The University of Manitoba

A STUDY OF BENZENE SOLVENT-INDUCED SHIFTS IN THE PROTON MAGNETIC RESONANCE SPECTRA OF SOME SUBSTITUTED BENZENES

by

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ABSTRACT

The benzene solvent-induced shifts in the proton magnetic resonance spectra of some substituted benzenes were examined. These solvent shifts, $\Delta^{C_6H_{12}}_{C_6D_6}$, for the ring protons of a number of substituted benzene compounds were observed to be additive. That is, incremental solvent shifts can be ascribed to a ring proton which has a given spatial relationship with a substituent. These empirically derived parameters, Δ^{X}_{o}, Δ^{X}_{m}, and Δ^{X}_{p} which represent the effect of a substituent X on the solvent shift at a proton ortho, meta, or para to it, are quite useful in revealing the nature of solute - benzene solvent interactions. From linear plots of Δ^{X}_{m} and Δ^{X}_{p} versus Taft's substituent constants σ^{o}_{m} and σ^{o}_{p}, it is concluded that simple electrostatic charge effects are most important in determining both the magnitude and sign of the solvent shift. In certain cases steric effects are evident but are of secondary importance.

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CHAPTER I

INTRODUCTION

The basic theory of proton magnetic resonance has been discussed in several books (1-3).

It is known (3) that the magnetic shielding constant of a nucleus in a dissolved molecule differs from its value in the free molecule (gaseous state). For example, the applied field strength necessary to produce proton magnetic resonance at a fixed frequency in methane gas is diminished by 1.99 ppm on dissolving it in carbon disulfide (4). Thus, the observed screening constant, σ_{total}, for a particular proton of the solute molecule is the sum of a screening constant for the isolated molecule and a contribution due to the surrounding medium. If the screening constant for the isolated molecule is approximated by that measured in the gas phase at low pressure, then

$$\sigma_{total} = \sigma_{gas} + \sigma_{solvent} \qquad (I-1)$$

The screening constant, $\sigma_{solvent}$, can be written as the following sum (4):

$$\sigma_{solvent} = \sigma_b + \sigma_e + \sigma_w + \sigma_a + \sigma_c \qquad (I-2)$$

where σ_b is the contribution of the bulk magnetic susceptibility of the medium, σ_e refers to the contribution to $\sigma_{solvent}$ made by the intermolecular electric fields created by permanent or induced electric moments in the solvent molecules. Such fields are probably only of significance when the solute molecule possesses a large electric dipole moment and the solvent has a fairly large dielectric constant. σ_e is usually negative. σ_w is due to the van der Waals forces between the solute and solvent. This term is always present, though usually small and normally negative. σ_a refers to the magnetic fields at the solute nuclei arising from the magnetic anisotropy of the solvent molecules. It is generally

accepted that "rod-shaped" solvent molecules (e.g., CS_2) produce a negative σ_a; "disk-shaped" solvent molecules (e.g., benzene) produce a positive σ_a. σ_c is the shielding due to specific molecular interactions between the solvent and solute molecules.

At this point the reader is reminded that the shielding constant of a particular proton is always measured relative to that of some reference proton, most commonly the protons of tetramethylsilane (TMS). Therefore the quantity which will be referred to as σ_{total} in this thesis is actually the difference in the total shielding constant between the proton(s) of the molecule under consideration and of some reference.

Unfortunately it is usually experimentally impossible to measure σ_{gas} directly. Therefore a direct calculation of $\sigma_{solvent}$ is seldom possible. Most NMR solvent effect work has been concerned with differences in the observed shielding for a particular proton, that is, a total shielding constant of the proton is measured in solvent i , and compared with the same measurement in solvent j .

$$\Delta^{i}_{j} = \sigma^{\text{in solvent i}}_{\text{total}} - \sigma^{\text{in solvent j}}_{\text{total}} \qquad \text{(I-3)}$$

Both measurements of σ_{total} should be carried out under the same experimental conditions. For example, the concentrations of solute in each solvent should be the same and sufficiently small to approximate the chemical shifts at infinite dilution. If this condition is not met one cannot assume that solute-solute interactions are negligibly small. For a given proton of a solute molecule, equation (I-3) may be written

$$\Delta^{i}_{j} = \Delta_b + \Delta_e + \Delta_w + \Delta_a + \Delta_c \qquad \text{(I-4)}$$

where $\Delta_b = \sigma_b^{\text{in solvent i}} - \sigma_b^{\text{in solvent j}}$, etc.

In the remainder of this thesis, solvent i will be referred to as a reference solvent. The properties of the ideal inert reference solvent have been discussed by Laszlo (5). It has been concluded that cyclohexane, n-hexane, neopentane, and tetramethylsilane ought to be preferred to carbon tetrachloride as inert solvents (5,6). Furthermore, the use of carbon disulfide , chloroform, or deuterochloroform as inert solvents is not recommended. $\Delta^{\text{inert reference solvent}}_{\text{aromatic solvent}}$ values are often referred to as "aromatic solvent induced shifts", abbreviated as ASIS.

By making the proper choice of solvents and by using an internal reference one can approximately eliminate certain terms in equation (I-4). In this particular study, $\Delta^{\text{cyclohexane}}_{\text{benzene}}$ values for ring protons of numerous substituted benzenes have been obtained. For this pair of solvents it will be shown that

$$\Delta^{\text{cyclohexane}}_{\text{benzene}} \simeq \Delta_a + \Delta_c \qquad \text{(I-5)}$$

if an internal reference is used.

Before discussing the terms of equation (I-2) further, the history and applications of ASIS will be briefly mentioned. Also, the purpose of this thesis will be mentioned.

In 1957, Bothner-By and Glick (7) and Zimmerman and Foster (8) first showed that an environment of aromatic molecules tends to lead to an increased solute screening constant whose magnitude varies widely from one solute to another. It is now accepted that these high field shifts arise predominantly from the large diamagnetic anisotropy of aromatic solvent molecules (9), which in turn owes its origin to the

relatively free circulation of π-electrons in the molecular plane induced by a magnetic field (10). Early work pertaining to ASIS has been discussed by Pople, Schneider, and Bernstein (11) and by Emsley, Feeney, and Sutcliffe (3). More recently, solvent effects in proton magnetic resonance have been reviewed by Laszlo (5) and by Ronayne and Williams (9).

Benzene solvent-induced shifts have been used as an aid in the simplification of complex NMR spectra, in structural elucidation, and in stereochemical studies. Only a few examples will be cited here; the reader is referred elsewhere for discussions of the applications of ASIS (5, 9, 12).

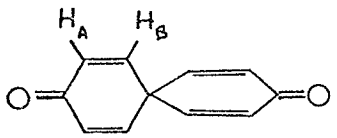
Sometimes the nuclear resonances for two types of nuclei in the same molecule, which are not isochronous by symmetry, will accidentally display the same chemical shift. This apparent degeneracy can often be removed by recourse to solvent effects. For example, the two different types of protons in the spiro molecule (I) appear isochronous in carbon tetrachloride, deuterochloroform, or trifluoroacetic acid solution, whereas they become nonequivalent in benzene (13).

Schaefer and Schneider have utilized ASIS to determine the relative signs of the cis and trans coupling constants in vinyl bromide (14).

By measuring the ASIS for a large variety of monocyclic and polycyclic ketones, Connolly and McCrindle (15, 16) have established that in the case of an isolated carbonyl group, the benzene-induced solvent shift ($\Delta^{CCl_4}_{C_6H_6}$ or $\Delta^{CDCl_3}_{C_6H_6}$) will be positive for protons lying behind a plane drawn through the carbonyl carbon atom and perpendicular to the

TABLE I

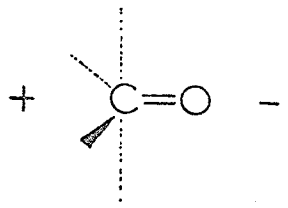
Solvent Shifts for the Protons of Molecule:



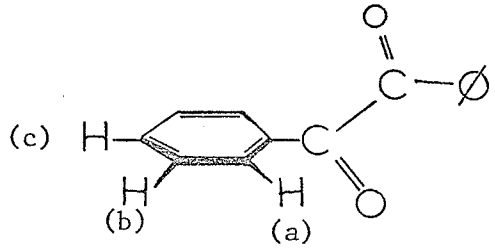
I

SOLVENT	H_A (ppm)	H_B (ppm)
CCl_4	6.42	6.42
$CDCl_3$	6.48	6.48
CFCOOH	6.80	6.80
C_6H_6	5.49	6.07

direction of the C-O bond (II); protons lying in front of the plane will have a negative shift, and protons lying very near, or in the reference plane will have a small or zero shift. For example, consider benzil (see III) (17).



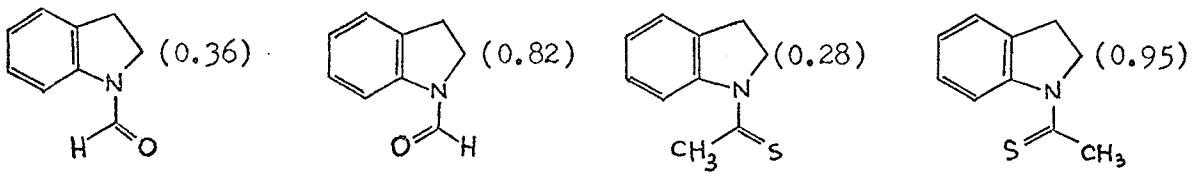
II



III

The ortho-protons (a) must be almost in front of the carbonyl group as the ASIS is only +0.01 ppm. The other protons have the same ASIS (+0.50 ppm) and cannot be distinguished by this method. The "carbonyl plane rule" has found wide applicability in the field of structure elucidation (18, 19).

In benzene solutions of amides it has been demonstrated that the substituent proton trans to the oxygen is shielded to a greater extent than the substituent cis to the oxygen (9). The ASIS of the 2-CH_2 protons of some N-formyl and N-thioacetylindolenes allows one to distinguish between conformational isomers (see IV - VII; the solvent shifts $\Delta^{CDCl_3}_{C_6H_6}$ are shown in parentheses) (20).



IV V VI VII

In using the solvents benzene and cyclohexane with an internal reference, one might expect no net ASIS due to the Δ_a term in equation (I-4), since the reference protons should experience the same differential shielding, Δ_a, as the solute protons. However, the space and time-averaged magnetic environment experienced by the solute molecules, due to the magnetic anisotropy of the benzene solvent molecules, will be different from that experienced by the TMS internal reference molecules. Specific interactions between the solute and solvent molecules are thought to lead to this difference (21). The main purpose of this thesis is to investigate further the nature of these specific interactions in a series of substituted benzenes. In particular, the effect of the size, shape, and electronic properties of the substituent groups on the ASIS of the ring protons will be of interest. Any correlations between substituent properties and the ASIS would be of empirical use

in structure determinations by NMR and may also serve as a guide to an eventual theoretical elucidation of the observed effects.

CHAPTER II

THE SHIELDING CONSTANT, $\sigma_{solvent}$

A. INTRODUCTION

The understanding of the shielding constant, $\sigma_{solvent}$, is facilitated by the following somewhat arbitrary breakdown,

$$\sigma_{solvent} = \sigma_b + \sigma_e + \sigma_w + \sigma_a + \sigma_c \qquad (I\text{-}2)$$

In this chapter the origin of the first four terms of equation (I-2) will be discussed briefly, but pertinent references will be given. The magnitude of some of the terms in equation (I-4), where i = cyclohexane, and j = benzene, will also be discussed.

$$\Delta^i_j = \Delta_b + \Delta_e + \Delta_w + \Delta_a + \Delta_c \qquad (I\text{-}4)$$

The specific solute-solvent interaction, σ_c, will be dealt with separately in the following chapter.

B. THE BULK SUSCEPTIBILITY TERM, σ_b

For a diamagnetic substance, the magnetization per unit volume induced by a magnetic field, H , is $\underline{M} = \chi_v \underline{H}$, where χ_v is a proportionality factor called the magnetic susceptibility per unit volume. The magnitude of χ_v is dependent on the particular material.

If an internal reference substance is used, no correction is necessary because the solute and reference molecules both experience the bulk susceptibility of the solution. Thus the σ_b term in equation (I-2) is zero.

However, if an external reference is used, χ_v (solute + solvent) $\neq$ χ_v (external reference). Therefore, the magnetic field experienced by a molecule in the sample will be slightly different from that experienced by a molecule in the reference. It can be shown that for a cylindrical sample (4),

$$\sigma \text{ total (corrected for bulk susceptibility)} = \sigma \text{ total (observed)} + \frac{2\pi}{3} \Delta\chi \qquad \text{(II-1)}$$

where $\Delta\chi = \chi_{\text{solvent}} - \chi_{\text{reference}}$.

Lussan has pointed out that if the chemical shifts are desired within 10^{-2} ppm, the values of the susceptibilities ought to be determined with a comparable absolute precision, which implies better than 0.25 % relative accuracy (22). Since it is difficult to obtain accuracies of better than 2 %, it is preferable to use internal referencing provided one carefully checks that the chosen

reference does not interact with the solvent (5).

In this particular study the TMS reference certainly experiences a solvent shift on going from cyclohexane to benzene as solvent. However, it is probably valid to assume that $\Delta^{C_6H_{12}}_{C_6D_6}$ is a constant for TMS in each solution studied, since solute-reference interactions would be very small and approximately constant. In the opinion of the author, external referencing would be more meaningful if proper bulk susceptibility corrections could be made.

C. THE REACTION FIELD TERM, σ_R

For polar solutes, large solvent shifts can often be attributed chiefly to the effect of the reaction field. When a polar solute molecule is dissolved in a polar or polarizable solvent, it polarizes the surrounding medium. This polarization leads to a secondary electric field, the "reaction field", which in turn modifies the electron distribution of the solute. If the solute molecule is sufficiently symmetrical, the mean reaction field is parallel and proportional to its dipole moment.

Buckingham has developed a theory based on the Onsager model (23) to account for the effect of the reaction field on chemical shifts. In this treatment the entire solute molecule is represented by a point dipole at the centre of a sperical cavity of radius r , surrounded by an isotropic, homogeneous, continuous medium with uniform dielectric constant ε . The reaction field, $\underline{R}$,is

$$\underline{R} = \frac{2(\varepsilon-1)}{2\varepsilon+1} \cdot \frac{\underline{m}}{r^3} \qquad \text{(II-2)}$$

where $\underline{m} = \mu + \alpha\underline{R}$ is the total dipole moment of the solute in the medium. The polarizability of a sphere, as given by the Clausius-Mossotti equation, is

$$\alpha = \frac{n^2-1}{n^2+2} \cdot r^3 \qquad \text{(II-3)}$$

where n is the refractive index of the pure solute (as a liquid or solid) for the Na - D line. Solving for $\underline{R}$ and simplifying gives

$$\underline{R} = Z(\varepsilon)(n^2 - 1) \cdot \frac{\mu}{\alpha} \qquad \text{(II-4)}$$

where $Z(\varepsilon)=2(\varepsilon-1)/3(2\varepsilon+n^2)$. For most solutes $n \sim 1.5$ and equation (II-4) reduces to

$$\underline{R} = \frac{\varepsilon - 1}{2\varepsilon + 2.5} \cdot \frac{\mu}{\alpha} \qquad \text{(II-5)}$$

Marshall and Pople (24) and Buckingham (23) have shown that the magnetic shielding of a particular nucleus should depend upon the component of the local electric field along the X - H bond direction. That is,

$$\sigma_e = - AE \cos\theta - BE^2 \qquad \text{(II-6)}$$

where $E \cos\theta$ is the projection of the local electric field, E, on the bond direction, and A and B are constants characteristic of the X - H covalent bond (for C - H bonds, $A \sim 2 \times 10^{-12}$ cm^2/e.s.u., and $B \sim 10^{-18}$ cm^4/(e.s.u.)^2).

Equations (II-5) and (II-6) yield a contribution to the shielding of the X - H proton due to the reaction field $\underline{R}$ of

$$\sigma_e = - \frac{2}{3} A Z(\varepsilon)(n^2 - 1)\frac{\mu}{\alpha} \cos\theta \qquad \text{(II-7)}$$

Since the E^2 term can be neglected, the observed chemical shift of a given solute is expected to correlate linearly with $Z(\varepsilon)$ with a slope of $-\frac{2}{3} A(n^2-1)\mu \cos\theta/\alpha$.

In order to take into account the shape of the solute molecule, Diehl and Freeman described a model based on an ellipsoidal cavity and showed that

$$\sigma_e = -A\frac{3\mu}{abc} \cdot \cos\theta\, \xi_a \left[1+(n^2+1)\xi_a\right] \frac{\varepsilon - 1}{\varepsilon + \beta} \qquad \text{(II-8)}$$

where $\beta = n^2 \xi_a / (1-\xi_a)$, ξ_a is a shape factor, and a,b, and c are the ellipsoidal semi-axes.

In the presence of two equal and opposed bond dipoles a quadrupolar reaction field may arise. The reaction field gradient of a quadrupolar moment, R' , is given by (23)

$$R' = \left[6(\varepsilon-1) / (3\varepsilon+2)\right] r^{-5} \Phi \qquad \text{(II-9)}$$

where Φ is the molecular quadrupole moment. For a molecule with two opposed dipoles of moment, μ , separated by a distance, d , $\Phi = 2d$. The magnitude of r^{-5} is readily obtained if the assumption is made that the molecule is spherical and completely fills the Onsager cavity.

The difficulty in obtaining the reaction field shift and testing the validity of the above model often lies in correcting for other factors which contribute to the total solvent shift.

The experimental results of several works have been reviewed by Laszlo (5) and Ronayne and Williams (9). Laszlo concludes that all experiments converge towards the idea that the reaction field exists and is apparent in NMR shifts. Also, he concludes that it is much more specific an effect than expected from the simple theory (II-7).

Many of the reported correlations of σ versus $Z(\varepsilon)$ exhibit considerable curvature as ε increases (9). Recently, Schaefer and Macdonald have suggested that this curvature may be the result of specific solute-solvent interactions in solvents of higher dielectric constant (25).

Kuntz and Johnson have proposed that most, if not all, the

"polar solvent effects" can be treated by specific interaction models where the lifetime of the complex is very short - of the order of the collision times in liquids (10^{-11} sec). The "ordering" of the liquid associated with the interactions is thought to be both short term and short range (nearest neighbour) (26).

Similarly, Goldstein and coworkers have found the Onsager model unsatisfactory for solvents of high dielectric constant (27). On the basis of a two-body interaction the influence of "polar effects" on chemical shifts was satisfactorily calculated using a virial-type expression involving a Stockmayer intermolecular potential energy.

On the assumption that σ_e is given by equation (II-7), it can easily be shown that σ_e is small in this particular study. The dielectric constants of benzene and cyclohexane are 2.284 (20° C) and 2.023 (20° C), respectively. Considering chlorobenzene as solute, $\mu = 1.60 \times 10^{-18}$ e.s.u.-cm, $n_D = 1.5248$, and $\alpha = 84.0$ cm^3. Substituting the appropriate values into equation (II-4), one obtains a reaction field of 6.71×10^3 e.s.u./cm^2 in benzene and 5.68×10^3 e.s.u./cm^2 in cyclohexane. Taking $\cos\theta = +1$, and $A = -2 \times 10^{-12}$ cm^2/e.s.u., the reaction field chemical shift of chlorobenzene is $\sigma_e = -0.0134$ ppm in benzene and -0.0114 ppm in cyclohexane. Thus $\sigma_e \simeq 0.002$ ppm for chlorobenzene.

D. THE VAN DER WAALS TERM, σ_w

For simple non-polar organic compounds, a change from the gaseous to the liquid state is accompanied by a shift to low field in excess of that calculated using the classical bulk susceptibility correction (4). For a symmetrical non-polar molecule such as methane, this low field shift is attributed to van der Waals interactions (dispersion forces).

In an early attempt to illustrate the effect of dispersion forces, Buckingham et al. obtained a fairly linear plot of the proton resonance shift of methane in dilute solution in various "inert" solvents against the heat of vaporization of the solvent at the boiling point (4).

Although the heat of vaporization is a measure of the interaction between like solvent molecules, a close proportionality of the corresponding interaction of the solvent molecules with the common solute molecule, CH_4, may be expected if the interactions are of the simple van der Waals type.

The mechanism of the shielding change due to van der Waals interactions is understood at the present time as involving a fluctuating electric field originating in the solvent molecule (28). Although the average magnitude of this field is zero over a period of time, the time-average value of its square is nonzero. This causes an expansion of the electron cloud of the solute proton and therefore a reduction in the shielding (which outweighs the increase in shielding caused by contraction of the cloud due to repulsive forces).

Raynes, Buckingham, and Bernstein have developed a semi-empirical statistical method which has been applied successfully in the cases of gases (binary collisions only) and gaseous solutions (29).

Linder, Howard, and Emerson have attempted to calculate σ_w by extending the Onsager continuum model to non-polar molecules (30, 31). In this model, one molecule is singled out and treated explicitly while the others are replaced by a uniform dielectric medium.

Consider the "centre" molecule to have a moment $\underline{M}$ with a frequency of oscillation ν_i (denoted $\underline{M}(\nu_i)$). This moment gives rise to an electric field at a distance r_K from the centre, which may be written,

$$\underline{E}_K = (3\underline{M}(\nu_i)\cdot r_K/r_K^5)\ \underline{r}_K - \underline{M}(\nu_i)/r_K^3 \qquad \text{(II-10)}$$

This field will fluctuate with the same frequency as $\underline{M}(\nu_i)$ and induces a moment in each molecule of the dielectric. For the K^{th} molecule the moment is

$$M_K = \alpha_K^* E_K \qquad \text{(II-11)}$$

where the asterisk serves to indicate that the polarizability is not static. Each moment $\underline{M}_K$ gives rise to a field $\underline{E}_K'$ at the centre of the Onsager cavity. This resultant field, $\sum_K \underline{E}_n'$, is the analogue of the reaction field of a dipole. It can be shown that this electric field is equivalent to

$$E^2 = \frac{3}{4} hg \frac{\nu_1 \nu_2}{\nu_1 + \nu_2} \qquad \text{(II-12)}$$

From equation (II-6), the shift due to the dispersion effect is

$$\sigma_w = \frac{3}{4} Bhg \frac{\nu_1 \nu_2}{\nu_1 + \nu_2} \qquad \text{(II-13)}$$

where $$g = \left[(2n^2-2) \,/\, (2n^2+1) \right] / r^3, \qquad \text{(II-14)}$$

n is the refractive index of the solvent, and r the radius of the solute which can be deduced from its molar volume; h is Planck's constant. A mean absorption frequency, ν , (the subscripts 1 and 2 refer respectively to solvent and solute) can be calculated from the relations

$$\nu = I / h \qquad \text{(II-15)}$$

where I is the ionization potential, or from

$$\nu = - \frac{4m_e c^2}{hN\alpha} \cdot \chi_M \qquad \text{(II-16)}$$

where α is the polarizability and χ_M is the molar diamagnetic susceptibility; m_e is the mass of the electron, and c is the velocity of light.

Lumbroso, Wu, and Dailey have used the above model to calculate the gas to solvent chemical shifts for six non-polar molecules in a range of solvents (32). The calculated shifts are much too small.

De Montgolfier (33) has attempted to improve the model of Linder et al.

The calculated σ_w shifts using the above models are invariably too small by a factor ranging from 2 to 10. Also, these models do not distinguish between the solvent effects for chemically different protons in the solute. By treating the solute's environment as consisting of a discrete number of solvent molecules, Rummens, Raynes, and Bernstein have presented a "binary collision gas" model, as well as a "cage" model for estimating σ_w (34). To account for the different van der Waals

shifts of the peripheral CH_3 groups and inner CH_2 groups of $Si(CH_2CH_3)_4$ in various solvents, a site-factor correction was introduced. Although good results were obtained for the compounds $X(CH_3)_4$, where X = C, Si, Ge, Sn, and Pb, the theory is really only valid for small molecules.

Raynes and Raza have found that there is no simple proportionality between observed σ_w values and the solvent molecule's polarizability (28). They concluded that σ_w is caused mainly by localized interactions since it has an r^{-6} dependence.

Kromhout and Linder have attempted to calculate σ_w using quantum mechanical perturbation theory and standard statistical averaging procedures (35). The theory was developed for closed shell atoms and crude modifications are introduced to permit application to CH_4 and CF_4. The agreement between observed and calculated σ_w values for these two molecules is only fair.

Since all calculations of σ_w have been concerned with non-polar solutes in non-polar solvents, it is difficult to estimate Δ_w for substituted benzenes in the solvents benzene and cyclohexane. However it is expected that Δ_w can be neglected in this study (36).

Hutton, Bock, and Schaefer have obtained a linear plot of the Si-F coupling constants in SiF_4 versus the heat of vaporization, H_b, of the solvent at its boiling point (37). From this plot it was concluded that the solvent dependence of the coupling in SiF_4 arises from dispersion interactions. The value of the Si-F coupling was the same in C_6H_{12} and C_6H_6 suggesting that the dispersion interaction of the solute with these two solvents was the same.

Using equation (II-13) Homer calculated the contribution to

the shielding constant of TMS arising from dispersion interactions (38). The value for benzene as solvent differed from the value for cyclohexane as solvent by only 0.005 ppm.

E. THE ANISOTROPY TERM, σ_a

The large high-field shifts commonly observed between non-polar solutes in aromatic and non-aromatic "inert" solvents can be attributed mainly to σ_a. Becconsal (39) has measured the chemical shifts of the solutes methane, cyclohexane, and tetramethylsilane relative to an external reference in the solvents benzene and carbon tetrachloride. All shifts were measured in dilute solutions (all below 0.1% w/w). The experimental σ_a values given in Table II are $\sigma_{loc}(C_6H_6) - \sigma_{loc}(CCl_4)$ values, where σ_{loc} values have been corrected only for bulk susceptibilities. Thus contributions from electric fields, van der Waals effects, and molecular association have been neglected.

TABLE II

Experimental Anisotropic Benzene Solvent Shifts

SOLUTE	EXPERIMENTAL σ_a (ppm)
Methane	0.536
Cyclohexane	0.490
Tetramethylsilane	0.452

This assumption is probably valid so that σ_a is correct to within $\pm$ 0.010 ppm. In this section a few of the models which have been directed at obtaining the magnitude of σ_a will be mentioned.

The magnetic anisotropy of the benzene molecule is well known and has been reviewed (2). The benzene rings have large induced magnetic moments only when the ring is at right angles to the field. It is this

induced magnetic field (illustrated in Figure 1 below) which leads to the deshielding of the ring protons of benzene relative to the ethylenic protons of cyclohexadiene-1,3. By assuming this ring current shift to be 1.50 ppm, Johnson and Bovey (40) have calculated the "isoshielding" lines shown in Figure 2.

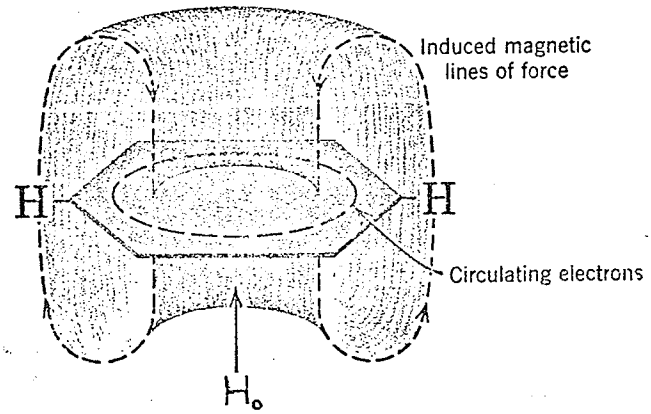


Figure 1. Ring current effects in benzene .

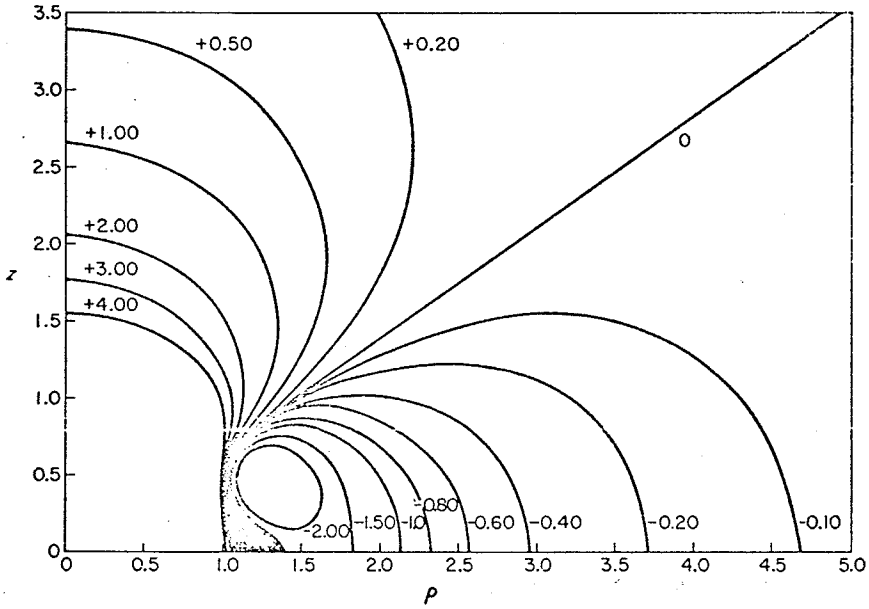
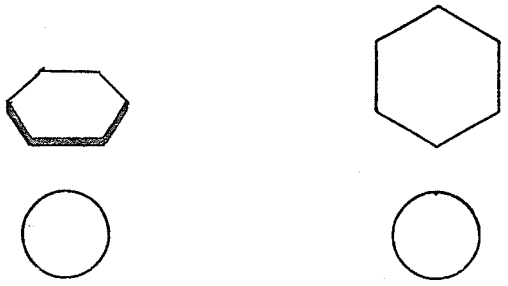


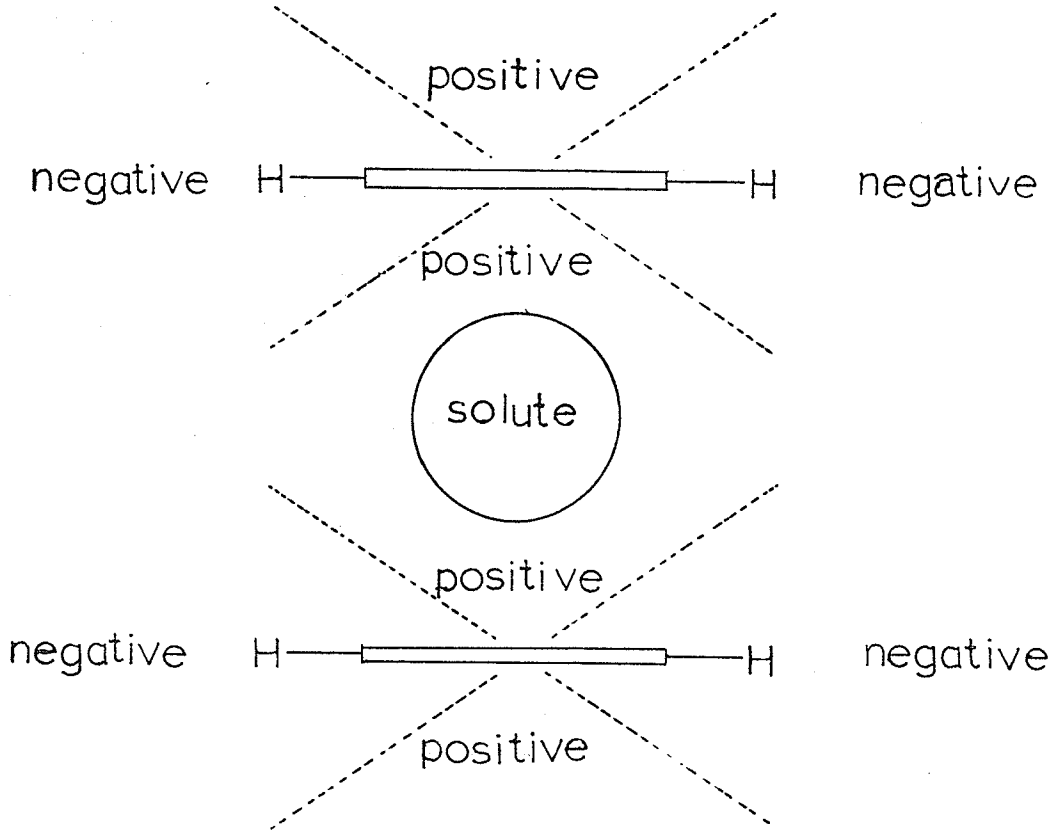
Figure 2. Effect on the chemical shifts of a nucleus at various positions due to the ring current of benzene. The plot represents one quadrant of a plane passing normally through the centre of the ring, which lies horizontally. A positive sign denotes an upfield contribution to the chemical shift; ρ and Z are in units of the benzene C-C distance, 1.39 Å.

High-field benzene solvent-induced shifts can be qualitatively explained as follows. In the absence of any specific solute-solvent interactions, a benzene molecule can approach solute molecules more closely along the benzene six-fold axis than in its molecular plane. Thus a configuration of the type VIII would be expected to be the preferred time-averaged orientation of benzene and solute as opposed to configuration IX.



VIII IX

It can be shown that to a first approximation the magnitude of the secondary magnetic field at distance R from the point (0,0) of Figure 2, varies approximately as the inverse third power of R (4). Because of the R^{-3} dependence, high-field benzene solvent-induced shifts can be "rationalized" by the importance of interactions of the type shown in (X). Notice that the solute molecule is shielded, thus "explaining" the relative sign of the observed σ_a values given in Table I.



X

From a statistical mechanical calculation in which the solute molecule is treated as a point, Stephen (41) and Buckingham et al. (4) obtained

$$\sigma_a = -n\left[(\chi_{\parallel} - \chi_{\perp})/3R^3 \right] \left[3 \cos^2\theta - 1 \right] \qquad \text{(II-16)}$$

where R is the magnitude of the vector between the origin of the solvent molecule (benzene) and the solute molecule,

θ is the angle between $\underline{R}$ and the axis of the solvent molecules,

$\chi_{\parallel}$ is the magnetic susceptibility along the principal axis of the solvent molecule; $\chi_{\perp}$ is the value perpendicular to it, and

n is the number of molecules in the relevant range of R.

Using equation (II-16), Buckingham, Schaefer, and Schneider calculated σ_a = 1.3 ppm for methane dissolved in benzene (4). In this calculation the following assumptions were made: $(\chi_{\parallel} - \chi_{\perp}) = 9 \times 10^{-29}$ erg gauss^{-2}, $n \sim 2$, and R = 4.5 Å.

Abraham (42) has considered the anisotropic solvent molecule as a cylinder of effective radius r(Å) and height 2h(Å) with different magnetic susceptibilities $\chi_{\parallel}$ and $\chi_{\perp}$ along and perpendicular to the axis of the cylinder. The resulting equation is

$$\sigma_a = 10^{30} \times \frac{2}{3} (\chi_{\perp} - \chi_{\parallel}) \frac{r + h}{(r + 2h)(r^2 + h^2)^{3/2}} \qquad \text{(II-17)}$$

Unfortunately this equation only provides an estimate of the shielding from a single anisotropic molecule, thus making a comparison of observed and calculated values difficult.

Schug (43) has presented a similar model, which accounts for all anisotropic molecules in the solution, rather than nearest neighbours only. The calculation is based on the assumption of complete randomness in the liquid state. The result is

$$\sigma_a = \left(\frac{2\pi}{3}\right)\left(\frac{\Delta\chi}{V}\right) \frac{\left[\sqrt{2}\,(4r^2 + h^2)^{\frac{1}{2}} - 2h\right]}{(4r^2 + h^2)^{\frac{1}{2}}} \qquad \text{(II-18)}$$

where $\Delta\chi$, r, and h are defined in the same way by Schug and Abraham. V is the molar volume. Using the following parameters for benzene: $\Delta\chi = 8.16 \times 10^{-29}$ erg gauss^{-2}, r = 4.3 Å, h = 4.8 Å, and V = 147.7 Å^3; Schug calculated a high field shift of 0.5 ppm for a solute in benzene. This is in good agreement with the values in Table I.

Recently, Becconsal (39) has derived expressions for calculating solvent anisotropy shifts (σ_a) for non-polar spherical solute molecules. The most important points resulting from this model are:

1. As a result of random tumbling, the anisotropy contribution, σ_a, to the nuclear screening is independent of the position of the nucleus within the solute molecule, being equal to that calculated for a nucleus at the centre of the molecule.
2. $|\sigma_a|$ decreases with increasing solute molecular radius.

The expressions obtained for σ_a are cumbersome. Observed results for the solutes of Table I are about one half the predicted value.

By using an internal reference in the present study one may expect the solute molecule (a substituted benzene) and the reference (TMS) to experience approximately the same σ_a. The term $\sigma_{solvent}$ of substituted benzene would be approximately zero in both solvents benzene and cyclohexane, and therefore $\Delta^{C_6H_{12}}_{C_6D_6} \simeq 0.00$ ppm. However this would be the case only if the orientation of solvent molecules surrounding the solute and reference molecules were completely random (i.e. no specific interactions). Since solvent shifts, $\Delta^{C_6H_{12}}_{C_6D_6}$ values, of between -0.25 and 1.03 ppm have been observed in the present study, it is concluded that solvent shifts arise from non-random orientations of the benzene solvent molecules in the vicinity of the solute. This non-random orientation of the benzene solvent molecules has been attributed to specific solute-solvent interactions. Different hypotheses concerning the nature of this interaction will be discussed in the following chapter.

CHAPTER III

SPECIFIC INTERACTIONS: σ_c

A. INTRODUCTION

Some type of specific interaction, σ_c, must be postulated to rationalize observed aromatic solvent induced shifts. Although the mechanism of this interaction is not well understood several useful empirical correlations between solute properties and ASIS exist (5, 9). The purpose of this chapter is to point out some of these correlations. Also an attempt will be made to show that the simplest model commonly used to interpret ASIS, the 1:1 complex, is obsolete. This chapter is not intended to be a comprehensive review of the specific interaction term.

B. CORRELATIONS

1. Correlation of the ASIS with the Solute Dipole Moment

Schneider (21) obtained a linear plot of μ/V versus ASIS, where μ is the dipole moment and V is the molecular volume of various solutes used (see Figure 3). Modest deviations in this plot probably reflect poor estimates of the quantity V. The large ASIS for chloroform is attributed to hydrogen bonding with the aromatic π-electrons.

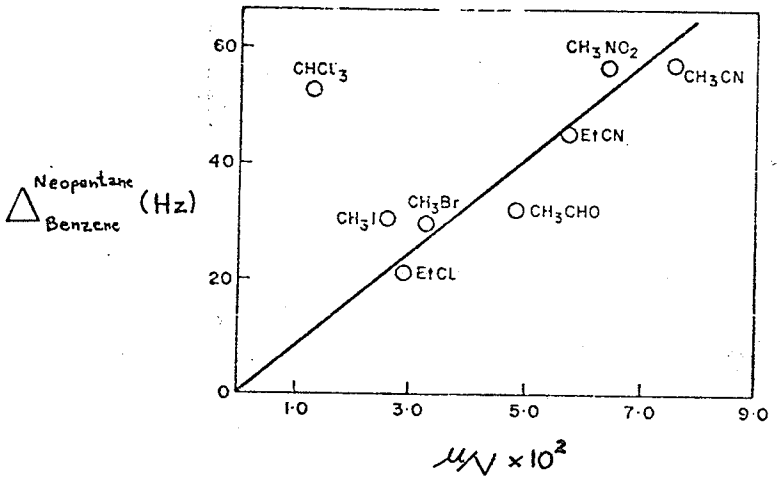


Figure 3. Plot of proton solvent shifts versus μ/V (From Schneider (21)).

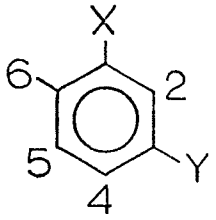
Brown and Stark (44) have shown that the dipole moments of organometallic compounds of the type $(CH_3)_nSnX_{4-n}$ (X=Cl, Br, and I), can be fairly accurately determined from the solvent shift (ASIS) of the methyl protons.

Diehl (45) has correlated the ASIS at the meta position of substituted benzenes with the substituent dipole moment, the slope being -0.14 ppm/Debye.

2. Additivity of ASIS

Diehl has demonstrated the additivity of ASIS for disubstituted

benzenes (46). Additivity implies that in a substituted benzene derivative, the ASIS of a given proton is a linear superposition of contributions from the individual substituents, X. Let Δ_i^X represent the contribution of substituent X to the total ASIS, Δ, for a proton in position i relative to substituent X (i = ortho, meta, or para). For example, in the case of a 1,3-disubstituted benzene (XI), the solvent shifts (relative to an internal reference) for the protons 2 and 4 are:



XI

$$\Delta(H_2) = \Delta_o^X + \Delta_o^Y \qquad \text{(III-1)}$$

$$\Delta(H_4) = \Delta_p^X + \Delta_o^Y \qquad \text{(III-2)}$$

$$\Delta(H_5) = \Delta_m^X + \Delta_m^Y \qquad \text{(III-3)}$$

The values of the parameters Δ_i^X which Diehl calculated from his experimental results are given in Table III.

TABLE III

Incremental ASIS in the Benzene Series (Hz at 60 MHz)

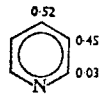
SUBSTITUENT X	Δ_o^X	Δ_m^X	Δ_p^X
NH_2	4.2	-6.0	
OH^2	9.6	6.0	
OMe	-4.2	-3.0	-4.2
F	3.6	13.8	
Me	-1.2	-3.0	
Cl	5.4	15.6	15.6
Br	5.4	16.2	16.2
I	5.4	5.4	
CN	22.2	31.8	
NO_2	15.6	36.6	

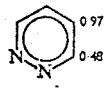
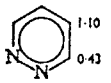
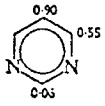
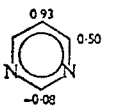
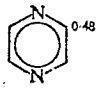
Using these values, one calculates the following ASIS for 1-nitro-3-chlorobenzene: 21.0 (H_2); 52.2 (H_5); 31.2 (H_6). The

observed values are: 18.30 (H_2); 50.40 (H_5); and 30.00 (H_6). Deviations from additivity occur however, when substituents are accumulated in adjacent positions, as in 1,2-dichlorobenzene and 1,2,3-trichlorobenzene.

Laszlo and Soong (47) have discussed the additivity of ASIS for the cyclazines. Consider Table IV.

TABLE IV OBSERVED AND CALCULATED VALUES OF THE ASIS FOR THE CYCLAZINES



Calculated	Observed	Deviations
		+0.13
		−0.05
		+0.03
		−0.05
		−0.14
		+0.02

Additivity of solvent shifts has also been reported in the steroid series (5, 12). For instance, Williams and Bhacca have demonstrated that under certain conditions, increments can be assigned for the ASIS due to the introduction of a carbonyl group in various positions of the steroidal framework. The agreement between observed and calculated ASIS is good.

3. Other Correlations

Diehl has shown that the ASIS in m- and p- positions of benzene derivatives are proportional to the Hammett Parameters of the substituents in question (46). From a plot of the Hammett parameter $\sigma_I + \frac{1}{2}\sigma_R$ vs. Δ^X_m;

a slope of 0.74 ppm/Hammett unit was obtained.

Bowie, Ronayne, and Williams (48) have tried to show that the solvent shift ($\Delta^{CCl_4}_{C_6H_6}$) for the methoxyl resonance of para substituted anisole derivatives (X= NO_2, COMe, CNO, Br, SMe, H, Me, OMe, NH_2, NMe_2) depends on the polarity of the solute molecule. They plotted Δ vs. σ_p as well as Δ vs. dipole moment of solute. These plots are certainly not linear but they indicate that Δ is related to some "electronic" property of X. Similar plots have been attempted for ortho and meta substituted anisoles (49).

Schwenk (36) has found that benzene solvent shifts ($\Delta^{C_6H_{12}}_{C_6H_6}$) for ring protons in polyhalobenzene derivatives correlate well with μ/r functions. μ is the dipole moment of, and r is the C-X bond length in, the phenyl halides. The following halogen-substituent solvent shift parameters, Δ_o^X, Δ_m^X, and Δ_p^X were derived from plots of $F(\mu/r)$ vs. $\Delta^{C_6H_{12}}_{C_6D_6}$ (Table V).

TABLE V

ASIS Parameters For Polyhalobenzenes
(Hz at 60 MHz)

HALOGEN	Δ_o	Δ_m	Δ_p
F	12.72	6.36	0
Cl	10.38	5.22	0
Br	9.36	4.68	0
I	7.56	3.78	0

After the addition of a stacking parameter, Δ', (which is the $\Delta^{C_6H_{12}}_{C_6D_6}$ value for benzene as solute), the solvent shift for a

polyhalobenzene with no ortho hydrogens was calculated using the following equation

$$\Delta^{C_6H_{12}}_{C_6D_6} = \sum_{o} \Delta_o + \sum_{m} \Delta_m + \Delta' \qquad \text{(III-4)}$$

For example, consider the ASIS of H_4 in 3,5-dichlorobenzene. One calculated $\Delta(H_4) = 0.173 + 0.173 + 0.062 = 0.408$ ppm. The observed value of $\Delta(H_4)$ is 0.393 ppm.

C. THE MECHANISM OF BENZENE-INDUCED SOLVENT SHIFTS

The nature of the specific interactions, σ_c, has been widely discussed (5, 9). The simplest and most convenient model posits a 1:1 association between solvent and solute molecules. The validity of the model may be considered in terms of the following points: 1. the nature of the interaction (the relative orientation of solute and solvent molecules in the postulated complex), 2. the stoichiometry of the interaction, and 3. the strength of the collision complex. Each of these points is discussed briefly in this section.

1. The Nature of the Interaction

For polar alkyl and vinyl derivatives as solutes, the magnitude of $\Delta^{\text{neopentane}}_{\text{benzene}}$ evidently depends on the magnitude of the molecular dipole moment as well as on the molecular volume (Figure 3). Schneider (21) interpreted these results in terms of a dipole-induced dipole interaction, leading to the solute-solvent orientation depicted for acetonitrile (Figure 4). This model seems reasonable because benzene is more polarizable in the molecular plane than normal to it ($\alpha_\perp$ =6.35 Å^3, $\alpha_\parallel$ = 12.3 Å^3) (44); further, a close approach to the solute molecules can be made in this configuration. In the orientation shown below, the methyl group is shielded by the ring currents of benzene, thus the large positive Δ value of 0.94 ppm is accounted for. Also, notice that the benzene solvent molecules lie relatively far from the region of high electron density in acetonitrile.

Using this model, Schneider was unable to account for:

1. $\Delta^{C_6H_{12}}_{C_6D_6}$ for the ring protons of the non-dipolar solute, p-benzoquinone, is 0.50 ppm;
2. $\Delta^{C_6H_{12}}_{C_6D_6}$ values for the ring protons of aniline and NN-dimethylaniline, are negative.

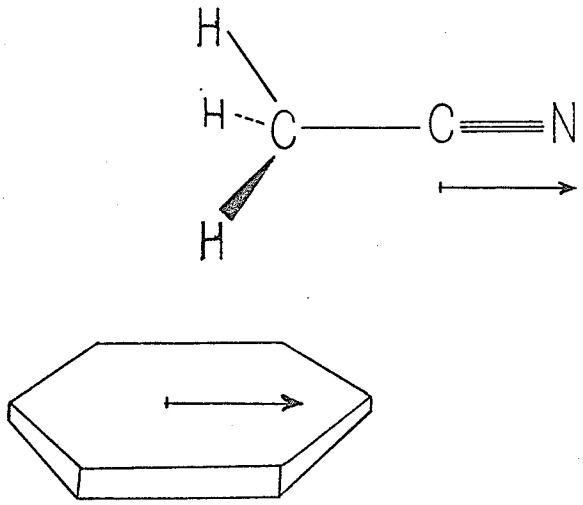


Figure 4. Interaction of Acetonitrile with the Benzene π -Electrons.

ASIS results ($\Delta^{CDCl_3}_{C_6D_6}$ values) for aromatic aldehydes, were rationalized by Klinck and Stothers (50) in terms of a specific solute-solvent interaction in which the site of association is governed by the electron distribution in the solute molecule (see Figure 5). Notice that the benzene solvent appears to solvate electron deficient sites in the solute molecule.

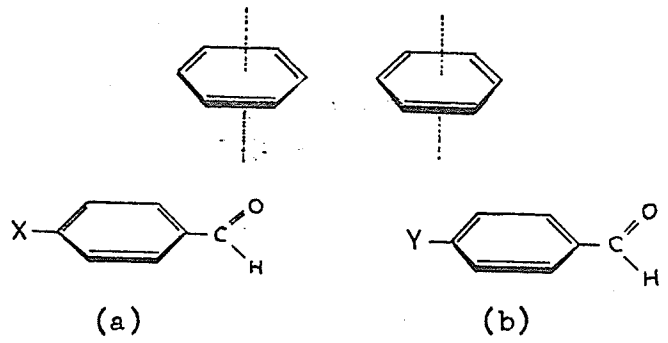
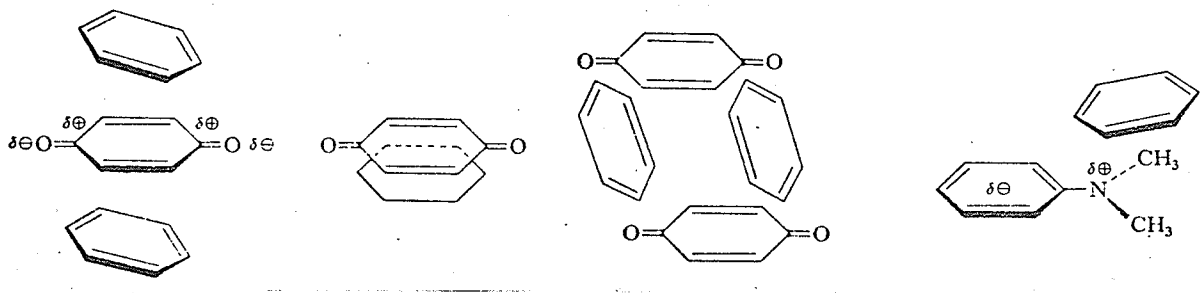


Figure 5. Schematic representations of a possible solute-solvent interaction for substituted benzaldehydes in benzene: (a) electron-withdrawing substituent, (b) electron-releasing substituent.

It has been suggested that a benzene molecule interacting with the partial positive charge of a local dipole will probably be oriented in a nonplanar "collision complex" so that the benzene ring lies as far as possible from the negative end of the dipole (51).

Assuming a nonplanar "collision complex" Ronayne and Williams (51) claim to understand Schneider's ASIS results (21) for p-benzoquinone and N,N-dimethylaniline with the aid of the diagrams shown below (XII-XIII).



XII-A XII-B XII-C XIII

The literature abounds with diagrams such as these. For example, Ledaal (52) has measured ASIS values ($\Delta^{CCl_4}_{C_6D_6}$) for approximately 80 different solutes and proposed a geometry of the "collision complex" for each. The procedure here is to calculate the ring current shifts (Δ values) using the Johnson-Bovey tables (40) for different relative orientations of an isolated pair of solute and solvent molecules. The orientation which gives best agreement between calculated and observed ASIS values is then proposed as the geometry of the "collision complex". However, Baldwin (53) has pointed out that five parameters are required to define the coordinates of the associating molecules. Thus for a solute molecule where less than five different ASIS values are available, there may be many different geometries which will simultaneously fit the experimental results. Therefore the majority of figures purporting to illustrate the relative orientations of solute and solvent have no physical significance. Even if five different parameters can be assigned, it is ridiculous to isolate one solute and one solvent molecule and to calculate their relative geometries. Surely more than one benzene solvent molecule is situated in the immediate vicinity of a solute molecule.

From the foregoing discussion it should be evident that at present there is no easy way of determining the geometry of a simple "1:1 complex". Also, it seems that the π-clouds of the benzene molecules tend to "solvate" electron deficient centres. Having established that charge effects are important in determining the magnitude of the ASIS it is of interest to consider the steric effect.

If the approach of solvent molecules to a solute proton is inhibited by steric effects, one expects the "surface protons" of the internal reference (usually tetramethylsilane) to be affected more by the σ_a and/or σ_w terms of a given solvent than the sterically hindered protons of the solute; i.e., the sterically hindered protons have an environment which approximates more nearly that in the gas phase. Therefore, as the environment of a given solute proton becomes more sterically hindered, relative to internal TMS, benzene is expected to cause an apparent downfield shift of the solute proton (largely a σ_a effect).

To test these predictions, several authors have studied the benzene-induced solvent shifts in various alkyl substituted benzenes (46,54, 55, 56).

Diehl (46) has observed that the magnitude of ASIS is reduced by a factor of 0.7 for the ring protons meta or para to the substituent in mesitylenes and durenes compared with the monosubstituted benzene derivative.

Williams et al. (54) have studied the ASIS of the aromatic protons of benzene, 1,4-dimethylbenzene, 1,3,5-trimethylbenzene, 1,4-di-t-butylbenzene, 1,3,5-tri-isopropylbenzene, and 1,3,5-tri-t-butylbenzene (Figure 6).

Wilson and Williams (55) have completed a thorough study of charge and steric effects by studying the temperature dependence of toluene-induced solvent shifts of various polyalkylbenzene derivatives. They found that with electron-donating substituents (NH_2, NMe_2, and OMe) when the principal site of "association" is thought to be in the region

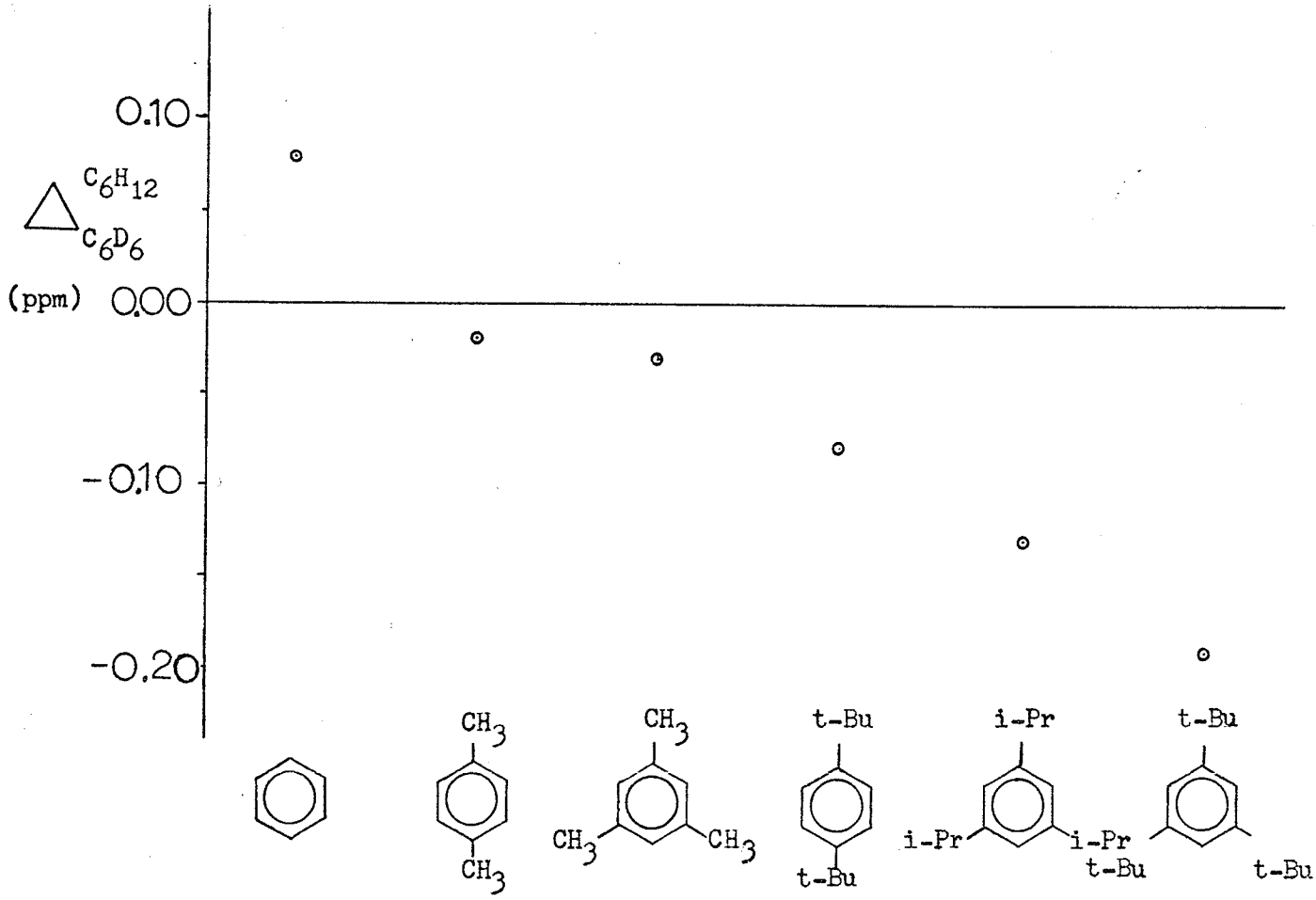
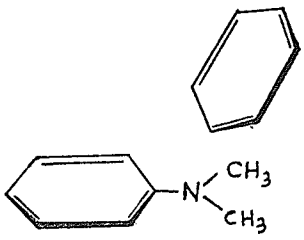


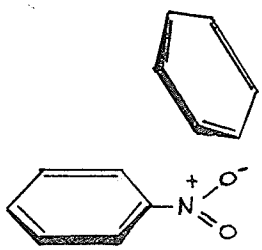
Figure 6. ASIS for Alkyl-Benzenes (ppm)

of the substituent group, appreciable inhibition of "association" appears to occur if there is steric inhibition of π -electron donation by the substituent group. With electron-withdrawing substituents (NO_2 and Br) when the principal site of association is thought to be over the benzene ring, the solvent shifts of the aromatic protons decrease in magnitude as the apparent steric factor increases. Also, it was concluded that solvent shifts are frequently surprisingly insensitive to steric factors.

Nomura and Takeuchi (56) have recently discussed the benzene-induced solvent shifts, $\Delta^{C_6H_{12}}_{C_6D_6}$, of monosubstituted (poly) methylbenzenes in terms of collision complexes of the general geometry proposed by Ronayne and Williams (57). They conclude that for electron-donating substituents (complex XIV), the geometry of the complex remains unchanged by the presence of meta and para methyl groups.



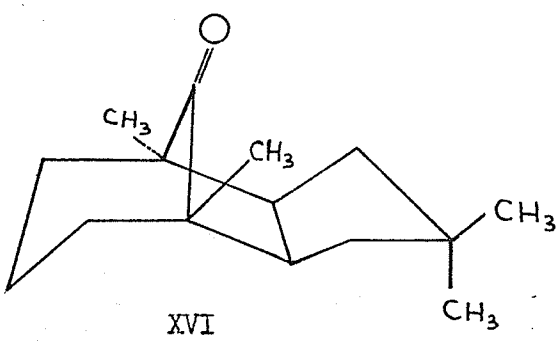
XIV



XV

For electron-withdrawing substituents, they suggest that formation of a complex of geometry (XV) will be made difficult by the presence of methyl groups regardless of their position.

Laszlo has stated that the interpretation based on steric hindrance is erroneous (5). For example, Connolly and McCrindle (15) have shown that the protons of the geminal methyl groups in the tricyclic ketone (XVI) have appreciable solvent shifts ($\Delta^{CDCl_3}_{C_6D_6}$ = 0.13 and 0.14 ppm).



XVI

A study of models indicates severe steric hindrance to the approach to the solvent to the rear of the carbonyl group. Laszlo concludes that the solvent shift appears to be characteristic of the precise geometrical position of a given proton, or methyl group, with respect to the carbonyl group, irrespective of the steric environment of the former or the latter.

The author of this thesis feels that steric effects are important in certain extreme cases but that in general they are small. Several workers have partly misinterpreted their experimental results by ignoring the charge effects. For example, consider the results given in Figure 6. Since the methyl group is electron-donating (Hammett σ_m = -0.069 and σ_p = -0.170) one could argue that the " π -electron cloud" of the benzene solvent molecule tends to avoid "solvating" the ring protons of 1,4-dimethylbenzene relative to benzene. Since the t-butyl group (σ_m = -0.100 and σ_p = -0.197) is a stronger electron-donating group than the methyl group, a similar argument could be used to rationalize the observed decrease in Δ for 1,4-di-t-butylbenzene relative to 1,4-dimethylbenzene.

Schwenk (36) has attempted to illustrate the steric effect from a plot of the solvent shift, Δ , for H_2 in 1-X, 3,4-dichlorobenzenes versus the van der Waals radius of the substituent X, where X = F, Cl, Br, and I. In the opinion of the author such a plot is meaningless since the solvent shifts of H_2 are not independent of other substituent properties such as electronegativity.

2. The Stoichiometry of the Interaction

It is assumed (58, 59, 60) that the stoichiometry of the benzene-solute collision complex is 1:1. The observation that the solvent shift of a given solute at various concentrations of benzene in an inert solvent is approximately proportional to the mole fraction of benzene is consistent with the above assumption. However, a linear relationship between Δ and concentration of benzene is not a proof of complex formation (61). Ronayne and Williams (57) point out that both aromatic and polyfunctional aliphatic solute molecules may undergo solvation by benzene at many sites and yet Δ would still be proportional to the mole fraction of benzene (added to an inert solvent).

Assuming the reversible equilibrium,

$$\text{solute} + \text{solvent} \rightleftharpoons \text{complex} \qquad \text{(III-5)}$$

Laszlo and Williams (62) used the dilution technique of Foster and Fyfe (63) to obtain an equilibrium constant of $K = 0.201/M$ at 33° C for 5α-androstan-17-one in toluene. This value is in fair agreement with the results of an alternative temperature method (see the next section of this thesis) applied to steroids of similar structure.

The conclusion from this section is that the dilution experiments cannot demonstrate the existence of a "1:1 complex". Probably it is most reasonable to assume a wide spectrum of aggregates, ranging from 1:1 in certain isolated cases, to something best described as a solvent cage. The author of this thesis feels that in the case of aromatic solutes where charges may be extensively delocalized, it is unreasonable to ascribe specific stoichiometries and geometries to the interaction of solute and solvent.

3. The Strength of the "Collision Complex"

By assuming a transient 1:1 association one can obtain thermodynamic parameters which give a measure of the strength of benzene-solute interactions. Since the energies of the unassociated solute and the "complex" would be expected to differ, the equilibrium (Equation III-5) will be temperature dependent. On the basis of a 1:1 "complex", Abraham (42) has developed a method by which enthalpy and entropy of formation together with the equilibrium constant of the complex may be approximated. If a fraction P of the solute is complexed at a temperature T , the equilibrium constant, K , for a dilute solution is given by,

$$K = \frac{P}{1 - P} \qquad \text{(III-6)}$$

The value of P is calculated from the expression

$$P = \frac{\nu_T - \nu_o}{\nu_c - \nu_o} \qquad \text{(III-7)}$$

where ν_T is the chemical shift of the proton in question at temperature T , and ν_c and ν_o are the chemical shifts of that proton in the pure complex and the complex-free solution respectively. Since

$$K = \exp\left(\Delta S/R\right)\exp\left(-\Delta H/RT\right) \qquad \text{(III-8)}$$

a plot of log K vs. 1/T should be linear with a slope of $-\Delta H/R$ and intercept $\Delta S/R$.

In this procedure, the position of the resonance in an "inert" solvent is taken to give ν_o , and is arbitrarily taken as zero, thus simplifying eauation (III-7). Estimates of ν_c are made by measuring ν_T as a function of temperature and extrapolating to 0°K. At

this temperature it is assumed that all of the solute molecules are complexed.

The results obtained by several authors (5, 9) indicate that the enthalpy of formation for the benzene-solute interaction is of the order of 1 Kcal/mole.

The significance of the thermodynamic parameters obtained in this way has been questioned in view of the assumption of a 1:1 collision complex, and of the gross approximations involved in the calculation. The observed temperature dependence of Δ might after all be accounted for by a simple packing effect. At low temperatures the benzene solvent molecules simply move closer to the solute molecules in a more ordered fashion. In any event the procedure of Abraham is useful in establishing the weak nature of benzene-solute interactions.

D. CONCLUSION

In this chapter, the model of a 1:1 dipole-induced dipole complex has been presented. This simple model has been successful in providing a qualitative understanding of most of the reported experimental results. It has led to several interesting new experiments, which have provided additional questions to answer and it has suggested a number of useful correlations. However, this model is too simple to adequately explain all experimental ASIS results. Laszlo concludes his review (5) by saying that the 1:1 complex model has done no harm to science, but that now it is clearly obsolete, and a more sophisticated model will have to be constructed.

Although this chapter has been mainly concerned with the 1:1 complex model, other models have been reported. They have been adequately reviewed elsewhere (5, 9) with the exception of the model of Matsuo (64, 65). He suggests that the attraction between solute and solvent molecules is due to the van der Waals interactions and partly to the charge-transfer interaction.

The following summarizes some of the important empirical observations concerning ASIS:

1. Remarkable additivity.
2. On a time average, the benzene molecules "solvate" positive centres, avoiding the negative centres of the solute.
3. If association occurs between one molecule of solute and one molecule of solvent, the lifetime of such an association is very small, certainly much smaller than 10^{-2} sec.

CHAPTER IV

EXPERIMENTAL

A. MATERIALS

1,2,3,4-tetramethoxybenzene, 1,2,4,5-tetramethoxybenzene, and pentamethoxybenzene were obtained from Dr. Arnold Zweig, American Cyanamid Company, Stamford, Connecticut. All other compounds used in this study were obtained from the following companies: (1) Aldrich Chemical Co., Inc.; (2) Ansul Chemical Company; (3) Columbia Organic Chemicals, Co., Inc.; (4) Eastman Organic Chemicals; (5) K & K Laboratories Inc.; (6) Koch-Light Laboratories, Ltd.; (7) Matheson, Coleman and Bell; (8) Merck, Sharp and Dohme, Ltd.; and (9) Pierce Chemical Company. They were used without further purification, since any peaks due to impurities would have been easily recognised.

B. PREPARATION OF SAMPLES

The compounds were normally prepared as 3 mole % solutions in benzene - d_6 and cyclohexane. In the case of 2,6-dimethoxytoluene, 1,2-dimethoxybenzene, 2,5-dichloroaniline, and 1,3-dichlorobenzene, 5 mole % solutions were required to aid the spectral analysis (the signal to noise ratio was increased). Approximately 7 - 11 drops of tetramethylsilane (TMS) was added to each solution as an internal reference. The samples were contained in glass tubes of 4 mm. inner diameter, and 5 mm. outer diameter. All solutions were degassed on a vacuum line by the freeze-pump-thaw technique.

C. MEASUREMENT OF SPECTRA

The spectra were measured and calibrated by period averaging in the frequency sweep mode of either a Varian DA-60-I or a Varian HA-100 spectrometer locked to internal TMS. The spectra were recorded at either 0.05 Hz/sec or 0.02 Hz/sec. The temperature of the sample was $28.5 \pm 1.0^{\circ}$ C as determined using an ethylene glycol sample and a calibration graph of internal shift versus temperature. The spectrum of each sample was measured and calibrated at least four times. The peak positions found by this procedure were almost always obtained with a precision of better than 0.05 Hz (at 60 MHz).

D. ANALYSIS OF SPECTRA

Most nontrival spectra were analyzed with the aid of the LAOCN 3 program (66, 67) on an IBM 360/65 computer. In some cases 3-spin systems were analyzed using LAOCN 3 as well as the method of Castellano and Waugh (68) and Cavanaugh (69). The RMS errors calculated by LAOCN 3 were almost always between 0.004 and 0.025 Hz. In order to compare experimental and calculated spectra, computed spectral curves were frequently obtained.

A brief discussion follows of spectral types which presented some problems of analysis.

2,5-Dichloronitrobenzene. In both benzene-d_6 and cyclohexane solutions this compound gives rise to a typical, deceptively simple ABX spectrum (70, 71) in which $2D_- \simeq J_{ab}$ (at 60 MHz), that is, $(\nu_A - \nu_B) \simeq \frac{1}{2}(J_{AX} - J_{BX})$. At 29.92 MHz the complete spectrum consists of five lines (72), at 60 MHz, seven lines, and at 100 MHz, nine lines are resolvable.

In analyzing such a spectrum, one first attempts a hand-analysis (70, 71). The coupling constants obtained by this procedure are then compared with those derived by the additivity scheme of Schaefer et al. (72) which is capable of giving ortho coupling constants to the nearest 0.05 Hz and meta coupling constants to the nearest 0.09 Hz. The parameter $\nu_A - \nu_B$ can be obtained most accurately by generating a series of calculated spectra (via LAOCN 3) and comparing these with the experimental spectra. The above procedure was used in the case of 2,5-dichloronitrobenzene.

2,3-Dichloronitrobenzene. In benzene solution this compound gives rise to an ABC spectrum. The parameters obtained from analyses using LAOCN 3 and Cavanaugh's 3-Spin Program agree to ± 0.01 Hz.

In cyclohexane solution the spectrum of 2,3-dichloronitrobenzene is AA'B $[\nu(H_4) \simeq \nu(H_6)]$ at both 60 and 100 MHz. The spectrum was analyzed as an A_2B spectrum to obtain the chemical shifts. Using the coupling constants obtained in the benzene solution several attempts were made to obtain a set of "best values" using the iteration option of LAOCN 3. It was not possible to obtain a satisfactory iteration.

1,2,4-Trimethoxybenzene. The ring proton spectrum of this compound is complicated by long-range coupling between the methoxy-group and ring proton(s) (74- 76). Because of this long-range coupling the para ring proton coupling was not observable and was set equal to 0.22 (J_{para} in 1,2-dimethoxybenzene is 0.227 Hz and J_{para} in 2,5-dimethoxychlorobenzene is 0.226 Hz). The coupling constants for this compound are probably accurate to the nearest 0.1 Hz. A more accurate analysis could be obtained by studying a more concentrated solution and by decoupling the two ortho methoxy groups.

2,5-Dimethoxychlorobenzene. The spectrum of this compound illustrates the important point that even though the ratio $J_{AX}/\delta\nu_{AX}$ is much greater than ten, one can not always measure J_{AX} directly (first order assumption). In cyclohexane solution, J_{OCH_3, H_3} appears to be approximately equal to 0.19 Hz, whereas in benzene this same coupling constant is approximately equal to 0.26 Hz. Since this long-range coupling constant was expected to be equal within experimental error in the two solutions, it was decided to generate calculated spectra (via

LAOCN 3) which would include the long-range coupling. Briefly, the long-range coupling constant J_{OCH_3, H_3} is apparently smaller in magnitude in cyclohexane because the protons H_3 and H_4 are more tightly coupled in the cyclohexane solution than in the benzene solution.

2,6-Dimethoxytoluene. The accurate analysis of a 3 mole % solution of this compound in cyclohexane was attempted, however it was not possible to decouple the methyl group without "jumping lock". Using a 5 mole % sample, the signal to noise ratio was significantly increased and the centres of the broad ring proton transitions were all determined to a precision of less than 0.06 Hz. The spectrum was then analyzed as an A_2B spectrum.

2,6-Dichloroaniline and 2,6-dibromoaniline. Solutions of these compounds were analyzed as A_2BX_2 spectra (77, 78).

2,5-Dichloroaniline. The 100 MHz spectrum of this compound is an excellent example of an ABX spectrum in which $\nu_A - \nu_B \simeq \frac{1}{2}(J_{AC} - J_{BC})$. In this case the AB region gives rise to five lines instead of eight. The two combination lines in the X region of the ABX spectrum appear outside the X quartet at 100 MHz, and within the X quartet at 60 MHz. The position of these combination lines depends critically on $(\nu_A - \nu_B)$ and $(J_{AX} - J_{BX})$, thus it was of interest to determine whether combination lines could always be distinguished from X lines. Several calculated spectra were generated by varying $\nu_A - \nu_B$ and and keeping J_{AX} and J_{BX} fixed; it was shown that it is not always possible to distinguish between X lines and combination lines via LAOCN 3.

o-Dimethoxybenzene (veratrole). A 5 mole % solution of veratrole in benzene gives rise to an $AA'BB'$ spectrum in which the chemical shift difference, $\nu_o \delta_{AB}$ is 9.34 Hz at 60 MHz. The two protons which are chemically equivalent and ortho to the methoxy groups give rise to peaks which are broadened by long-range coupling to the methoxy group. The results of Grant, Hirst, and Gutowsky (79) were of great assistance in this particular analysis.

The complete ring proton spectrum of a 5 mole % solution of o-dimethoxybenzene in cyclohexane consists essentially of a triplet in which the intensity of the central peak is much greater than that of the outer two peaks. The outer two peaks of this triplet are separated by approximately 1.1 Hz at 60 MHz; thus all four ring protons are practically chemically equivalent. Since the high-field peak of the triplet was much broader than the low-field peak, it was assumed that the protons ortho to the methoxy group resonate to high field of the other two ring protons. By using the coupling constants obtained from the analysis of the benzene solution, calculated spectra were generated with different values of the chemical shift difference, $\nu_o \delta_{AB}$, until a reasonable fit was obtained. It was found that $\nu_o \delta_{AB} = 1.40 \pm 0.05$ Hz at 60 MHz.

m-Dichlorobenzene. The 100 MHz spectrum of a 5 mole % solution of m-dichlorobenzene in cyclohexane is a tightly coupled A_2BX spectrum. LAOCN 3 was used to aid in the analysis of this spectrum.

E. EXPERIMENTAL ERRORS

The author of this thesis feels that the chemical shifts obtained for the protons of any given sample he prepared are reproducible to better than ± 0.20 Hz (at 60 MHz). This error is largely due to calibration techniques and is negligible compared to the errors caused by dilution shifts.

1. TMS Dilution Shift

a. In benzene solutions. In benzene solutions, one expects the chemical shifts of solute protons which experience large ASIS values to depend on the concentration of TMS added as reference to the benzene solution. To measure this TMS dilution shift a 3 mole % solution of 2,3,5,6-tetrachloronitrobenzene was prepared. The solvent shift for the proton H_4 in this solution is approximately 62 Hz at 60 MHz. From the slope of a plot of chemical shift versus the number of drops of TMS added to the 3 mole % solution mentioned above, a TMS dilution shift of approximately 0.17 Hz/drop of TMS was calculated. Since TMS may be considered an "inert"solvent similar to cyclohexane, the TMS dilution shift is proportional to the benzene induced solvent shift, $\Delta^{C_6H_{12}}_{C_6D_6}$. One could easily correct observed $\Delta^{C_6H_{12}}_{C_6D_6}$ values for TMS dilution shifts if the exact number of drops of TMS added to the benzene solution were known. However, assuming that 7 to 11 drops of TMS were added to each benzene solution, the calculated TMS dilution shift for any given solute proton is 2.46 ± 0.55 % of its benzene-induced solvent shift. In conclusion, observed chemical shifts of solute protons in benzene solution

are to low field of their "real" chemical shift values if $\Delta^{C_6H_{12}}_{C_6D_6}$ is positive, and to high field of their "real" chemical shift values if $\Delta^{C_6H_{12}}_{C_6D_6}$ is negative. The TMS dilution shifts could have been adequately accounted for if a standard stock solution of TMS and benzene - d_6 had been used throughout the study.

b. In cyclohexane solutions. Since both cyclohexane and TMS are "inert" solvents, the chemical shifts of a given proton do not change significantly whether 7 or 11 drops of TMS are added to the cyclohexane solution.

2. Infinite Dilution Chemical Shifts

Because of the importance of solute-solute interactions, it is often desirable to measure the chemical shift at several concentrations and extrapolate to infinite dilution. The importance of solute-solute interactions for 3 mole % solutions will be briefly mentioned.

a. Benzene solutions. From the work of Kotowycz (80) it is evident that dilution shifts may be as large as 2.7 Hz at 60 MHz for the protons of substituted benzenes on going from a 3 mole % solution to infinite dilution in benzene. For example consider the solvent and dilution shifts of 3,5-dichlorosalicylaldehyde (Table VI). A positive dilution shift indicates that the observed solute chemical shifts in 3 mole % benzene solution are to low field of their chemical shift value at infinite dilution in benzene.

In order to be able to predict the magnitude of infinite dilution chemical shifts, one must know something about the solvent properties of the solute. Schneider (21) and Schwenk (36) have studied

TABLE VI

Solvent and Dilution Shifts for 3,5-Dichlorosalicylaldehyde (Hz at 60 MHz)

	Solvent Shift $X=\Delta^{C_6H_{12}}_{C_6D_6}$ 2.5 mole% at 30°C	Dilution Shift Y= Chem. Shift at 2.5mole% in benzene - Chem. Shift at inf. dil. in benzene	(Y/X)×100
H_4	26.34	0.60	2.28
H_6	53.16	2.70	5.07
Aldehyde Proton	60.18	2.64	4.38
Phenol Proton	-8.64	-0.96	11.10

the solvent shifts of the solute benzene in various substituted benzene solvents. Table VII summarizes some of their results.

TABLE VII

Solvent Shifts of Benzene in Various Substituted Benzene Solvents (Hz at 60 MHz)

Solvent - X	$\Delta^{X}_{\text{cyclohexane}}$ (benzene)*
Cyclohexane	0.00
Benzene - d_6	3.72
Hexafluorobenzene	1.68
1,2,3,4-Tetrafluorobenzene	-3.06
1,2,4-Trichlorobenzene	-1.26
2,5-Dichloroiodobenzene	-2.64
Nitrobenzene	-12.90
N,N-Dimethylaniline	2.40

* $\Delta^{X}_{\text{cyclohexane}}(\text{benzene}) = \begin{pmatrix}\text{chemical shift of benzene}\\ \text{in cyclohexane solution}\end{pmatrix} - \begin{pmatrix}\text{chemical shift of}\\ \text{benzene in solvent}\end{pmatrix}$

Schwenk (36) observed that the solvent shifts in halobenzene solutions, $\Delta^{X}_{\text{cyclohexane}}$(benzene) were negative except for hexafluorobenzene and pentafluorobenzene solvents. It is evident that the polar halobenzene solvents do not behave as the non-polar anisotropic benzene solvent.

From the limited data given in Table VI it appears that one may be able to make a "first order" correction for dilution shifts in benzene by adding 5% of the magnitude and sign of $\Delta^{\text{benzene}}_{\text{cyclohexane}}$(observed) to the observed solvent shift, that is,

$$\Delta^{\text{benzene}}_{\text{cyclohexane}}(\text{corrected}) = \Delta^{\text{benzene}}_{\text{cyclohexane}}(\text{observed}) + 0.05\ \Delta^{\text{benzene}}_{\text{cyclohexane}}(\text{observed}) \qquad \text{(IV-1)}$$

Notice that the $\Delta^{\text{benzene}}_{\text{cyclohexane}}$(observed) value is the observed solvent shift for a 3 mole % solution.

b. Cyclohexane solutions. The solvent shift imparted to a solute proton by substituted benzene solvents is not understood. Thus with the limited data available even a first order correction for infinite dilution shifts in cyclohexane is difficult.

3. Summary of Experimental Errors

In order to illustrate the important experiment errors discussed in this section, a specific example will be considered. The observed benzene solvent induced shift, $\Delta^{C_6H_{12}}_{C_6D_6}$ (3 mole % solutions containing 9 ± 2 drops of TMS) of proton H_4 in 2,5-dichloroaniline is about 25 Hz at 60 MHz. The dilution shift in cyclohexane solution for H_4 was found to be 0.90 Hz. Assuming nine drops of TMS were added to the benzene solution, the calculated TMS dilution shift for H_4 is 0.60 Hz. The first

order correction for the dilution shift error of H_4 in benzene is 1.25 Hz. Figure 7 summarizes these contributions. For this particular example, the corrected ASIS is approximately 11 % larger than the observed value. Although this estimated experimental error is large, the following points must be considered:

a. The TMS dilution shift error is a systematic error,

$$\Delta^{C_6H_{12}}_{C_6D_6}\left(\begin{matrix}\text{corrected for TMS}\\ \text{dilution shift}\end{matrix}\right) = 0.0246 \pm 0.0055\Delta^{C_6H_{12}}_{C_6D_6}(\text{observed}) + \Delta^{C_6H_{12}}_{C_6D_6}(\text{observed}) \qquad \text{(IV-2)}$$

b. The infinite dilution shift errors in benzene appear reasonably systematic (see equation (IV-1)).

c. Although there is a lack of experimental data, the infinite dilution shift errors in cyclohexane are probable fairly systematic.

The experimental errors in the ASIS values measured in this study are reasonably systematic. For example, consider any two observed ASIS values, X and Y, which have experimental errors of 9 and 12 % of their respective observed values. When comparing the ASIS values of X and Y, the total error in this comparison is not 21 %, but 3 %; that is, the experimental errors are approximately systematic since the observed ASIS values are always greater than the corrected ASIS values. The author feels that any conclusions made by comparing ASIS values will not be strongly influenced by experimental errors.

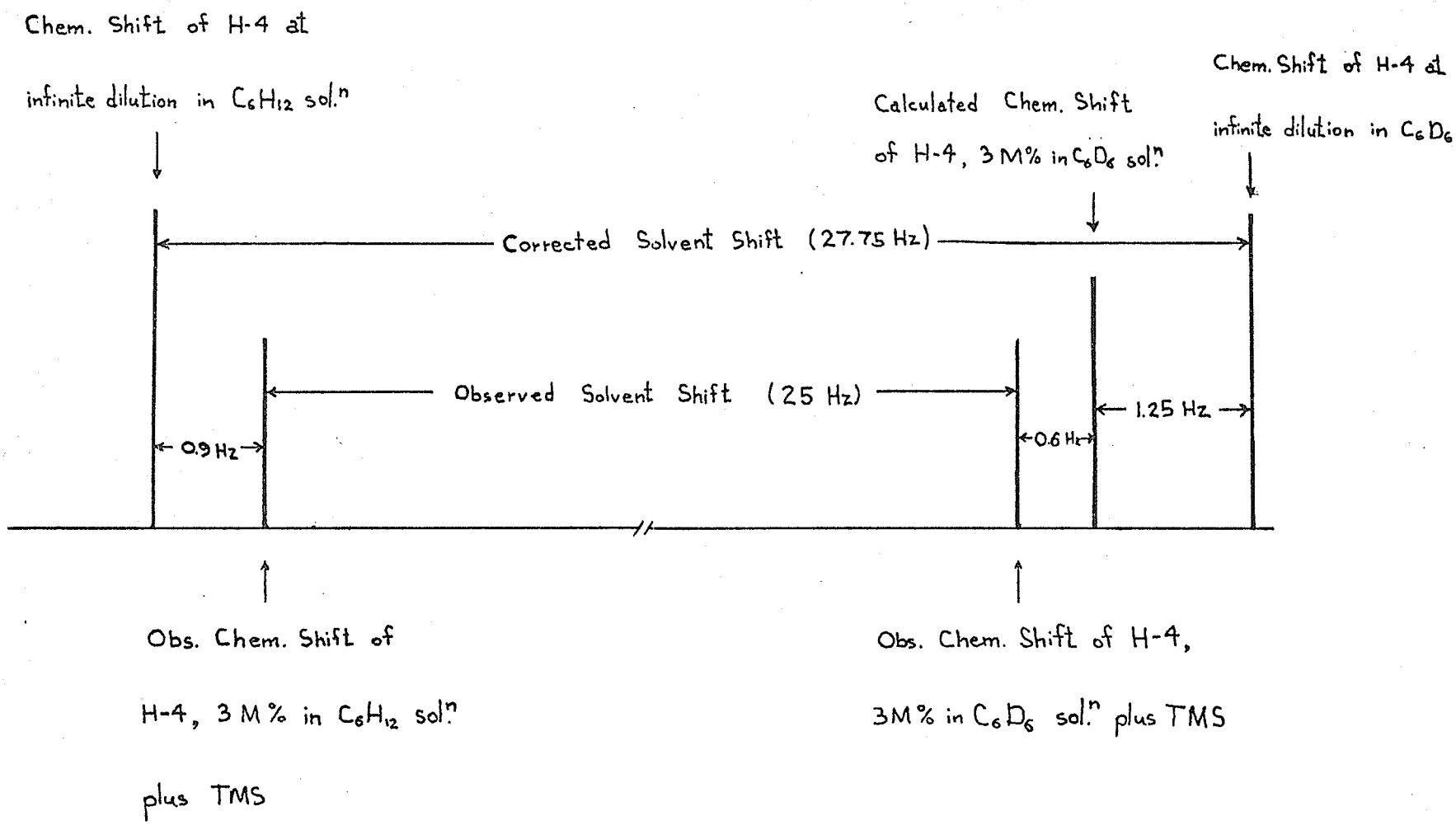


Figure 7. Observed and corrected solvent shifts for H_4 in 2,5-dichloroaniline (Hz at 60 MHz).

CHAPTER V

RESULTS

In Table VIII the proton chemical shift(s) (Hz to low field of TMS at 60 MHz) of 55 substituted benzenes in C_6H_{12} and in C_6D_6 are given, along with their $\Delta^{C_6H_{12}}_{C_6D_6}$ values. For convenience all solvent shifts discussed in the remainder of this thesis are in Hz at 60 MHz. Since Schwenk and Richardson (36, 81) and Nomura and Takeuchi (56) have made the same measurements under similar experimental conditions for several substituted benzenes not included in Table I, their results will also be considered in this thesis. Their results are given in Appendix I.

The ring proton-ring proton coupling constants measured by the author are reported and briefly discussed in Appendix II.

In Figure 8, the observed and calculated (ring) proton spectra of a 3 mole % solution of 2,5-dimethoxychlorobenzene in cyclohexane are given.

TABLE VIII

Proton Chemical Shifts of Substituted Benzenes

(Hz to Low Field of TMS at 60 MHz)

COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(1) 2,4-Dichloronitrobenzene	H_3	446.603	404.064	42.54
	H_5	434.837	382.760	52.08
	H_6	463.205	411.998	51.20
(2) 2,5-Dichloronitrobenzene	H_3	440.33	386.64	53.69
	H_4	439.77	387.72	52.05
	H_6	464.56	424.75	39.81
(3) 3,4-Dichloronitrobenzene	H_2	495.247	462.678	32.57
	H_5	449.364	395.922	53.44
	H_6	478.083	434.379	43.70
(4) 1,2,4-Trimethoxybenzene	H_3	382.82	390.21	-7.39
	H_5	374.08	377.57	-3.49
	H_6	398.25	398.55	-0.30

Table VIII (continued)

COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(5) 2,3-Dichloronitrobenzene	H_4	451.15	402.397	48.75
	H_5	431.04	370.131	60.91
	H_6	451.15	405.730	45.42
(6) 1,2,3-Trimethoxybenzene	H_4	385.96	382.94	3.02
	H_5	406.56	409.85	-3.29
	H_6	385.96	382.94	3.02
(7) 2,5-Dimethoxychlorobenzene	H_3	400.819	384.157	16.66
	H_4	395.885	393.088	2.79
	H_6	410.258	416.408	-6.15
(8) 3-Chloro-4-fluoronitrobenzene	H_2	495.57	461.182	34.39
	H_5	428.44	369.364	59.08
	H_6	483.91	437.530	46.38
(9) 2,6-Dimethoxytoluene	H_3	382.22	381.83	0.39
3 mole % in C_6D_6 5 mole % in C_6H_{12}	H_4	416.42	422.29	-5.87
	H_5	382.22	381.83	0.39
(10) 2,6-Dichloroaniline	H_3	422.08	411.08	11.00
	H_4	387.12	367.52	19.60
	H_5	422.08	411.08	11.00

Table VIII (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(11)	2,6-Dibromoaniline	H_3	434.00	422.315	11.68
		H_4	379.06	359.38	19.68
		H_5	434.00	422.315	11.68
(12)	3,5-Dichloroaniline	H_2	382.116	358.31	23.81
		H_4	398.22	398.52	-0.30
		H_6	382.116	358.31	23.81
(13)	2,5-Dichloroaniline	H_3	419.83	405.681	14.15
	(5 mole % in both C_6D_6 and C_6H_{12})	H_4	391.61	381.765	9.85
		H_6	393.95	369.880	24.07
(14)	3,5-Dichlorobenzaldehyde	H_2	457.43	428.84	28.59
		H_4	448.72	421.18	27.54
		H_6	457.43	428.84	28.59
(15)	3-Chloro-4-bromonitrobenzene	H_2	493.166	461.172	32.00
		H_5	460.991	407.694	53.30
		H_6	472.228	428.618	43.61
(16)	2,4-Dichloroaniline	H_3	428.020	424.307	3.71
		H_5	413.320	404.088	9.23
		H_6	387.817	353.883	33.94

Table VIII (continued)

COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(17) 3,5-Dichlorobenzonitrile	H_2	444.35	396.44	47.91
	H_4	447.97	409.33	38.64
	H_6	444.35	396.44	47.91
(18) 2,6-Dichlorobenzaldehyde	H_3	434.72	403.02	31.70
	H_4	431.58	386.14	45.44
	H_5	434.72	403.02	31.70
(19) 1,2-Dimethoxybenzene (5 mole % in both C_6D_6 and C_6H_{12})	H_3, H_6	403.58	398.927	4.65
	H_4, H_5	404.98	408.271	-3.29
(20) 1,3-Dichlorobenzene	H_2	436.68	425.82	10.86
	H_4, H_6	426.59	407.21	19.38
	H_5	423.74	391.15	32.59
(21) 3,5-Dichloronitrobenzene	H_2, H_6	482.56	449.38	33.18
	H_4	453.44	410.74	42.70
(22) 3,5-Dichlorophenol	H_2, H_6	397.25	373.66	23.59
	H_4	411.72	404.44	7.28
(23) 1-Bromo-2,4,5-trichlorobenzene	H_3	445.87	412.77	33.10
	H_6	456.33	424.71	31.62
(24) 1-Fluoro-2,4,5-trichlorobenzene	H_3	443.44	409.51	33.93
	H_6	427.91	389.48	38.43

Table VIII (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(25)	1-Iodo-2,4,5-trichlorobenzene	H_3	444.32	412.77	31.55
		H_6	469.23	440.90	28.33
(26)	2,6-Dichloro-3-nitrotoluene	H_4	444.37	400.69	43.68
		H_5	436.31	392.53	43.78
(27)	2,3,6-Trichlorotoluene	H_4	425.57	399.98	25.59
		H_5	425.57	399.98	25.59
(28)	2,4,5-Trichloronitrobenzene	H_3	452.43	400.02	52.41
		H_6	474.07	424.96	49.11
(29)	3,5-Dimethylaniline	H_2, H_6	366.50	362.57	3.93
		H_4	376.10	381.34	-5.24
(30)	2-Ethyl-4,5-dimethylphenol	H_3	404.72	408.17	-3.45
		H_6	380.36	369.55	10.81
(31)	2,4,5-Trimethylbromobenzene	H_3	411.30	400.50	10.80
		H_6	431.03	433.47	-2.44
(32)	2,4,5-Trichlorotoluene	H_3	439.87	424.20	15.67
		H_6	431.25	403.26	27.99
(33)	2,4-Dichloro-5-ethyl-3-methylphenol	H_6	403.01	396.46	6.55
		Methyl	145.19	135.27	9.22

Table VIII (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(34)	2,4-Dichloro-3-ethyl-5-methylphenol	H_6	401.92	392.52	9.40
		Methyl	135.68	121.42	14.26
(35)	2,4,6-Trimethoxytoluene	H_3,H_5	359.76	368.39	-8.63
(36)	2,4,6-Trimethylaniline	H_3,H_5	395.94	402.84	-6.90
(37)	2,4-Dibromo-3,6-Dichloroaniline	H_5	444.15	422.87	21.28
(38)	1,2,4,5-Tetramethylbenzene	H_3,H_6	405.43	410.67	-5.24
(39)	2,3,5,6-Tetrafluoroanisole	H_4	394.59	360.41	34.18
(40)	Pentamethylbenzene	H_1	400.35	407.24	-6.89
(41)	1.4-Dibromobenzene	H_2,H_3,H_5,H_6	433.96	409.03	24.93
(42)	1,3,5-Trimethoxybenzene	H_2,H_4,H_6	357.65	372.22	-14.57
(43)	1,3,5-Trifluorobenzene	H_2,H_4,H_6	389.95	368.42	21.53
(44)	1,2,3,4-Tetramethylbenzene	H_5,H_6	405.07	412.95	-7.88
(45)	2,3,5,6-Tetrafluorotoluene	H_4	403.63	374.12	29.51
(46)	1,2,3,5-Tetramethylbenzene	H_4,H_6	401.13	405.39	-4.26
(47)	4-Chloro-2,3,5- trimethylphenol (1.5 mole % in C_6H_{12}; 3 mole % in C_6D_6)	H_6	380.03	354.44	25.59
(48)	2,4,6-Trichlorotoluene	H_3,H_5	432.00	416.19	15.81

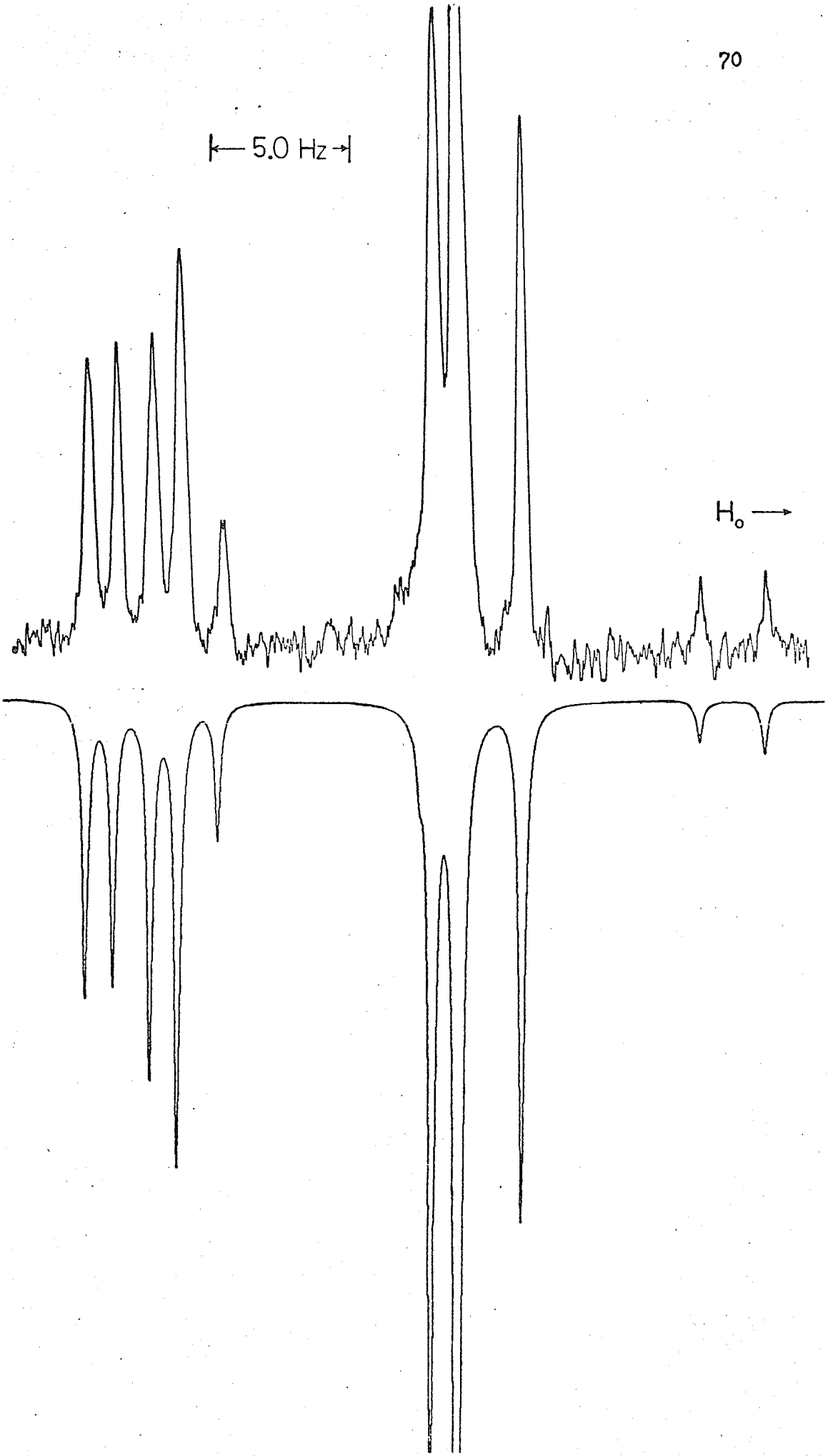
Table VIII (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$
(49)	2,3,5,6-Tetrafluoroaniline	H_4	374.29	352.02	22.27
(50)	2,3,5,6-Tetrafluorophenol	H_4	387.67	357.38	30.29
(51)	2,3,5,6-Tetrafluorothiophenol	H_4	402.09	360.61	41.48
(52)	2,4,6-Trichloroaniline	H_3, H_5	424.68	411.35	13.33
(53)	1,2,3,4-Tetramethoxybenzene*	H_5, H_6	385.2	382.02	3.2
(54)	1,2,4,5-Tetramethoxybenzene*	H_3, H_6	385.8	389.77	-4.0
(55)	Pentamethoxybenzene*	H_6	370.2	368.82	1.4

* Inert solvent used was carbon tetrachloride instead of cyclohexane.

Figure 8. 60 MHz experimental and calculated ring proton NMR spectrum of a 3 mole % solution of 3,5-dimethoxychlorobenzene in cyclohexane. The experimental spectra were analysed with the aid of the LAOCN 3 programme using an IBM 360/65 computer. The final calculated points of coordinates ν_i and I_i were interpolated by lorentzian curves using a Calcomp 562 graph plotter.

The rms error between experimental and calculated frequencies was 0.012 Hz.


5.0 Hz
H_o

CHAPTER VI

DISCUSSION

A. ADDITIVITY

As already mentioned, Diehl (46) has demonstrated the additivity of ASIS for disubstituted benzenes.

In demonstrating additivity of ASIS for trisubstituted benzenes the observed ASIS value of any given proton is divided into contributions from the individual substituents. Since Diehl (46) observed departures from additivity when substituents were accumulated in adjacent positions, the ASIS values of 1,2,3-substituted benzenes were not used in the derivation of individual substituent contributions in this study. The calculated incremental benzene solvent induced shifts of several substituents are given in Table IX.

TABLE IX

Incremental ASIS in the Benzene Series (Hz at 60 MHz)

Substituent X	Δ^X_o	Δ^X_m	Δ^X_p
NH_2	4.44	-6.12	-8.20
CH_3	-0.44	-2.71	-1.74
OH	7.30	-1.77	1.07
F	6.10	13.96	12.73
Cl	3.61	15.13	15.88
Br	2.61	14.50	17.73
I	1.14	14.40	14.08
CN	25.37	31.53	30.85
NO_2	17.13	34.39	33.31

The results of Nomura and Takeuchi (Appendix I) were used in the derivation of Δ^{CH_3}, Δ^{OH}, and Δ^{CN} values. The Δ^{OH} values are not very reliable since thy are derived from only three compounds. This is also the case for the Δ^{CN} values. All other substituent contributions were derived from several compounds. It was not possible to derive consistent parameters for the methoxy group.

The substituent increments given in Table IX are in good qualitative agreement with those derived by Diehl (Table III). It is of interest to mention that Diehl used an external reference in his study.

Using the substituent parameters in Table IX, benzene-induced solvent shifts were calculated for over eighty compounds. The observed and calculated solvent shifts of all trisubstituted benzenes which do not have three adjacent substituents are compared in Table X. Notice that the results of Schwenk and Richardson (36, 81) and Nomura and Takeuchi (56) are also used in this comparison. The mean deviation of the differences between 107 calculated and observed ASIS values is 1.5 Hz. Since the solvent shifts of these trisubstituted benzenes vary from -8.4 to 53.7 Hz, a total range of 62.1 Hz, the mean deviation is 2.4 % of the total range. Although the additivity is reasonably good, the author does not claim that the substituent increments given in TableIX are unique.

An apparently simple steric effect occurs when a nitro group and a bulky ortho substituent are present. In the presence of an ortho group, $\Delta_o^{NO_2} \approx 21.01$ Hz while in the absence of an ortho group, $\Delta_o^{NO_2} \approx 13.59$ Hz. These observations are consistent with the crystallographic results summarized by Holden and Dickinson (82). It is

TABLE X

Observed and Calculated ASIS Values for some Trisubstituted Benzenes (Hz at 60 MHz)

	COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION*
(1)	2,4-Dichloronitrobenzene	H_3	42.54	41.61	0.93
		H_5	52.08	53.88	-1.80
		H_6	51.20	47.39	3.81
(2)	2,5-Dichloronitrobenzene	H_3	53.69	53.13	0.56
		H_4	52.05	52.05	0.00
		H_6	39.81	35.87	3.94
(3)	3,4-Dichloronitrobenzene	H_2	32.57	35.87	-3.30
		H_5	53.44	53.13	0.31
		H_6	43.70	48.14	-4.44
(4)	3-Chloro-4-fluoronitrobenzene	H_2	34.39	34.70	-0.31
		H_5	59.08	55.62	3.46
		H_6	46.38	46.97	-0.59

Table X (continued)

COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION *
(5) 3,5-Dichloroaniline	H_2, H_6	23.81	23.93	-0.12
	H_4	-0.30	-0.98	0.68
(6) 2,5-Dichloroaniline	H_3	14.15	12.80	1.35
	H_4	9.85	10.72	-0.87
	H_6	24.07	23.18	0.89
(7) 3-Chloro-4-bromonitrobenzene	H_2	32.00	35.24	-3.24
	H_5	53.30	52.13	1.17
	H_6	43.61	47.51	-3.90
(8) 2,4-Dichloroaniline	H_3	3.71	1.10	2.61
	H_5	9.23	13.37	-4.14
	H_6	33.94	34.70	-0.76
(9) 3,5-Dichlorobenzonitrile	H_2, H_6	47.91	44.86	3.05
	H_4	38.64	38.07	0.57

Table X (continued)

	COMPOUND	PROTON	Δ(obs.)	Δ(calc.)	DEVIATION*
(10)	1,3-Dichlorobenzene	H_2	10.86	7.22	3.64
		H_4, H_6	19.38	19.49	-0.11
		H_5	32.59	31.76	0.83
(11)	3,5-Dichloronitrobenzene	H_2, H_6	33.18	36.62	-3.44
		H_4	42.70	40.53	2.23
(12)	1,3,5-Trichlorobenzene	H_2, H_4, H_6	23.10	23.10	0.00
(13)	1,3,5-Tribromobenzene	H_2, H_4, H_6	21.72	22.95	-1.23
(14)	1,3,5-Trifluorobenzene	H_2, H_4, H_6	21.53	24.93	-3.40
(15)	3,5-Dichlorobromobenzene	H_2, H_6	22.56	22.10	0.46
		H_4	23.58	24.95	-1.37
(16)	1-Bromo-3-chloro-5-iodobenzene	H_2	22.80	20.30	2.50
		H_4	22.80	22.48	0.32
		H_6	21.36	19.63	1.73

Table X (continued)

	COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION *
(17)	1,2,4-Trichlorobenzene	H_3	22.86	22.35	0.51
		H_5	34.62	34.62	0.00
		H_6	33.36	33.87	-0.51
(18)	1,2,4-Tribromobenzene	H_3	20.16	19.72	0.44
		H_5	36.24	34.84	1.40
		H_6	31.38	31.61	-0.23
(19)	1-Bromo-2,5-dichlorobenzene	H_3	30.96	33.24	-2.28
		H_4	37.02	36.47	0.55
		H_6	21.18	21.35	-0.17
(20)	1-Bromo-3,4-dichlorobenzene	H_2	22.56	21.35	1.21
		H_5	35.52	33.24	2.28
		H_6	32.82	33.62	-0.80
(21)	1-Iodo-2,4-dichlorobenzene	H_3	18.60	21.62	-3.02
		H_5	32.52	33.89	-1.37
		H_6	32.82	31.40	1.42

Table X(continued)

	COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION *
(22)	1-Iodo-2,5-dichlorobenzene	H_3	34.02	33.14	0.88
		H_4	32.82	32.82	0.00
		H_6	18.96	19.88	-0.92
(23)	1-Iodo-3,4-dichlorobenzene	H_2	21.00	19.88	1.12
		H_5	36.84	33.14	3.70
		H_6	29.46	32.15	-2.69
(24)	1-Fluoro-3,4-dichlorobenzene	H_2	24.54	24.84	-0.30
		H_5	33.60	32.78	0.82
		H_6	34.02	37.11	-3.09
(25)	1-Fluoro-2,4-dibromobenzene	H_3	21.18	19.18	2.00
		H_5	33.42	34.30	-0.88
		H_6	37.50	35.10	2.40
(26)	3,5-Difluoroiodobenzene	H_2, H_6	21.18	19.97	1.21
		H_4	25.32	26.28	-0.96

Table X (continued)

	COMPOUND	PROTON	Δ(obs.)	Δ(calc.)	DEVIATION*
(27)	3,5-Dichlorotoluene	H_2, H_6	17.76	19.05	-1.29
		H_4	4.74	5.48	-0.74
(28)	3,5-Dimethylaniline	H_2, H_6	3.00	2.26	0.74
		H_4	-7.20	-9.08	1.88
(29)	3,5-Dimethylchlorobenzene	H_2, H_6	1.80	1.43	0.37
		H_4	13.80	15.00	-1.20
(30)	3,5-Dimethlybromobenzene	H_2, H_6	2.40	0.43	1.97
		H_4	15.60	16.85	-1.25
(31)	3,5-Dimethyliodobenzene	H_2, H_6	3.00	-1.04	4.04
		H_4	16.80	13.20	3.60
(32)	3,5-Dimethylbenzonitrile	H_2, H_6	24.00	23.19	0.81
		H_4	29.40	29.97	-0.57
(33)	3,5-Dimethylnitrobenzene	H_2, H_6	11.40	14.95	-3.55
		H_4	33.60	32.43	1.17

Table X (continued)

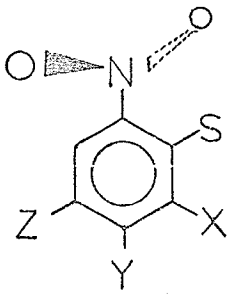
COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION*
(34) 2,4-Dimethylaniline	H_3	-4.80	-7.00	2.20
	H_5	-8.40	-8.30	-0.10
	H_6	-1.20	-0.98	-0.22
(35) 2,4-Dimethylchlorobenzene	H_3	13.80	14.25	-0.45
	H_5	10.80	12.95	-2.15
	H_6	-2.40	-1.81	-0.59
(36) 2,4-Dimethylbromobenzene	H_3	14.40	13.62	0.78
	H_5	11.40	12.32	-0.92
	H_6	-1.20	-2.81	1.61
(37) 2,4-Dimethyliodobenzene	H_3	16.80	13.52	3.28
	H_5	13.80	12.22	1.58
	H_6	-1.20	-4.28	3.08
(38) 2,4-Dimethylbenzonitrile	H_3	30.60	30.65	-0.05
	H_5	29.40	29.35	0.05
	H_6	16.80	19.95	-3.15

Table X (continued)

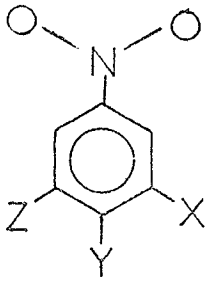
	COMPOUND	PROTON	$\triangle$(obs.)	$\triangle$(calc.)	DEVIATION*
(39)	2,4-Dimethylnitrobenzene	H_3	32.40	33.51	-1.11
		H_5	28.20	32.21	-4.01
		H_6	7.80	11.71	-3.91
(40)	1,3,5-Trimethylbenzene	H_2, H_4, H_6	-2.22	-2.62	0.44
(41)	3,5-Dichlorophenol	H_2, H_6	23.59	26.79	-3.20
		H_4	7.28	8.29	-1.01
(42)	3,5-Dimethylphenol	H_2, H_6	6.6	5.12	1.48
		H_4	1.2	0.19	1.01
(43)	2,4-Dimethylphenol	H_3	-3.0	-2.65	-0.35
		H_5	-3.6	-3.95	0.35
		H_6	3.6	1.88	1.72

*DEVIATION = $\triangle$(obs.) - $\triangle$(calc.) where $\triangle = \triangle^{C_6H_{12}}_{C_6D_6}$

well known that an unhindered aromatic nitro group lies approximately in the plane of the ring to which it is attached because the stabilization energy due to resonance interactions is greatest for a coplanar configuration. However, since the stabilization energy diminishes as the cosine or square of the cosine of the angle between aromatic and nitro group planes, an 18° rotation would reduce the energy by only 5 or 10 % (83). Therefore, in the presence of a bulky ortho substituent it is not surprising that nitro groups are often rotated. For example, in o-nitrobenzaldehyde, the nitro group is rotated by 27°. In



XVII. The plane of the nitro group is twisted out of the aromatic ring plane by X.



XVIII. The nitro group lies in the same plane as the aromatic ring.

compounds such as XVII, the proton ortho to the nitro group (H_6) is more readily "solvated" by benzene solvent molecules than is H_6 in XVIII, because H_6 in XVII is further away from the negative oxygen atom of the nitro group. Since the benzene solvent molecules tend to avoid negative centres, the calculated $\Delta_o^{NO_2}$ values are in qualitative agreement with this explanation. Using these modified $\Delta_o^{NO_2}$ values the differences between observed and calculated ASIS values are significantly reduced compared to those given in Table X (see Table XI).

TABLE XI

Observed and Calculated ASIS Values for Proton(s) Ortho to a Nitro Group for some Trisubstituted Benzenes (Hz at 60 MHz)

Compound	Proton	Δ(obs)	Δ(calc.)	Deviation (obs)- (calc.)
2,4-Dichloronitrobenzene	H_6	51.20	51.27	-0.07
2,5-Dichloronitrobenzene	H_6	39.81	39.75	0.06
3,4-Dichloronitrobenzene	H_2	32.57	32.33	0.24
	H_6	43.70	44.60	-0.90
3-Chloro-4-bromonitrobenzene	H_2	32.00	31.70	0.30
	H_6	43.61	43.97	-0.36
3,5-Dichloronitrobenzene	H_2,H_6	33.18	33.08	0.10
3,5-Dimethylnitrobenzene	H_2,H_6	11.40	11.41	-0.01
2,4-Dimethylnitrobenzene	H_6	7.80	15.59	-7.79
3-Chloro-4-fluoronitrobenzene	H_2	34.39	31.16	3.23
	H_6	46.38	43.43	2.95

Two compounds for which this modified additivity scheme does not work are 2,4-dimethylnitrobenzene and 3-chloro-4-fluoronitrobenzene.

A steric effect analogous to the one for the nitro group is apparently not important for the smaller amino group (see Table X).

The calculated and observed solvent shifts of some disubstituted, tetrasubstituted and pentasubstituted benzenes are given in Table XII. Trisubstituted benzenes with three adjacent substituents are also included in this table. It is interesting to notice that the calculated solvent shifts of almost all tri-, tetra-, and

pentasubstituted benzenes given in this table are larger than their corresponding observed ASIS values. Since one would expect benzene solvent molecules to experience steric hindrance in their approach to the solute protons of a tetra- and pentasubstituted benzene, the above observations can be partly explained. However, if such steric effects are important the author would expect the observed solvent shifts of ring protons in trisubstituted benzenes with three adjacent substituents to be larger than the calculated values.

The 1,4-dihalobenzenes all have larger observed solvent shifts than calculated. This deviation between observed and calculated ASIS increases on going from 1,4-difluorobenzene to 1,4-diiodobenzene which is contrary to what one would expect on the basis of a simple steric effect.

TABLE XII

Compounds for which the Additivity Scheme is Unsatisfactory

	COMPOUND	PROTON	$\triangle$(obs.)	$\triangle$(calc.)	DEVIATION*
(1)	2,3-Dichloronitrobenzene	H_4	48.75	52.05	-3.30
		H_5	60.91	65.40	-4.49
		H_6	45.42	48.14	-2.72
(2)	2,6-Dichloroaniline	H_3, H_5	11.00	13.37	-2.37
		H_4	19.60	22.06	-2.46
(3)	2.6-Dibromoaniline	H_3, H_5	11.68	14.22	-2.54
		H_4	19.68	20.80	-1.12
(4)	2,3-Dichloroiodobenzene	H_4	28.26	32.83	-4.57
		H_5	39.66	45.41	-5.75
		H_6	27.18	32.15	-4.97
(5)	1,2,3-Trichlorobenzene	H_4, H_6	28.62	34.62	-6.00
		H_5	41.22	46.14	-4.92

Table XII (continued)

COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION*
(6) 1,2,4,5-Tetrafluorobenzene	H_3, H_6	41.70	40.12	1.58
(7) 1,2,4,5-Tetrachlorobenzene	H_3, H_6	35.04	37.48	-2.44
(8) 1,2,4,5-Tetrabromobenzene	H_3, H_6	31.74	34.22	-2.48
(9) 1-Fluoro-2,4,5-trichlorobenzene	H_3	33.93	36.31	-2.38
	H_6	38.43	39.97	-1.54
(10) 1-Bromo-2,4,5-trichlorobenzene	H_3	33.10	36.85	-3.75
	H_6	31.62	36.48	-4.86
(11) 1-Iodo-2,4,5-trichlorobenzene	H_3	31.55	36.75	-5.20
	H_6	28.33	35.01	-6.68
(12) 2,4,5-Trichloronitrobenzene	H_3	52.41	56.74	-4.33
	H_6	49.11	51.00	-1.89
(13) 2,4,5-Trichlorotoluene	H_3	15.67	19.64	-3.97
	H_6	27.99	33.43	-5.44

Table XII (continued)

	COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION*
(14)	2,4,6-Tribromoiodobenzene	H_3, H_5	27.00	37.35	-10.35
(15)	1,4-Difluoro-2,5-dibromobenzene	H_3, H_6	38.88	37.17	1.71
(16)	1,2,3,5-Tetrafluorobenzene	H_4, H_6	32.28	38.89	-6.61
(17)	1,2,3,4-Tetrofluorobenzene	H_5, H_6	44.70	46.75	-2.05
(18)	1,2,3,4-Tetrachlorobenzene	H_5, H_6	41.40	49.75	-8.35
(19)	2,6-Dichloro-3-nitrotoluene	H_4	43.68	45.65	-1.97
		H_5	43.78	51.17	-7.39
(20)	2,3,6-Trichlorotoluene	H_4	25.59	32.13	-6.54
		H_5	25.59	31.91	-6.32
(21)	2,4,5-Trimethylbromobenzene	H_3	10.80	10.91	-0.11
		H_6	-2.44	-3.25	0.81
(22)	2,4,6-Trimethylaniline	H_3, H_5	-6.90	-8.74	1.84

Table XII (continued)

	COMPOUND	PROTON	△(obs.)	△(calc.)	DEVIATION*
(23)	1,2,4,5-Tetramethylbenzene	H_3, H_6	-5.24	-6.30	1.06
(24)	1,2,3,4-Tetramethylbenzene	H_5, H_6	-7.88	-7.60	-0.28
(25)	1,2,3,5-Tetramethylbenzene	H_4, H_6	-4.26	-5.33	1.07
(26)	Pentamethylbenzene		-6.89	-8.04	1.15
(27)	2,3,5,6-Tetrafluoroaniline		22.27	31.92	-9.65
(28)	2,3,5,6-Tetrafluorotoluene		29.51	38.38	-8.87
(29)	2,3,5,6-Tetrafluorophenol		30.29	41.19	-10.90
(30)	Pentafluorobenzene		51.90	52.85	-0.95
(31)	Pentachlorobenzene		40.80	53.36	-12.56
(32)	2,4-Dibromo-3,6-dichloroaniline	H_5	21.28	32.96	-11.68
(33)	2,4,6-Trichlorophenol	H_3, H_5	22.86	21.33	1.53
(34)	2,4,6-Trichlorophenol	H_3, H_5	17.76	14.59	3.17

Table XII (continued)

	COMPOUND	PROTON	$\triangle$(obs.)	$\triangle$(calc.)	DEVIATION*
(35)	2,6-Dinitro-4-chlorophenol	H_3, H_5	52.26	52.28	-0.02
(36)	2,3,5,6-Tetrachloronitrobenzene	H_4	61.98	70.79	-8.81
(37)	2,4,6-Trichloroaniline	H_3, H_5	13.33	16.98	-3.65
(38)	1,4-Difluorobenzene		21.12	20.06	1.06
(39)	1,4-Dichlorobenzene		24.18	18.74	5.44
(40)	1,4-Dibromobenzene		24.93	17.11	7.82
(41)	1,4-Diiodobenzene		24.30	15.54	8.76

*DEVIATION = $\triangle$(obs.) - $\triangle$(calc.) where $\triangle = \triangle^{C_6H_{12}}_{C_6D_6}$

B. OTHER CORRELATIONS

As mentioned earlier, it is difficult to demonstrate the importance of steric effects on ASIS. In compounds such as the 3,5-dichloro-X-benzenes one expects the ASIS values of H_4 to be independent of steric effects and mainly dependent on charge effects.

1. Hammett's σ Constant

As a measure of substituent effects in the benzene ring system we have Hammett's σ constants. If these constants are related to the electron densities at the meta and para carbon atoms, one might expect Hammett σ constants (or the modified resonance and inductive components of the σ constants as proposed by Taft (84)) to correlate with the ^{13}C and ^{1}H chemical shifts of the nuclei involved. Many investigators have attempted to show that such a correlation exists (84-91). For example, Hayamizu and Yamamoto (91) have shown that the para-proton chemical shift in a monosubstituted benzene is given by the following linear relationship:

$$\delta_{para} = -0.45\ \sigma_I - 1.14\ \sigma_R^{o} + 0.08 \quad (ppm) \qquad (VI-1)$$

where σ_I and σ_R^{o} are the inductive and resonance contributions of the substituent. For the 15 monosubstituted benzenes studied by Hayamizu and Yamamoto the r.m.s. error was ± 0.04 ppm, which corresponds to 4 % of the range in the para-proton shift. Since the error in Taft's σ constants is ± 0.03 (91), which is about 4 % of the range of the σ constants, this empirical relation seems excellent.

The Hammett equation can be expressed as (VI-2), in which the

regular Hammett σ constant is equal to $\sigma_I + \sigma_R$, the inductive and resonance substituent constants, respectively.

$$\log K/K_o = (\sigma_I + \sigma_R)\rho \qquad \text{(VI-2)}$$

can be obtained separately for the para and meta positions,

$$\sigma_R^p = \sigma_p - \sigma_I \quad \text{and} \quad \sigma_R^m = \sigma_m - \sigma_I \qquad \text{(VI-3)}$$

for which it is assumed that σ_I is the same for the two positions (92).

For reactions in which (a) there is essentially no resonance between the substituent and the reaction centre, and (b) the first atom of the side chain of reaction site does not bear a formal charge and thereby does not produce any significant polarization of the substituent, one may write equation (VI-4) (92).

$$\log K/K_o = \sigma^o\rho = (\sigma_I + \sigma_R^o) \qquad \text{(VI-4)}$$

σ_R^o is a substituent constant reflecting the resonance interaction of the substituent with the ring. The substituent constants, σ^o, are often referred to as Taft's substituent constants. Taft has evaluated these constants from the ionizations of phenylacetic and phenylpropionic acids and from the rates of saponification of ethylphenylacetates and benzylacetates (93). σ_I values from three sources are given and discussed by Ritchie and Sager (93). σ_R^o values can be approximately derived from the σ^o and σ_I values (93).

The Taft σ constants of interest in this thesis are given in Table XIII.

TABLE XIII

Taft σ Constants (from Ritchie and Sager (93))

Substituent	σ^{o}(meta)	σ^{o}(para)
$N(CH_3)_2$	-0.15	-0.44
NH_2	-0.14	-0.38
OH	0.04	-0.13
OCH_3	0.13	-0.12
CH_3	-0.07	-0.15
SCH_3	0.09	-0.03
H	0.00	0.00
F	0.35	0.212
Cl	0.37	0.27
Br	0.38	0.26
I	0.35	0.27
$COCH_3$	0.34	0.46
COOR	0.36	0.46
CHO	-	0.43
CN	0.62	0.69
NO_2	0.70	0.82

The σ^{o} value for the para-fluoro group was taken from the results of Niwa (94). The Taft σ constant for the formyl group, p-CHO, was taken to be equal to its ordinary Hammett σ_p value (95). This approximation is probably good since σ_p equals 0.50 and 0.45 for the p-$COCH_3$ and p-COOR groups, while σ^{o} is 0.46 for both groups.

The importance of charge effects in benzene solvent induced shifts may be demonstrated by plotting ASIS values of H_4 in the 3,5-dichloro-X-benzenes versus X's σ°-substituent constant (see Figure 9). The correlation coefficient for this plot is 0.9966, and the slope is 37.50 Hz/Taft unit. An analogous plot for a series of 3,5-dimethyl-X-benzenes is shown in Figure 10. It is interesting to notice that the ASIS values of the methyl group protons in the p-X-toluene series are also linearly related to the σ° values of X (see Figure 11).

Following the work of Diehl (46) the incremental solvent shifts, Δ_X^p and Δ_X^m (see Table IX) were plotted against $\sigma_I + 0.50\ \sigma_R^\circ$ (Figures 13 and 14). Also, Δ_X^p and Δ_X^m were plotted against $\sigma_I + 0.75\ \sigma_R^\circ$, σ° and $0.50\ \sigma_I + \sigma_R^\circ$ (Figures 15 to 20). The necessary values of Taft's constants σ_I and σ_R°, were taken from Hayamizu and Yamamoto (91). The author feels that plots of the type where some property of a substituent X is plotted against $\alpha\ \sigma_I + \beta\ \sigma_R^\circ$ often have little significance when α and β are empirical scaling factors.

From the limited data available, the ASIS of H_4 in the 2,3,5,6-tetrafluoro-X-benzenes also appears to be related to the σ° values of substituent, X (see Figure 21).

Although the reason for the linearity of the plots shown in Figures 9 to 21 is not completely understood two important conclusions may be stated: (a) the origins of ASIS for proton(s) para to substituent X in 3,5-dichloro-X-benzenes, 3,5-dimethyl-X-benzenes, and in p-X-toluenes must be similar; (b) the magnitude of the benzene solvent induced shift for any given proton appears to be linearly related to the electron density at that proton. For example, the incremental solvent shifts, Δ_p^X,

for a substituent X para to a particular proton is given by the expression:

$$\Delta^{X}_{para} = 35.83\ \sigma^{o}_{para,X} \pm 1.30\ \sigma^{o}_{para,X} + 5.39 \pm 0.55 \text{ Hz} \qquad \text{(VI-5)}$$

Figure 9. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 3,5-dichloro-X-benzenes versus Taft's sigma para (σ^{o}_{para}) value for X.

Parameters Calculated from the above Plot:

Y-Intercept = 12.25 Hz

Variance of the Y-Intercept = $\pm$ 0.50 Hz

Slope = 37.50 Hz/Taft's sigma para value

Variance of the Slope = $\pm$ 1.17 Hz/Taft's sigma para value

Correlation Coefficient = 0.9966

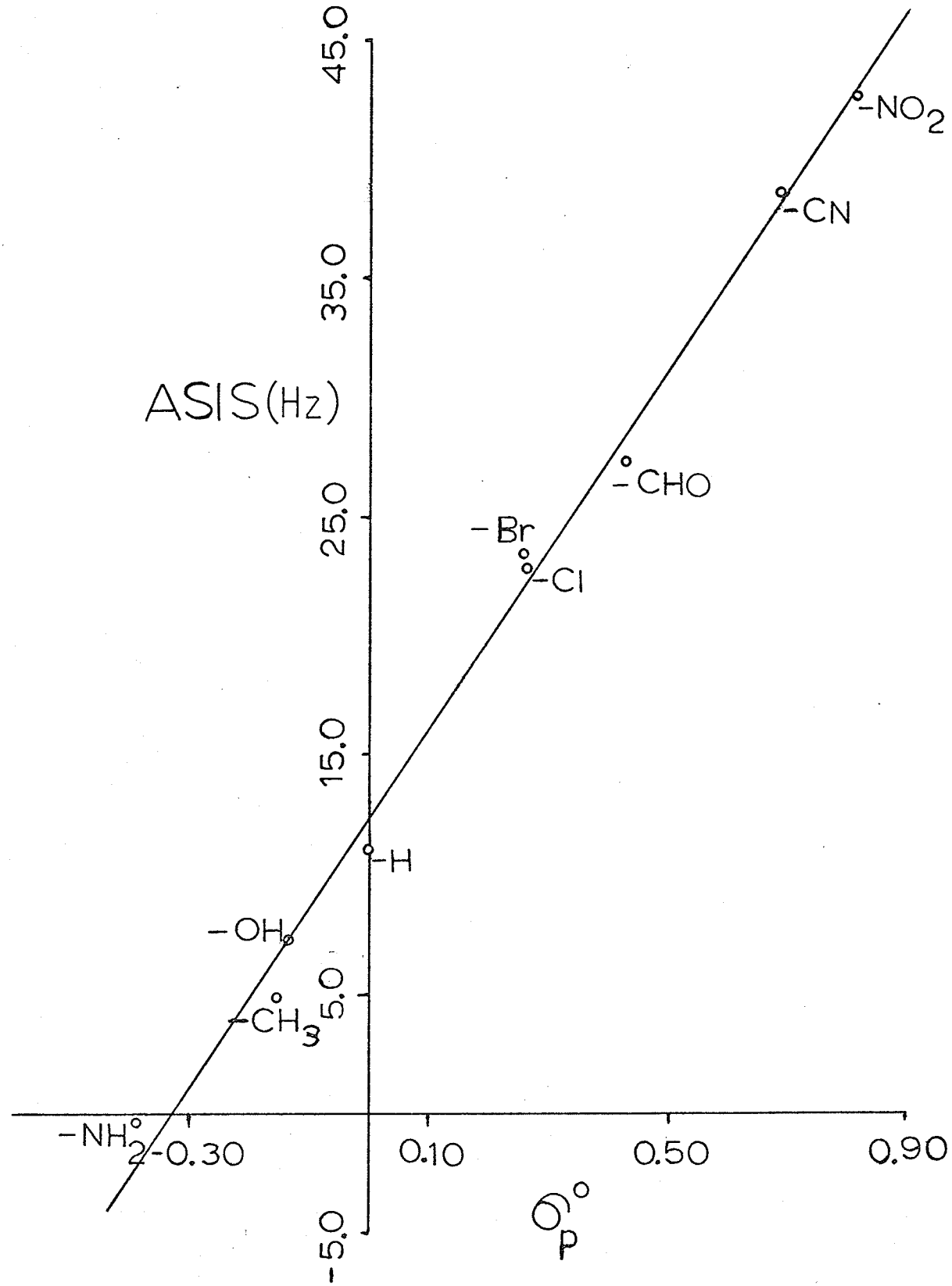

45.0
35.0
25.0
15.0
5.0
-5.0
ASIS(Hz)
-NO2
-CN
-CHO
-Br
-Cl
-H
-OH
-CH3
-NH2
-0.30
0.10
0.50
0.90
σp°

Figure 10. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 3,5-dimethyl-X-benzenes versus Taft's sigma para (σ^{o}_{para}) value for X.

Parameters Calculated from the above Plot:

Y-Intercept = 3.92 Hz

Variance of the Y-Intercept = $\pm$ 0.86 Hz

Slope = 35.21 Hz/Taft's sigma para value

Variance of the Slope = $\pm$ 2.13 Hz/Taft's sigma para value

Correlation Coefficient = 0.9821

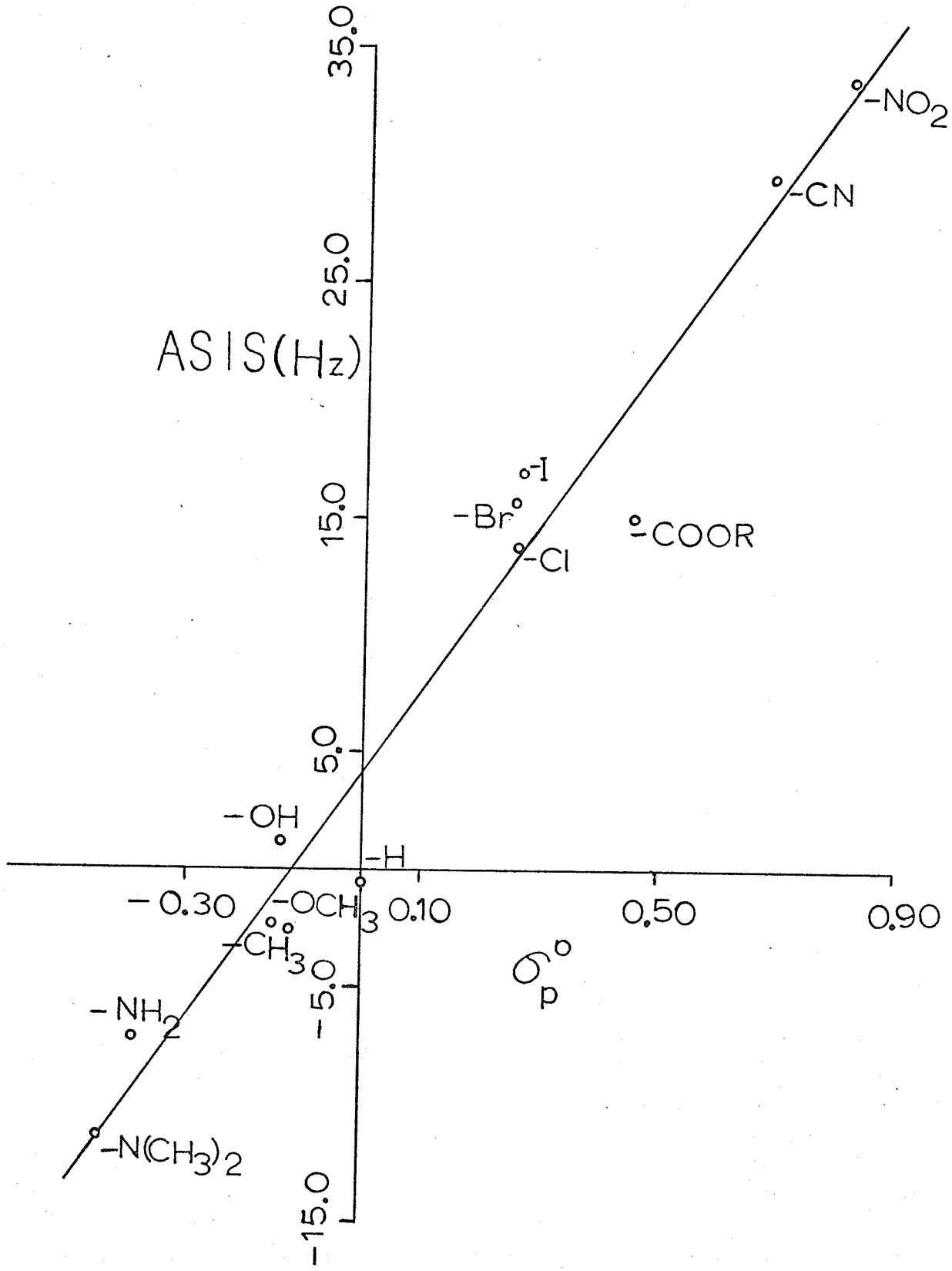

ASIS(Hz)
35.0
25.0
15.0
5.0
-5.0
-15.0
-NO2
-CN
-I
-Br
-Cl
-COOR
-OH
-H
-0.30
-OCH3
0.10
0.50
0.90
-CH3
-NH2
-N(CH3)2
σp

Figure 11. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for the methyl protons in some parasubstituted toluenes versus Taft's sigma para (σ^{o}_{para}) value for X.

Parameters Calculated from the above Plot:

Y-Intercept = 11.36 Hz

Variance of the Y-Intercept = $\pm$ 0.77 Hz

Slope = 28.84 Hz/Taft's sigma para value

Variance of the Slope = $\pm$ 1.84 Hz/Taft's sigma para value

Correlation Coefficient = 0.9822

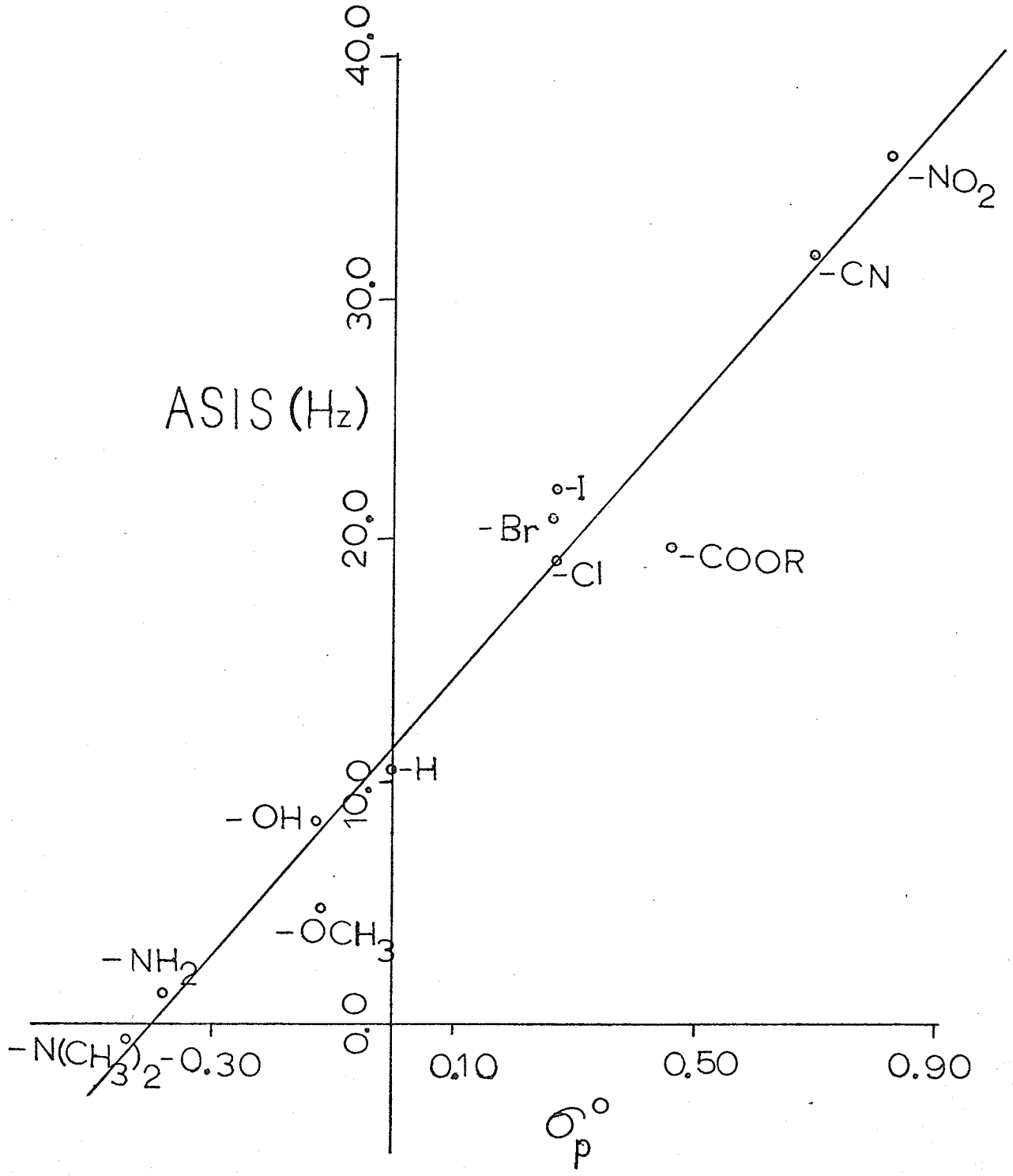

40.0
30.0
20.0
10.0
0
ASIS (Hz)
-NO2
-CN
-I
-Br
-Cl
-COOR
-H
-OH
-OCH3
-NH2
-N(CH3)2
-0.30
0.
0.10
0.50
0.90
σp°

Figure 12. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 3,5-dichloro-X-benzenes versus $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 3,5-dimethyl-X-benzenes.

<u>Parameters Calculated from the above Plot:</u>

Y-Intercept = 7.09 Hz

Variance of the Y-Intercept = $\pm$ 0.38 Hz

Slope = 1.07

Variance of the Slope = $\pm$ 0.02

Correlation Coeffient = 0.9991

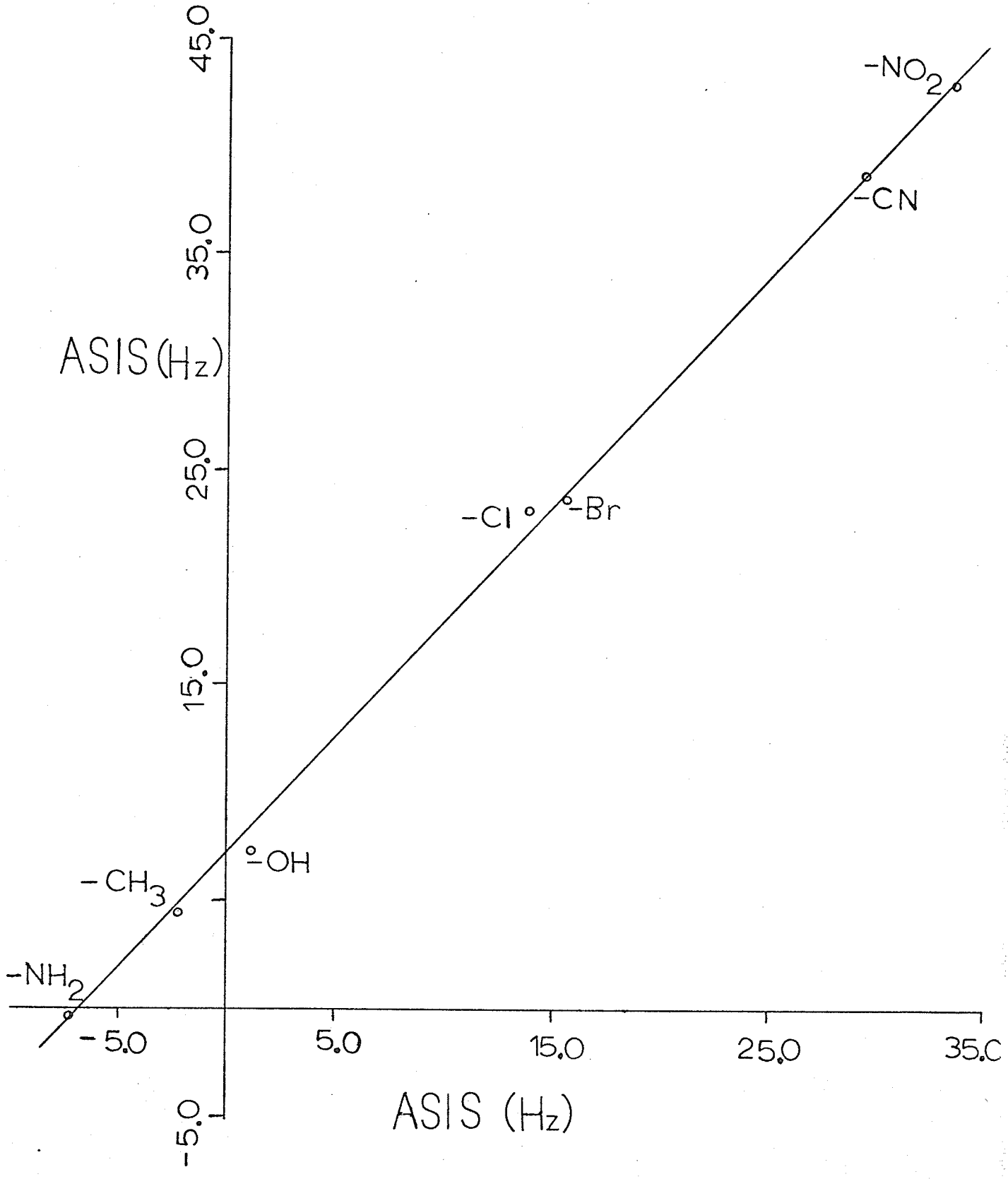

45.0
35.0
25.0
15.0
-5.0
ASIS (Hz)
-NO2
-CN
-Cl
-Br
-OH
-CH3
-NH2
-5.0
5.0
15.0
25.0
35.0
ASIS (Hz)

Figure 13. A plot of Δ^{X}_{meta} (defined in text) in Hz at 60 MHz versus $\sigma_I + 0.5\ \sigma_R^{o}$. The substituent constants σ_I and σ_R^{o} are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = -0.86 Hz

Variance of the Y-Intercept = 1.00 Hz

Slope = 47.11 Hz/sigma value

Variance of the Slope = 2.48 Hz/sigma value

Correlation Coefficient = 0.9904

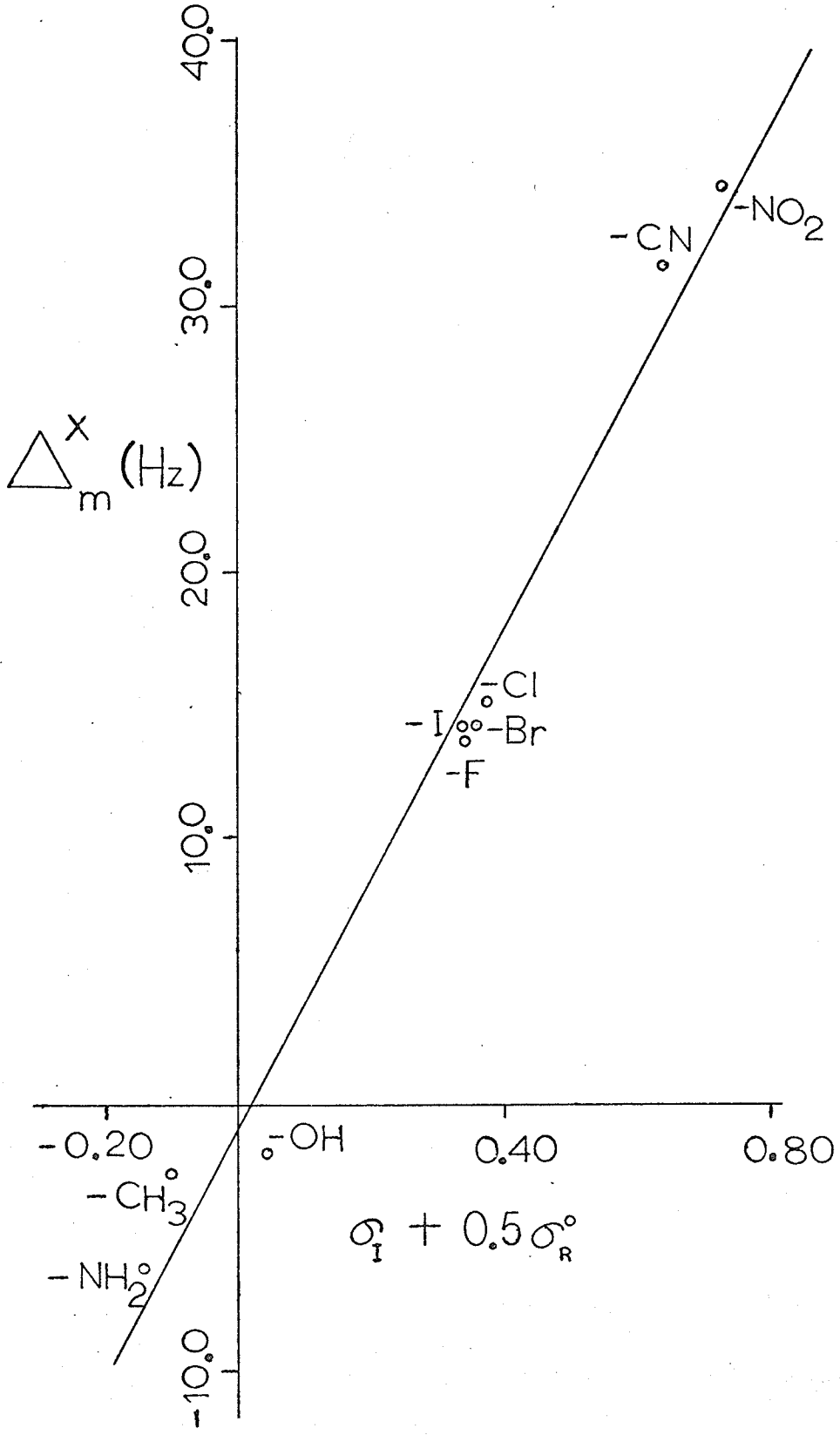

40.0
30.0
20.0
10.0
-10.0
Δ^{X}_{m} (Hz)
-CN
-NO2
-Cl
-I
-Br
-F
-0.20
-OH
0.40
0.80
-CH3
-NH2
$\sigma_I + 0.5\sigma_R^\circ$

Figure 14. A plot of Δ^{X}_{para} (defined in text) in Hz at 60 MHz versus $\sigma_I + 0.5\ \sigma_R^{o}$. The substituent constants σ_I and σ_R^{o} are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = -0.32 Hz

Variance of the Y-Intercept = $\pm$ 0.94 Hz

Slope = 46.16 Hz/sigma value

Variance of the Slope = $\pm$ 2.34 Hz/sigma value

Correlation Coefficient = 0.9911

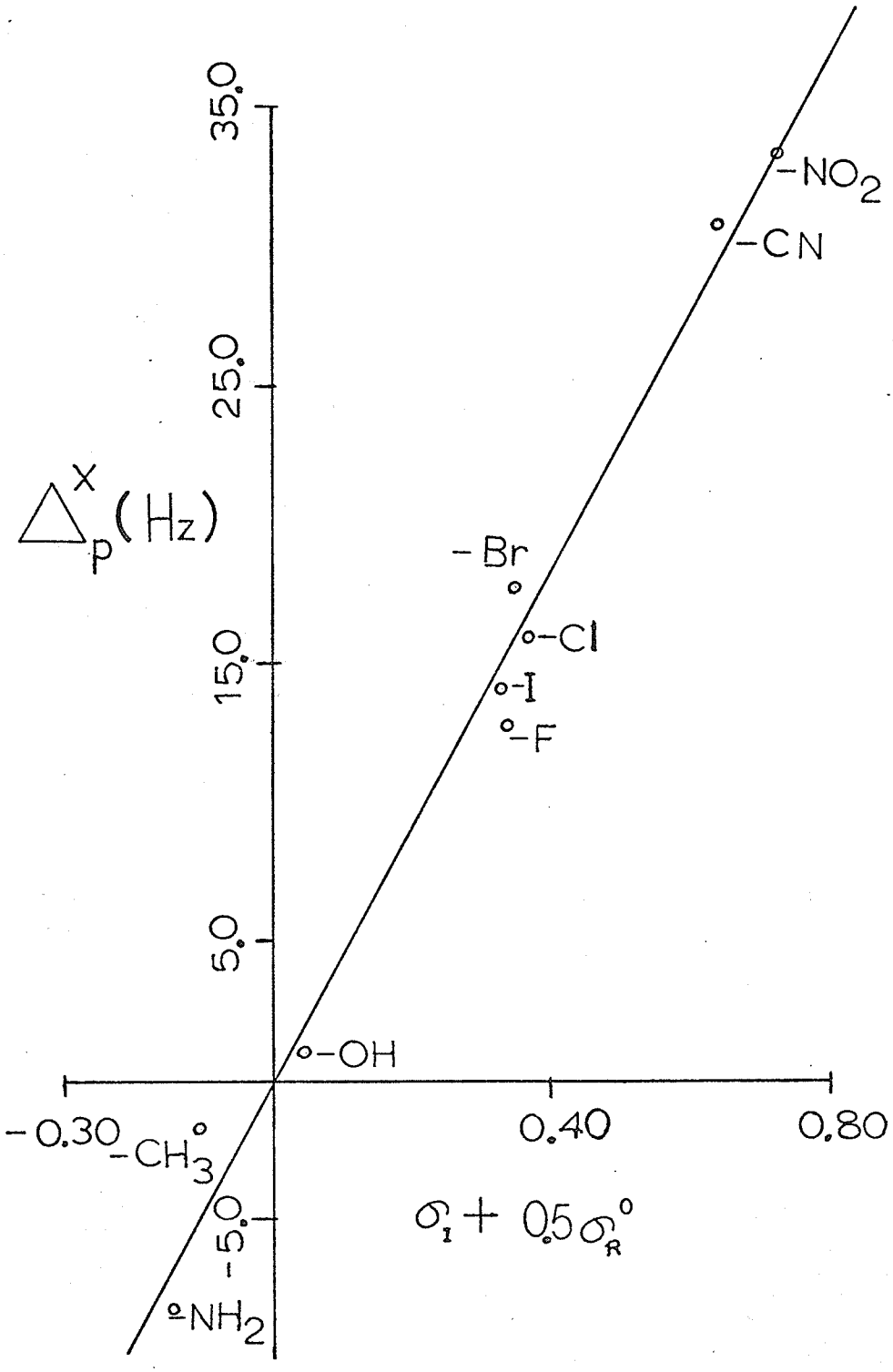

35.0
25.0
15.0
5.0
-5.0
Δ_p^X (Hz)
-NO2
-CN
-Br
-Cl
-I
-F
-OH
-NH2
-0.30
-CH3
0.40
0.80
$\sigma_I + 0.5\sigma_R^0$

Figure 15. A plot of Δ^{X}_{meta} (defined in text) in Hz at 60 MHz versus $\sigma_I + 0.75\ \sigma_R^{\circ}$. The substituent constants σ_I and σ_R° are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = 2.46 Hz

Variance of the Y-Intercept = $\pm$ 0.60 Hz

Slope = 41.43 Hz/sigma value

Variance of the slope = 1.47 Hz/sigma value

Correlation Coefficient = 0.9956

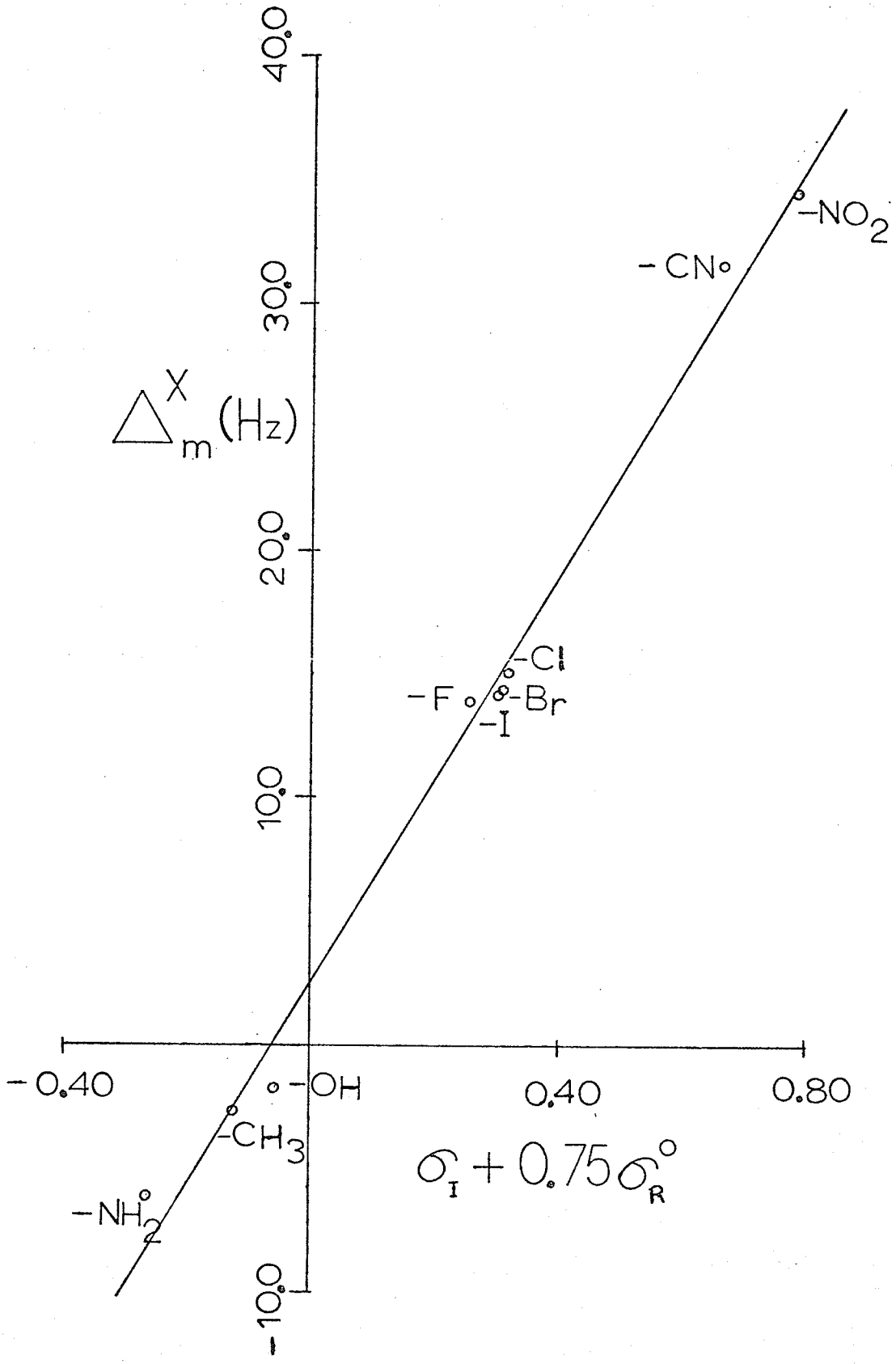

40.0
30.0
20.0
10.0
-10.0
Δ^{X}_{m}(Hz)
-NO2
-CN
-Cl
-F
-Br
-I
-0.40
-OH
0.40
0.80
-CH3
-NH2
$\sigma_I + 0.75\sigma_R^{\circ}$

Figure 16. A plot of Δ^{X}_{para} (defined in text) in Hz at 60 MHz versus $\sigma_I + 0.75 \quad \sigma_R^{o}$. The substituent constants σ_I and σ_R^{o} are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = 2.93 Hz

Variance of the Y-Intercept = $\pm$ 0.50 Hz

Slope = 40.62 Hz/sigma value

Variance of the Slope = $\pm$ 1.22 Hz/sigma value

Correlation Coefficient = 0.9969

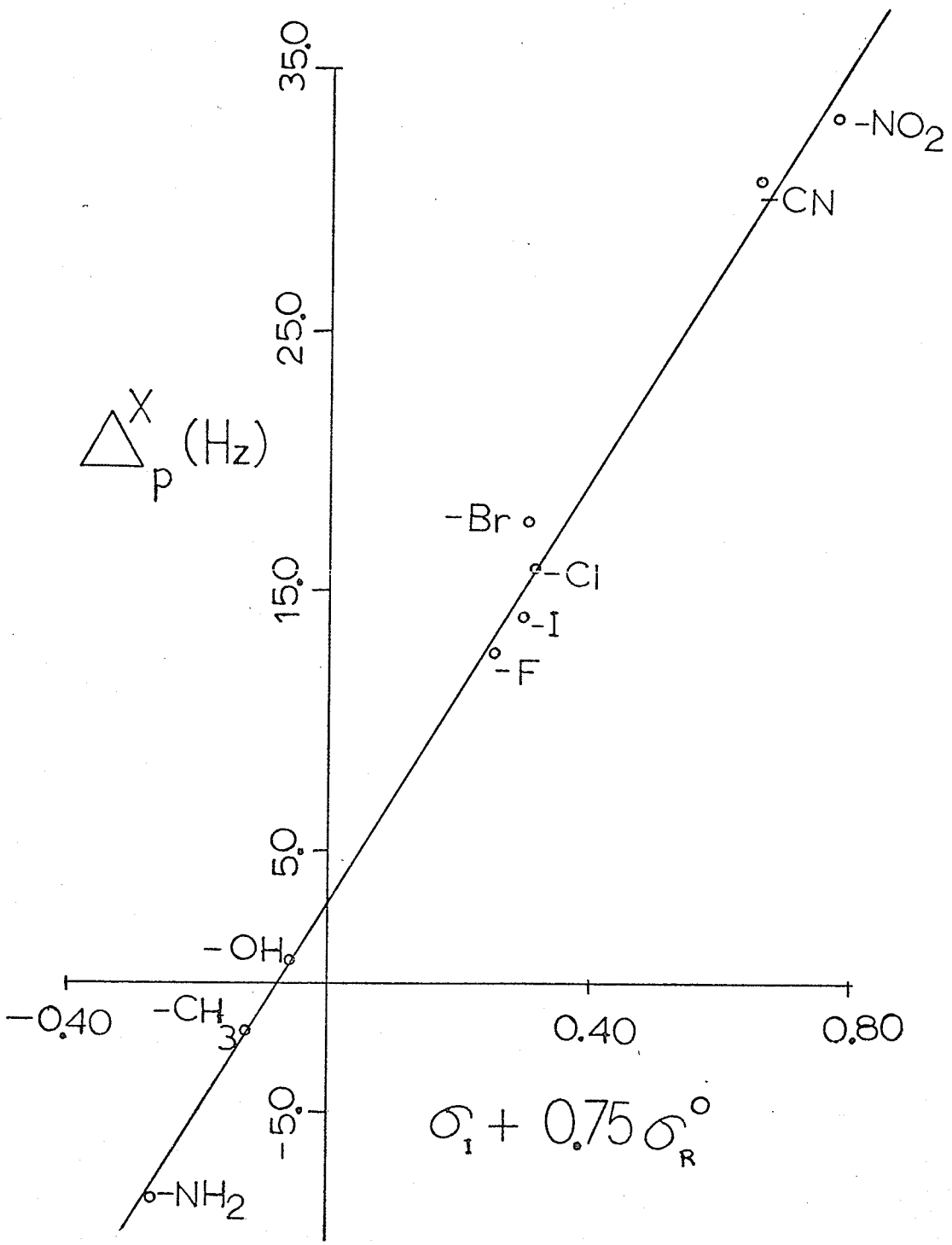

35.0
25.0
15.0
5.0
-5.0
Δ^X_p (Hz)
-NO2
-CN
-Br
-Cl
-I
-F
-OH
-CH3
-NH2
-0.40
0.40
0.80
$\sigma_I + 0.75\sigma_R^\circ$

Figure 17. A plot of Δ^{X}_{meta} (defined in text) in Hz at 60 MHz versus Taft's sigma meta (σ^{o}_{meta}) value for X.

Parameters Calculated from the above Plot:

Y-Intercept = -1.48 Hz

Variance of the Y-Intercept = $\pm$ 1.13 Hz

Slope = 48.69 Hz/Taft's sigma meta value

Variance of the Slope = $\pm$ 2.83 Hz/Taft's sigma meta value

Correlation Coefficient = 0.9884

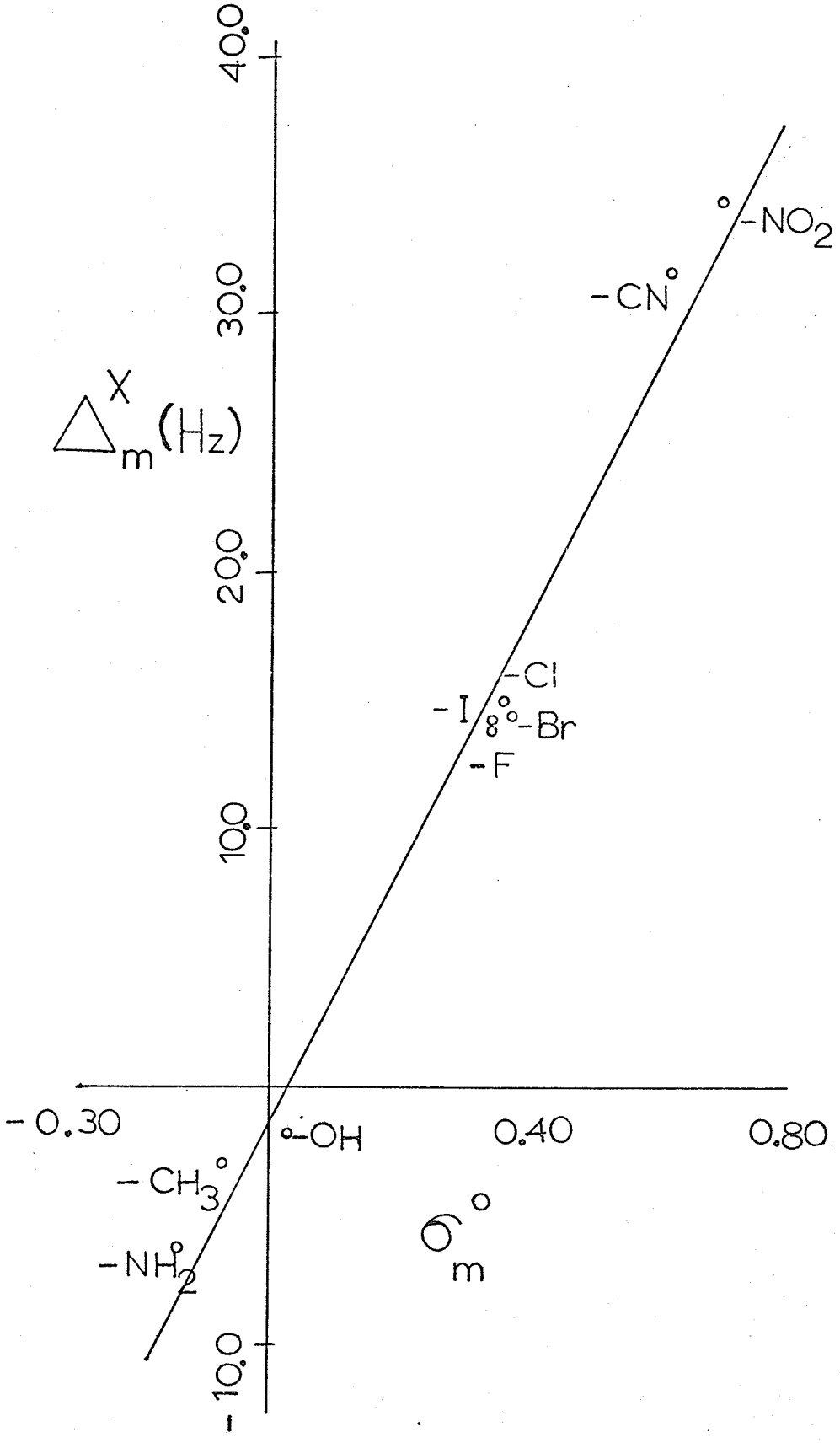

40.0
30.0
20.0
10.0
-10.0
Δ^{X}_{m}(Hz)
-NO2
-CN
-Cl
-I
-Br
-F
-0.30
-OH
0.40
0.80
-CH3
-NH2
σ_m

Figure 18. A plot of $\triangle^{X}_{para}$ (defined in text) in Hz at 60 MHz versus Taft's sigma para (σ^{o}_{para}) value for X.

Parameters Calculated from the above Plot:

Y-Intercept = 5.39 Hz

Variance of the Y-Intercept = $\pm$ 0.55 Hz

Slope = 35.83 Hz/Taft's sigma para value

Variance of the Slope = $\pm$ 1.30 Hz/Taft's sigma para value

Correlation Coefficient = 0.9948

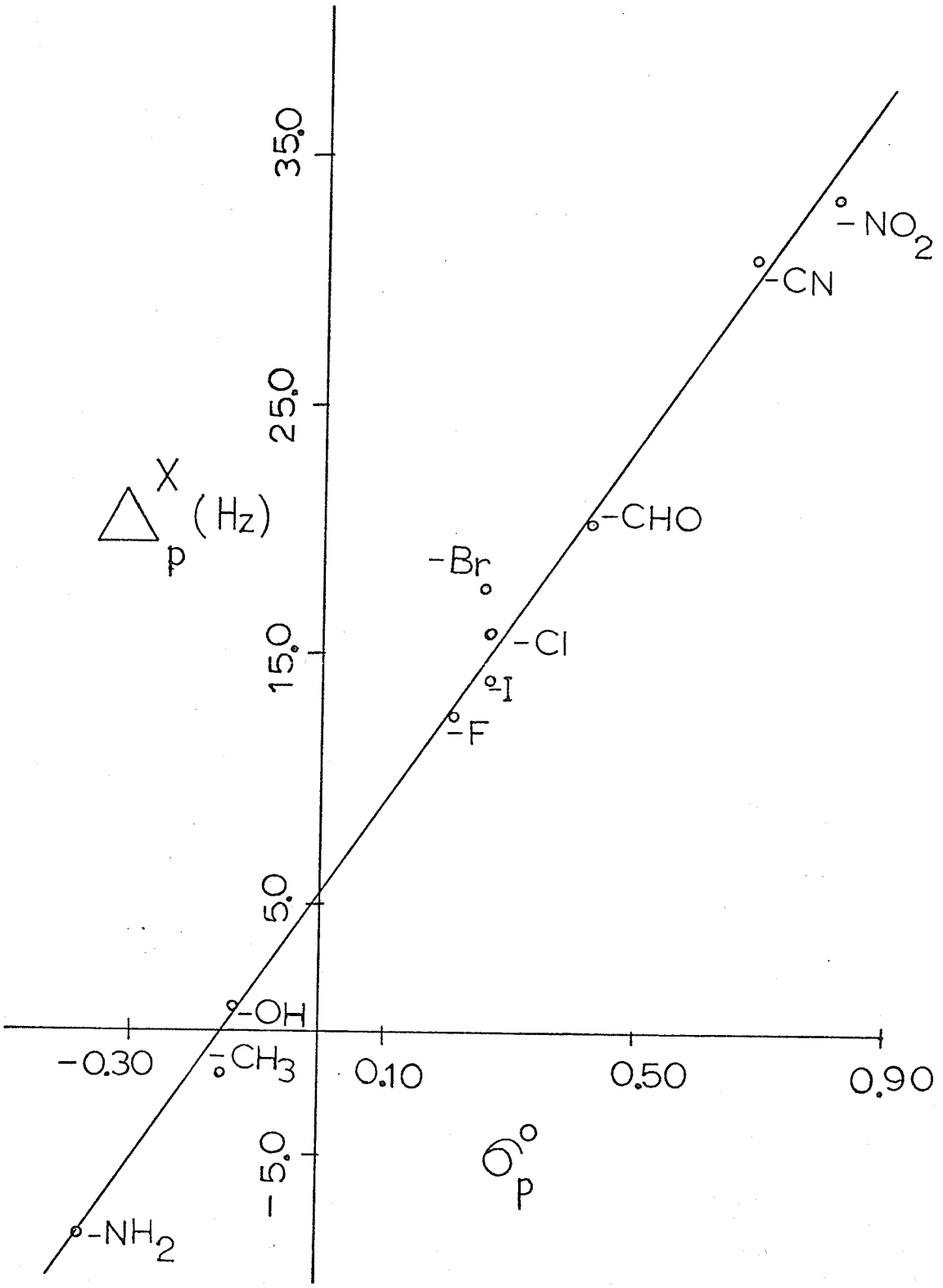

35.0
25.0
15.0
5.0
-5.0
Δ^{X}_{p} (Hz)
-NO2
-CN
-CHO
-Br
-Cl
-I
-F
-OH
-CH3
-NH2
-0.30
0.10
0.50
0.90
σ°_{p}

Figure 19. A plot of Δ^{X}_{meta} (defined in text) in Hz at 60 MHz versus $0.5\ \sigma_I + \sigma_R^{\circ}$. The substituent constants σ_I and σ_R° are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = 11.87

Variance of the Y-Intercept = $\pm$ 1.45

Slope = 45.99 Hz/sigma value

Variance of the Slope = $\pm$ 5.14 Hz/sigma value

Correlation Coefficient = 0.9589

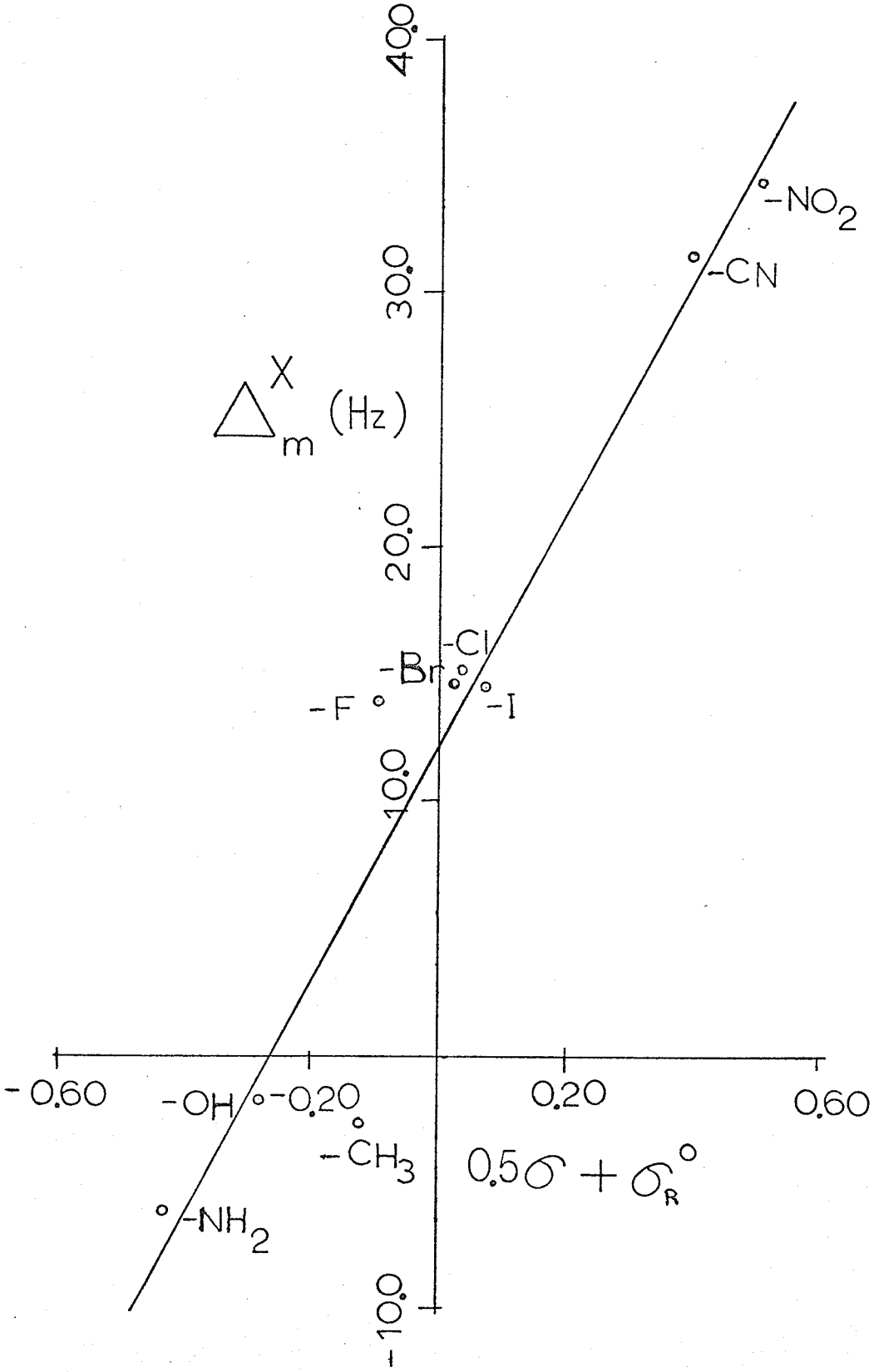

40.0
30.0
20.0
10.0
-10.0
Δ^{X}_{m} (Hz)
-NO2
-CN
-Cl
-Br
-I
-F
-0.60
-OH
-0.20
0.20
0.60
-CH3
-NH2
0.5σ + σR°

Figure 20. A plot of Δ^{X}_{para} (defined in text) in Hz at 60 MHz versus $0.5\ \sigma_I + \sigma_R^{\circ}$. The substituent constants σ_I and σ_R° are taken from reference 91.

Parameters Calculated from the above Plot:

Y-Intercept = 11.63 Hz

Variance of the Y-Intercept = $\pm$ 1.42 Hz

Slope = 42.91 Hz/sigma value

Variance of the Slope = $\pm$ 4.95 Hz/sigma value

Correlation Coefficient = 0.9506

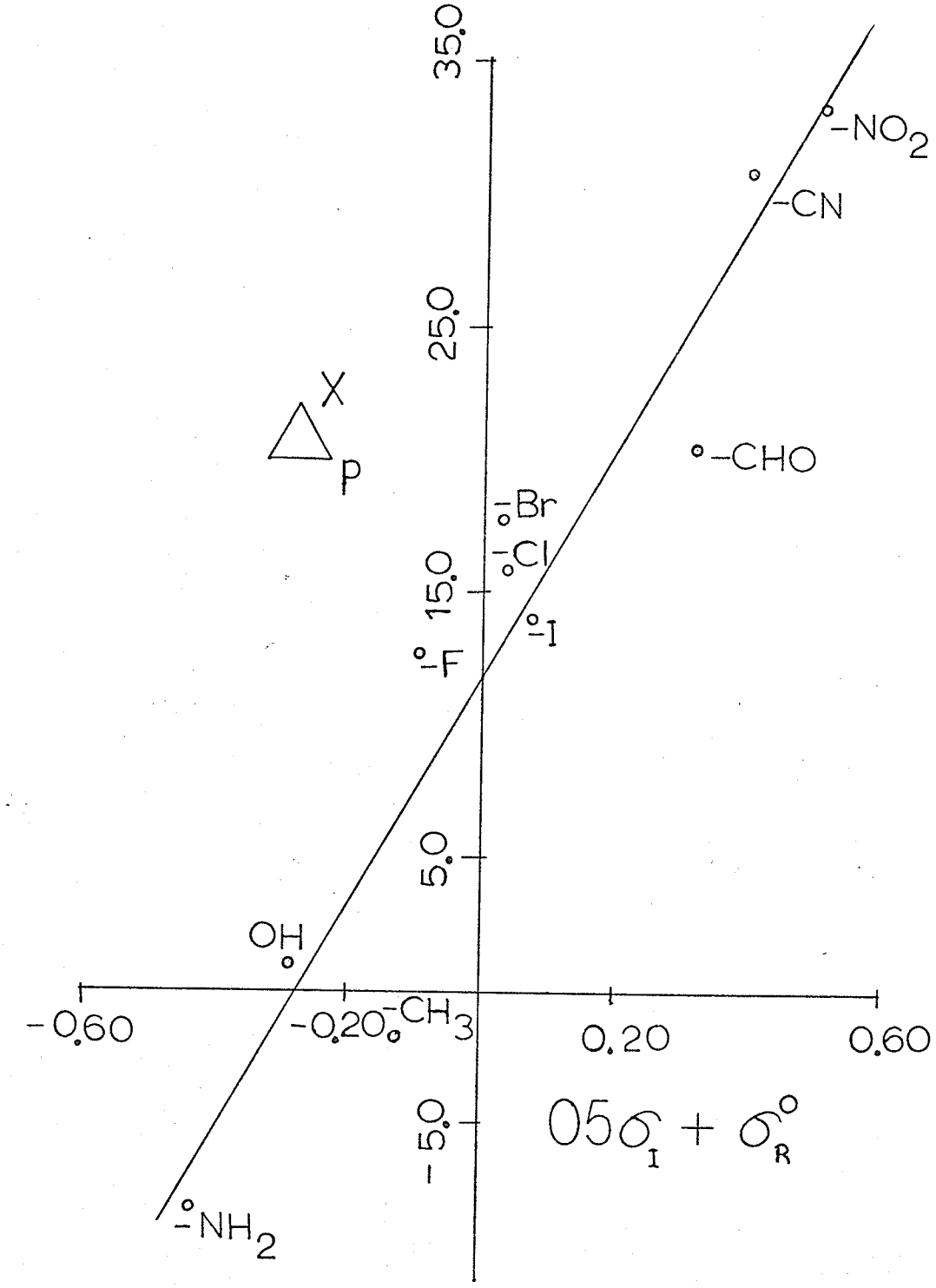

35.0
25.0
15.0
5.0
-5.0
X
P
-NO2
-CN
-CHO
-Br
-Cl
-I
-F
OH
-NH2
-0.60
-0.20
-CH3
0.20
0.60
0.5σI + σR°

Figure 21. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 2,3,5,6-tetrafluoro-X-benzenes versus Taft's sigma para (σ^{o}_{para}) value for X.

Parameters Calculated from the above Plot:

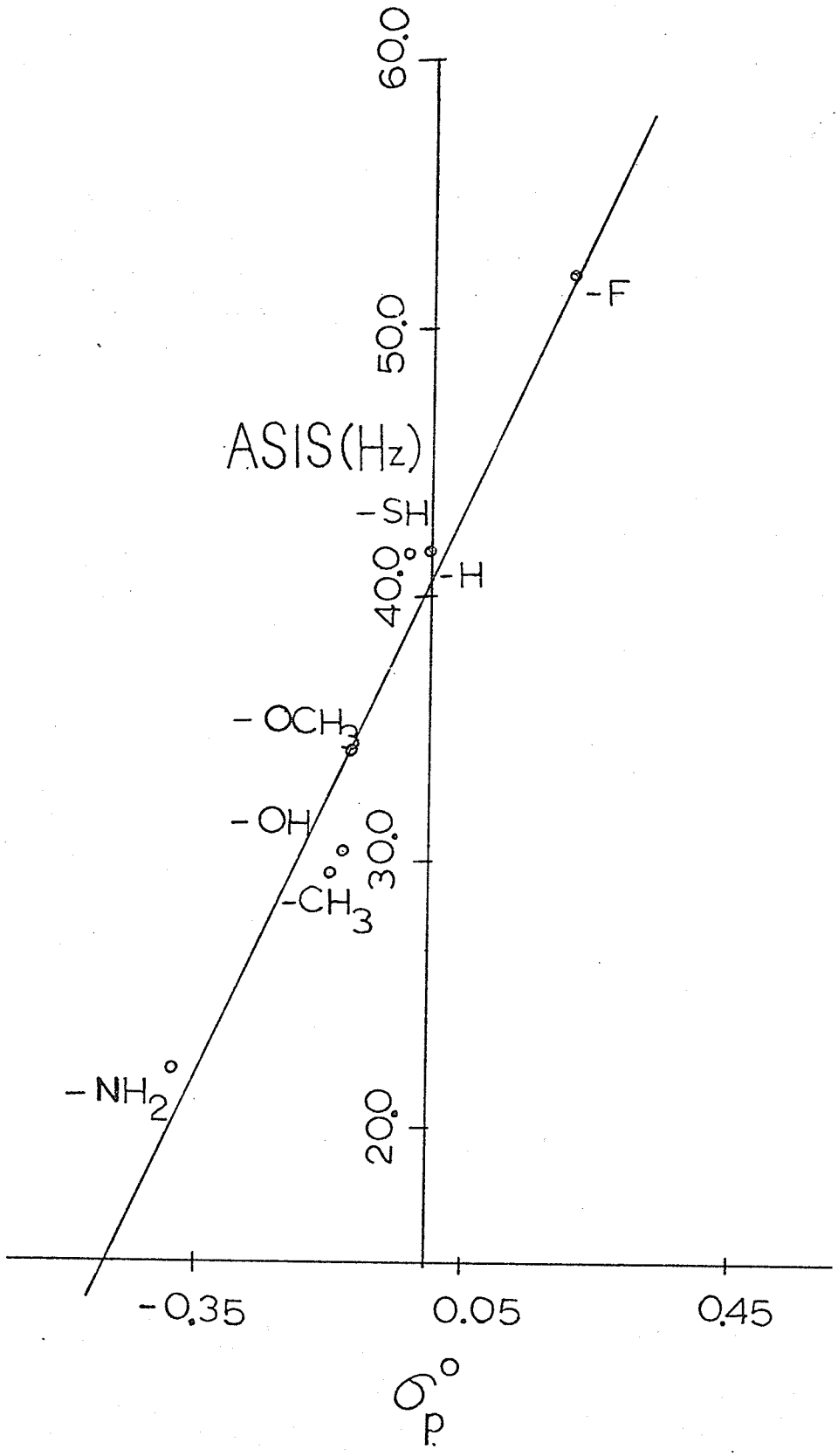
Y-Intercept = 40.46 Hz

Variance of the Y-Intercept = $\pm$ 1.07 Hz

Slope = 53.38 Hz/Taft's sigma para value

Variance of the Slope = $\pm$ 5.75 Hz/Taft's sigma para value

Correlation Coefficient = 0.9722


60.0
50.0
ASIS(Hz)
40.0
30.0
20.0
-F
-SH
-H
-OCH3
-OH
-CH3
-NH2
-0.35
0.05
0.45
σp°

2. Dipole Moments

As mentioned in Chapter III, several investigators have shown that the ASIS of a particular solute proton is linearly related to the dipole moment of the solute. Whether or not this linearity is indicative of a dipole-induced-dipole mechanism is open to question.

In the case of 3,5-dichloro-X-benzenes, a plot of the dipole moment of the X-mono-substituted benzenes (96) versus ASIS of H_4 shows some degree of linearity (Figure 22). The author feels that the linearity of this plot is a reflection of the electronic charge density at H_4. The effect of a substituent X on the charge density at various positions in a monosubstituted benzene may be roughly represented by μ/r. Here μ is the dipole moment of the molecule, and r is the length of the dipole. Although it is readily possible to determine the dipole moment of a molecule, the separation of the latter into the components, the charge (e) and the distance (r), is far more arbitrary. Essentially this is a consequence of the non-localized form of the electric charge. In the case of monosubstituted benzenes one does not have two point charges, thus any attempt to give μ a numerical value may be expected to lead to erroneous results.

For solute molecules which contain no ortho hydrogens, Schwenk has used the function

$$F(\mu/r) = \left[\sum_{o} \frac{\mu}{r}\right]_{\substack{\text{MESO.}\\\text{IND.}}} + \frac{1}{2}\left[\sum_{m} \frac{\mu}{r}\right]_{\text{IND.}} + \frac{1}{3}\left[\left(\frac{\mu}{r}\right)_{p}\right]_{\text{MESO.}} \quad \text{(VI-6)}$$

as an approximation to the change in the charge distribution induced by the substituent (36). Here μ is the dipole moment of the C-X bond, and r is the C-X bond length. For $-N(CH_3)_2$ and $-NO_2$ only the C-N bond

distance was used for the r value. Substituents which are mainly inductive contributors were considered when they were situated ortho or meta to the proton in question, while substituents which are mainly mesomeric contributors were considered only when they were placed ortho or para to the proton in question.

By taking the slope of an amazingly linear plot of solvent shifts, $\Delta^{C_6H_{12}}_{C_6D_6}$, for polyhalobenzenes in which no protons occur ortho to each other, versus $F(\mu/r)$, Schwenk (36) obtained the additivity parameters given in Table V. Notice that Δ^X_p is zero, and Δ^X_m is one-half Δ^X_o for any halogen substituent X. Although this scheme seems to work well for halobenzenes with no ortho protons, the author feels it is not generally applicable to substituted benzenes containing substituents other than halogens.

For example, Schwenk (36) has suggested the following groups be considered only when placed ortho or para to the proton in question: OH, NH_2, OCH_3, CHO, CN, and NO_2. He calculates a $F(\mu/r)$ value of 1.86 e.s.u. for H_3 and H_5 in 2,4,6-trichlorophenol. That is, he predicts the same solvent shift for this compound as for H_2 in 1,3-dichlorobenzene. However, $\Delta(H_2)$ = 10.86 Hz in 1,3-dichlorobenzene while $\Delta(H_3)$ and $\Delta(H_5)$ = 22.86 Hz in 2,4,6-trichlorophenol. Similarly, equation (VI-6) predicts the ASIS of proton H_3 in 2,4-dichloroaniline and 2,4-dichloronitrobenzene to be equal , but $\Delta(H_3)$ equals 3.71 and 42.54 Hz, respectively. These results demonstrate that one cannot ignore the inductive effects of mainly mesomeric groups when they are placed meta to the proton in question.

Finally it is of interest to note that the ASIS of proton H_2

in 1,3-dichlorobenzene and 1,3,5-trichlorobenzene are 10.86 and 23.10 Hz, respectively. Schwenk's additivity model would predict equal $\triangle(H_2)$ values in these compounds. The author would like to point out that because $\triangle(H_2)$ in 1,3,5-trichlorobenzene is much greater than $\triangle(H_2)$ in 1,3-dichlorobenzene, does not necessarily imply that the inductive effect of the chlorine atom is operative at the para position (i.e., over five bonds). The inductive effect of a chlorine atom on two meta-Cl atoms must also be considered.

Figure 22. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for H_4 in some 3,5-dichloro-X-benzenes versus the dipole moment of the X-monosubstituted benzenes. The dipole moments are taken from reference 96.

Parameters Calculated from the above Plot:

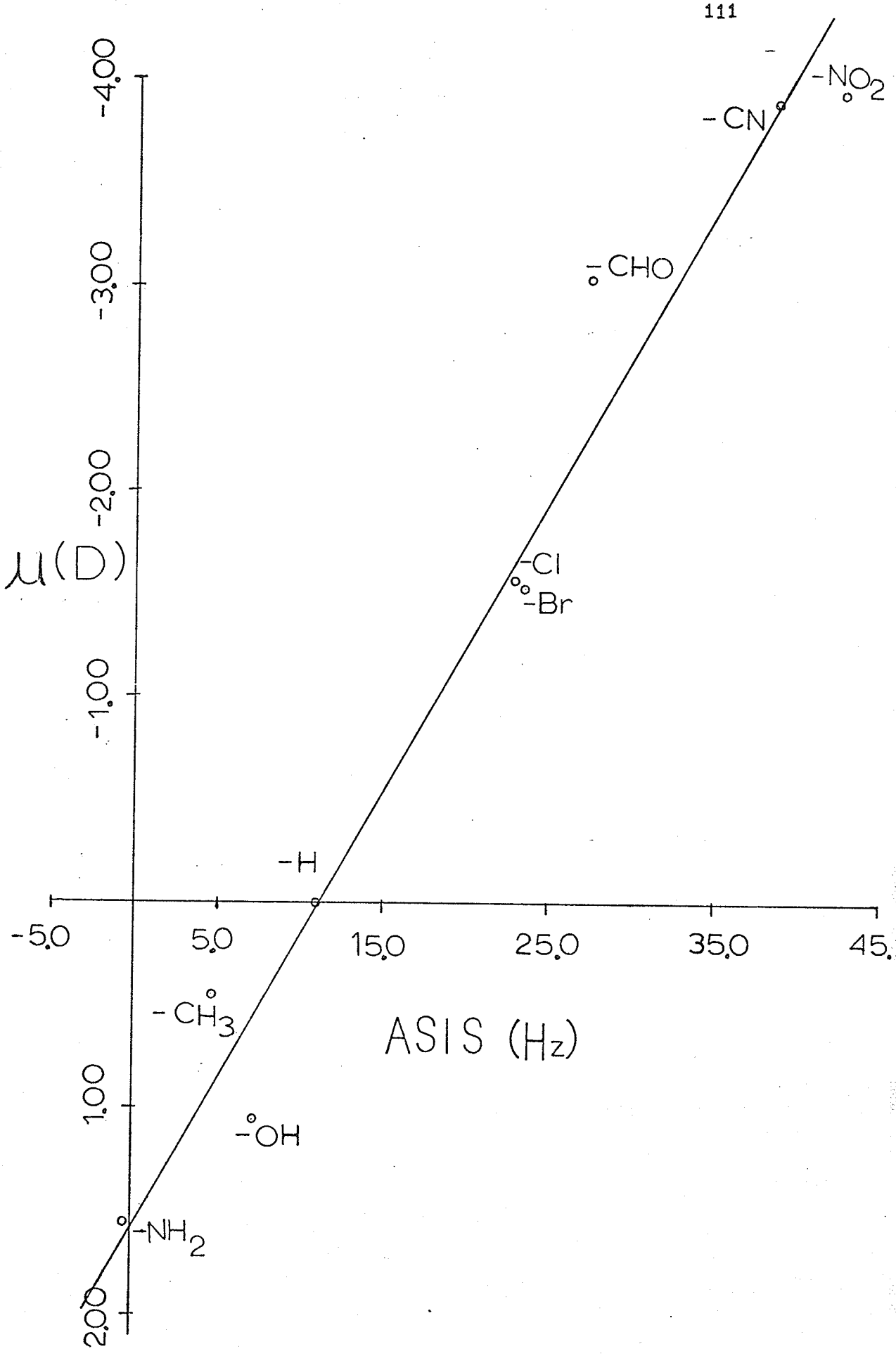
Y-Intercept = 11.23 Hz

Variance of the Y-Intercept = $\pm$ 1.22 Hz

Slope = -7.08 Hz/Debye

Variance of the Slope = $\pm$ 0.52 Hz/Debye

Correlation Coefficient = 0.9814


-4.00
-3.00
-2.00
-1.00
1.00
2.00
μ(D)
-5.0
5.0
15.0
25.0
35.0
45.
ASIS (Hz)
-NO2
-CN
-CHO
-Cl
-Br
-H
-CH3
-OH
-NH2

3. π-Electron Densities

In Chapter III, the attempts of various authors to illustrate the importance of steric effects in determining the magnitude of ASIS were criticized because investigators have failed to isolate the steric from the charge effect of a substituent.

Zweig, Lehnser, Lancaster, and Meglia (97) have shown that the respective ring proton chemical shifts of the methoxybenzenes are approximately proportional to the calculated π-electron densities on the ring carbon atoms. From 19 nonequivalent aromatic protons in the set of compounds considered, a chemical shift of 9.95 ppm per unit of π-electron density was calculated. This value is in good agreement with the value obtained by Schaefer and Schneider (98).

Having established that ASIS values are related to charge distributions (i.e., Taft's σ constants), it is of interest to determine whether the ASIS values for the aromatic ring protons of methoxybenzenes are linearly related to the π-electron density on the attached ring carbon sites. If the ASIS of a given ring proton is dependent only on the π-electron density at the carbon it is attached to, one expects a linear plot of ASIS versus π-electron density. One may attribute any non-linearity in this plot to effects other than charge effects, that is, steric effects. The ASIS values and π-electron densities of nine methoxybenzenes are given in Table XIV.

The NMR spectra of methoxybenzene and 1,3-dimethoxybenzene were not analyzed due to time limitations. Also, the last three compounds listed in Table XIV were insolubie in cyclohexane, therefore the results from carbon tetrachloride solutions were used (97).

TABLE XIV*

ASIS Values (Hz at 60 MHz) of Aromatic Protons and π-Electron Densities at the Attached Ring Sites in the Methoxybenzenes

COMPOUND	POINT	PROTON	In C_6H_{12}	In C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$	π-ELECTRON DENSITY
1,2-Dimethoxybenzene	1	H_3, H_6	403.58	398.93	4.65	1.040
	2	H_4, H_5	404.98	408.27	-3.29	1.026
1,4-Dimethoxybenzene	3	H_2, H_3, H_5, H_6	400.86	404.28	-3.42	1.037
1,2,3-Trimethoxybenzene	4	H_4, H_6	385.96	382.94	3.02	1.066
	5	H_5	406.56	409.85	-3.29	1.024
1,2,4-Trimethoxybenzene	6	H_3	382.82	390.21	-7.39	1.079
	7	H_5	374.08	377.57	-3.49	1.066
	8	H_6	398.25	398.55	-0.30	1.037
1,3,5-Trimethoxybenzene	9	H_2, H_4, H_6	357.65	372.22	-14.57	1.109
1,2,3,4-Tetramethoxybenzene	10	H_5, H_6	385.2	382.02	3.2	1.064

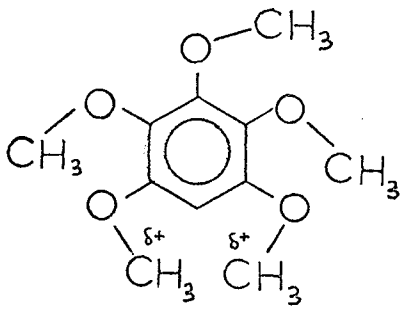
TABLE XIV (continued)

COMPOUND	POINT	PROTON	In C_6H_{12}	In C_6D_6	$\Delta^{C_6H_{12}}_{C_6D_6}$	π -ELECTRON DENSITY
1,2,4,5-Tetramethoxybenzene	11	H_3, H_6	385.8	389.77	-4.0	1.078
Pentamethoxybenzene	12	H_6	370.2	368.82	1.4	1.104

* (1) Shifts are relative to TMS.

(2) All compounds which dissolved in C_6H_{12} and C_6D_6 were 3 mole % samples except for o-dimethoxybenzene which was 5 mole %.

Figures 23 and 24 show plots of aromatic proton chemical shifts in cyclohexane and ASIS against calculated charge densities at attached ring positions in methoxybenzenes. Although the ring proton chemical shifts of the methoxybenzenes in cyclohexane appear to be linearly related to the π-electron density at the attached ring position, no such relationship between ASIS values and π-electron densities is evident. This writer contends that little can be concluded from these results for the following reasons: First, the electron densities on all atoms immediately adjacent to the ring proton in question must be considered. For example, the methyl groups of the methoxybenzenes will be somewhat positive centres, thus attracting the benzene solvent molecules. One may attribute the large observed ring-proton solvent shift of pentamethoxybenzene (point 12 in Figure 24) to a structure such as XIX. Similarly, the negative solvent shifts observed



XIX

for protons H_4 and H_5 in 1,2-dimethoxybenzene (point 2 in Figure 24) and for proton H_5 in 1,2,3-trimethoxybenzene (point 5 in Figure 24) may be attributed to the absence of an ortho-methoxy group, that is, the absence of a relatively positive centre. Secondly, the experimental error involved in the determination of ASIS values for methoxybenzenes

is large since they equal the difference of two large numbers of comparable magnitude. And thirdly, π-electron densities calculated by Huckel molecular orbital theory without overlap sometimes have limited significance.

Figure 23. A plot of aromatic ring proton chemical shifts (Hz at 60 MHz) versus the calculated charge densities at attached ring positions in methoxybenzenes.

Parameters Calculated from the above Plot:

Y-Intercept = 930.41 Hz

Variance in the Y-Intercept = ± 57.78 Hz

Slope = -511.31 Hz per unit of π-electron density

Variance in the Slope = ± 54.45 Hz per unit of π-electron density

Correlation Coefficient = -0.9472

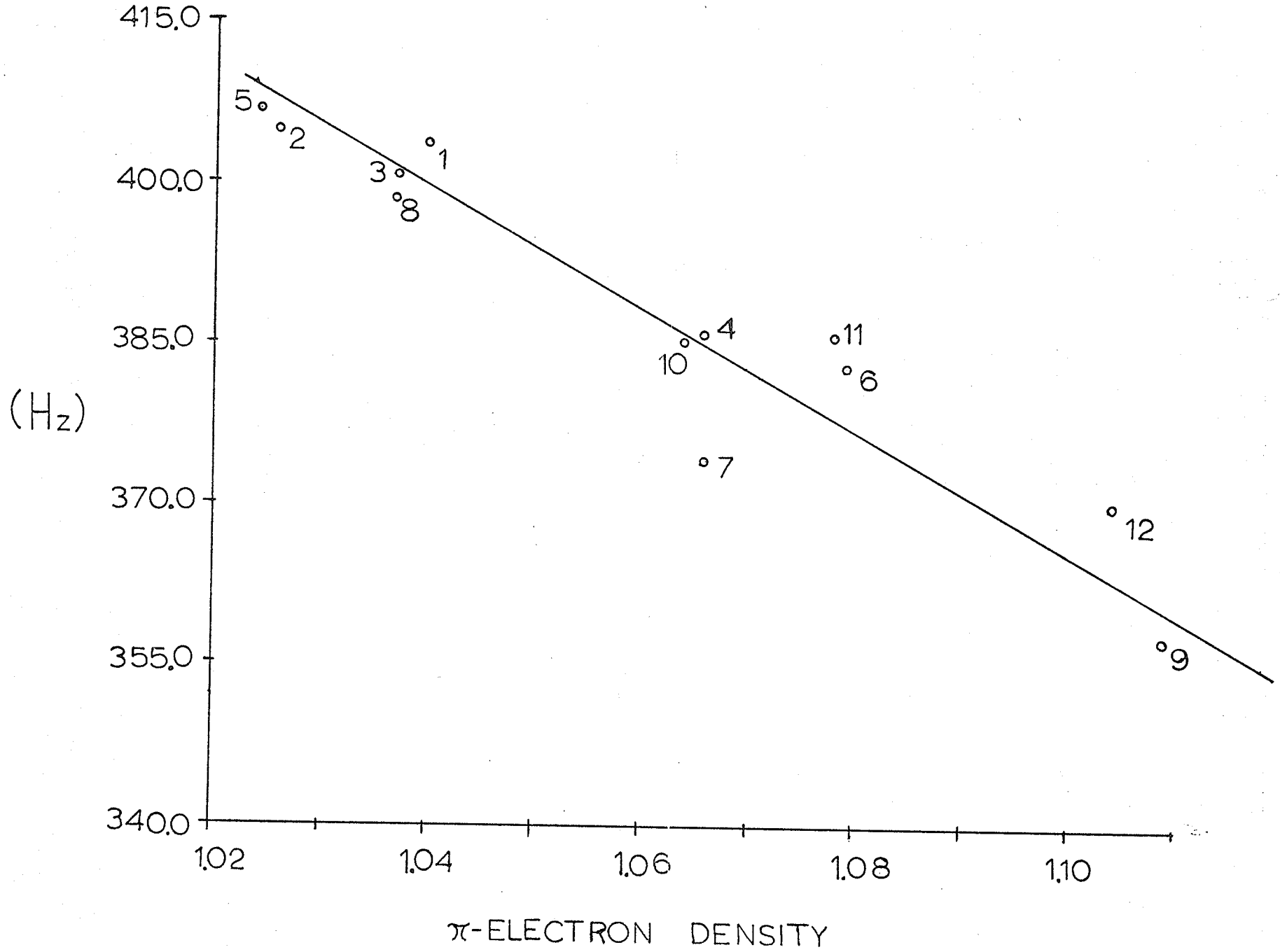

415.0
400.0
385.0
370.0
355.0
340.0
(Hz)
1.02
1.04
1.06
1.08
1.10
π-ELECTRON DENSITY
1
2
3
4
5
6
7
8
9
10
11
12

Figure 24. A plot of $\Delta^{C_6H_{12}}_{C_6D_6}$ in Hz at 60 MHz for aromatic protons in methoxybenzenes versus the calculated charge densities at attached ring positions.

<u>Parameters Calculated from the above Plot:</u>

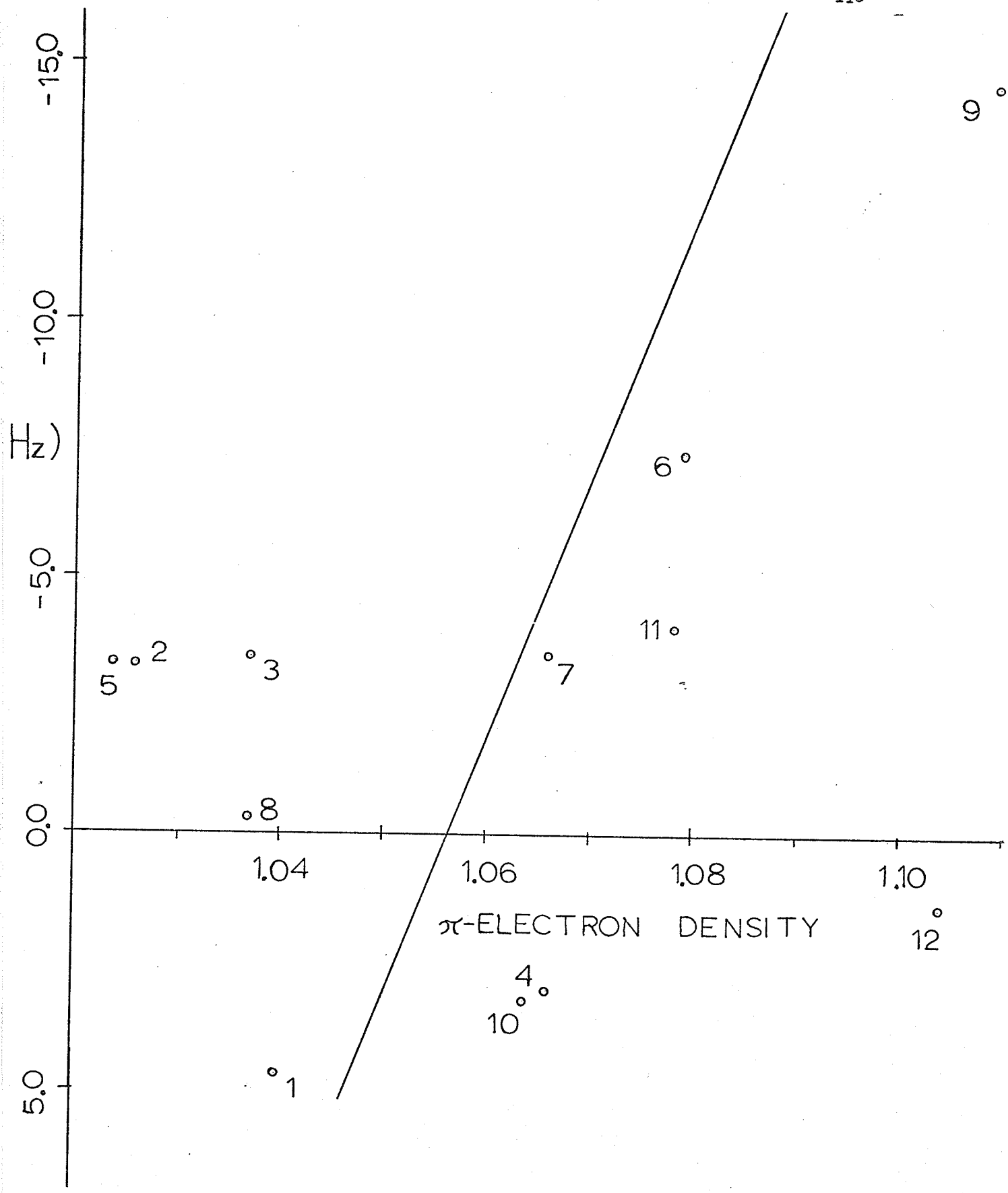
Y-Intercept = 69.45 Hz

Variance in Y-Intercept = $\pm$ 57.82 Hz

Slope = -67.62 Hz per unit π-electron density

Variance in the Slope = $\pm$ 54.48 Hz per unit π-electron density

Correlation Coefficient = -0.3654

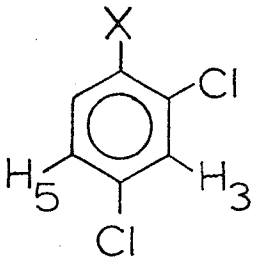

-15.0
-10.0
-5.0
0.0
5.0
H/N)
1.04
1.06
1.08
1.10
π-ELECTRON DENSITY
1
2
3
4
5
6
7
8
9
10
11
12

4. Steric Effects

Since steric effects are electronic in nature, it is somewhat difficult to formally distinguish between charge and steric effects. The term steric effect is used in this thesis to designate the situation where the approach of benzene solvent molecules to a solute proton is sterically inhibited. That is, because of spatial crowding about the solute proton, the approach of the benzene solvent molecules is inhibited (see Chapter IV).

As mentioned in Chapter IV, Nomura and Takeuchi (56) have discussed the ASIS of monosubstituted (poly)methylbenzenes by considering the effect of methyl substituent(s) on the geometry of the 1:1 complex between the solute and benzene solvent molecule. Since the author of this thesis does not believe that substituted benzene solute molecules are "solvated" by only one benzene solvent molecule at any given time (see Chapter IV), the term "steric effect" will not be used to designate modifications of the geometry of the hypothetical 1:1 complex.

In order to demonstrate the relative importance of charge and steric effects, consider the following compounds (XX)*. On the basis of

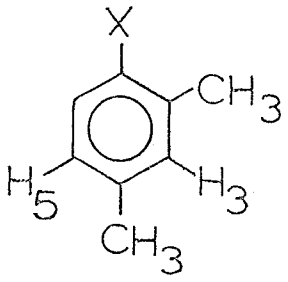


XX

X	$\Delta(H_3)$	$\Delta(H_5)$	$\Delta(H_5)/\Delta(H_3)$
NH_2	3.71	9.23	2.49
H	10.86	19.38	1.79
I	18.60	32.52	1.75
Cl	22.86	34.62	1.51
NO_2	42.54	52.08	1.22

*All ASIS values are $\Delta^{C_6H_{12}}_{C_6D_6}$ values (Hz at 60 MHz).

spatial crowding the author would expect $\triangle(H_5) > \triangle(H_3)$, and this is in fact observed. However, as the electron withdrawing power of X increases, the ratio $\triangle(H_5)/\triangle(H_3)$ decreases. If a steric effect were the only factor determining the ASIS shifts of H_3 and H_5, the ratio, $\triangle(H_5)/\triangle(H_3)$ should be approximately constant for all X substituents, provided that X influences the ASIS values of H_3 and H_5 equally. In connection with these observations, consider the following results of Nomura and Takeuchi (XXI) (56)*.



XXI

X	$\triangle(H_3)$	$\triangle(H_5)$
NH_2	-4.8	-8.5
Cl	13.8	10.8
I	16.8	13.8
NO_2	32.4	28.2

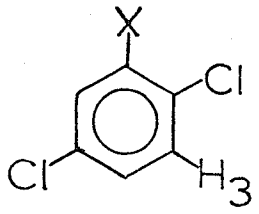
* All ASIS values are $\triangle^{C_6H_{12}}_{C_6D_6}$ values (Hz at 60 MHz).

Steric factors imply that $\triangle(H_5) > \triangle(H_3)$. However, $\triangle(H_3)$ is more positive than $\triangle(H_5)$ in all cases for series XXI. Nomura and Takeuchi (56) have given the following explanation for the apparent anomaly: "The 2-methyl group pushes the overlying solvent molecule aside, causing the slant of the plane of the solvent molecule out of that of the solute, thus the 5-proton is more deeply immersed in the paramagnetic region of the solvent than the 3-proton". Such an argument is erroneous. Since the van der Waals radius of a chlorine atom is approximately equal to that of a methyl group, one expects the ASIS values of H_3 and H_5 in series XX and XXI to show similar trends on the

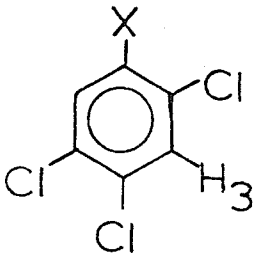
basis of the explanation of Nomura and Takeuchi. Opposite trends are observed. This can be explained by noting that, in general, chlorine atoms will behave as negative centres relative to methyl groups because of the relatively large electronegativity of chlorine atoms. Thus, in the case of 2,4-dichloro-X-benzenes, the benzene solvent molecules tend to avoid the H_3 region relative to the H_5 region. However, in the case of 2,4-dimethyl-X-benzenes the benzene solvent molecules tend to "solvate" the "positive" methyl groups, thus $\triangle(H_3) > \triangle(H_5)$. The decrease of the ratio $\triangle(H_5)/\triangle(H_6)$ with increasing electron withdrawing power of X in the series XX can also be explained by charge effects. When X = NO_2, the electron density at the 2-chlorine atom is reduced considerably relative to the case where X = NH_2. Thus with X = NO_2, the benzene solvent molecules tend to solvate H_3 and H_5 to the same extent. However with X = NH_2, the highly electronegative chlorine atom ortho to the amino group will behave as a negative centre relative to H_6, thus benzene solvent molecules "solvate" H_5 to a much greater extent than H_3.

Finally, it must be stressed that the above interpretation given to explain the ASIS values of compounds XX and XXI does not preclude the presence of a steric effect. However, the author contends that the steric effects in compounds XX and XXI are overshadowed by the negative charge on the chlorine atoms and the positive charge on the methyl groups.

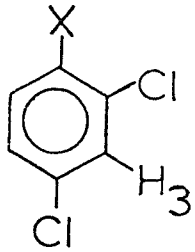
Before concluding this section, an example which further demonstrates the relative importance of charge and steric effects is discussed. Consider the following series of compounds:



XXII



XXIII



XXIV

X	$\Delta(H_3)$	$\Delta(H_3)$	$\Delta(H_3)$
H	24.18	22.86	10.86
Cl	33.36	35.04	22.86
Br	30.96	33.10	-
I	34.02	31.55	18.60
NO_2	53.69	52.41	42.54

* All ASIS values are $\Delta^{C_6H_{12}}_{C_6D_6}$ values (Hz at 60 MHz).

Notice that even though protons H_3 in compounds XXIII and XXIV are expected to be spatially crowded to approximately the same extent, $\Delta(H_3)$ in series XXIII is greater than $\Delta(H_3)$ in series XXIV. These observations can be explained by charge effects since in the case of XXIII, the additional electronegative chlorine atom in the 5 position will decrease the electron density on atoms adjacent to H_3 in compounds XXIII relative to compounds XXIV. Thus H_3 is "solvated" by the benzene solvent molecules to a greater extent in XXIII than in XIV. On the basis of steric effects one would expect $\Delta(H_3)$ in XXII to be greater than $\Delta(H_3)$ in XXIII, but in fact, $\Delta(H_3)$ is approximately the same in XXII and XXIII. These observations show that the steric effect, if important

at all in these compounds, is definitely overshadowed by charge effects.

5. Unsatisfactory Correlations

Attempts were made to correlate the ASIS of H_4 in 3,5-dichloro-X-benzenes with the para proton (H^1), para fluorine (F^{19}), and para carbon (C^{13}) chemical shifts of the mono-X-substituted benzenes. Although these plots show some degree of linearity, none compare with the plot of $\triangle(H_4)$ versus σ° (Figure 9).

C. SUMMARY AND CONCLUSIONS

In summary, this work has shown:

1. that the electron density at and in the immediate vicinity of a given proton is related to its observed ASIS value,

2. that observed benzene solvent-induced shifts appear to be surprisingly insensitive to steric effects,

3. that the equation proposed by Schwenk (36), equation (VI-6), is not generally applicable to substituted benzenes,

4. the importance of dilution shifts in determining the magnitude of experimental errors in ASIS studies, and

5. the presence of long-range spin-spin coupling constants (99, 100) which previously had not been reported.

This study has yielded no evidence for complex formation between solvent benzene molecules and substituted benzene solute molecules. In the case of substituted benzenes as solutes it is probably most logical to think of the anisotropic benzene molecules as preferentially "solvating" electron deficient regions while avoiding regions of larger electron density. On the NMR time scale the observed solvent shifts must correspond to the time average of many such "solvating" events.

Finally, this work has provided new questions to be answered.

D. SUGGESTIONS FOR FUTURE RESEARCH

The benzene-induced solvent shifts of protons in substituted benzenes are related to electron density. To put this relationship on firmer grounds it would be valuable to study solute molecules for which reliable calculations of electron density are available. The vinyl protons of 4-substituted styrenes should be examined in this connection. Wehrli, Pretsch, and Simon (101) have calculated electron densities at the vinyl carbon atoms for the substituents Br, Cl, F, Me, OMe, H, NMe_2, and NO_2 in 4-substituted styrenes. Also, Hamer and Reynolds (102) have carefully measured the vinyl proton chemical shifts of several 4-substituted styrenes in cyclohexane. Calculated π-electron densities are also available for several heterocyclic compounds (103 - 105).

The complete proton NMR spectra of several monosubstituted benzenes have been satisfactorly analyzed in carbon tetrachloride solutions (91, 106 - 112). With the availability of a 100 MHz NMR spectrometer and improving computer facilities, a careful study of ASIS in monosubstituted benzenes should be feasible in this laboratory.

The magnetic anisotropy of fluorobenzene has been shown to be practically identical to that of benzene (113). It would be interesting to compare the solvent shifts induced by fluorobenzene and benzene, however one would expect the measurements in fluorobenzene to be complicated by the reaction field term in equation (I - 4).

APPENDIX I

SOLVENT SHIFT DATA FROM THE WORK OF SCHWENK AND RICHARDSON (36, 81) AND NOMURA AND TAKEUCHI (56)

TABLE XV A.

Proton Chemical Shifts of Polyhalosubstituted Benzenes

(Hz to Low Field of TMS at 60 MHz)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	△
(1)	Benzene	—	432.66	428.94	3.72
(2)	1,4-Difluorobenzene	—	412.14	391.02	21.12
(3)	1,4-Dichlorobenzene	—	428.76	404.58	24.18
(4)	1,4-Dibromobenzene	—	433.96	409.03	24.93
(5)	1,4-Diiodobenzene	—	437.88	413.58	24.30
(6)	1,3,5-Trichlorobenzene	—	429.78	406.68	23.10
(7)	1,3,5-Tribromobenzene	—	451.26	429.54	21.72
(8)	1,2,3,4-Tetrafluorobenzene	—	405.66	360.96	44.70
(9)	1,2,3,4-Tetrachlorobenzene	—	429.72	388.32	41.40
(10)	1,2,4,5-Tetrafluorobenzene	—	413.22	371.52	41.70
(11)	1,2,4,5-Tetrachlorobenzene	—	445.92	410.88	35.04
(12)	1,2,4,5-Tetrabromobenzene	—	466.08	434.34	31.74
(13)	1,4-Difluoro-2,5-dibromobenzene	—	432.36	393.48	38.88
(14)	1,2,3,5-Tetrafluorobenzene	—	395.58	363.30	32.28
(15)	2,4,6-Tribromoiodobenzene	—	456.30	429.30	27.00

Table XV A. (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	Δ
(16)	Pentafluorobenzene	—	403.14	351.24	51.90
(17)	Pentachlorobenzene	—	444.42	403.62	40.80
(18)	1,2,3-Trichlorobenzene	H_4, H_6	433.50	404.88	28.62
		H_5	416.70	375.48	41.22
(19)	3,5-Dichlorobromobenzene	H_2, H_6	439.50	416.94	22.56
		H_4	432.18	408.60	23.58
(20)	1-Bromo-3-chloro-5-iodobenzene	H_2	442.02	419.22	22.80
		H_4	442.02	419.22	22.80
		H_6	449.04	427.68	21.36
(21)	1,2,4-Trichlorobenzene	H_3	441.30	418.44	22.86
		H_5	422.52	387.90	34.62
		H_6	433.38	400.02	33.36
(22)	1,2,4-Tribromobenzene	H_3	460.92	440.76	20.16
		H_5	428.94	392.70	36.24
		H_6	439.86	408.48	31.38
(23)	1-Bromo-2,5-dichlorobenzene	H_3	433.62	402.66	30.96
		H_4	425.16	388.14	37.02
		H_6	451.98	430.80	21.18

Table XV A. (continued)

	COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	Δ
(24)	1-Bromo-3,4-dichlorobenzene	H_2	450.78	428.22	22.56
		H_5	429.84	394.32	35.52
		H_6	431.22	398.40	32.82
(25)	1-Iodo-2,4-dichlorobenzene	H_3	466.26	447.66	18.60
		H_5	423.00	390.48	32.52
		H_6	436.98	404.16	32.82
(26)	1-Iodo-2,5-dichlorobenzene	H_3	432.78	398.76	34.02
		H_4	427.14	394.32	32.82
		H_6	466.32	447.36	18.96
(27)	1-Iodo-3,4-dichlorobenzene	H_2	461.88	440.88	21.00
		H_5	420.60	383.76	36.84
		H_6	442.80	413.34	29.46
(28)	1-Iodo-2,3-dichlorobenzene	H_4	437.82	409.56	28.26
		H_5	402.42	362.76	39.66
		H_6	459.48	432.30	27.18
(29)	1-Fluoro-3,4-dichlorobenzene	H_2	425.04	400.50	24.54
		H_5	436.08	402.48	33.60
		H_6	406.92	372.90	34.02

Table XV A. (continued)

COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	Δ
(30) 1-Fluoro-2,4-dibromobenzene	H_3	456.72	435.54	21.18
	H_5	435.72	402.30	33.42
	H_6	409.62	372.12	37.50
(31) 3,5-Difluoroiodobenzene	H_2, H_6	429.90	408.72	21.18
	H_4	398.88	373.56	25.32

TABLE XV B.

Proton Chemical Shifts of Various Polysubstituted Benzenes

(Hz to Low Field of TMS at 60 MHz)

COMPOUND	PROTON	IN C_6H_{12}	IN C_6D_6	Δ
(1) Toluene	ring	423.06	423.90	-0.84
(2) p-Xylene	ring	415.38	417.48	-2.10
(3) Mesitylene	ring	400.32	402.54	-2.22
(4) p-Dimethoxybenzene	ring	400.86	404.28	-3.42
(5) p-Dinitrobenzene	—	494.94	441.78	53.16
(6) 2,4,6-Trichlorophenol	ring	429.18	406.32	22.86
(7) 2,4,6-Triiodophenol	ring	471.90	454.14	17.76
(8) 2,6-Dinitro-4-chlorophenol	ring	487.26	435.00	52.26
(9) 2,3,5,6-Tetrachloronitrobenzene	—	454.32	392.34	61.98
(10) 3,5-Dichlorotoluene	H_2, H_6	416.82	399.06	17.76
	H_4	424.92	420.18	4.74

TABLE XVI A.

Solvent Shifts ($\triangle^{C_6H_{12}}_{C_6D_6}$) of 1-Substituted-4-methylbenzenes (Hz at 60 MHz)

SUBSTITUENT	$\triangle$(Me (4))
NMe_2	-0.6
NH_2	1.2
OMe	4.8
OH	8.4
H	10.2
Cl	19.2
Br	21.0
I	22.2
CO_2Me	19.8
CN	31.8
NO_2	36.0

TABLE XVI B.

Solvent Shifts ($\Delta^{C_6H_{12}}_{C_6D_6}$) of 1-Substituted-3,5-dimethylbenzenes (Hz at 60 MHz)

SUBSTITUENT	$\Delta(H_2, H_6)$	$\Delta(H_4)$
NMe_2	-6.6	-11.4
NH_2	3.0	-7.2
OMe	-6.6	-2.4
OH	6.6	1.2
Cl	1.8	13.8
Br	2.4	15.6
I	3.0	16.8
CO_2Me	12.6	15.0
CN	24.0	29.4
NO_2	11.4	33.6

TABLE XVI C.

Solvent Shifts ($\Delta^{C_6H_{12}}_{C_6D_6}$) of 1-Substituted-2,4-dimethylbenzenes (Hz at 60 MHz)

SUBSTITUENT	$\Delta(H_3)$	$\Delta(H_5)$	$\Delta(H_6)$
NH_2	-4.8	-8.4	-1.2
OH	-3.0	-3.6	3.6
OCH_3	-1.8	-5.4	1.2
Cl	13.8	10.8	-2.4
Br	14.4	11.4	-1.2
I	16.8	13.8	-1.2
CN	30.6	29.4	16.8
NO_2	32.4	28.2	7.8

APPENDIX II

COMPILATION OF COUPLING CONSTANTS

Spin-spin coupling constants measured and calculated by the author are given in Table XVIII. Coupling constants were calculated by assuming additivity of substituent effects (73, 114). In Table XVII the differences $\triangle J$ between the coupling constants in the monosubstituted benzenes (10 w/w % solutions in carbon tetrachloride (108 - 112)) and benzene (115) are given.

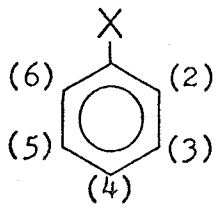
TABLE XVII

Effect of substituents on the proton coupling constants in monosubstituted benzenes

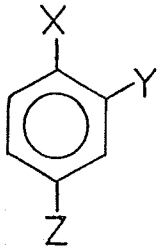
X*	$\triangle J_{23}$	$\triangle J_{34}$	$\triangle J_{24}$	$\triangle J_{26}$	$\triangle J_{35}$	$\triangle J_{36}$
CN	0.26	0.12	-0.10	0.41	-0.07	-0.01
I	0.39	-0.07	-0.23	0.51	0.38	-0.23
Br	0.51	-0.10	-0.25	0.75	0.41	-0.23
Cl	0.50	0.07	-0.26	0.86	0.25	-0.13
F	0.82	-0.07	-0.30	1.37	0.45	-0.26
NO_2	0.82	-0.07	-0.19	1.03	0.11	-0.14
NH_2	0.48	-0.15	-0.27	1.16	0.23	-0.22
OH	0.63	-0.14	-0.28	1.34	0.37	-0.20
OCH_3	0.76	-0.18	-0.35	1.37	0.39	-0.25
CH_3	0.10	-0.01	-0.12	0.49	0.13	-0.08
CHO	0.20	-0.07	-0.05	0.38	-0.11	-0.04

*Numbering begins with the substituent.
Defined as $J_X - J_b$ where J_B are the couplings ($\pm$ 0.04 Hz) in benzene: $J_o = 7.54$, $J_m = 1.37$, $J_p = 0.69$ Hz (115).
In Hz with a probable error of not more than 0.05 Hz, derived from monosubstituted benzenes in CCl_4 (108 - 112).

For example, for the 1-X-2-Y-4-Z-benzenes (formula XXVI) the predicted coupling constants can be written with reference to the monosubstituted



XXV



XXVI

benzenes (formula XXV):

$$J_o = J_{56} = \Delta J_{23}^{X} + \Delta J_{34}^{Y} + \Delta J_{23}^{Z} + J_o^{B}$$

$$J_m = J_{35} = \Delta J_{35}^{X} + \Delta J_{24}^{Y} + \Delta J_{26}^{Z} \quad J_m^{B}$$

$$J_p = J_{36} = \Delta J_{36}^{X} \quad \Delta J_{36}^{Y} \quad \Delta J_{36}^{Z} \quad J_p^{B}$$

where J_o^{B}, J_m^{B}, J_p^{B} are the unperturbed couplings in benzene. Using this procedure Schaefer, Kotowycz, Hutton, and Lee (73) have shown that ortho coupling constants of 1-X-2-Y-4-Z-benzenes are well reproduced (root mean square deviations = 0.05 Hz) while meta and para couplings show saturation effects.

The average deviation between the calculated and measured ortho coupling constants given in Table XVIII is 0.17 Hz.

TABLE XVIII

Coupling Constants in some Substituted Benzenes (Hz)*

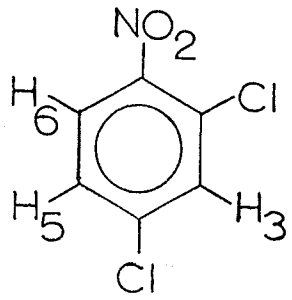
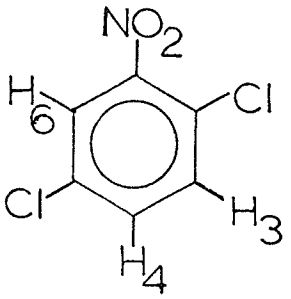
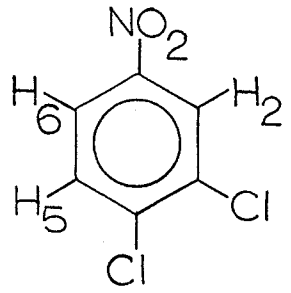
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(1) 2,4-Dichloronitrobenzene 	J_{35}	2.152	2.213	2.08
	J_{36}	0.340	0.299	0.29
	J_{56}	8.727	8.713	8.93
(2) 2.5-Dichloronitrobenzene 	J_{34}	8.41	8.52	8.47
	J_{36}	0.31	0.31	0.29
	J_{46}	2.53	2.54	2.29
(3) 3.4-Dichloronitrobenzene 	J_{25}	0.312	0.313	0.29
	J_{26}	2.532	2.595	2.39
	J_{56}	8.807	8.817	8.93

Table XVIII (continued)

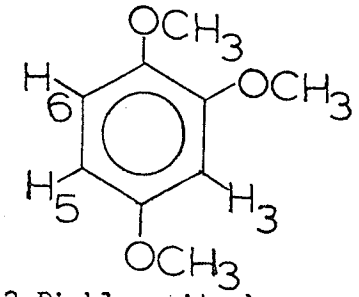
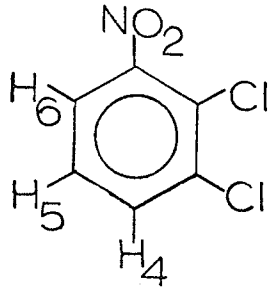
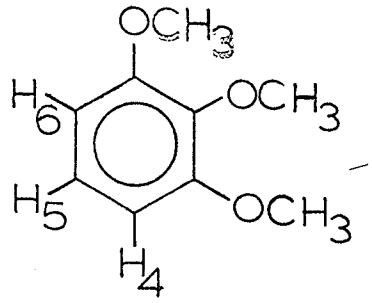
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(4) 1,2,4-Trimethoxybenzene	J_{35}	2.696	2.806	2.78
	J_{36}	0.222	0.222	-0.06
	J_{56}	8.666	8.754	8.88
(5) 2,3-Dichloronitrobenzene	J_{45}	-	8.173	8.04
	J_{46}	-	1.512	1.17
	J_{56}	-	8.190	8.50
(6) 1,2,3-Trimethoxybenzene	J_{45}	8.343	8.387	7.94
				

Table XVIII (continued)

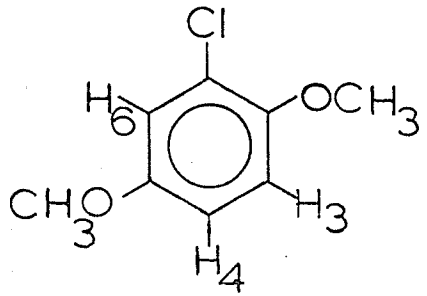
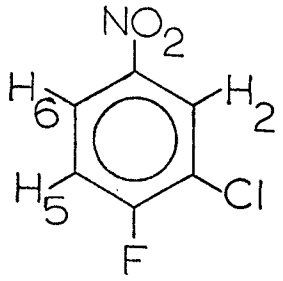
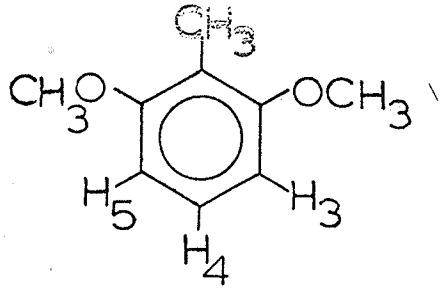
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(7) 2,5-Dimethoxychlorobenzene	J_{34}	8.973	8.987	9.13
	J_{36}	0.313	0.226	0.06
	J_{46}	2.987	3.038	2.87
(8) 3-Chloro-4-fluoronitrobenzene	J_{25}	0.305	0.308	0.16
	J_{26}	2.735	2.778	2.59
	J_{56}	9.027	9.027	9.25
	J_{H_2F}	6.294	6.357	-
	J_{H_5F}	7.777	8.115	-
	J_{H_6F}	4.071	4.150	-
(9) 2,6-Dimethoxytoluene	J_{34}	8.34	8.33	8.11
				

Table XVIII (continued)

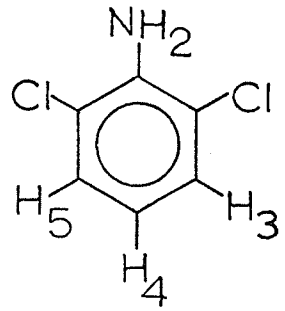
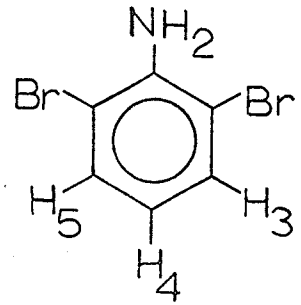
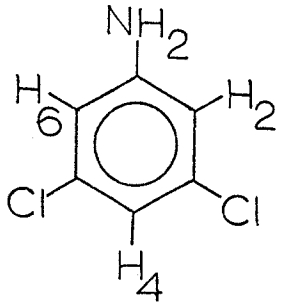
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(10) 2,6-Dichloroaniline 	J_{34}	8.05	8.08	7.96
(11) 2,6-Dibromoaniline 	J_{34}	8.02	7.98	7.80
(12) 3,5-Dichloroaniline 	J_{24}	1.731	1.789	1.70

Table XVIII (continued)

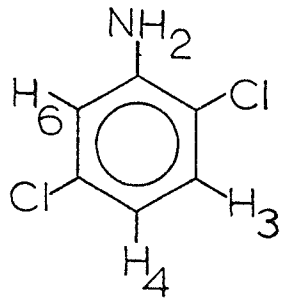
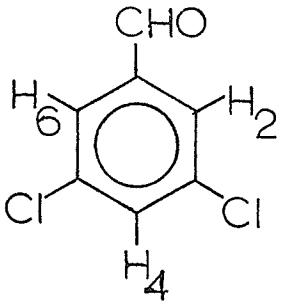
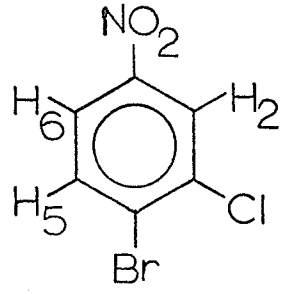
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(13) 2,5-Dichloroaniline 	J_{34}	8.48	8.477	8.39
	J_{36}	0.30	0.267	0.21
	J_{46}	2.35	2.401	2.21
(14) 3,5-Dichlorobenzaldehyde 	J_{24}	1.97	1.94	1.92
(15) 3-Chloro-4-Bromonitrobenzene 	J_{25}	0.308	0.311	0.19
	J_{26}	2.563	2.599	2.55
	J_{56}	8.764	8.784	8.94

Table (continued)

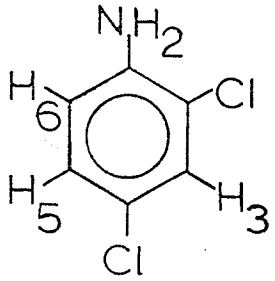
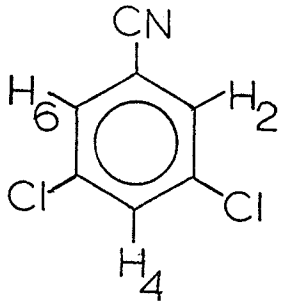
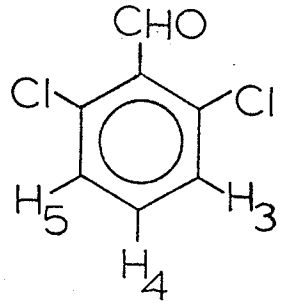
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(16) 2,4-Dichloroaniline 	J_{35}	2.356	2.369	2.20
	J_{36}	0.281	0.280	0.21
	J_{56}	8.548	8.586	8.59
(17) 3,5-Dichlorobenzonitrile 	J_{24}	1.90	1.95	1.87
(18) 2,6-Dichlorobenzaldehyde 	J_{34}	-	8.10	8.04

Table XVIII (continued)

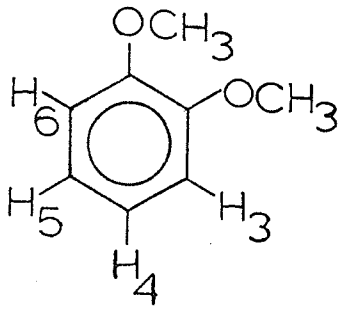
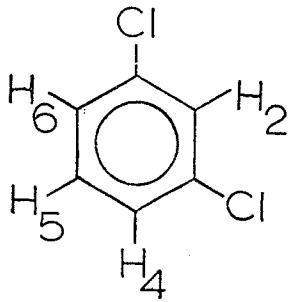
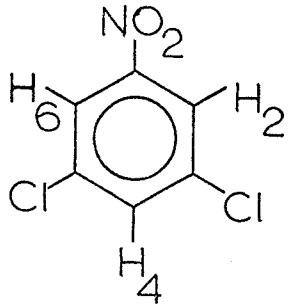
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(19) 1,2-Dimethoxybenzene 	J_{34}, J_{56}	-	8.029	8.12
	J_{35}, J_{46}	-	1.524	1.41
	J_{36}	-	0.227	0.19
	J_{45}	-	7.577	7.18
(20) 1,3-Dichlorobenzene 	J_{24}	1.99	2.00	1.97
	J_{25}	0.35	0.35	0.43
	J_{45}	8.09	8.12	8.11
(21) 3,5-Dichloronitrobenzene 	J_{24}	1.86	1.87	1.78

Table XVIII (continued)

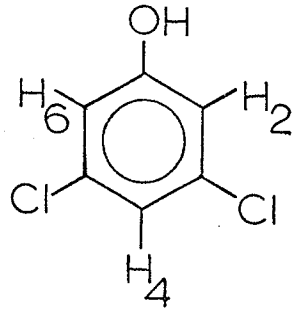
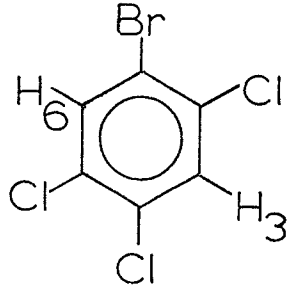
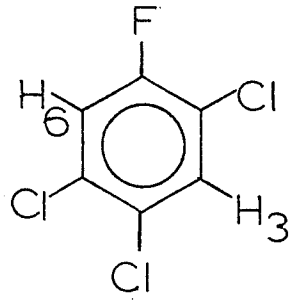
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(22) 3,5-Dichlorophenol	J_{24}	1.76	1.78	1.69
				
(23) 1-Bromo-2,4,5-trichlorobenzene	J_{36}	0.30	0.30	0.07
				
(24) 1-Fluoro-2,3,4-trichlorobenzene	J_{36}	0.36	0.36	0.04
	$J_{F,\ H_3}$	6.99	7.06	-
	$J_{F,\ H_6}$	8.17	8.39	-

Table XVIII (continued)

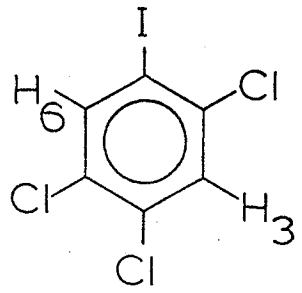
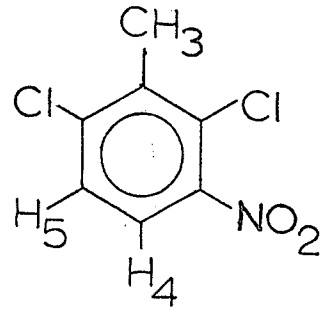
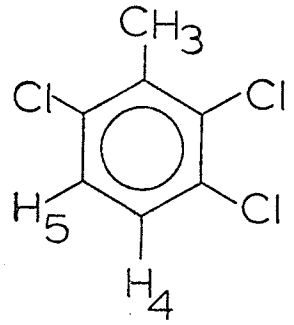
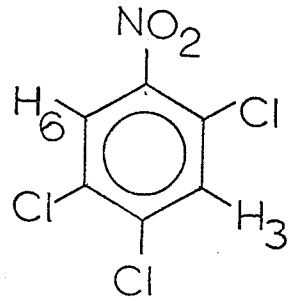
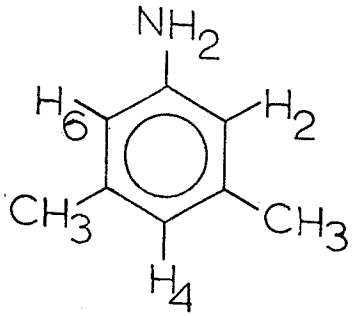
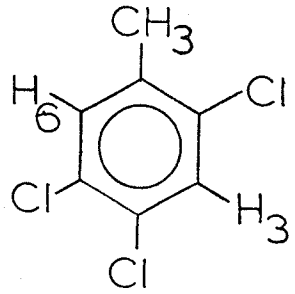
COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(25) 1-Iodo-2,4,5-trichlorobenzene 	J_{36}	0.24	0.25	0.07
(26) 2,6-Dichloro-3-nitrotoluene 	J_{45}	8.70	8.73	8.92
(27) 2,3,6-Trichlorotoluene 	J_{45}	-	-	8.60

Table XVIII (continued)

COMPOUND	J	J(In C_6H_{12})	J(In C_6D_6)	J(calculated)
(28) 2,4,5-Trichloronitrobenzene 	J_{36}	0.36	0.35	0.16
(29) 3,5-Dimethylaniline 	J_{24}	(1.32)	(1.52)	1.47
(30) 2,4,5-Trichlorotoluene 	J_{36}	0.30	0.31	0.22

* Standard deviations are in most cases less than ± 0.03 Hz.

BIBLIOGRAPHY

1. E.D. Becker, "High Resolution NMR", Academic Press, New York, 1969.

2. J.D. Memory, "Quantum Theory of Magnetic Resonance Parameters", McGraw-Hill Book Company, New York, 1968.

3. J.W. Emsley, J. Feeney, and L.H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance", Vols. I and II, Pergamon Press Ltd., Oxford, 1965.

4. A.D. Buckingham, T. Schaefer, and W.G. Schneider, J. Chem. Phys., 32, 1227 (1960).

5. P. Laszlo in "Progress in Nuclear Magnetic Resonance Spectroscopy", Vol. III, Pergamon Press Ltd., Oxford, 1967.

6. T. Schaefer, B. Richardson, and R. Schwenk, Can. J. Chem., 46, 2775 (1968).

7. A.A. Bothner-By and R.E. Glick, J. Chem. Phys., 26, 1651 (1957).

8. J.R. Zimmerman and M.R. Foster, J. Phys. Chem., 61, 282 (1957).

9. J. Ronayne, and D.H. Williams in "Annual Review of NMR Spectroscopy", Vol. II, Academic Press, New York, 1969.

10. B.P. Dailey, J. Chem. Phys., 41, 2304 (1964).

11. J.A. Pople, W.G. Schneider, and H.J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill Book Company, Inc., New York, 1959.

12. N.C. Bhacca and D.H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day Inc., San Francisco, 1964, Chapter VII.

13. G. Farges and A.S. Dreiding, Helv. Chim. Acta, 49, 552 (1966).

14. T. Schaefer and W.G. Schneider, Can. J. Chem., 38, 2066 (1960).

15. J.D. Connolly and R. McCrindle, Chem. Ind., 379 (1965).

16. J.D. Connolly and R. McCrindle, Chem. Ind., 2066 (1965).

17. J.H. Bowie, G.E. Gream, and M.H. Laffer, Aust. J. Chem., 21, 1799 (1968).

18. W. Cocker, P.V.R. Shannon, and P.A. Staniland, J. Chem. Soc. (C), 485 (1967).

19. K. Tori, Pharm. Bull. (Japan), 12, 1439 (1964).

20. K. Nagarajan and M.D. Nair, Tetrahedron, 23, 4493 (1967).

21. W.G. Schneider, J. Phys. Chem., 66, 2653 (1962).

22. C. Lussau, J. Chim. Phys., 61, 462 (1964).

23. A.D. Buckingham, Can. J. Chem., 38, 300 (1960).

24. T.W. Marshall and J.A. Pople, Mol. Phys., 1, 199 (1958).

25. C.J. MacDonald and T. Schaefer, Can. J. Chem., 45, 3157 (1967).

26. I.D. Kuntz, Jr., and M.D. Johnston, Jr., J. Amer. Chem Soc., 89, 6008 (1967).

27. R.J. Schmidt, R.S. Butler, and J.H. Goldstein, J. Phys. Chem., 73, 1117 (1969).

28. W.T. Raynes and M.A. Raza, Mol. Phys. 17, 157 (1969).

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

30. B. Linder, J. Chem. Phys., 33, 668 (1960).

31. B. Linder, B. Howard, and M. Emerson, J. Chem. Phys., 36, 485 (1962).

32. N. Lumbroso, T.K. Wu, and B.P. Dailey, J. Phys. Chem., 67, 2469 (1963).

33. P. DeMontgolfier, J. Chim. Phys., 64, 639 (1967).

34. F.H.A. Rummens, W.T. Raynes, and H.J. Bernstein, J. Phys. Chem., 72, 2111 (1968).

35. R.A. Kromhout and B. Linder, J. of Magnetic Resonance, 1, 450 (1969).

36. R.J. Schwenk, M.Sc. Thesis, University of Manitoba, 1968.

37. H.M. Hutton, E. Bock, and T. Schaefer, Can. J. Chem., 44, 2772 (1966).

38. J. Homer, Tetrahedron, 23, 4065 (1967).

39. J.K. Becconsall, Mol. Phys., 15, 129 (1968).

40. C.E. Johnson and F.A. Bovey, J. Chem. Phys., 29, 1012 (1958).

41. M.J. Stephen, Mol. Phys., 1, 223 (1958).

42. R.J. Abraham, Mol. Phys., 4, 369 (1961).

43. J.C. Schug, J. Phys. Chem., 70, 1816 (1966).

44. T.L. Brown and K. Stark, J. Phys. Chem., 69, 2679 (1965).

45. P. Diehl, J. Chim. Phys., 61, 199 (1964).

46. P. Diehl, Helv. Chim. Acta, 45, 568 (1962).

47. P. Laszlo and J.L. Soong, Jr., J. Chem. Phys., 47, 4475 (1967).

48. J.H. Bowie, J. Ronayne, and D.H. Williams, J. Chem. Soc. (B), 785 (1967).

49. J.H. Bowie, J. Ronayne, and D.H. Williams, J. Chem. Soc (B), 535 (1967).

50. R.E. Klinck and J. B. Stothers, Can. J. Chem., 40, 1071 (1962).

51. J. Ronayne and D.H. Williams, Chem. Comm., 712 (1966).

52. T. Ledaal, Tetrahedron Letters, 1683 (1968).

53. J.E. Baldwin, J. Org. Chem. 30, 2423 (1965).

54. D.H. Williams, J. Ronayne, and R.G. Wilson, Chem. Comm., 1089 (1967).

55. R.G. Wilson, and D.H. Williams, J. Chem. Soc. (B), 1163 (1968).

56. Y. Nomura and Y. Takeuchi, Tetrahedron, 25, 3825 (1969).

57. J. Ronayne and D.H. Williams, J. Chem. Soc. (B), 540 (1967).

58. R.E. Klinck and J.B. Stothers, Can. J. Chem., 40 2339 (1962).

59. K.M. Baker and B.R. Davis, J. Chem. Soc. (B), 261 (1968).

60. J. Homer, and M.C. Cooke, J. Chem. Soc. (A), 777 (1969).

61. R.C. Fort, Jr. and T.R. Lindstrom, Tetrahedron, 23, 3227 (1967).

62. P. Laszlo and D.H. Williams, J. Amer. Chem. Soc., 88, 2799 (1966).

63. R. Foster and C.A. Fyfe, Trans. Faraday Soc., 61, 1629 (1965).

64. T. Matsuo, T. Yoshida, and O. Higuchi, Bull. Chem. Soc. Jap., 40, 2526 (1967).

65. T. Matsuo, J. Phys. Chem., 72, 1819 (1968).

66. S. Castellano and A.A. Bothner-By, J. Chem. Phys., 41, 3863 (1964).

67. A.A. Bothner-By and S. Castellano, LAOCN 3, Mellon Institute, Pittsburgh, Pa., 1966.

68. S. Castellano and J.S. Waugh, J. Chem. Phys. 34, 295 (1961).

69. J.R. Cavanaugh, J. Chem. Phys. 39, 2378 (1963).

70. R.J. Abraham and H.J. Bernstein, Can. J. Chem. 39, 216 (1961).

71. G. Slomp, Applied Spectroscopy Reviews, 2, 263 (1969).

72. R.E. Richards and T. Schaefer, Mol. Phys. 1, 331 (1958).

73. T. Schaefer, G. Kotowycz, H.M. Hutton, and J.W.S. Lee, Can. J. Chem., 46, 2531 (1968).

74. S. Forsén and R.A. Hoffman, J. Mol. Spectrosc., 20, 168 (1966).

75. H. Angad Gaur, J. Vriend, and W.G.B. Huysmans, Tetrahedron Letters, 1999 (1969).

76. R.W. Crecely, K.W. McCracken, and J.H. Goldstein, Tetrahedron, 25A, 877 (1969).

77. J.A. Pople and T. Schaefer, Mol. Phys., 3, 547 (1960); P. Diehl and J.A. Pople, ibid., 3, 557 (1960).

78. R.C. Hirst, D.M. Grant, E.G. Paul, J. Chem. Phys., 44, 4305 (1966).

79. D.M. Grant, R.C. Hirst, and H.S. Gutowsky, J. Chem. Phys., 38, 407 (1963).

80. G. Kotowycz, Ph.D. Thesis, University of Manitoba, Winnipeg, Manitoba, 1967.

81. B.W. Richardson, M.Sc. Thesis, University of Manitoba, Winnipeg, Manitoba, 1967.

82. J.R. Holden and C. Dickinson, J. Phys. Chem., 73, 1199 (1969).

83. "Progress in Stereochemistry ", Vol. II, Edited by W. Klyne and P.B.D. de la Mare, Butterworths, London, 1958, p. 102.

84. R.W. Taft, J. Amer. Chem. Soc., 79, 1045 (1957).

85. P.C. Lauterbur, J. Amer. Chem. Soc., 83, 1846 (1961).

86. P. Diehl, Helv. Chim. Acta, 49, 829 (1961).

87. G.W. Smith, J. Mol. Spectry., 12, 146 (1964).

88. I.D. Rae and L.K. Dyall, Aust. J. Chem., 19, 835 (1966).

89. S.H. Marcus, W.F. Reynolds, and S.I. Miller, J. Org. Chem., 31, 1872 (1966).

90. J.G. Traynham and F.A. Knesel, J. Org. Chem., 31, 3350 (1966).

91. K. Hayamizu and O. Yamamoto, J. Mol. Spectry., 29, 183 (1969).

92. L.N. Ferguson, "The Modern Structural Theory of Organic Chemistry", Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1963, p. 412.

93. C.D. Ritchie and W.F. Sager in "Progress in Physical Organic Chemistry", Vol. II, Edited by S.G. Cohen, A. Strietwieser, and R.W. Taft, Interscience Publishers, New York, 1964, p.323.

94. J. Niwa, Bulletin Chem. Soc. of Japan, 42, 1926 (1969).

95. A.A. Humffray, J.J. Ryan, J.P. Warren, and Y.H. Yung, Chemical Communications, 1965, p.610.

96. J.W. Smith, "Electric Dipole Moments", Butterworths Scientific Publications, London, 1955, p. 203.

97. A. Zweig, J.E. Lehnsen, J.E. Lancaster, and M.T. Meglia, J. Amer. Chem. Soc., 85, 3940 (1963).

98. T. Schaefer and W.G. Schneider, Can. J. Chem., 41, 966 (1963).

99. R. Wasylishen and T. Schaefer, Can. J. Chem., (in press).

100. T. Schaefer and R. Wasylishen, Can. J. Chem., (in press).

101. F.W. Wehrli,, E. Pretsch, and W. Simon, Helvetica Chimica Acta, 50, 2189 (1967).

102. G.K. Hamer and W.F. Reynolds, Can. J. Chem., 46, 3813 (1968).

103. L. Salem, "The Molecular Orbital Theory of Conjugated Sustems", W.A. Benjamin, New York, 1966.

104. M.J.S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, 1969.

105. Quantum Chemistry Symposium, Tetrahedron, Vol. XIX, Suppl. 2, August, 1963.

106. K. Hayamizu and O. Yamamoto, J. Mol. Spectry., 28, 89 (1968).

107. K. Hayamizu and O. Yamamoto, J. Mol. Spectry., 25, 422 (1968).

108. S. Castellano, R. Kostelnik, and C. Sun, Tetrahedron Letters, 46, 4635 (1967).

109. S. Castellano, C. Sun, and R. Kostelnik, Tetrahedron Letters, 50, 5205 (1967).

110. M.P. Williamson, R.J. Kostelnik, and S. Castellano, J. Chem. Phys., 49, 2218 (1968).

111. R.J. Kostelnik, M.P. Williamson, D.E. Wisnosky, and S.M. Castellano, Can. J. Chem., 47, 3313 (1969).

112. "Nuclear Magnetic Resonance Spectra and Chemical Structure", Vol. I, Compiled by W. Brügel, Academic Press, New York, 1967.

113. W. Huttner and W.H. Flygare, J. Chem. Phys., 50, 2863 (1969).

114. S. Castellano and R. Kostelnik, Tetrahedron Letters, 51, 5211 (1967).

115. J.M. Read and J.H. Goldstein, J. Mol. Spectry., 23, 179 (1967).