The Calculation of Nuclear Magnetic Resonance Spectra by Semiempirical Methods. I. Proton Chemical Shifts in Hydrocarbons[1,2]

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Abstract: Using the basic formalism of Zürcher which includes considerations of bond anisotropies expressed by the McConnell equation as modified by ApSimon, together with consideration of a van der Waals dispersion effect, we have been able to devise a way to calculate the chemical shifts of hydrocarbons in a very general way. The parameters needed have been deduced by a least squares fitting to 18 resonances in 7 simple hydrocarbons. These data are fit with an average deviation of 0.058 ppm. When these methods and parameters are then applied to the calculation of 46 resonance lines from a diverse variety of hydrocarbons, the data are reproduced with an average deviation of 0.097 ppm.

Since the inception of nuclear magnetic resonance (nmr) as a structural tool for the study of organic compounds, interest has been evidenced in the calculation of nmr spectra for predictive purposes. For several years now, the quantum mechanical methods for the solution of this problem have been refined to the point that *replication* of a spectrum can often be performed with great precision;[5] however, the *prediction* of the observed absorptions (chemical shifts and coupling constants) by means of quantum mechanical methods has not yet reached a similar level of efficacy.[6] Researchers have hence turned to other, more empirical methods, which have met with a moderate degree of success in limited areas, but which have usually been based on shaky theoretical foundations.

We have approached the calculation of chemical shifts from a classical direction in an attempt to be theoretically plausible, though empirical, and at the same time increase our understanding of some of the more important phenomena involved. Several papers dealing with the theoretical aspects of this problem have appeared. We will discuss only chemical shifts here; a later paper will discuss coupling constants. The ideas presented here have been employed before; however, previous studies have been very limited in scope, really only special cases. The objective here is a study of the problem in a very general way.

In connection with chemical shifts, the chapter by Zürcher[7b] is of singular interest. This was a moderately successful attempt to calculate the relative chemical shifts of protons from expressions describing the contributions of the magnetic anisotropic, electric field, and van der Waals dispersion forces. This chapter[7b] forms a starting point for our calculations, although we have modified some of the details for the purpose of increasing generality, accuracy, and theoretical soundness, and have investigated other methods for calculating the above effects, in addition to those originally cited.

Theory. The calculation of the effective magnetic field which a proton experiences ($\mathbf{H}_{\text{local}}$) in the nmr spectrometer can be formulated as depending on the applied magnetic field (**H**) and a screening constant (σ), the latter being a result of the magnetic field introduced by the molecular electron cloud. Thus, for the protons of a molecule in the gas phase

$$\mathbf{H}_{\text{local}} = \mathbf{H} - \sigma_{\text{av}} \cdot \mathbf{H} \qquad (1)$$

where the term $-\sigma_{\text{av}} \cdot \mathbf{H}$ is the average chemical shift expressed in gauss.

The shielding theory of chemical shifts[8] considers the proton in a molecule as being shielded from the applied magnetic field by both its own electron cloud and by other electrons from neighboring atoms within the molecule such that

$$\sigma = \sigma_{\text{localized}} + \sigma_{\text{distant}} \qquad (2)$$

It is often convenient to express the effects of distant shielding in terms of either atoms or bonds. Although the concept of a molecular electronic cloud is a more accurate description of this type of shielding, the dissection of the cloud into bond components would be expected to be a good approximation for most molecules.[9] The contribution of the localized electron cloud of a proton to shielding the proton itself is not a directly measurable quantity; thus, the discussion of chemical shifts is relative rather than absolute. However, the assumption that this type of shielding is nearly identical for all protons in a hydrocarbon[8] is probably not a bad one, and it has been used extensively in the literature. Keeping the above assumption in mind, we might hope that it would be possible to assign magnetic screening properties to neighboring atoms and/or bonds, and to calculate accurate "chemical shift" values resulting from the effects of neighboring shielding alone.

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[1] This is paper LXXI in the series "Conformational Analysis." Paper LXX: N. L. Allinger, B. J. Gorden, I. J. Tyminski, and M. T. Wuesthoff, *J. Org. Chem.*, **36**, 739 (1971).

[2] This work was supported in part by Grant AM-5836 from the National Institute of Arthritis and Metabolic Diseases.

[3] National Institutes of Health Postdoctoral Fellow, 1968–1970.

[4] Correspondence concerning this paper should be addressed to this author.

[5] See, for example, Y. K. Pan and M. T. Rogers, *Rev. Pure Appl. Chem.*, **18**, 17 (1968).

[6] (a) W. N. Lipscomb, *Advan. Magn. Resonance*, **2**, 137 (1966); (b) J. I. Musher, *ibid.*, **2**, 177 (1966); (c) H. Katô, H. Kato, and T. Yonezawa, *Bull. Chem. Soc. Jap.*, **43**, 1921 (1970).

[7] (a) R. F. Zürcher in "Nuclear Magnetic Resonance in Chemistry," B. Pesce, Ed., Academic Press, New York, N. Y., 1965, pp 45–51; (b) R. F. Zürcher in "Progress in Nuclear Magnetic Resonance Spectroscopy," J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Ed., Vol. 2, Chapter 5, Pergamon Press, New York, N. Y., 1967, pp 205–257.

[8] P. T. Narasimhan and M. T. Rogers, *J. Chem. Phys.*, **31**, 1302 (1959).

[9] S. Diner, J. P. Malrieu, F. Jordan, and P. Claverie, *Theoret. Chim. Acta*, **18**, 86 (1970), and other papers in this series.

The values would be valid, of course, only if the model was able to account for all important interaction mechanisms.

Zürcher[7] has chosen three types of additive mechanisms for intramolecular screening of the proton as magnetic, electric, and van der Waals shieldings, and has included an intermolecular solvent effect as well. These contributions can be illustrated in terms of the δ chemical shift scale as

$$\delta_{\text{total}} = \delta_{\text{magnetic}} + \delta_{\text{electric}} + \delta_{\text{van der Waals}} + \delta_{\text{solvent}} \quad (3)$$

The fact that magnetic screening properties are approximately additive quantities has been shown through various independent observations of empirical group contributions[10] to the chemical shift, as well as in previous theoretical studies.[11] In addition, there is an intermolecular solvent contribution which must be considered for absolute comparisons on this scale.[12] This intermolecular factor is neglected at this time, however, because of the lack of a sufficiently good theory or enough experimental data to deal with the problem in a reasonable way. We have tried to minimize the difficulty by utilizing only data on hydrocarbons obtained in very dilute solutions of chloroform or carbon tetrachloride for our parameter determinations.

Of the three remaining effects which require attention, one of these should be negligible when considering hydrocarbons. The term δ_{el} measures the influence of the electric field produced by the various bond dipoles within the molecule upon the total chemical shift. The bond dipole moment for the C–H bond in hydrocarbons is very small, *i.e.*, from −0.3 to +0.4 D, with most chemists[13] accepting the 0.0 to +0.3 D range; thus the δ_{el} term will also be small for hydrocarbons. For substituents other than H, this effect can be of major importance,[14] and it will be evaluated later for other types of molecules.

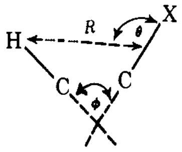
For the sake of completeness, we include here the equation used for the calculation of δ_{el}, the contribution of dipolar effects to the chemical shift (δ). This equation will be used later in the evaluation of the importance of this effect in the calculation of the chemical shifts of hydrocarbons

$$E^{\text{total}} = \frac{\mu(1 + 3\cos^2\theta)^{1/2}}{R^3} \quad (4)$$

where E^{total} is the electrical field in the area of the proton, μ is the electric dipole moment of the C–X bond, R is the distance between the proton and the center of the dipole, and θ is the angle between R and the vector of μ. E_z, the component along the C–H bond, is given by the equation

$$E_z = E^{\text{total}} \cos\phi \quad (5)$$

where ϕ is the angle between the C–H bond and the vector E



$$\delta_{\text{el}} = AE_z \quad (6)$$

where A is an empirical constant, to be determined from available experimental data.

In the past, a problem has arisen due to the fact that shielding mechanisms have generally not been studied in a simultaneous manner; each researcher has instead usually isolated for pragmatic reasons one mechanism as the exclusive agent for the shieldings under consideration.[8,14–16] However, evidence is now available that any one of these mechanisms is not adequate for the complete description of proton chemical shifts.[8,17] Other problems have been the lack of accurate molecular geometries on which to base the calculations, and the mathematical functions have often been used beyond their limitations.

In 1957, McConnell[18] published an extensive derivation for the magnetic shielding effect of a distant bond (possessing axial symmetry) on an isolated proton. His equation is the first bracketed term of eq 7. Until recently, the unlimited utilization of this equation has been hindered by the inclusion in the derivation of the point-dipole approximation, which is accurate only for interatomic distances greater than about 3 Å.[19] Ap-

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(10) (a) H. Primas, R. Arndt, and R. Ernst, *Advan. Mol. Spectrosc.*, **3**, 1246 (1962); (b) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry. Illustrations from the Steroid Field," Holden-Day, San Francisco, Calif., 1964, Chapter II, pp 13 ff; (c) K. L. Williamson and T. A. Spencer, *Tetrahedron Lett.*, 3267 (1965); (d) D. E. O'Reilly in "Progress in NMR Spectroscopy," J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Ed., Vol. II, Pergamon Press, New York, N. Y., 1967, pp 1–59; (e) R. F. Zürcher, *Helv. Chim. Acta*, **44**, 1380 (1961); (f) *ibid.*, **46**, 2055 (1963).

(11) (a) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, Chapter 7, pp 112–130, and references therein; (b) P. Laszlo and A. Speert, *J. Chem. Phys.*, **51**, 1677 (1969); (c) see also the arguments of Zürcher,[7b] Musher,[15f] and Pople[15g] based upon Pascal's additive constants for magnetic susceptibilities (A. Pacault, *Rev. Sci.*, **86**, 38 (1948))

(12) (a) J. K. Becconsall, *Mol. Phys.*, **15**, 129 (1968); (b) J. Ronayne and D. H. Williams in "Annual Review of NMR Spectroscopy," Vol. 2, E. F. Mooney, Ed., Academic Press, New York, N. Y., 1969, pp 83–124.

(13) J. W. Smith, "Electric Dipole Moments," Butterworths, London, 1955, p 92.

(14) (a) J. W. Emsley, *Mol. Phys.*, **9**, 381 (1965); (b) J. Feeney, L. H. Sutcliffe, and S. M. Walker, *ibid.*, **11**, 117, 129, 137 (1966).

(15) (a) J. Guy and J. Tillieu, *J. Chem. Phys.*, **24**, 1117 (1956); (b) J. Tillieu, *Ann. Phys.*, **2**, 471, 631 (1957); (c) A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.*, **80**, 1728 (1958); (d) A. A. Bothner-By and C. Naar-Colin, *Ann. N. Y. Acad. Sci.*, **70**, 833 (1958); (e) J. I. Musher, *J. Chem. Phys.*, **35**, 1159 (1961); (f) J. I. Musher, *Mol. Phys.*, **6**, 93 (1963); (g) J. A. Pople, *J. Chem. Phys.*, **37**, 53, 60 (1962); (h) J. A. Pople, *Discuss. Faraday Soc.*, **34**, 68 (1962); (i) D. W. Davies, *Mol. Phys.*, **6**, 489 (1963); (j) A. G. Moritz and N. Sheppard, *ibid.*, **5**, 361 (1962).

(16) (a) J. W. ApSimon, W. G. Craig, P. V. Demarco, D. W. Mathieson, L. Saunders, and W. B. Whalley, *Tetrahedron*, **23**, 2339, 2357 (1968); (b) J. W. ApSimon, W. G. Craig, P. V. Demarco, D. W. Mathieson, and W. B. Whalley, *ibid.*, 2375 (1968); (c) J. W. ApSimon, P. V. Demarco, D. W. Mathieson, W. G. Craig, A. Karim, L. Saunders, and W. B. Whalley, *ibid.*, **26**, 119 (1970); (d) J. Homer and D. Callaghan, *J. Chem. Soc. A*, 439 (1968); (e) J. Elguero and A. Fruchier, *Bull. Soc. Chim. Fr.*, 496 (1970).

(17) (a) N. Muller and W. C. Tosch, *J. Chem. Phys.*, **37**, 1167 (1962); (b) G. E. Hawkes and J. H. P. Utley, *Chem. Commun.*, 1033 (1969); (c) G. P. Ceasar and B. P. Dailey, *J. Chem. Phys.*, **50**, 4200 (1969); (d) E. Doomes and N. H. Cromwell, *J. Org. Chem.*, **34**, 310 (1969); (e) N. C. Baird and M. A. Whitehead, *Theoret. Chim. Acta*, **6**, 167 (1966).

(18) H. M. McConnell, *J. Chem. Phys.*, **27**, 226 (1957).

(19) A referee has questioned also the assumption that in a molecule, the amplitudes of the molecular orbitals of an interacting group are of zero amplitude at the nucleus under consideration. It is always possible to recast the atomic orbitals in orthogonalized form (Lowdin orbitals) and these do not differ much from ordinary Slater orbitals; this is an argument for the validity zero-differential overlap approximation now widely used in calculations of the Pariser–Parr–Pople or CNDO type. This approximation therefore seems reasonable [R. G. Parr, *J. Chem. Phys.*, **33**, 1184 (1960); I. Fischer-Hjalmars, *ibid.*, **42**, 1962 (1965); J. A. Pople, D. P. Santry, and G. A. Segal, *ibid.*, **43S**, 129 (1965); **43S** 136 (1965); **44**, 3289 (1966)].

Simon and coworkers[16a–c] have recently refined this approach by introducing a correction term which better accounts for the induced magnetic dipole occurring at distances closer than 3 Å. The complete expression is

$$\delta_{\mathrm{mag}} = \left[\frac{\Delta\chi}{3}\frac{(1 - 3\cos^2\theta)}{R^3}\right] + \frac{S^2}{R^5}\left[\frac{-(\chi_{\mathrm{L}} + 2\chi_{\mathrm{T}})}{2} + 5(\chi_{\mathrm{L}}\cos^2\theta + \chi_{\mathrm{T}}\sin^2\theta) - 5.833(\chi_{\mathrm{L}}\cos^4\theta + \chi_{\mathrm{T}}\sin^4\theta)\right] \quad (7)$$

where χ_{L} is the magnetic susceptibility of the bond along its symmetry axis, χ_{T} is the magnetic susceptibility along any direction normal to the symmetry axis, and $\Delta\chi$ is the magnetic anisotropy of the bond ($\chi_{\mathrm{L}} - \chi_{\mathrm{T}}$). S, an arbitrary parameter, is one-half the length of the induced bond dipole, R is the distance between the proton and the induced magnetic dipole of the bond, and θ is the angle between the vector R and the bond symmetry axis. One might question the assumption made in the derivation that the induced magnetic field can be approximated by a physical dipole of length $2S$. The correction term is generally small, but our results indicate that it is necessary for a successful general treatment of diverse hydrocarbons (*vide infra*). This result is in contrast to the more limited studies by Homer and Callaghan[16d] or Elguero and Fruchier.[16e]

ApSimon[16a] has used the above relationship to calculate the chemical shift differences between the methine protons in cyclohexanols and norborneols. There is some question as to the validity of comparing chemical shifts in compounds containing such a highly polarizable group as the hydroxyl, since the electrical field effect of this group will significantly affect the shifts of the methine proton in the substituted and unsubstituted molecules as their true geometries are varied through steric interaction. And too, the geometries that were used for these molecules by ApSimon were certainly approximate, and can well account for some of the error reported.

Recently Homer and Callaghan[16d] have deduced bond anisotropies for the C–C and C–H bonds from the chemical shifts of the rigid molecule norbornane using the McConnell equation. These authors have pointed out that there is a disturbingly large range of previous determinations of these bond anisotropies, and have suggested from their own results that the theoretical method, and even the bond anisotropy concept itself, is in doubt. Other remonstrances to this effect have been voiced.[17a,20] Another possibility, of course, is that other effects are mixed in with the anisotropies,[16d] and until they are disentangled, the measured anisotropies will remain functions of the measurement and system studied.

The inclusion of a van der Waals term in the calculation of the chemical shifts is a result of several observations:[10c,17d,21] in general, protons placed in a sterically hindered position exhibit chemical shifts far downfield from where bond anisotropy calculations alone predict. For example, Anet[21e] observed anomalous downfield shifts of greater than 1 ppm in some birdcage compounds under study. These extremely crowded molecules provide good models for such calculations. Similarly, Schaefer[21c] and Castellano, *et al.*,[21p] estimated that in several instances, chemical shifts due to dispersion effects are at least as important as those due to magnetic anisotropies.

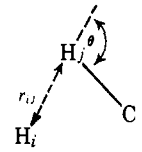
Zürcher[7] has presented the following equation for the calculation of van der Waals dispersion effects, based upon the work of Bothner-By,[22] and by Raynes, Buckingham, and Bernstein[23]

$$\delta_{\mathrm{VDW}} = -3B\alpha I/R^6 \quad (8)$$

where B = the dispersion constant (herein defined), α = the static polarizability of the substituent, I = the first ionization potential of the substituent, and R = the distance between the substituent and the proton. Another equation for calculating the effects of intramolecular steric interactions has recently been suggested by Cheney[21f]

$$\delta_{\mathrm{VDW}} = \mathrm{V}_{(\mathrm{H})}\sum \cos\theta \exp(-2.671 r_{ij}) \quad (9)$$

where $\mathrm{V}_{(\mathrm{H})}$ is an empirical constant, r_{ij} is the distance between protons H_i and H_j, and θ is the angle between the extension of the vector r_{ij} and the C–H bond. This equation was originally derived empirically from ^{13}C chemical shift data and has been used to calculate steric shifts in a few compounds.



Unfortunately, Zürcher was forced to abandon all van der Waals interaction calculations in order to obtain reasonable agreement with experiment. His use of the simplified McConnell equation for the calculation of δ_{mag} may account for some of this discrepancy, and the universal value of 20 × 10^{-12} erg for the ionization constant of all substituents may also be questioned.[24] Errors in geometry in these and other calculations appear to be largely responsible for the limited success of these early studies. For example, the assumption of tetrahedral angles[15j] or the measurements of bond lengths and interatomic distances from models[16] are clearly rough approximations. Since the δ values are affected by high powers (3 or 6) of distances, small

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(20) (a) N. Muller and O. R. Hughes as quoted by (b) A. Segre and J. I. Musher, *J. Amer. Chem. Soc.*, **89**, 706 (1967); (c) J. B. Lambert and Y. Takeuchi, *Org. Magn. Res.*, **1**, 345 (1969).

(21) (a) C. Reid, *J. Mol. Spectrosc.*, **1**, 18 (1957); (b) T. W. Marshall and J. A. Pople, *Mol. Phys.*, **3**, 339 (1960); (c) T. Schaefer, W. F. Reynolds, and T. Yonemoto, *Can. J. Chem.*, **41**, 2969 (1963); (d) V. M. S. Gil and W. A. Gibbons, *Mol. Phys.*, **8**, 199 (1964); (e) F. A. L. Anet, A. J. R. Bourn, P. Carter, and S. Winstein, *J. Amer. Chem. Soc.*, **87**, 5247, 5249 (1965); (f) B. V. Cheney, *ibid.*, **90**, 5386 (1968); (g) B. B. Howard, B. Lindler, and M. T. Emerson, *J. Chem. Phys.*, **36**, 485 (1962); (h) T. B. Cobb and J. D. Memory, *ibid.*, **47**, 2020 (1967); (i) H. P. Figeys, *Tetrahedron Lett.*, 4625 (1966); (j) W. Nagata, T. Terasawa, and K. Tori, *J. Amer. Chem. Soc.*, **86**, 3746 (1964); (k) S. J. Brois, *Tetrahedron*, **26**, 227 (1970); (l) J. G. Lindberg and A. G. Pinkus, *J. Magn. Res.*, **1**, 652 (1969); (m) E. Pretsch, H. Immer, C. Pascual, K. Schaffner, and W. Simon, *Helv. Chim. Acta*, **50**, 105 (1967); (n) K. D. Bartle and D. W. Jones, *J. Chem. Soc. A*, 437 (1969); (o) K. D. Bartle, P. M. G. Bavin, D. W. Jones, and R. L'amie, *Tetrahedron*, **26**, 911 (1970); (p) S. Castellano, H. Günther, and S. Ebersole, *J. Phys. Chem.*, **69**, 4166 (1965).

(22) A. A. Bothner-By, *J. Mol. Spectrosc.*, **5**, 52 (1960).

(23) W. T. Raynes, A. D. Buckingham, and H. J. Bernstein, *J. Chem. Phys.*, **36**, 3481 (1962).

(24) D. W. Turner in "Advances in Physical Organic Chemistry," Vol. 4, V. Gold, Ed., Academic Press, New York, N. Y., 1966, p 31.

errors in distance yield sizable errors in δ. Much of the success of both ApSimon's and Zürcher's work is a result of the absorption of geometrical errors into other parameters. This procedure can be expected to work well within a limited series of compounds where errors tend to be held constant, but it cannot be expected to be nearly as good when applied to molecules in general.

Although many discrepancies have been pointed out in the *application* of the Zürcher formulation, moderate success has been achieved using some rather crude approximations.[7b] We have been able to resolve some of these problems and also achieve a higher degree of accuracy through the following refinements: (1) inclusion of the ApSimon correction term for the nonpoint dipole calculation, (2) inclusion of van der Waals contribution calculations as basic to the chemical shift calculation, (3) utilization of accurate geometries for all calculations. With respect to this latter point, we have previously developed a method[25] of calculation of minimum energy geometries for organic compounds using a molecular mechanics approach.[26] Accuracies of bond lengths to 0.01 Å and bond angles to 1° have been demonstrated to be possible for the most part. The only other general method for determining geometry at present (except for small molecules and special cases) is by X-ray diffraction (better, neutron diffraction) of crystals. Protons are not usually accurately located in such studies, and the geometry of the molecule in the crystal may differ from that in solution. (The geometry in the gas phase, which is what the calculation determines, may also differ from that in solution, but the difference in the latter case is likely to be smaller, and easier to allow for).

In a preceding paper[27] we reported the development of a new force field which was used to calculate the geometries used in the present work.[28] There is, of course, some difficulty in describing a dynamic system with a static model. For example, the problem of rotating methyl groups has been treated here by averaging the results for the three appropriate static protons. ApSimon and coworkers[16a] have used a different approach to this problem. Another difficulty is that the chemical shifts for the axial and equatorial protons in cyclohexane are experimentally observed as an average value due to rapid inversion of the ring at room temperature. We have elected to use the low temperature measurements of Garbisch and Griffith[29] for the chemical shifts of these two types of protons in the "frozen" conformer, which should not differ significantly from the room temperature observation, if such were possible.

Method and Results

In our first attempts at the calculation of proton chemical shifts, we were unable to find any consistent set of C–C and C–H bond anisotropies–susceptibilities for use in the McConnell or extended McConnell equation which could reasonably reproduce the large body of available data listed in Table III. These parameter sets have been discussed in some detail by Homer and Callaghan.[16d] A crucial compound is norbornane, whose spectrum has been carefully analyzed and contains several unusual features.[30] Because of the general failure of any one of these earlier studies to yield useful results, we decided to develop our own method based on the Zürcher formalism and to answer, if possible, several other questions which have been the topics of recent investigations: (1) whether the ApSimon correction term is necessary for successful calculations; (2) which other phenomena are (or are not) required to adequately represent proton shielding in hydrocarbons; and (3) which model (expressions and parameters) best represents the selected phenomena.

Our method of investigation involves the linear least squares optimization of several variables simultaneously in the following general manner

$$\delta_{\text{obsd}} = ax_1 + bx_2 + cx_3 \cdots$$

where δ_{obsd} is the observed chemical shift (parts per million, infinite dilution), a, b, and c $\cdots$ are geometrical factors, and x_1, x_2, and x_3 $\cdots$ are the physical phenomena or proportionality numbers such as bond anisotropies or susceptibilities (eq 7), van der Waals dispersion constant (eq 8), empirical van der Waals constant (eq 9), or electrical constant (eq 6). With enough accurate data, this approach should lead to physically meaningful results.

We were not restrictive in our investigation of the various physical phenomena known to affect proton shielding, and included magnetic anisotropic, van der Waals, and dipolar electrical effects in various combinations in our survey, as listed in Table I.

Table I. Evaluation of the Importance of Various Effects upon the Calculation of Chemical Shifts

Run no.	Magnetic anisotropy + other phenomena[e]	S_{18}[a]	S_{46}[b]	N[c]
1	① + ③	0.067	0.184	3
2	① + ⑥	0.073	0.201	3
3	① + ④	0.070	0.219	3
4	① + ④ + ⑤	0.068	0.202	4
5	②	0.099	0.330	4
6[d]	② + ③	0.064	0.150	5
7	② + ⑥	0.056	0.258	5
8	② + ④	0.063	0.312	5
9	② + ④ + ⑤	0.060	0.225	6
10	② + ④ + ⑥	0.058	0.199	6
11	② + ③ + ⑥	0.056	0.258	6

[a] S_{18} = standard deviation (parts per million) based on the 18 chemical shifts used in the least squares basis set (seven hydrocarbons). [b] S_{46} = standard deviation (parts per million) based on the 46 chemical shifts listed in Table III (basis set + 10 other hydrocarbons) using the parameters from the corresponding basis set. [c] N = number of adjustable parameters in each approach. [d] Selected parameter set for the results cited in Tables II and III. [e] See text for description of notation.

We decided that a standard basis set of compounds must be chosen from which comparative evaluations of

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(25) (a) N. L. Allinger, M. A. Miller, F. A. Van-Catledge, and J. A. Hirsch, *J. Amer. Chem. Soc.*, **89**, 4345 (1967); (b) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. Van-Catledge, *ibid.*, **90**, 1199 (1968); (c) N. L. Allinger, J. A. Hirsch, M. A. Miller, and I. J. Tyminski, *ibid.*, **90**, 5773 (1968).

(26) See, for example, J. E. Williams, P. J. Stang, and P. von R. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968).

(27) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Amer. Chem. Soc.*, **93**, 1637 (1971).

(28) The geometries of the four isomeric androstanes will be the subject of a forthcoming paper.

(29) E. W. Garbisch, Jr., and M. G. Griffith, *J. Amer. Chem. Soc.*, **90**, 6543 (1968).

(30) (a) K. Tori, K. Aono, Y. Hata, R. Muneyuki, T. Tsuji, and H. Tanida, *Tetrahedron Lett.*, 9 (1966); (b) E. Pretsch, H. Immer, C. Pascual, K. Schaffner, and W. Simon, *Helv. Chim. Acta*, **50**, 105 (1967).

the above phenomena could be made. We therefore chose the 18 resonance values in ethane, propane, isobutane, isopentane, neopentane, cyclohexane, and methylcyclohexane for this purpose. These experimental values represent what we feel to be a balanced set of accurately determined methyl, methylene, and methine proton shifts. An additional 28 resonances (listed in Table III) were used to test the parameters selected from each analysis of the basis set data.

From the analysis of the data listed in Table I, we found that several combinations of phenomena could reproduce the data for the basis set alone, but when the additional resonance values from the larger compound set were considered, we were able to select one set as being superior.

The various terms used in the calculations in Table I are as follows: ① McConnell equation using $\Delta\chi^{C-C}$ and $\Delta\chi^{C-H}$ (first term of eq 7), ② McConnell equation with ApSimon correction term using $\chi_L{}^{C-C}$, $\chi_T{}^{C-C}$, $\chi_L{}^{C-H}$, and $\chi_T{}^{C-H}$ (eq 7), ③ Buckingham van der Waals dispersion equation (eq 8), ④ Cheney empirical van der Waals equation for hydrogen (eq 9), ⑤ Cheney-type empirical van der Waals equation for carbon (eq 9), ⑥ dipolar electrical equation (eq 6).

Each run (1–11) consists of a certain combination of the above terms as shown below. For each run, all of the parameters in the equations were optimized by the least squares method for the basis set of 18 chemical shifts (seven hydrocarbons), and the chemical shifts for the expanded set of 46 resonances (17 compounds) were then computed using these parameters. The results are given in terms of the standard deviation of the calculated chemical shifts from the experimental values.

For parameter sets 1–4 the combination of C–C and C–H anisotropies, coupled with Buckingham's van der Waals effect (set 1), gave the best description of both the 18 and the 46 chemical shift sets.

Comparing sets 5–11, the results are not as clear-cut, but it is apparent that for the 46 chemical shift set that parameter set 6, the system analogous to the one selected before, but this time including the ApSimon correction term, provides the best overall description of the entire spectrum of chemical shifts. Other effects such as Cheney's empirical van der Waals equation for hydrogens only (sets 3 and 8) and for both hydrogen and carbon (sets 4 and 9) did not significantly improve matters. Other combinations which included the dipolar electrical effect of the C–H bond ($\mu_{C-H} = 0.5$ D) similarly were not helpful. The following description is based on our best efforts to calculate hydrocarbon chemical shifts using parameter set 6.

The complete expression which we use in the calculation of ^{1}H chemical shifts (on the δ scale) for hydrocarbons consists of the combination of eq 7 and 8. In the first equation there are four unknowns—the magnetic susceptibilities (longitudinal and transverse) of the C–C and C–H bonds. In eq 8 the dispersion constant B must also be evaluated. In a reduced form the combination of eq 7 and 8 may be thought of in terms of five additive unknowns, each of which is accompanied by a multiplicative geometrical factor as illustrated in eq 10–13. Symbols for these latter equations are the same as those defined for eq 7 and 8

$$\delta = \mathbf{V}\cdot\chi_L{}^{C-C} + \mathbf{W}\cdot\chi_T{}^{C-C} + \mathbf{X}\cdot\chi_L{}^{C-H} + \mathbf{Y}\cdot\chi_T{}^{C-H} + \mathbf{Z}\cdot B \qquad (10)$$

where **V**, **W**, **X**, **Y**, and **Z** are the geometrical factors associated with $\chi_L{}^{C-C}$, $\chi_T{}^{C-C}$, $\chi_L{}^{C-H}$, $\chi_T{}^{C-H}$, and B.

$$\mathbf{V} \text{ and } \mathbf{X} = \frac{1 - 3\cos^2\theta}{3R^3} + \frac{S^2}{R^5} - \frac{1}{2} + 5\cos^2\theta - 5.833\cos^4\theta \qquad (11)$$

$$\mathbf{W} \text{ and } \mathbf{Y} = -\frac{(1 - 3\cos^2\theta)}{3R^3} + \frac{S^2}{R^5} - 1 + 5\sin^2\theta - 5.833\sin^4\theta \qquad (12)$$

$$\mathbf{Z} = -\frac{3\alpha I}{R^6} \qquad (13)$$

The following values in eq 4 and 5 were used in our calculations: for the magnetic anisotropic calculation the length of the point dipole (S) for C–C bonds has been taken to be 75% of one-half the bond length.[31] For C–H bonds we take the point dipole to be located 0.50 Å from the carbon atom.[32] Using this value instead of one-half the bond length, the value of S for C–H bonds is automatically set at 0.375 Å. In the van der Waals calculation the static polarizability for carbon is taken as 1.019×10^{-24} cm^3 and that of hydrogens as 0.406×10^{-24} cm^3;[33] the first ionization potentials are taken as 18.03×10^{-12} erg and 20.8104×10^{-12} erg for carbon and hydrogen, respectively.[24]

We have evaluated the five unknown quantities, $\chi_L{}^{C-C}$, $\chi_T{}^{C-C}$, $\chi_L{}^{C-H}$, $\chi_T{}^{C-H}$, and B, simultaneously using the most accurate experimental data available (18 chemical shifts) and the geometries of the corresponding seven hydrocarbons as given by molecular mechanics. In addition, we have included 28 chemical shift values from ten additional hydrocarbons as an independent comparison of experimental and theoretical parameters. The shifts for the protons of a methyl group were calculated independently and later averaged. The above unknown quantities were evaluated through solution of the simultaneous equations by the least squares criteria. These parameters are shown in Table II. The results of the above calculations gave the following values: $\Delta\chi^{C-C} = 9.93 \times 10^{-6}$ cm^3/mol;[34] $\chi_L{}^{C-C} = 10.75 \times 10^{-6}$ cm^3/mol; $\chi_T{}^{C-C} = 0.82 \times 10^{-6}$ cm^3/mol; $\Delta\chi^{C-H} = 0.84 \times 10^{-6}$ cm^3/mol; $\chi_L{}^{C-H} = 8.50 \times 10^{-6}$ cm^3/mol; $\chi_T{}^{C-H} = 7.66 \times 10^{-6}$ cm^3/mol; $B = 0.27 \times 10^{-18}$ esu. Previous literature values[15,16a,b] for the C–C bond anisotropy vary from 1.31 to 11.0×10^{-6} cm^3/mol and from 0.0 to 6.80×10^{-6} cm^3/mol for the C–H value.

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(31) ApSimon[16a] has shown that the determination of bond anisotropies is not sensitive to the value of the S parameter, which, for C–C bonds, is approximately 75% of one-half the bond length.

(32) From our earlier work[25] we have found it expeditious to offset the position of the electronic cloud of the hydrogen atom in the C–H bond closer to the carbon atom by an amount equivalent to 8% of the C–H bond length. This distance is approximately 1.01 Å from the carbon atom on the average. We have therefore taken 0.5 Å or one-half of this distance to represent the position of the point dipole in this bond. ApSimon[16a] has used the values of $S^{C-C} = 0.60$ Å, $S^{C-H} = 0.25$ Å, and the position of the point dipole on the C–H bond located 0.67 Å from the carbon atom.

(33) Atomic polarizabilities (α) are calculated from the atomic refractivities (d) by the expression $\alpha = 3d/4\pi N$, where N = Avogadro's number. Atomic refractivities are from R. J. W. LeFevre, *Advan. Phys. Org. Chem.*, 3, 1 (1965).

(34) One of the referees has suggested that our value for the anisotropy of the C–C bond is in opposition to the statement by Bothner-By and Pople [*Annu. Rev. Phys. Chem.*, 16, 43 (1965)] that $\Delta\chi^{C-C}$ should not exceed a value of 4.5×10^{-6} cm^3/mol in order to be consistent with magnetic susceptibility measurements. This statement is based on the explanation of magnetic phenomena in terms of C–C anisotropy alone, and is not appropriate to the work described in the present paper.

Table II. Parameters Used in Least Squares Determination of $\chi_L{}^{C-C}$, $\chi_T{}^{C-C}$, $\chi_L{}^{C-H}$, $\chi_T{}^{C-H}$, and B

Run no.	Compound	δ[a]	Geometrical factors				
			V	W	X	Y	Z
1	Ethane, CH_3	−0.856	−0.04437	0.06441	0.00732	0.01615	−2.35870
2	Propane, CH_3	−0.906	−0.04156	0.06032	0.00737	0.01595	−2.44630
3	Propane, CH_2	−1.343	−0.07808	0.12112	0.04473	−0.04437	−2.37750
4	Isobutane, CH_3	−0.890	−0.03785	0.05442	0.00901	0.01395	−2.56630
5	Isobutane, CH	−1.740	−0.09744	0.16656	0.06202	−0.08170	−2.41570
6	Neopentane, CH_3	−0.927	−0.03326	0.04626	0.01370	0.00838	−2.71380
7	Isopentane, CH_3	−0.860	−0.03204	0.04750	0.00265	0.02010	−2.61780
8	Isopentane, $(CH_3)_2$	−0.940	−0.03316	0.04793	0.00617	0.01673	−2.65630
9	Cyclohexane, *ax*-H	−1.137	−0.03637	0.07349	−0.00326	0.00403	−2.67440
10	Cyclohexane, *eq*-H	−1.616	−0.11125	0.15075	0.08652	−0.08793	−2.39660
11	*eq*-Methylcyclohexane, CH_3	−0.920	−0.05536	0.07093	0.03617	−0.01330	−2.59490
12	1-*ax*-H	−1.317	−0.05809	0.11940	0.01869	−0.03651	−2.71930
13	2-*eq*-H	−1.683	−0.09508	0.13241	0.07624	−0.07774	−2.58010
14	2-*ax*-H	−0.867	−0.02238	0.05626	−0.01194	0.01485	−2.84000
15	3-*eq*-H	−1.717	−0.11531	0.15494	0.09518	−0.09710	−2.41510
16	3-*ax*-H	−1.200	−0.05067	0.08725	0.01840	−0.01571	−2.68330
17	4-*eq*-H	−1.667	−0.11740	0.15674	0.09791	−0.09969	−2.41110
18	4-*ax*-H	−1.100	−0.04471	0.08199	0.01014	−0.00810	−2.66750

[a] δ is the observed chemical shift of the appropriate proton(s) in parts per million downfield from tetramethylsilane (a negative value indicates downfield). **V**, **W**, **X**, **Y**, and **Z** are geometrical factors explained in the text for eq 10–13. Experimental chemical shift values are referenced in Table III.

Literature values[7b,14b,23,35] for the dispersion constant range from 0.15 to 1.35 × 10^{-18} esu, and have been evaluated primarily from intermolecular solvent effect data.

From the values computed above for the anisotropies and dispersion constant we calculate the chemical shifts for the compounds in Table III.

Discussion

In our present calculations, the magnitude of the dispersion constant (0.27 × 10^{-18} esu) ensures a large van der Waals shift for every proton (of the order of −0.50 to −0.80 ppm). It is the variable magnetic effect, however, which causes the difference observed in the chemical shifts for methyl, methylene, and methine protons.

In all previous work on the magnetic anisotropic contributions to the chemical shift, the anisotropy of the C–C bond has always been larger than that of the C–H bond by a substantial amount. Our calculations, which now include van der Waals dispersion effects, still confirm this trend. Thus, for the magnetic contribution to the chemical shift, the C–C bonds should dominate the effect and the C–C bonds closest to the proton under consideration should determine the magnitude and sign of the total magnetic shift.

Some interesting trends can be seen from the data presented in Table III. For most compounds the van der Waals contribution is the predominant term in the chemical shift for methyl protons. It is of the same order of magnitude as the magnetic contribution for methylene protons, and it is usually overshadowed by the magnetic contribution for methine protons. This result is somewhat unexpected, since much of the earlier work on the magnetic anisotropic contribution to the chemical shift was done in terms of the methyl shifts in such compounds as ethane, propane, isobutane, neopentane, etc. Our calculations indicate that the chemical shifts for these compounds are almost entirely the result of dispersion interactions.

Another interesting observation concerns the androstane isomers. The 18-methyl protons in α,α- and β,α-androstane and the 19-methyl protons in α,α- and α,β-androstane contain net magnetic contributions which *shield* the protons. The total downfield shift for these methyl groups is a result of the large van der Waals dispersion terms. On all other molecules which we have studied, the magnetic contribution to the chemical shift is deshielding.

For cyclohexane, the axial and equatorial protons have approximately the same van der Waals shift (−0.65 ppm) and the observed lower shift of the equatorial proton over that of the axial is the result of an extremely large deshielding magnetic effect for the equatorial one (δ_{mag} for the axial proton is −0.31 ppm, whereas it is −1.11 ppm for the equatorial one).

The major influence upon the δ_{mag} shielding of the axial and equatorial protons is from the C1–C2 and C1–C6 bonds which cause both protons to be shifted downfield by 0.90 ppm. This observation had previously been described by Moritz and Sheppard.[15j] It is the C2–C3 and C5–C6 bonds, however, which seem to determine the positions of these absorptions relative to each other, since the axial proton is shifted by these bonds *upfield* 0.23 ppm while the equatorial one is shifted downfield 0.37 ppm. Magnetic effects upon the axial proton are approximately the same as the van der Waals contributions, but in the equatorial case, the magnetic contributions are approximately twice as great as the van der Waals ones. These latter observations may be contrasted with the reversal of importance of these effects in the androstane series in which VDW shifts dominate. We conclude from these results that the van der Waals shifts are not at all negligible and usually predominate in these compounds.

The first 18 resonances listed in Table III are those quantities used in the least squares parameterization procedure. These resonances represent what we feel are a balance between some of the best experimental data available and a general selection of methyl, methylene, and methine shifts. The chemical shift difference between the axial and equatorial protons in cyclo-

(35) (a) T. W. Marshall and J. A. Pople, *Mol. Phys.*, 1, 199 (1958); (b) F. H. A. Rummens and H. J. Bernstein, *J. Chem. Phys.*, 43, 2971 (1965); (c) R. A. Kromhout and B. Linder, *J. Magn. Resonance*, 1, 450 (1969).

Table III. Chemical Shift Calculations[a]

Compound	δ_{mag}	δ_{VDW}	δ_{calcd}	δ_{obsd}	$\delta_{\mathrm{calcd}} - \delta_{\mathrm{obsd}}$	Ref
Ethane, CH_3[b]	−0.238	−0.617	−0.856	−0.856	0.000	15j
Propane, CH_3[b]	−0.213	−0.641	−0.854	−0.906	0.052	15j
CH_2[b]	−0.700	−0.628	−1.328	−1.343	0.015	15j
Isobutane, CH_3[b]	−0.179	−0.673	−0.852	−0.890	0.038	15j
CH[b]	−1.010	−0.645	−1.654	−1.740	0.086	15j
Neopentane, CH_3[b]	−0.139	−0.713	−0.852	−0.927	0.075	15j
Isopentane, CH_3[b]	−0.129	−0.690	−0.819	−0.860	0.041	*c, d*
$(CH_3)_2$[b]	−0.136	−0.699	−0.836	−0.940	0.104	*c, d*
Cyclohexane, *ax*-H[b]	−0.311	−0.708	−1.019	−1.137	0.118	29
eq-H[b]	−1.011	−0.634	−1.644	−1.616	−0.028	29
eq-Methylcyclohexane, CH_3[b]	−0.331	−0.681	−1.012	−0.920	−0.092	33
1-*ax*-H[b]	−0.647	−0.727	−1.374	−1.317	−0.057	*e*
2-*eq*-H[b]	−0.861	−0.683	−1.544	−1.683	0.139	*e*
2-*ax*-H[b]	−0.182	−0.753	−0.935	−0.867	−0.068	*e*
3-*eq*-H[b]	−1.067	−0.639	−1.686	−1.717	0.031	*e*
3-*ax*-H[b]	−0.437	−0.711	−1.148	−1.200	0.052	*e*
4-*eq*-H[b]	−1.065	−0.637	−1.702	−1.667	−0.035	*e*
4-*ax*-H[b]	−0.389	−0.707	−1.096	−1.100	0.004	*e*
Norbornane, bridge CH_2	−0.548	−0.647	−1.195	−1.21	0.015	30a
CH	−1.675	−0.537	−2.120	−2.20	0.080	30a
endo-H	−0.602	−0.654	−1.257	−1.18	0.077	30a
exo-H	−0.690	−0.651	−1.341	−1.49	0.149	30a
Hexamethylethane, CH_3	−0.107	−0.795	−0.902	−0.87	−0.032	15j
α,α-Androstane, 18-CH_3	0.145	−0.843	−0.697	−0.692	0.005	10b
19-CH_3	0.133	−0.900	−0.767	−0.792	0.025	10b
α,β-Androstane, 18-CH_3	−0.197	−0.774	−0.972	−0.992	0.020	10b
19-CH_3	0.121	−0.889	−0.768	−0.767	−0.001	10b
β,α-Androstane, 18-CH_3	0.167	−0.841	−0.674	−0.692	0.018	10b
19-CH_3	−0.179	−0.848	−1.027	−0.925	−0.102	10b
β,β-Androstane, 18-CH_3	−0.176	−0.774	−0.950	−0.992	0.042	10b
19-CH_3	−0.197	−0.843	−1.040	−0.900	−0.140	10b
tert-Butylcyclohexane, $(CH_3)_3$	−0.200	−0.772	−0.972	−0.852	0.122	*f*
1,3,5-*eq*-Trimethylcyclohexane						
1-*ax*-H	−0.889	−0.729	−1.617	−1.40	−0.217	21b
2-*eq*-H	−0.794	−0.727	−1.520	−1.64	0.120	21b
2-*ax*-H	−0.067	−0.812	−0.870	−0.47	−0.400	21b
CH_3	−0.360	−0.686	−1.045	−0.86	−0.185	21b
1-*ax*-3,5-*eq*-Trimethylcyclohexane						
1-*eq*-H	−1.312	−0.681	−1.993	−2.00	0.007	21b
2-*eq*-H	−0.781	−0.724	−1.505	−1.52	0.015	21b
2-*ax*-H	−0.350	−0.783	−1.134	−1.01	−0.124	21b
3-*ax*-H	−0.648	−0.776	−1.424	−1.52	0.096	21b
4-*eq*-H	−0.735	−0.727	−1.462	−1.53	0.068	21b
4-*ax*-H	−0.057	−0.813	−0.870	−0.47	−0.400	21b
1-*ax*-CH_3	−0.179	−0.731	−0.910	−0.97	0.060	21b
3,5-*eq*-CH_3	−0.344	−0.688	−1.031	−0.83	−0.201	21b
Adamantane, CH_2	−0.563	−0.729	−1.292	−1.78	0.488	*g*
CH	−1.420	−0.649	−2.069	−1.88	−0.189	*g*

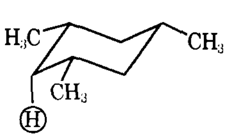
[a] A negative chemical shift refers to a position downfield from the internal standard, tetramethylsilane (in parts per million, infinite dilution). [b] Resonances used in the least-squares parameterization procedure. [c] H. Conroy, *Advan. Org. Chem.*, **2**, 265 (1960). [d] G. V. D. Tiers, "Characteristic Nuclear Magnetic Resonance (NMR) 'Shielding Values' (Spectral Positions) for Hydrogen in Organic Structures," Central Research Department, Minnesota Mining and Manufacturing Co., St. Paul, Minn., Project 737602, March 28, 1958. [e] J. D. Remijnse, H. van Bekkum, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **89**, 658 (1970). [f] W. D. Wilk, A. L. Allred, B. A. Koven, and J. A. Marshall, *J. Chem. Soc. B*, 565 (1969). [g] R. C. Fort, Jr., and P. von R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965).

hexane is calculated to be slightly larger (0.63 ppm) than the observed difference (0.47 ppm). Methylcyclohexane was included in the basis set because of some anomalous shifts observed in some other methylated cyclohexane derivatives (*vide infra*). Overall, the chemical shifts of methylcyclohexane are well reproduced. The largest error in the entire basis set (0.14 ppm) is found for the 2-equatorial proton in this compound, however.

We have found the nmr spectrum of norbornane to be a critical test in evaluating the several test parameter sets listed in Table I. Only the present method reproduces the unusual observation of almost identical shifts for the bridgehead methylene protons and the 2-endo protons. Even so, we calculate the 2-exo proton too far upfield by 0.15 ppm.

The four isomeric androstanes make interesting test compounds. The geometries of these large molecules are not entirely known experimentally, but we feel that our computed geometries are quite accurate. The 18- and 19-methyl proton shifts are well reproduced by our method, and the relative comparison of these shifts in each compound is exactly reproduced with the exception of those in β,β-androstane, in which the calculated order of absorptions is reversed. Since the 19-methyl absorption is in error by −0.14 ppm in this compound, we are not sure whether the method or some structural irregularity is responsible for the discrepancy observed in this unusual isomer.

There have been cited in the literature recently several examples of "anomalous" chemical shifts observed primarily in some methylated cyclohexanes. For example, Musher[20b] has shown that the axial protons situated between two equatorial methyl groups absorb at the unusually high field position of −0.47 ppm.



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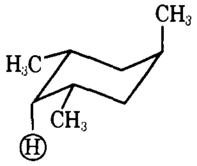
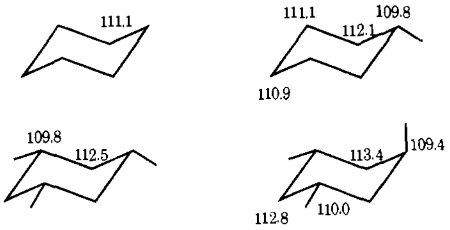


II

Our calculations place these absorptions in I and II both at −0.87 ppm, a position which is not unreasonable considering the absorption of the 2-axial proton in methylcyclohexane at −0.935 ppm. This discrepancy is apparently not just a geometrical problem. Our geometries computed for both *cis,cis*-1,3,5- and *cis,trans*-1,3,5-trimethylcyclohexane (I and II, respectively) show the cyclohexane ring only slightly flattened from that of methylcyclohexane or cyclohexane itself. Apparently the addition of the second equatorial methyl group produces a unique situation for the central axial proton which our present calculations do not deal with adequately.



Ring Angles in Some Cyclohexane Derivatives

Another problem with this same set of compounds is associated with the resonance of the equatorial methyl groups. The calculated positions of these methyls in I and II are at −1.045 and −1.031 ppm, respectively. These values, again, are quite reasonable when compared to the methyl resonance in methylcyclohexane of −1.012 ppm. Musher's observed values for these protons are −0.86 and −0.83 ppm, respectively, however.

Our calculations do throw some interesting light on one aspect of this problem. Wepster, *et al.*,[36] have suggested that the equatorial methyl proton has a considerable effect on an adjacent axial proton as witnessed by the difference in chemical shifts for the axial protons in cyclohexane (−1.137 ppm) and the 2-axial proton in methylcyclohexane (−0.867). These authors suggest an explanation for the unusual high field absorptions of the equatorial methyl groups in I and II by assuming that the effect is doubled when an axial proton is flanked by two equatorial methyl groups.

Our calculations, on the other hand, indicate that the second methyl group has very little additional effect, and instead, the decreased magnetic anisotropic effect coupled with an increased van der Waals effect results in a very little calculated difference between the methyl protons in methylcyclohexane, I, or II.

Adamantane, too, is a compound whose nmr spectrum is not satisfactorily calculated by our method, nor, insofar as we are aware, by any method. None of the variants we examined improved this situation.

Conclusions

(1) Within the framework of the McConnell approach[18] to chemical shift calculations, the inclusion of the ApSimon correction term[16a] for the non-point dipole is important for the general calculation of chemical shifts.

(2) A second effect, which we include as a van der Waals term, is also necessary and we have found Buckingham's equation for this mechanism[23] to better fit the data than the empirical one of Cheney.[21f] van der Waals effects are found to predominate in some cases and are in no way negligible.

(3) There are several sets of parameters which give essentially the same results for our basis set (ethane, propane, isobutane, neopentane, isopentane, cyclohexane, and methylcyclohexane), but only the set used in this work can reproduce the spectrum of norbornane to any acceptable degree.

(4) The anomalous spectra of *cis,cis*-1,3,5- and *cis,-trans*-1,3,5-trimethylcyclohexane, and adamantane, are not well reproduced in any of the studies which we have made, and variation of parameters does not change the situation.

We believe that the geometries used in the calculation are sufficiently accurate, and that the experimental data are valid. Using all of the data we have at hand (46 chemical shifts in 17 hydrocarbons), the largest deviation between the calculated and experimental values is 0.49 ppm, the second largest is 0.22 ppm. The standard deviation is 0.15 ppm, and the average deviation is 0.097 ppm. The errors are not just a scatter, but rather there are large errors in only a few structural types. This suggests that the theoretical equations are incomplete, and that (within the framework of the present model) a specific effect is being omitted in the calculation.

[36] See Table III, footnote *e*.