a decrease of the rank of the equation system, and

¹ COSMOS is available for MS-DOS and MS-Windows systems from COSMOS Software GbR, Johann-Griesbach-Straße 26, D-07743 Jena, Germany. The authors provide a free BONDPOL software package (C++) which includes all routines for chemical-shift and atomic charge calculations. Further information can be obtained by email from COSMOS@fiasko.physik.uni-jena.de or from the WorldWideWeb via <http://www.uni-jena.de/chemie>.

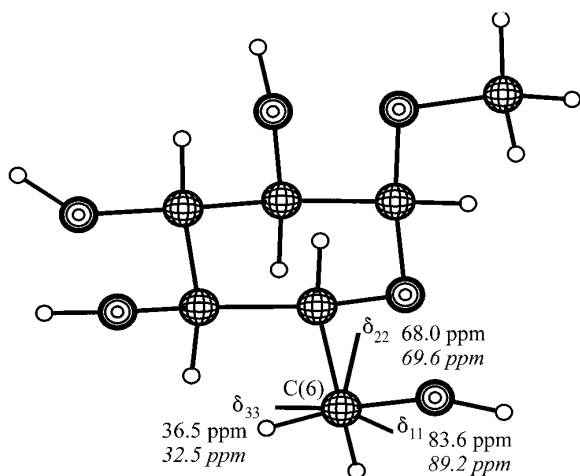


FIG. 3. Molecule of methyl- α -D-glucopyranoside with calculated principal axes and principal values of the ^{13}C chemical-shift tensor of C(6). The experimental principal values from (16) are given in italics for reference.

thus this parameter cannot be determined from this set of equations alone. The result would rather depend on the small deviations from the bond symmetry, possibly caused by small random errors in the given atomic coordinates. Therefore, the bond contribution of $\sigma_{33}^{\sigma_i}$ was set to a fixed value of -13.5 ppm (chemical-shift scale convention, i.e., upfield is negative) which was the average of values taken from *ab initio* calculations by Schindler (45). The inner shell contribution was -21.92 ppm on the chemical-shift scale relative to TMS. This value is based on an inner shell shielding of 206.02 and 184.1 ppm absolute shielding of TMS (46).

RESULTS AND DISCUSSION

The bond-polarization parameters for sp^3 hybridized carbons for C–C, C–H, C–O, and C–N σ bonds and for sp^2

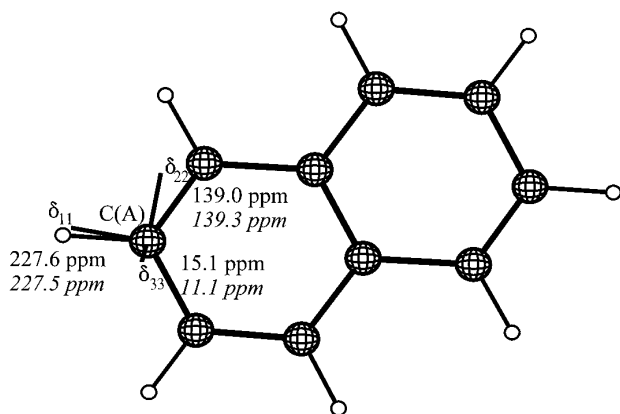


FIG. 4. Molecule of naphthalene with calculated principal axes and principal values of the ^{13}C chemical-shift tensor of C(A). The molecular structure was taken from a neutron diffraction study of the deuterated form (21). The experimental values from Ref. (12) are given in italics.

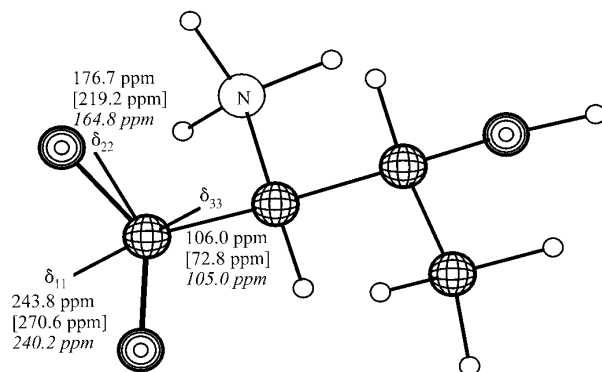


FIG. 5. Molecule of the zwitterionic solid amino acid L-threonine. The principal axes and principal values of the ^{13}C chemical-shift tensor of the carboxy group were calculated with inclusion of the surrounding unit cells. The principal values in square brackets were calculated for an isolated molecule with the same structure. The principal axes were removed for clarity (see Table 5 for exact comparison of tensors). Numbers in italics denote the experimental values from Ref. (30).

hybridized carbons for C–C and C–H σ and C–C π bonds were calculated by the least-squares method from a set of 516 equations [17] derived from the experimental data for the substances in Table 1. The resulting parameters are given in Table 2. A general comparison between experimental and calculated tensor components is shown in Fig. 1. The coefficient of determination R^2 is 0.984, which is a quite good agreement between experimental and calculated shift values if the great variation of the substances is considered ranging from sugars to amino acids or to aromatic compounds. The mean deviation of the calculated shift tensor components from the experimental values is 7.73 ppm.

The δ_{yy} component of C(1) of methyl- α -D-glucopyranoside shows, with an error of 31 ppm, by far the biggest deviation of a single tensor component (for better comparison, the tensors were transformed back to the Cartesian coordinate system here). The C(1) carbon is connected to two oxygen atoms which causes an atypical behavior regarding the molecular structure, known as the anomeric effect (47). Apparently, this effect cannot be described by the bond-polarization theory very well since the anomeric carbons appearing in other sugar molecules cause relatively large errors as well, ranging from 18 ppm (δ_{xy} component, methyl- α -galactopyranoside) to 14 ppm (δ_{xx} component of C(2') in sucrose).

Additionally, the bond-polarization parameters for the C–O bonds of sp^2 carbons were obtained from a second set of 90 equations. The calculated parameters are listed in Table 2 as well. The correlation coefficient is $R^2 = 0.974$, and the mean deviation of the calculated from the experimental values is 14.8 ppm.

Besides the inaccuracy of the structural data, another source of error appears when the bond directions differ too much from the usual sp^3 or sp^2 geometry. This is only a

TABLE 3
Calculation Time for all Atomic Charges and All ^{13}C Chemical-Shift Tensors of *p*-Tolyl Ether (14 C Atoms, 1 O Atom, 14 H Atoms)

Processor type	Charge calculation	^{13}C chemical shift tensor calc.
386 SX 16 MHz	9.2 s	11.7 s
486 DX 33 MHz	1.5 s	1.8 s
Pentium 75 MHz	0.3 s	0.4 s

minor effect in the substances of our data set, and therefore these deviations could be neglected. A solution to this problem will be discussed in a later publication.

The errors of the calculated isotropic shift values vs experimental shifts are presented in Fig. 2 to give an overview of the deviations in the individual substances. Some representatives of molecules with individual ^{13}C chemical-shift tensors are shown in Figs. 3–5 as examples. The directions of the principal axes and the corresponding principal values for a typical C site are given. The C(6) site of methyl- α -D-glucopyranoside (Fig. 3) is a typical example of a σ -bonded atom in a CH_2OH group. These atoms display a

relatively low shift anisotropy, and no preference of the tensor axes with respect to the bonds can be observed. In contrast to this situation, the shift tensor of the C(A) site of naphthalene (Fig. 4) is oriented with respect to the plane of the π system with a large shift difference between the in-plane and out-of-plane values. The next example is the COO^- group of the amino acid L-threonine (Fig. 5). Again, the tensor values are dominated by the delocalized π system, but in this case the polarization by surrounding molecules within the lattice is of major influence. The former examples in Figs. 3–5 belonged to the calibration set of molecules but the following calculations are extrapolations

TABLE 4
Principal Values of Calculated ^{13}C Shift Tensors of *p*-Tolyl Ether and Comparison with GIAO *ab Initio* Calculations and Experimental Values [from Ref. (47)]

C site	bond polarization model			GIAO calculation			experimental			
C ₂	222.0	170.4	72.7	276.2	173.6	70.5	239	161	74	
C ₉	222.1	168.7	74.7	276.1	161.8	69.5	238	147	74	
C ₅	208.0	164.0	7.4	268.5	179.9	12.5	228	153	14	
C ₁₂	223.9	147.3	11.2	271.3	184.3	11.6	233	160	8	
C ₇ ortho	225.3	128.4	20.9	213.8	139.2	-5.0	196	139	13	
C ₃	223.2	133.3	19.5	228.6	137.7	7.3	a	202	128	21
C ₁₀ ortho	224.5	129.5	21.1	233.0	139.6	6.5		204	140	18
C ₁₄	227.7	131.7	19.7	227.5	142.5	-0.6				
C ₄	224.8	139.7	14.9	252.2	139.8	11.5	a	226	143	24
C ₆ meta	223.0	138.5	15.5	250.7	142.2	4.2		228	144	23
C ₁₁	235.3	125.5	22.1	250.2	138.6	10.6				
C ₁₃	224.8	140.3	14.9	248.2	143.1	4.0				
C ₈ methyl	30.1	29.9	16.2	34.9	23.6	-5.9	a	34	23	0
C ₁₅	30.1	30.0	16.2	35.1	24.4	-5.5		39	25	3

^a Without knowledge of the tensor, the experimental shift tensors could not be assigned to a particular C site within the groups.

TABLE 5
¹³C Chemical-Shift Tensor Components of Threonine, Calculated Including or Excluding Crystal Lattice Influences Compared to Experimental Tensors

C site	tensor component	Calculation including neighbors	Calculation of single molecule	experimental values from ref. (30)
C ₀	xx	212.2	230.5	209.2
	yy	127.8	104.4	127.3
	zz	186.5	227.7	173.4
	xy	46.6	67.6	47.3
	yz	-18.6	-25.1	-16.4
	zx	-19.0	-12.0	-19.9
C(α)	xx	52.4	52.2	57.2
	yy	61.2	58.6	64.9
	zz	57.9	51.3	58.4
	xy	2.8	3.8	-2.8
	yz	12.7	15.8	6.6
	zx	5.2	4.0	1.6
C(β)	xx	54.8	53.2	50.7
	yy	72.2	71.4	72.5
	zz	75.9	75.8	73.0
	xy	-10.1	-10.3	-14.5
	yz	11.8	12.1	9.9
	zx	12.8	13.4	9.1
C(γ ₂)	xx	30.9	30.9	23.1
	yy	26.3	26.1	23.0
	zz	18.4	18.2	10.5
	xy	3.5	2.6	-0.02
	yz	6.8	7.2	13.2
	zx	-4.0	-3.9	-4.6

to other systems and are therefore better suited as test for the theory.

The estimated parameters can now be used to calculate ¹³C chemical-shift tensors very quickly. The full calculation including determination of charges takes only a few minutes on a PC when the exact structural data are given. As an example, the shift tensors of *p*-tolyl ether were calculated. Actual timing tests for this calculation are presented in Table 3.

The principal values of the experimental tensors and *ab initio* GIAO calculations were taken from Ref. (48) for comparison. This comparison is incomplete since only the principal values of the tensors are given and thus the orientation could not be considered. Nevertheless, the results in Table 4 demonstrate that the bond-polarization method can estimate the ¹³C chemical-shift tensors quite accurately, even for medium sized or larger molecules where the *ab initio* methods are limited due to the increasing number of atoms.

However, the semi-empirical model cannot reproduce some of the trends caused by nonpolarization effects that were discussed in Ref. (48), such as the characteristic decrease of the δ_{33} component for C₇.

For the calculation, the neighboring unit cells were again modeled, although their effect on the bond polarization has only a minor influence on the ¹³C chemical-shift tensors in this case. The differences of the net atomic charges in the aromatic ring structure are small, and thus the bond-polarization energy is low. In contrast, when the charge differences are higher, a considerable contribution of bond polarization would be expected.

For example, amino acids appear in solid phase in their zwitterionic form and hence the net atomic charges have the greatest values in the set of substances from Table 1. In order to demonstrate the influence of the neighboring molecules, the calculation of ¹³C shift tensors for threonine was carried

out on an isolated molecule (using the same molecular structure) considering only inner molecular polarization and neglecting neighboring molecules (Table 5). The biggest deviation occurred in case of the COO^- group, possibly because of the greater polarization response A^{CO} (especially for π bonds, but also for σ bonds). On the other hand, this carbon is situated in vicinity of the charged NH_3^+ groups of the neighboring molecule due to the formation of $\text{O} \cdots \text{H}$ bridges.

Basically, the same effect was described in connection with the calculation of ^{13}C chemical-shift tensors of amino acids by *ab initio* methods. De Dios *et al.* introduced point charges to substitute for the neighbors in a calculation of threonine and tyrosine shift tensors (49). Malkin *et al.* added as many as four neighboring molecules in a calculation of glycine (50).

CONCLUSIONS

The bond-polarization theory provides a method for the rapid calculation of ^{13}C chemical-shift tensors. One hurdle of the application of this model is the necessary calculation of semi-empirical bond polarization parameters. These parameters were presented for C–C, C–H, and C–O bonds of sp^3 and sp^2 and the C–N bonds of sp^3 carbons. The model has no limitations regarding the size of the molecular system and provides a simple approach for the inclusion of influences of the crystal lattice on the chemical shifts.

On the other hand, this method is well suited to calculate derivatives of the chemical shifts with respect to the coordinates of the nuclei. This feature is of great importance if chemical shifts are to be used as target functions in molecular mechanics calculations. The calculations can be carried out very quickly (a typical calculation within a crystal lattice part of 2000–3000 atoms including net atomic charges took only a few minutes on a PC computer).

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