Chapter 1

Recent Advances in Nuclear Magnetic Shielding Theory and Computational Methods

Cynthia J. Jameson

Department of Chemistry, University of Illinois at Chicago, Chicago, IL 60607

As the well-established methods employing multiple origins, GIAO, IGLO, LORG, IGAIM, and common origin CHF methods are applied to diverse molecular systems, using ever larger basis sets up to near Hartree-Fock limit, the limitations of calculations at the SCF level in accurately predicting the nuclear shielding becomes more evident. The challenge of applying ab initio methods and density functional methods to heavier nuclei or to nuclei having neighboring halogens and other atoms with large spin orbit coupling constants demanded the development of theoretical methods for improved description of shielding in systems where electron correlation is important, and systems where relativistic effects are important. At the same time, the calculations on small molecules have become sufficiently accurate that comparisons with experiment have to include accurate rovibrational averaging. This overview of the recent successes, new challenges, and new directions for the theory of nuclear magnetic shielding, provides only a hint of the new and exciting results that are reported in this Symposium.

The first conference devoted to the NMR chemical shift was held in Maryland, July 20-24, 1992, as a NATO Advanced Scientific Workshop on Nuclear Magnetic Shielding and Molecular Structure (*1*). Experimentalists measuring fundamental quantities such as the chemical shift tensor and its dependence on geometry and intermolecular interactions and theoreticians involved in computations of the nuclear magnetic shielding exchanged information on the state of the subject. At that time, the following was already known:

1. The use of distributed origins (IGLO, LORG, GIAO) leads to dramatic improvement in damping the errors arising from incomplete cancellation of long-range contributions due to basis set inadequacies.

2. At the CHF level, common origin calculations with large basis sets can yield results indistinguishable from distributed origins calculations with modest basis sets.
3. The full shielding tensor provides more complete information and more stringent tests of calculations than the isotropic shielding. Ingenious experimental techniques for single crystals in systems of up to 24 distinct ^{13}C nuclear sites are complemented by ab initio calculations of the shielding tensor, which are nearly indispensable in interpreting experimental data.
4. The dependence of the nuclear shielding on molecular geometry defines shielding surfaces. The shielding surface determines the experimentally observed thermal average shielding, the temperature dependence of the shielding, and the isotopic chemical shifts. Rovibrational averaging over the shielding surface are required for good comparisons of theoretical values with experimental values.
5. The intermolecular shielding surface and the effects of electric fields on shielding (shielding polarizabilities and hyperpolarizabilities) are useful in the interpretation of long-range intramolecular effects and in intermolecular effects on shielding.
6. Electron correlation is important for multiple bonded systems, especially when lone pairs are also involved, but the magnitude of the contribution from electron correlation is clouded by the use of modest basis sets in correlated calculations.
There are many unanswered questions about nuclei in the 3rd row and below in the Periodic Table, for transition as well as representative elements. Basis set development for such atoms are required before quantitative results for σ may be expected. The possible importance of relativistic effects, the unknown geometries (especially of complex ions) in solution, and the lack of absolute shielding scales for such nuclei makes any "good agreement" of small basis set uncorrelated calculations with chemical shifts observed in solution very suspect.

At the end of the conference the following directions for future work were discussed.
1. We need to optimize basis sets for 3rd and 4th row atoms in the Periodic Table.
2. How does one do relativistic calculations? Although two formalisms had been in the literature outlining relativistic approaches to shielding calculations, no calculations had been carried out for molecules.
3. Absolute shielding scales are not available for many interesting nuclei. In a relativistic system, is the relation between the spin-rotation tensor and the paramagnetic shielding derived in the nonrelativistic limit preserved? Instead, C. J. Jameson suggested using a linear molecule: measurement of $(\sigma_{\parallel}-\sigma_{\perp})$ together with theoretical $\sigma_{\parallel}^{d}$ gives absolute shielding tensor components.
4. There is a need of more gas phase data for accurate comparisons of ab initio calculations with experiments since the intermolecular effects present in condensed phases are especially large for nuclei having large numbers of electrons.
5. There is a need for rovibrational averaging of theoretical shielding prior to comparison of calculated values with experiment. This becomes even more important as the theoretical methods begin to yield more accurate results.
6. There is a need for shielding calculations including electron correlation at higher levels than have already been reported at the conference (MBPT2, SOPPA/SOLO) to really find out how large the electron correlations effects are in molecules such as N_2, HCN, CO.

7. Experimentalists are very interested in interpretation of the NMR chemical shifts observed in complex systems. How does one deal with computations of NMR chemical shifts in complex systems such as proteins, zeolites, and other extended networks?

These directions for future work have correctly predicted the multiple thrusts of theoretical computations of the NMR shielding from the summer of 1992 to the present time. There have been major theoretical developments in the following areas: (a) New treatments of the gauge origin problem, (b) development and widespread implementation of density functional methods for shielding calculations, (c) treatment of scalar and spin orbit relativistic effects on σ, (d) high-level electron correlated calculations of σ, (e) more efficient computations by using parallelized code in multiple processors, (f) an analysis of and demonstration of basis set convergence, (g) beginning calculations of σ for some heavy nuclei, (h) accurate rovibrational averaging of σ for small molecules, (i) supermolecule calculations of intermolecular shielding functions, other approaches to intermolecular effects, and ensemble averages including intermolecular effects on σ, (j) theoretical approach to calculations of shielding in proteins, (k) model calculations in zeolites and inorganic solids, and (l) fine geometry effects on shielding: NMR refinement of diffraction results. Probably the most important developments from the point of view of widespread applications of shielding calculations to new areas were the calculations of shielding surfaces for proteins and the calculations of average chemical shifts in adsorbed Xe in zeolites. With these applications, theoretical calculations of NMR chemical shifts have entered the mainstream of chemical tools, no longer a highly specialized activity for a selective few practitioners. The papers included in this Symposium proceedings, describing some of the recent developments listed above, demonstrate quite clearly that theoretical computation of the NMR chemical shift has finally reached a level of accuracy and efficiency that it has become a generally recognized tool in the elucidation of molecular structure and interactions.

New Treatments of the Gauge Origin Problem.

The CSGT (continuous set of gauge transformations) method introduced by Keith and Bader (*2*), more accurately renamed CTOCD (continuous transformations of the origin of the current density) by Lazzeretti et al. (*3-5*), uses a different gauge origin in real space for each point **r**; by using a shift function, one can empirically shift the gauge origin towards the nucleus nearest to the point **r**, for example. The paper by Paolo Lazzeretti in this Symposium demonstrates that one can choose to rigorously annihilate either the diamagnetic or the paramagnetic contribution to the first order induced current density. The first, annihilation of the diamagnetic contribution, turns out to be equivalent to Geertsen's polarization propagator-based procedure. Both methods have been applied to small molecules. Gauge-invariance tests of all the components of the shielding tensor is an important objective criterion for the robustness of a method of theoretical calculation of magnetic properties. The adequacy of the basis set used can be tested separately from the extent of electron correlation contributions. Such purely theoretical tests (as opposed to comparisons against experiments) are a particular emphasis in the work of Lazzeretti and co-workers.

Density Functional Methods for Shielding Calculations

Since the Maryland meeting, density functional theory has been developed as a major tool for shielding calculations (*6*). The pioneering studies by Malkin and Salahub (*7*) on one hand, were followed by independently developed methods by Handy et al. (*8*), Schreckenbach and Ziegler (*9*), Pulay et al. (*10*), and Cheeseman et al. (*11*) on the other hand. The practical utility of this method compared to ab initio methods is that correlation is intrinsically included in the exchange-correlation energy functional used, and once the functional is chosen, there are only basis set levels to choose for describing the electron density. Unlike the perturbation expansion approaches to electron correlation, MPn or MBPTn, the level of electron correlation in the DFT method is not a variable choice. The method is intrinsically efficient in incorporating correlation as the size of the system increases. The disadvantage is that results depend on which functional is used in the calculation. Functionals used in calculations of magnetic properties should have an explicit dependence on the electron current density as well as the electron density itself, but neglect of this may be a minor problem (*8*).

Existing field-free exchange correlation (XC) functionals can be classified as local density approximations (LDA), or generalized gradient approximations, or hybrid functionals that incorporate part of the Hartree-Fock exchange. There are gradient corrected exchange functionals by Becke without (B) or with Hartree-Fock exchange (B3) which can be combined with correlation functionals by Lee, Yang, and Parr (LYP) or by Perdew (P86) or Perdew and Wang (PW91). Thus DFT calculations may use LDA, BP86, BLYP, or BPW91 or the hybrid B3LYP functionals. It has been shown that the simple LDA is insufficient for chemical shifts (*6*). There is yet no universal functional that works uniformly well for all shielding calculations. For example, hybrid functionals have been found to give inferior results compared to various generalized gradient approximations in the study of ^{17}O shielding in $[MO_4]^{n-}$ complexes (*12*), but hybrid functionals are clearly superior to generalized gradient functionals in recovering the full range of the ^{57}Fe and ^{103}Rh chemical shifts (*13*), although not for ^{95}Mo (Bühl, M. to be published). The main problem is that the functionals presently in use do not provide the correct asymptotic behavior in the immediate vicinity of the nucleus and are therefore intrinsically deficient for calculation of magnetic properties that involve the r^{-3} operators. Nevertheless, when differences in shielding (chemical shifts) rather than absolute shielding values are being compared with experiment, these intrinsic deficiencies appear not to be a significant problem. Earlier DFT calculations by Malkin et al. used IGLO local origins, but more recent DFT implementations use GIAOs. The latter present no ambiguities related to the localization methods used.

While DFT may or may not be more accurate than MP2 for absolute shielding calculations is debatable, the strength of the DFT method in calculations of shieldings is in the ability of DFT to provide a consistent picture over a wide range of chemical systems, since calculations can be done at a very modest computational cost compared to MP2. Among the successes of the method is in ligand chemical shifts in transition metal complexes. For example, ^{13}C, ^{17}O, ^{31}P and ^{1}H chemical shifts for oxo (*12,14,15*), carbonyl (*16-19*), interstitial carbide (*20*), phosphine (*21,22*), hydride (*23*), and other ligands have been successfully reproduced to within tens of ppm in

most cases. Other successes include ^{77}Se (*24*), and ^{125}Te (*25*) shieldings in a large number of chemical bonding situations. DFT methods have also been used to include relativistic corrections, as we see below.

Scalar and Spin Orbit Relativistic Effects on σ.

Fully relativistic methods based on four-component wavefunctions and the complete Dirac equation would be impractical. Several approaches have been used. One may neglect the spin orbit operator completely and find only "scalar" or "spin-free" relativistic effects. Since the mass-velocity and Darwin contributions may induce large perturbations in the electronic structure close to the nuclei, perturbation theory may not be adequate. To circumvent this difficulty, techniques such as the relativistic zeroth order Hamiltonian, quasirelativistic effective core potentials, or the frozen-core approximation have been used. Within the DFT method, one approach is a quasirelativistic theory in which the highly relativistic core is described with 4-component wavefunctions, from which are extracted the core electron density and potential (effective core potential, ECP), and these are used in molecular calculations (*15,26*). Another is a combination of a first order quasirelativistic approach with the frozen core approximation (*16,27*). The scalar relativistic effects have a large contribution to the absolute shieldings. The atomic core contributions to the diamagnetic part of the shielding are increased. When relative chemical shifts are considered however, the shielding contributions from the inner cores are quite similar in the various molecular environments and tend to cancel to a large extent in the chemical shift values. The valence MOs are orthogonalized against all core MOs; this ensures their correct asymptotic behavior near the nucleus. What gives rise to the scalar relativistic effects on the chemical shifts is that the core tails of the valence orbitals are shaped differently from one molecule to another.

The first attempts to calculate spin orbit contributions to the shielding with nonrelativistic wavefunctions used a third order perturbation treatment within a semiempirical theory. Recently, Nakatsuji et al. developed an approach using ab initio unrestricted Hartree-Fock wavefunctions and the finite field perturbation method with a common gauge origin (*28*). They applied this method to the calculation of halogen substitution-induced chemical shifts of ^{1}H, ^{13}C, ^{27}Al, ^{29}Si, ^{119}Sn and other nuclei (*28-31*). Later on, they included the scalar relativistic corrections, still using a common origin and no electron correlation (*32*). With this approach, significant cross terms between scalar relativistic effects and spin orbit coupling have been found for ^{199}Hg and ^{183}W chemical shifts (*33,34*). The halogen spin orbit contributions to the chemical shifts of neighboring nuclei are in the direction of increased shielding and is responsible for the so-called normal halogen dependence, in which the central atom shielding increases when going from Cl to Br to I substituents.

A DFT-based third order perturbation theory approach includes the FC term by FPT. Based on the perturbed nonrelativistic Kohn-Sham orbitals spin polarized by the FC operator, a sum over states treatment (SOS-DFPT) calculates the spin orbit corrections (*35-37*). This approach, in contrast to that of Nakatsuji et al., includes both electron correlation and local origins in the calculations of spin orbit effects on chemical shifts. In contrast to these approaches that employed the finite perturbation method the SO corrections to NMR properties can be calculated analytically from

quadratic response functions (*38,39*). The latter method using SCF and MCSCF wavefunctions have been used to calculate the ^{1}H shieldings in the hydrogen halides and the ^{13}C shielding in the methyl halides, including only SO corrections, without the scalar relativistic effects (*39*).

An analogy of the role of the Fermi contact (FC) operator in the spin orbit (SO) shifts to the FC role in spin spin coupling constants indicates that the higher the s character in the bond to the halogen, the greater the SO shifts (*37*). This provides understanding of experimentally observed facts: the large SO shifts for nuclei having a large s orbital participation in the bond (in ^{1}H, ^{13}C, ^{29}Si, in main group elements in high oxidation states, and in d^{10} transition metals). In contrast, a low s character of the bond leads to an inefficient FC mechanism, to small SO shifts, and thus to inverse halogen dependence, the usual situation when SO effects are not included, such as for early transition metals in high oxidation states, or for p-block main group elements in low oxidation states.

Electron Correlated Calculations of σ in Small Molecules.

What is the current state of shielding calculations for small molecules? This question can be asked in the context of state of the art calculations of shielding in molecules

Table I. ^{13}C Shieldings, ppm Relative to $^{13}CH_4$

^{13}C in Molecule	*SCF*[a]	*MBPT(2)*[a]	*Expt.*[b]
CH_3CH_3	11.7	13.5	14.2
$H_2C{=}CH_2$	135.8	130.3	130.6
$HC{\equiv}CH$	81.8	78.2	77.9
CH_3F	71.6	79.7	78.3
CH_3OH	52.0	59.3	58.5
CH_3NH_2	31.9	36.6	36.8
$\boldsymbol{C}H_3CHO$	33.5	38.7	37.9
$(\boldsymbol{C}H_3)_2CO$	32.2	37.0	37.1
$\boldsymbol{C}H_3CN$	4.8	7.9	7.4
CO	224.9	190.4	194.1
CO_2	147.9	138.0	136.3
H_2CO	205.0	194.8	
$CH_3\boldsymbol{C}HO$	211.3	200.3	201.8
$(CH_3)_2\boldsymbol{C}O$	218.8	207.3	208.2
HCN	127.5	114.2	113.0
$CH_3\boldsymbol{C}N$	135.1	125.4	121.3
$CH_2{=}\boldsymbol{C}{=}CH_2$	240.0	227.5	224.4
$\boldsymbol{C}H_2{=}C{=}\boldsymbol{C}H_2$	81.7	80.6	79.9
CF_4	116.4	137.1	130.6
C_6H_6	140.6	137.5	137.9

[a] Ref. (*42*).
[b] Ref. (*41*).

Table II. Calculated Shieldings in Small Molecules

METHOD	*^{13}C in CH_4*	*^{13}C in CO*	*^{13}C in HCN*	*^{15}N in NH_3*	*^{15}N in N_2*	*^{15}N in HCN*	*Ref.*
DFT	184.33	-15.35			-84.82		(*8*)
DFT	187.5	-17.7		259.2	-87.9		(*11*)
DFT	187.80	-12.27	71.74	259.42	-80.55	-43.47	(*10*)
DFT	191.2	-9.3	91.5	262.0	-72.9	8.4	(*9*)
SCF	194.8	-25.5	70.9	262.3	-112.4	-50.7	(*44*)
MBPT(2)	201.0	10.6	87.6	276.5	-41.6	-0.3	(*44*)
MBPT(3)	198.8	-4.2	80.0	270.1	-72.2	-26.2	(*44*)
MBPT(4)	198.6	4.1	84.3	269.9	-60.1	-14.9	(*44*)
MCSCF	198.2	8.22	86.76		-52.2	2.63	(*47,48*)
CCSD	198.7	0.8	84.1	269.7	-63.9	-16.7	(*46*)
CCSD(T)	198.9	5.6	86.3	270.7	-58.1	-13.6	(*46*)
Expt. σ_e [b]	198.7	3.2	84	273.3	-59.6	-15	(*51*)
	±1.2	±0.9	±1	±0.2	±0.2	±1	
Expt. σ_0 [a]	195.1	1.0	82.1	264.5	-61.6	-20.4	(*51*)
	±1.2	±0.9	±0.9	±0.2	±0.2	±0.2	

[a] These are absolute isotropic shielding values σ_0 which are the thermal averages in the gas at the zero pressure limit. The error bars are associated with the determination of the absolute scale based on the spin rotation constants for specific molecules (^{13}CO, $^{15}NH_3$, $H^{19}F$). References for the experimental values σ_0 and the calculations of the rovibrational corrections that lead from σ_0 to σ_e are given in Ref. (*51*).

[b] These are absolute isotropic shielding values σ_e for a molecule fixed at its equilibrium molecular geometry, with which the calculations are to be compared.

containing only 1-2 second row atoms. In another context, with modest effort, how closely can computations predict ^{13}C chemical shifts in simple organic compounds? Gauss's answer is, within 1.7% at MBPT(2) level or 0.8 ppm, with exceptions (*40*), in calculations for carbon in molecules where comparison of the isotropic shielding against either the absolute shielding scale or at least gas phase experiments (*41*) is possible. These are shown in Table I (*42*).

Gauss has derived shielding theory with electron correlated calculations in the Møller-Plesset expansion (*43,44*) and also in the coupled cluster approach (*45*). He has provided benchmark calculations on a set of small molecules shown in Tables II and III at the CCSD(T) level (*46*).

In these molecules the sign and magnitude of the contribution of electron correlation to ^{13}C, ^{15}N, ^{17}O, ^{19}F are found to be positive (except for F_2), as little as 4 ppm, as much as 54 ppm. How well can we do with including intermediate levels of electron correlation? Gauss finds that MBPT(2) or MP2 overcorrects, except in the case of F_2. For F_2 molecule the full CCSD(T) calculations and also rovibrational averaging have to be included before comparison with experiment is possible. In Tables II and III the various methods are compared with one another. All have used GIAOs as basis functions in the computations, so as not to cloud the comparisons. The signs and magnitudes of the electron correlation contribution to shielding in these molecules are finally settled. In 1992, the discrepancies were still large in the

calculated shieldings of the various heavy nuclei in the set of N_2, NH_3, HCN, NNO molecules or in the set of CH_4, CO, HCN molecules when compared with experimental absolute shieldings. It was suggested that something might be wrong with absolute shielding scales for ^{13}C and ^{15}N. It is obvious now that MBPT(2) level of theory is insufficient for some of these systems (*44*). At this time, the consensus is that the absolute shielding scales for ^{13}C and ^{15}N are fine. On the other hands, the ^{17}O absolute shielding is thought to be at the far edge of the rather large error bar associated with the reference molecule ($C^{17}O$) (*49*). How well did density functional theory do for these benchmark systems? Tables II and III show that, where there is little electron correlation, DFT did not do as well as SCF. Different exchange-correlation functionals give different answers. In some cases, DFT provided absolute shielding results that are not yet as accurate as MP2-level calculations.

Table III. Calculated Shieldings in Small Molecules

METHOD	*^{17}O in H_2O*	*^{17}O in CO*	*^{19}F in HF*	*^{19}F in F_2*	*Ref.*
DFT	317.86	-77.14	405.05	-271.70	(*8*)
DFT	324.8	-80.7			(*11*)
DFT	326.37	-73.60	410.87	-277.14	(*10*)
DFT	331.5	-68.4	412.5	-282.7	(*9*)
SCF	328.1	-87.7	413.6	-167.9	(*44*)
MBPT(2)	346.1	-46.5	424.2	-170.0	(*44*)
MBPT(3)	336.7	-68.3	417.8	-176.9	(*44*)
MBPT(4)	337.5	-52.0	418.7	-174.0	(*44*)
MCSCF	335.3	-38.92	419.6	-136.6	(*47*)
CCSD	336.9	-56.0	418.1	-171.1	(*46*)
CCSD(T)	337.9	-52.9	418.6	-186.5	(*46*)
Expt. σ_e [b]	357.6	-36.7	419.7	-192.8	(*51*)
	±17	±17	±6	±6	
Expt. σ_0 [a]	344.0	-42.3	410.0	-232.8	(*51*)
	±17.2	±17.2	±6	±6	

[a, b] The same footnotes as in Table II.

Full configuration interaction (CI) calculations for the shieldings in H_2 (*50*) and BH molecules have demonstrated that the CCSD(T) results are sufficiently close to the full CI results, so that for practical purposes, the CCSD(T) calculations may be considered as the benchmark calculations for each molecule, against which other methods such as density functional methods may be tested.

More Efficient Computations by Using Parallelized Code in Multiple Processors.

Single processor calculations of nuclear shielding at the SCF level are limited by practical computation times in most hardware to about 800 basis functions with no symmetry or 1600 with high symmetry. Thus, the obvious solution of the problem is parallel processing using an array of inexpensive workstations or PCs. In a significant breakthrough, Peter Pulay et al. have implemented the first parallel computation of

shielding (*52*). The program by Wolinski, Haacke, Hinton and Pulay uses the new integral program of Wolinski that calculates integrals in vectorized batches, increases efficiency, and simplifies parallelization. The self consistent field step includes a multi-Fock algorithm, i.e., the simultaneous calculation of several Fock matrices with the same integral set, increasing the efficiency of the direct SCF procedure. Replacing the SCF diagonalization by pseudo-diagonalization, a method widely used in semiempirical programs, provides further time savings. Including higher angular momentum functions in the basis sets is an important factor in calculations of shielding of heavier elements. By concentrating all logic in integer arrays, the program has in principle been made open ended with respect to angular momentum integrals. The results are very promising, presently a scaling of computational time to $N^{2.8}$, N being the number of basis functions, has been achieved toward the ultimate goal of N^2 scaling. The paper presented by Peter Pulay in this Symposium proceedings provides details and comparisons.

Basis Set Convergence.

A case study of the basis set dependence of the anisotropy and the isotropic shielding has been presented by Enevoldsen and Oddershede (*53*) for ^{19}F in the CH_3F molecule. The RPA (SCF level) results are shown in Tables IV and V.

Table IV. Calculation of $\Delta\sigma = (\sigma_{\parallel} - \sigma_{\perp})$ for ^{19}F in the CH_3F molecule.[a,b]

Basis set size	*LORG*	*Common origin*	*Geertsen method*	*CTOCD*	*GIAOs*
4-31G, (24)	29.34	5.91	53.61	19.38	-75.34
6-31G, (24)	21.21	-2.78	44.88	11.26	-74.14
D95, (26)	17.81	7.79	39.38	10.98	-80.84
6-31G+, (36)	-44.89	-65.47	-40.00	-47.78	-68.95
6-31G++,(45)	-49.03	-65.85	-42.48	-52.18	-67.42
75	20.51	10.22	40.03	-0.51	-86.11
132	-69.75	-70.17	-66.02	-71.90	-67.28
135	-67.44	-67.63	-63.52	-69.38	-67.78
141	-67.76	-67.96	-63.84	-69.71	-68.67
158	-67.69	-67.95	-66.82	-67.72	-68.58

[a]From Ref. (*53*).
[b]Experimental value is -60.86±15 ppm (*54*).

The conclusions are as follows: The basis set must include polarization functions. GIAOs converge fastest, better than LORG or IGLO. The inclusion of polarization functions in standard basis sets (6-31G+ and 6-31G++) do not guarantee convergence. The basis set may be considered converged (for 132 functions or more) when, using any method, only small basis set dependences are observed. These trends are the same both in RPA (equivalent to coupled Hartree-Fock) and SOPPA (second order polarization propagation approximation), although SOPPA results are not shown here. As expected, the Geertsen method is gauge invariant at all basis set levels. The full

tensor is more sensitive to deficiencies in the basis set than the isotropic average shielding.

Table V. Calculation of σ_{iso} for ^{19}F in the CH_3F Molecule.[a,b]

Basis set	*LORG*	*Common origin*	*CTOCD and Geertsen*	*GIAOs*
4-31G, (24)	404.11	420.55	-46.67	488.82
6-31G, (24)	405.58	422.24	-47.08	489.35
D95, (26)	407.05	425.69	-55.29	492.96
6-31G+, (36)	453.29	467.06	100.34	488.32
6-31G++, (45)	458.66	469.25	106.76	488.52
75	405.16	411.60	235.25	493.99
132	480.12	480.22	466.62	483.75
135	482.31	482.39	468.81	483.26
141	482.31	482.40	475.31	483.65
158	482.27	482.44	480.99	483.39

[a] From Ref. (*53*).
[b] Experimental value is 471 ppm (*55*).

Calculations of σ for Heavy Nuclei.

What is the current state for shielding calculations of nuclei in the third row of the Periodic Table? We illustrate the current state with two nuclei for which absolute shielding scales exist (*56,57*), ^{77}Se and ^{71}Ga, in Tables VI and VII. It has been found that, in addition to complications arising from relativistic corrections, electron correlation contributions can be large in heavy atoms, so the DFT method should have an advantage in large systems. For ^{77}Se the best calculations, which can be considered benchmarks, are the CCSD calculations by Gauss et al. (*58*). There are few experimental gas phase results for comparisons. For the O=C=Se molecule the experimental value of the absolute ^{77}Se shielding has been derived (see Table 8 of Ref. (*59*) from the measured ^{77}Se spin rotation tensor and the equilibrium molecular geometry. No error estimates were provided with the spin rotation tensor. On the optimistic side, we assign an uncertainty of about ± 60 ppm. For a linear molecule such as the Se=C=Se molecule, the absolute isotropic shielding can be obtained from the shielding anisotropy by a simple relation: $\sigma = \sigma_{\parallel}^{\ d} - (2/3)\Delta\sigma$. The nonrelativistic free atom value 2998 ppm (*61*), used in the Flygare approximation (*62*), including atom dipole correction terms equal to 9.6 ppm, gives $\sigma_{\parallel}^{\ d} = 3008$ ppm. From the experimental shielding anisotropy measured in liquid crystal solution (2210±120 ppm) (*60*) and the parallel component of the diamagnetic shielding, we estimate the absolute isotropic ^{77}Se shielding in liquid phase SeCSe = 1535±80 ppm, the uncertainty reflecting only that of the shielding anisotropy measurement. With an experimental gas-to-liquid shift of 73.7 ppm, between the liquid at 20°C and the gas at 90°C (*63*), the gas phase isotropic shielding is estimated to be 1610±80 ppm. Table VI shows us that calculated ^{77}Se shieldings are in reasonable agreement with the

absolute shielding values. There are still discrepancies which could be attributed to rovibrational effects.

Table VI. Absolute Shielding σ(^{77}Se) in Small Molecules

	H_2C=Se	*SeF_6*	*Me_2Se*	*MeSeH*	*H_2Se*	*O=C=Se*	*Se=C=Se*
DFT[a]		953	1668	1837	2093	2270	1441
CONV[g]			1905.4	1988.0	2156.7		
CONV[b]			1926.3	2015.7	2171.0		
SCF[c]			1927.0	2043.8	2178.5		
MP2[c]			1922.2	2093.0	2275.6		
SCF[d]	-1011.4	1320.6	1897.6	2027.6	2167.6	2261.6	1451.6
MP2[d]	-994.5	1147.5	1874.7	2054.5	2236.5	2406.5	1753.5
SCF[e]	-886		1894.1		2170	2291	1488
MP2[e]	-813		1895.4		2260	2418	1748
CCSD[e]	-741		1877.5		2213	2345	1596
Expt.	-900 ±200[f]	1138 ±64[g]	1756 ±64[h]	1911 ±64[h]	2101 ±64[g]	2348 ±60[i]	1610 ±80[d]

[a] Ref. (*24*).
[b] Ref. (*64*).
[c] Ref .(*65*).
[d] Ref. (*66*).
[e] Ref. (*58*).
[f] From Table 16 in Ref. (*67*), derived from ^{77}Se spin rotation tensor and rotational constants in high resolution microwave data of Ref. (*68*).
[g] From Ref. (*56*), the ^{77}Se absolute shielding scale, but without the relativistic corrections (300 ppm) in the diamagnetic shielding of the Se free atom used in Ref. (*56*).
[h] The chemical shifts between H_2Se vs. MeSeH and Me_2Se (all in the gas phase) from Ref. (*1*) were converted to absolute shieldings by using the absolute shielding σ(^{77}Se, H_2Se, gas) = 2101±64 ppm from Ref. (*56*), again leaving out the relativistic corrections.
[i] See the text for the determination of these experimental values.

Calculations on ^{125}Te shielding have been very successful in reproducing the 4000 ppm range of isotropic chemical shifts in a wide variety of compounds in solutions or neat liquids (*25*).although no corrections of medium effects had been made in comparing with experimental values.

For the ^{71}Ga nucleus, the availability of an absolute shielding scale also makes possible a comparison of calculated absolute shieldings with experimental values. The standard used experimentally, $[Ga(OH_2)_6]^{3+}$ in solution, is unsuitable as a theoretical reference due to the lack of consideration of water molecules beyond the first solvation shell in the calculations. On the other hand, there exists an absolute shielding scale for ^{71}Ga, based on the NMR measurement in an atomic Ga beam at the same time as in the ion at infinite dilution in a D_2O solution (*57*).

By using the calculated nonrelativistic diamagnetic shielding for the free Ga atom = 2638.6 ppm (*61*), it is found that,

$\sigma(^{71}Ga, [Ga(OD_2)_6]^{3+}$ infinitely dilute solution in $D_2O) = 1840(45)$ ppm.

With this value we can convert the experimental chemical shift measurements to absolute shieldings. Table VII shows that within the experimental errors, without taking into account the solvation effects, the agreement of the calculations of ^{71}Ga shielding at the MP2 level with experiment is reasonable. These three examples, ^{77}Se, ^{125}Te, and ^{71}Ga, provide convincing evidence that shielding calculations for heavy nuclei of representative elements are presently feasible.

Table VII. Absolute Shielding $\sigma(^{71}Ga)$

$\sigma(^{71}Ga)$	*MP2 calc*[a]	*exptl. (± 45 ppm)*[b]	*% recovery*
$GaMe_3$	1175.5	1120	105
$[GaCl_4]^-$	1613.2	1593	101
Ga_2Cl_6	1625.0	1598	102
$[Ga(OH)_4]^-$	1629.4	1620	100
$[GaH_4]^-$	1827.3	1730	106
$[Ga(OH_2)_6]^{3+}$	1930.4	1840	105
$Ga(C_5H_5)$	2593.2	2554	101

[a] From Ref. (*69*).

[b] The experimental chemical shifts (compiled by Ref. (*69*)) have been converted to absolute shielding, based on the σ (^{71}Ga, $[Ga(OD_2)_6]^{3+}$ infinitely dilute in D_2O) = 1840(45) ppm, as described in the text.

Rovibrational Averaging of σ for Small Molecules.

How large are the rovibrational corrections? How well can they be calculated? To do the rovibrational corrections, we need both the shielding surface for the nucleus and the potential energy surface for the molecule. The average is obtained from the shielding value at each point on the shielding surface weighted according to the probability of finding the molecular system at that nuclear configuration. There had been, prior to 1992, a large quantity of data on the rovibrational effects on the NMR shielding. Furthermore, the theoretical interpretation of the observed consequences of rovibrational averaging (temperature dependence of the molecule in the limit of zero pressure, and shielding changes upon isotopic substitution) were already well established (*70,71*). However, few accurate shielding surfaces had been calculated, for several diatomic molecules, and only for very few polyatomic molecules: H_2O (*72*), NH_3 (*73*), PH_3 (*74*), and CH_4 (*75*).

The developments since 1992 include very accurate calculations of the shielding surfaces in the immediate vicinity of the potential minimum for diatomic molecules. Rovibrational corrections to shielding calculated with these more accurate shielding surfaces (CCSD(T) level calculations) are shown in Table VIII.

Some of the shielding surfaces are found to have significant curvature at the equilibrium internuclear separation, so that it is important to evaluate higher than first derivatives of the surface at this configuration. In comparing with experimental data,

data from the full range of temperature should be used, rather than making a comparison between theoretical derivatives (σ_e', σ_e'') and experimental ones. For example, the empirical value for σ_e' in F_2 molecule was obtained from a single parameter fitting to the observed temperature dependence of the ^{19}F chemical shift in F_2 gas in the limit of zero pressure (*76*). Thus, the empirical parameter actually stands for the effects of both the first derivative (σ_e') and the second derivative (σ_e'') terms. The single parameter is found to be too large compared to current theoretical values for the first derivative of ^{19}F shielding (*49*), nevertheless, the change in the thermal average ^{19}F shielding over the range 230 to 350 K predicted from the theoretical

Table VIII. Magnitudes of Rovibrational Corrections to Shielding

System	$\langle\sigma\rangle_{v=0} - \sigma_e$	$\langle\sigma\rangle_{300\,K} - \langle\sigma\rangle_{v=0}$	$\langle\sigma\rangle_{300\,K} - \sigma_e$	$\langle\sigma\rangle_{300\,K} - \sigma_e$
	a	*a*	*a*	*EXPT*
^1H in H_2	-0.355	-0.014	-0.369	-0.303 [d,f], -0.375 [d,g]
^1H in HF	-0.323	-0.035	-0.358	-0.38 [i]
^{19}F in HF	-10.0	-0.42	-10.42	-9.75 [i], -10.5 [d,g]
^{13}C in CO	-2.24	-0.15, (-0.087) [b,c]	-2.39	-1.91 [d,h]
^{17}O in CO	-5.73	-0.35	-6.07	-4.88 [d,h]
^{15}N in N_2	-4.03	-0.24, (-0.255) [b,c]	-4.27	-3.49 [d,h]
^{19}F in F_2	-30.87	-4.69	-35.56	-40 [c,j]
^{17}O in H_2O	-9.85[e]	-0.36[e]	-10.22[e]	-13.0 [d,h]
^{33}S in H_2S			-16.4 [k, m]	
^{77}Se in H_2Se			-58.9 [n]	-56.9 [d,h]
^{15}N in NH_3			-8.81[p]	-8.3 [d,h]
^{31}P in PH_3			-12.78 [q]	-10.4 [d,h]
^{13}C in CH_4	-3.591	-0.104	-3.695[r]	-3.3 [d,g]

[a] Except where noted, the values are taken from Ref. (*49*).
[b] From Ref. (*77*).
[c] experimental estimate from the temperature dependence of the chemical shift in the gas phase at the zero-pressure limit.
[d] experimental estimate from the isotope shift.
[e] The more accurate values reported by W. T. Raynes at this Symposium. Earlier values were -13.116, -0.457, and -13.573 ppm respectively, from a CHF shielding surface Ref. (*78*).
[f] Ref. (*79*).
[g] Ref. (*80*).
[h] Ref. (*70*).
[i] Ref. (*81*).
[j] Ref. (*82*).
[k] Using shielding derivatives of Ref. (*83*).
[m] Ref. (*84*).
[n] Ref. (*85*), page 23.
[p] Ref. (*73*).
[q] Ref. (*74*).
[r] Ref. (*86*).

derivatives $\sigma_e'$and σ_e'', and the mean bond and mean square displacements, is in good agreement with experiment. The calculations for the H_2 molecule have been carried out with full configuration interaction, and the last remaining minor discrepancy with experiments, including the isotope shifts, have been accounted for (*50*).

For comparison, some polyatomic molecules have been included in Table VIII. The most recent more accurate shielding surface for H_2O is reported by W. T. Raynes in a paper at this Symposium, and an independent calculation by Vaara et al. has recently appeared (*87*). Both calculations use MCSCF wavefunctions, however, the calculations by Raynes et al. have the benefit of more accurate force constants and perhaps a more accurate shielding value at the equilibrium geometry. With increasing accuracy of the shielding calculations for small molecules, rovibrational corrections are increasingly important for comparison with absolute shielding scales. In addition, accurate recovery of the experimental isotope shifts provide a stringent test of the derivatives of the theoretical shielding surface.

Intermolecular Effects on σ

There are several approaches to the calculations of intermolecular effects on shielding. Where the experiment can measure binary collision effects, as in the dilute gas, or in a van der Waals complex in a beam, comparisons with experiment can be achieved by calculations of the binary complex supermolecule shielding surface accompanied by determination of the intermolecular potential surface. In doing supermolecule shielding surface calculations, it is very important to make counterpoise corrections at every configuration (*88*). The second virial coefficients of the shielding, i.e., the density coefficient of the intermolecular chemical shift as a function of temperature can be calculated by doing the integration of the shielding surface over all configurations, weighted by the intermolecular potential function. The experimental work done in gases in the early 1970s were quantitatively interpreted for the first time in 1992 (*88*), in which ab initio calculations on the rare gas atom pairs were scaled to the heavier rare gas atoms by a corresponding states analog. Recently, the intermolecular shielding functions for Xe-CO_2, Xe-CO, Xe-N_2 have been reported (*89*). These are the first complete configuration shielding surfaces involving molecules, providing for the first time, the shape of a atom-linear molecule shielding surface. The Xe-Xe shielding function obtained using very large basis sets on the Xe atom, compared with that obtained from scaling the Ar-Ar shielding function, demonstrated excellent agreement over the range of configurations sampled in the integration for the experimental temperature range ±100 K. The very recent CCSD(T) calculations on the Ne-Ne shielding surface established that there is a negligible effect of correlation on the shielding surface for this rare gas pair (Bühl, M.; Kaupp, M.; Malkin, V. G.; Malkina, O. L. *J. Comp. Chem.*, **1999**, in press.).

For Xe adsorbed in a zeolite, the system configurations involve variable occupancy so that a grand canonical ensemble average must be used in calculating the shielding. Here, one starts with a shielding surface which involves the Xe atom in question, all the atoms of the zeolite cage, plus a variable number of Xe atoms in the same cage. The approach that has been adopted for this system is to consider one rare gas atom in a supermolecule with a rigid fragment of the zeolite cage (*90*). The

shielding values obtained at a multitude of configurations of the supermolecule can be expressed in a functional form as pairwise sums of distance dependent atom-atom (Xe-O, Xe-Na^+, etc.) shielding functions. The Xe-Xe contributions for the n Xe atoms in the cage and adjacent cages are likewise treated as pairwise sums of the ab initio σ function of the Xe-Xe distance. By using periodic boundary conditions, the Xe configurations in the entire zeolite can be simulated. Monte Carlo methods are used to determine distributions of configurations to find the grand canonical ensemble average of $\sigma(^{129}Xe)$ in this environment (*91*). In this simulation approach all parts of the medium are treated as atoms with orbitals and electrons, and the framework atoms of the real zeolite are located in the known positions based on diffraction data. The experimental Xe chemical shifts in mixtures of Xe with other molecules within the zeolite cages have been reproduced in this way (*92*).

Other approaches do not consider the overlap/exchange/dispersion interactions of the molecule with the surrounding molecules, but only the electric fields and gradients generated by the molecules of the medium. The linear and quadratic response to external static electric fields **F** and field gradients ∇**F** were first introduced by Buckingham (*93*).

$$\sigma_{\alpha\beta}(\mathbf{F},\nabla\mathbf{F}) = \sigma_{\alpha\beta} + \sigma'_{\alpha\beta\gamma}\mathbf{F}_\gamma + (1/2)\sigma''_{\alpha\beta\gamma\delta}\mathbf{F}_\gamma\mathbf{F}_\delta + \sigma'_{\alpha\beta\gamma\delta}\mathbf{F}_{\gamma\delta} + \ldots \quad (1)$$

The physical picture is a simple one: a static homogeneous magnetic field and intrinsic nuclear magnetic moments induce stationary currents within the electronic charge distribution, whereas a static electric field polarizes it. Therefore, the distortion induced in the electron clouds by the latter gives rise to additional effects, which can be rationalized in terms of response tensors of higher rank. In one approach to intermolecular effects, Dykstra, Oldfield, and Pearson calculate the average shielding of a molecule in a liquid in a molecular dynamics simulation by using Eq. (1), with the shielding polarizability parameters as constants obtained from a previous ab initio calculation (*94,95*). Following this method, Mikkelsen et al. used molecular dynamics simulations to obtain the ensemble averages of the electric field and field gradient at the ^{17}O and ^{1}H nuclear sites as a function of temperature. In this approach, the surrounding water molecules are represented entirely by fields and field gradients, i.e., they possess no electrons with which to generate exchange and overlap contributions to shielding at the H_2O molecule of interest. Including the effects of the different average geometry in the liquid from that of an isolated H_2O, plus the total contribution calculated from Eq. (1) leads to only 28% and 16% of the experimental gas-to-liquid shift of the ^{17}O and ^{1}H, respectively. Further, the temperature coefficient of the chemical shifts in the liquid is found to have the correct sign, but too small a magnitude compared to experiment (*96*).

Another method of calculating the electric field and field gradient contributions to the shielding in a molecule in a liquid is to use a reaction field model. This idea was first introduced by Buckingham, using the Onsager dipole model (*93*). Mikkelsen et al. present an update of the Buckingham model, considering a molecule within a spherical cavity in a homogeneous isotropic and linear dielectric medium, and include higher multipole terms (*97,98*). This model accounts for only a small portion of the observed gas-to-solution shifts of ^{13}C and ^{1}H in CH_4 in solvents of various dielectric constants. The sign of the gas-to-liquid shift for ^{17}O in water calculated by this method is opposite to that observed experimentally (9.4 ppm increase in shielding rather than the observed 36 ppm decrease in shielding in going to the liquid) (*97*).

Results for ^{1}H improved by introducing the surrounding 4 water molecules into the cavity, but still only leads to 45% of the gas-to-liquid shift for the ^{17}O nucleus (*97*). Likewise, this method fails to account for all of the gas-to-liquid shift of ^{19}F in fluoromethanes (*99*) and of ^{77}Se in H_2Se (*100*). Clearly, medium effects can not be treated accurately by using a reaction field model. The major problem with the above two approaches is that only the electric polarization effects are included in the model.

For associated liquids such as the above examples, the best approach appears to be the quantum cluster equilibrium (QCE) theory of Farrar and Weinhold (*101*). In this method, σ is calculated in various stable clusters (n-mers of the molecule, typically, n = 2-6). Each cluster is geometry optimized via an *ab initio* method and the shielding is calculated at the optimized geometry for each of the clusters. Excellent tests for the geometry and electronic properties of the clusters have been made against spectroscopy of van der Waals complexes. Using standard statistical thermodynamics and employing energies (vibrational frequencies, etc.) obtained from *ab initio* calculations, partition functions are calculated and the distribution of molecules among the various clusters can be obtained. This distribution is then used for determining population-weighted NMR shieldings. This scheme has been applied to ammonia (*102,103*), N-methyl formamide(*104*), CH_3NC (*105*) and N-methyl acetamide (*106*). The success in reproducing the temperature dependence is an indication that most of the temperature dependence is in the changes in the distributions of the molecules among various clusters.

Ab Initio Calculations of Shielding in Proteins

The nuclei in the same amino acid residue in different parts of a protein exhibit uniquely different chemical shifts. Secondary structural information is therefore encoded in the NMR shifts. Herein lies the challenge: how to predict chemical shifts for given secondary (and tertiary) structures. Then, there is the even more difficult challenge of how to unencode the experimental chemical shifts to deduce or refine secondary structures of proteins. Earlier work on intermolecular effects had focused on electrostatic effects and magnetic anisotropy, and considered dispersion contributions to be paramount, using the Raynes, Buckingham, and Bernstein framework (*107*). Within this framework, research groups working on chemical shifts in proteins had been largely concerned with proton chemical shifts (*108*), particularly electrostatic effects, ring currents and magnetic anisotropy using parameterized empirical models. These magnetic anisotropy effects are of very little consequence for chemical shifts of nuclei other than protons. The earlier interpretations of protein chemical shifts reported at the Maryland conference were highly invested in the electric polarization idea, that the way to calculate these was by calculating shielding polarizabilities of the observed nuclei coupled with calculations of local electric fields and electric field gradients generated by all the atoms in the surroundings of the nucleus of interest, as in Eq. (1) (*94*).

An alternative approach is to consider the shielding surface, i.e., the nuclear magnetic shielding as a function of nuclear coordinates of a molecule (distances, bond angles, torsion angles, ...) and to calculate traces on the shielding hypersurfaces to elicit the main factors influencing chemical shifts in proteins. For a ^{13}C nucleus, for example, there was a hint already in experiments that the torsion angles were

important in distinguishing helix from sheet (*109*). Therefore, the model system had to permit exploration of the dependence of ^{13}C, ^{15}N, ^{17}O shielding on local geometry, especially torsion angles, as well as on hydrogen bonding. Furthermore, the effects of the more distant parts of the protein had to be taken into account.

Since the Maryland meeting, de Dios, Oldfield, and others have established that ab initio calculations of ^{13}C and ^{15}N (and ^{19}F) chemical shifts in proteins can be done successfully using a model system, specifically, a molecular fragment having the essential attributes of local geometry and short range interactions, including hydrogen-bonding, calculated at a sufficiently high ab initio level while surrounded by the rest of the protein represented with a simpler description such as point charges at atomic locations (*110-115*). In this approach to the calculation of a property, the local geometry and electronic structure (including a hydrogen bonding partner) are represented in the greatest detail by a judiciously chosen molecular fragment with locally enhanced basis sets, and good ab initio calculations at various local geometries (in the case of proteins the torsion angles phi and psi are paramount, but also chi has been considered). The remainder of the protein (or the remainder of the crystal in the case of amino acid shielding tensor calculations) is represented at a lower level of detail, the long range intermolecular effects treated by point charges at each atom of the residues located within a sphere, for example. All short range intermolecular effects are of course treated correctly ab initio within the fragment. Others who have later adopted the model originated by de Dios et al. have given this approach the name "embedded cluster", and of course, the model can and has been generalized to permit the surrounding framework to be treated by molecular mechanics, and to include even further out, the solvent molecules under molecular dynamics. Thus, the initial work in this area has influenced the direction of research in this and other fields, with other researchers adopting the approach and embellishing further. This approach to calculating chemical shifts in very large molecules (or networks) such as proteins is discussed with new examples in the paper by Oldfield in this Symposium proceedings.

The prediction that the component of the ^{13}C(alpha) shielding tensor in a peptide along the C-H bond has a larger range of values depending on the torsion angles phi, psi than the range of the isotropic shieldings for the same nucleus (*116*) has been corroborated experimentally by Bax et al. (*117*). This is an important development. First of all, theoretical calculations (*116*) have demonstrated that the experimental method of Bax et al. which depends on the cross relaxation terms involving chemical shift anisotropy and dipolar coupling does indeed lead to good values for the shielding component along the C-H bond direction. Second, the theoretical calculations demonstrate that this is more sensitively associated with the local geometry than is the isotropic shielding of the same ^{13}C nuclear site, thus providing complementary and more sensitive information for deducing structure.

Model Calculations in Zeolites and Inorganic Solids.

One of the most difficult challenges for theoretical treatments of the NMR chemical shift is in extended networks such as inorganic solids. Indeed, while the immediate future approaches to isolated small molecule chemical shifts were being laid out even at the time of the Maryland conference, the theoreticians attending did not have any

words of comfort for the experimentalists who brought fascinating trends and puzzles in covalent solids.

One approach to solids that are not molecular crystals is to carve out a fragment of the solid as a model system, with appropriate terminations of what would otherwise be dangling bonds This is a logical approach for an ionic solid, where replacing the distant neighbors by point charges is an excellent approximation. The paper by de Dios in this Symposium provides a very nice example for the theoretical predictions of trends in ^{87}Rb shielding in various Rb doped into alkali ion sites in various alkali halide crystals, using the full complement of nearest neighbors in the model fragment. In aluminosilicates the size of the model fragment used in the calculations of the ^{29}Si shielding tensor has varied from the very early 3 heavy atoms (one O and two T atoms) to the larger fragments containing up to 15 heavy atoms (*118-120*). There is a controversy about the extent to which geometry optimization of the model fragment should be carried out, or even whether it makes sense to use anything different than accurate experimental T-O distances and T-O-T bond angles in the actual aluminosilicate. Similarly, for the calculation of the ^{13}C shielding tensor of a small organic molecule (acetone) adsorbed in a zeolite, a model fragment that has been used to represent the HZSM5 zeolite has one central oxygen bridging the Si and Al moieties each of which is terminated with OSiH3 groups, i.e., the $(H_3SiO)_3SiOHAl(OSiH_3)_3$ fragment (*121*). In contrast to the more usual practice of using smaller terminating groups of the type $OSiH_3$, $OSi(OH)_3$ terminating groups have been used by Farrar et al. for aluminosilicate glasses (*122*). In the model fragment used in this work, the central Si or Al is surrounded by four groups of the type $OSi(OH)_3$ or $OAl(OH)_3$ or OH, and counter ions to balance the charge. The calculated ^{29}Si and ^{27}Al shielding in various clusters representative of the Q^n species (Q is the central tetrahedral Al or Si and *n* is the number of oxygens that bridge the central atom to tetrahedral Al or Si sites) in aluminosilicate glasses can accurately predict experimentally observed trends in these glasses (*122*).

In inorganic solids like carbides and nitrides, Tossell has found that the theoretical shielding results are sensitive to the second nearest neighbors in the solid (*123*), i. e., these systems demand a larger fragment that includes not only the nearest neighbors but also the second nearest neighbors. Tossell has calculated the effects arising from second nearest neighbors on the ^{15}N shielding in crystalline α- and β-Si_3N_4 are as large as 80 ppm (*123*). The shielding calculated with the largest fragment, $Si_9N_9H_{21}$, is still 50 ppm more shielded than the experimental shielding in β-Si_3N_4, indicating that the this size fragment is still an inadequate model system.

A completely different approach is to start with basis functions that already have the periodic nature of the solid and extend indefinitely, for example, using basis functions of plane waves. This method has been used very successfully for calculations of electric field gradients (*124*) and has only very recently been applied to shielding (*125*).

Fine Geometry Effects on Shielding, NMR Refinement of Diffraction Results.

Complete assignment of ^{13}C shielding tensors in the entire molecule from single crystal studies has been developed to the highest level by D. M. Grant and co-workers. Single crystal NMR measurements provide complete tensor information and

the increased resolution in the 2D chemical shift-chemical shift correlation method and the multiple-axis sample reorientation mechanism developed in this group permits the study of crystals containing 50-100 magnetically different nuclei per unit cell. The redundant data provided by the crystal symmetry increases the number of independent observations of a given shift tensor, enabling the calibration of the magnetic field directions in the single crystal sample and improving the precision of the shift measurements to better than 0.5 ppm. These experimental techniques are combined with ab initio calculations which provides a high level of agreement between calculated and experimental tensors for ^{13}C in a large number of polycyclic aromatic compounds and sugars. Only the structural parameters (bond distances and angles) limit the level of agreement. This means that *ab initio* calculations and measurements together can be used to address certain fine details of solid-state structure, surpassing the accuracy of x-ray data. In a dramatic application of ab initio calculations toward the elucidation of the shielding tensor and its dependence on molecular geometry, it has been shown that the departures from D_{2h} symmetry observed in the experimental chemical shift tensor components of naphthalene in the single crystal (leading to the reduced symmetry, C_i) could be accounted for entirely by small geometrical variations that are smaller than the error bars of the x-ray diffraction parameters (*126*). This leads to the conclusion that solid state NMR methods can be used for refining structural data, especially in those cases where imperfections such as translational disorder or occlusion of molecular impurities degrade diffraction data while having no effect on chemical shift data (*127*).

In summary, the challenges in the computations of nuclear magnetic shielding are being met, and the rich and diverse structural and dynamical NMR chemical shift data are beginning to yield to rigorous, accurate interpretation. This Symposium presents some of the most recent breakthroughs in the field.

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