

The University of Manitoba

THE CORRELATION OF PROTON CHEMICAL SHIFTS IN POLYHALO  
SUBSTITUTED BENZENES USING AN ADDITIVITY RELATIONSHIP

by

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- TO MY PARENTS -

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- ABSTRACT -

The proton chemical shifts and coupling constants of twenty-three polyhalosubstituted benzenes have been determined in cyclohexane and carbon tetrachloride. A rough correlation of the chemical shifts with the sum of the Q's of the ortho substituents was found; it is not, however, useful as an empirical tool. Attempts to predict the chemical shifts on the basis of previously proposed additivity constants failed.

Assuming the additivity principle, the chemical shifts are correlated by introducing a new "ortho-meta" constant,  $\Delta(X-Y)$ , which pairs the substituents X, ortho to, and Y, meta to the proton. In this way it was possible to take into account the steric interaction which must be operating in molecules as highly substituted as these.

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## Chapter I

### - INTRODUCTION -

## INTRODUCTION

The basic theory of nuclear magnetic resonance (NMR) is covered in many books (1-5)\*. A brief review will be presented in this chapter.

The phenomenon of magnetic resonance can be observed only if the nucleus has a spin  $I$  and a magnetic moment  $\mu$ .  $I$ , known as the spin quantum number, is the maximum measurable component of the angular momentum resulting from a circulation of mass about a given axis.  $I$  may have values  $0, 1/2, 1, 3/2, \dots$ .  $\mu$ , known as the nuclear magnetic moment, arises from an associated circulation of charge and is given, in vector form, by

$$\mu = \gamma \hbar I = \mu_0 g I \quad (1-1)$$

where  $\gamma$  is the magnetogyric ratio.  $\gamma = 0$  for nuclei with even mass number and even atomic number.  $I$  is the spin vector,  $\mu_0$  is the nuclear magneton and  $g$  is the nuclear equivalent of the Landé  $g$  factor for electrons. Hence a spinning nucleus can be regarded as a tiny bar magnet placed along the spin axis, the so-called nuclear magnet.

In field-free space, the orientations of the spinning nuclei will be random but the angular momentum vector must still be such that its components along a particular reference direction are given by  $I, I-1, I-2, \dots, 0, \dots, -(I-2), -(I-1), -I$ . The

\* These can be considered general references, from which much of the first three chapters find their substance.

energies of these  $2I+1$  orientations are degenerate. The application of a magnetic field  $\underline{H}_0$  defines the reference direction and lifts the degeneracy. The splitting of the energy levels in a magnetic field is known as the nuclear Zeeman splitting. This is illustrated for  $I = 1$  in Fig. 1.

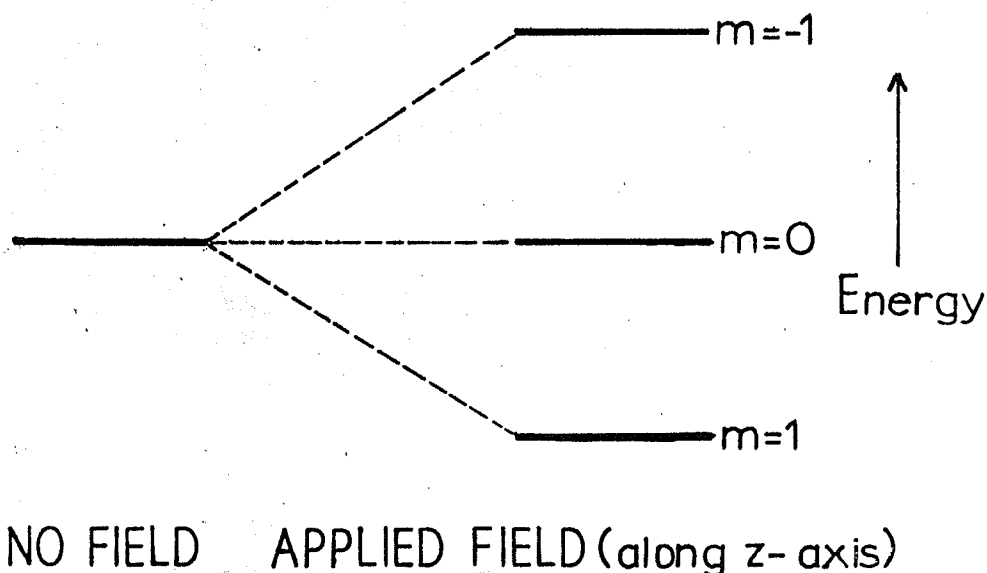


Fig. 1: The splitting of the energy levels in a magnetic field for a nucleus with  $I = 1$ .

The energy of interaction between the nuclear magnet and the magnetic field is

$$E = -\underline{\mu} \cdot \underline{H}_0 \quad (1-2)$$

or

$$E = -\mu_H H_0 \quad (1-3)$$

where  $\mu_H$  is the component of  $\underline{\mu}$  along  $\underline{H}_0$ . The magnetic moment  $\underline{\mu}$  is at all times collinear with the angular momentum vector and its magnitude is given by  $m\mu_{\max}/I$  where  $m$ , the magnetic quantum number, can assume values  $I, I-1, \dots, 0, \dots, -(I-1), -I$ . Therefore,

following from equation (1-1),

$$\mu_H = mg\mu_o \quad (1-4)$$

and the potential energy of the magnet in the field is

$$E = -mg\mu_o H_o \quad (1-5)$$

The separation of adjacent nuclear energy levels is then

$$\Delta E = g\mu_o H_o = \gamma h H_o \quad (1-6)$$

Subject to the selection rule  $\Delta m = \pm 1$  (6), transitions can occur

when the nucleus absorbs electromagnetic radiation of frequency  $\nu$

such that the Bohr frequency condition is satisfied

$$\nu = g \frac{\mu_o H_o}{h} = \frac{\gamma H_o}{2\pi} \quad (1-7)$$

This is the resonance equation which applies to NMR.

Classically, the magnetic momentum vector  $\underline{\mu}$  precesses about the magnetic field vector  $\underline{H}_o$  as a result of the torque exerted by  $\underline{H}_o$ , tending to align  $\underline{\mu}$  with  $\underline{H}_o$ , and its intrinsic mechanical spin, counteracting this tendency. The angular frequency of precession is given by

$$\omega_o = 2\pi\nu = \gamma H_o \quad (1-8)$$

which is precisely equal to the frequency of electromagnetic radiation necessary to induce a transition on quantum mechanical grounds.

A second magnetic field,  $\underline{H}_1$ , applied perpendicularly to  $\underline{H}_o$ , will change the precession into a nutation. If  $\underline{H}_1$  rotates at the same angular frequency as the magnetic momentum vector, the angle  $\theta$  between  $\underline{\mu}$  and  $\underline{H}_o$  will increase constantly until the nucleus will "tip" into a new orientation with respect to  $\underline{H}_o$  and an absorption of energy occurs, giving rise to an NMR signal.

## Chapter II

### - THE CHEMICAL SHIFT -

A- INTRODUCTION

In Chapter I it was tacitly assumed that we were dealing with a bare nucleus, stripped of its electron(s) - a situation that is not realized in practice. The extranuclear electrons undergo Larmor precession about the direction of the applied field and shield the nucleus so that the field "felt" by the nucleus,  $H_{\text{local}}$ , will be less than the field applied to the molecule,  $H_0$ . This can be stated (7) as

$$H_{\text{local}} = H_0(1 - \sigma) \quad (2-1)$$

where  $\sigma$  is the shielding constant, a positive quantity which depends on the electronic environment. Reference to equation (2-1) shows that the resonance frequency of a particular nucleus will vary from one environment to another. This difference or shift in the resonance frequencies is known as the chemical shift. It is seen from equation (2-1) that the chemical shift depends on the electron density about the nucleus, characterized by  $\sigma$ , and the applied field  $H_0$ .

The resonance line positions are usually specified with respect to some reference. Today the most commonly used reference in proton magnetic resonance is tetramethylsilane (TMS). It is convenient (8) to express the chemical shift as a dimensionless parameter,  $\delta$  (in units of parts per million), defined by

$$\delta_{rs} = \frac{H_s - H_r}{H_r} \quad (2-2)$$

when  $H_s$  and  $H_r$  are the resonant fields of the sample and the reference respectively. This avoids the necessity of stating the applied field

at which the experiment is being carried out. The chemical shift can also be expressed in terms of the shielding constants (9), namely

$$\delta_{rs} = \sigma_r - \sigma_s \quad (2-3)$$

The sign convention for  $\delta$  is reversed from that of  $\sigma$  (10).

Tiers has introduced a system of  $\tau$ -values (11) for use instead of  $\delta$ , where

$$\tau = 10 - \delta \quad (2-4)$$

Chemical shifts were first observed in 1949 by Knight (12) who found differences in the  $P^{31}$  resonance positions in several salts. Similar effects were found by Proctor and Yu (13) when they observed two peaks for the  $N^{14}$  nucleus in  $NH_4NO_3$ . Dickenson (14) found related effects for  $F^{19}$  resonance and Lindstrom (15) and Thomas (16) first observed the chemical shift for protons.

B - THE ORIGINS OF THE CHEMICAL SHIFT

The theory is actually an extension by Ramsey (17) and Pople (18) of the theory of diamagnetic susceptibilities. All theoretical attempts so far have been concerned with the mathematical formulation of  $\sigma$ , the shielding constant. Following a method used recently (19),  $\sigma$  can be decomposed into several contributions as follows:

$$\sigma = \sigma_G + \sigma_B + \sigma_A + \sigma_W + \sigma_E + \sigma_C \quad (2-5)$$

where  $\sigma_G$  is the contribution of an isolated gaseous molecule;  $\sigma_B$ , the contribution due to the bulk diamagnetic susceptibility of the solvent;  $\sigma_A$ , the contribution due to the anisotropy in the susceptibility of the solvent;  $\sigma_W$ , the contribution from van der Waals interactions;  $\sigma_E$ , the contribution from the reaction field effect, and  $\sigma_C$ , the contribution due to complex formation. The last five contributions to  $\sigma$  were first suggested by Buckingham, Schaefer and Schneider (20).

All except  $\sigma_G$  are seen to be solvent or intermolecular effects and will not be discussed further. The experimental conditions used are such that the solvent effects should be minimized and essentially constant.  $\sigma_G$  has been further decomposed (21) into four contributions as

$$\sigma_G = \sigma_{GG}^d + \sigma_{GG}^p + \sum_{G \neq B} \sigma_{GB} + \sigma_{G,ring} \quad (2-6)$$

where  $\sigma_{GG}^d$  and  $\sigma_{GG}^p$  are the diamagnetic and paramagnetic contributions from the electrons of atom G;  $\sigma_{GB}$  is the contribution from



the B substituent anisotropy and  $\sigma_{G,ring}$  is the contribution due to ring currents. These ideas will be expanded further in the remainder of this section.

### 1. Lamb's Formula

Lamb (22) first attempted to calculate the screening constant for a free atom in an S state. A diamagnetic circulation of the electrons about the nucleus is produced upon application of the magnetic field. Associated with this is a secondary magnetic field at the nucleus, directed oppositely to the applied field. The end result of such a calculation is

$$\sigma = \frac{4\pi e^2}{3mc^2} \int_0^\infty r \rho(r) dr \quad (2-7)$$

where  $\rho(r)$  is the electron density at a distance  $r$  from the nucleus.

$\sigma$  here corresponds to  $\sigma_{GG}^d$  in equation (2-6). This is known as Lamb's formula and is only true for atoms with no resultant orbital or spin angular momentum.

### 2. Ramsey's Formula

Ramsey (17) carried out a second-order perturbation calculation which considered the magnetic interactions between the electrons and nuclei of an isolated molecule placed in a uniform static magnetic field. Equation (2-8) is a simpler and less accurate expression for Ramsey's formula.

$$\sigma_{zz} = \frac{e^2}{2mc^2} \int \frac{x^2+y^2}{r^3} \rho dr + \frac{e^2 \hbar^2}{m^2 c^2 \Delta E} \left\langle 0 \left| \sum_{jk} r_k^{-3} \frac{\partial^2}{\partial \phi_j \partial \phi_k} \right| 0 \right\rangle \quad (2-8)$$

where  $\Delta E$  is the mean excitation energy for an electron,  $e$  and  $m$  are the electronic charge and mass respectively,  $c$  is the speed of light,

$\rho$  is the charge density,  $r$  is the distance from the nucleus in question,  $\hbar$  is Planck's constant divided by  $2\pi$ ,  $\frac{\partial}{\partial \phi}$  is the operator for angular momentum about the z axis. The two terms in his formula correspond to "diamagnetic" and "paramagnetic" shieldings. The first term resembles Lamb's formula and is a measure of the shielding if the whole electronic structure of the molecule rotated about the nucleus in question. The second term accounts for the lack of spherical symmetry in a molecule and corrects for the hindrance of the electronic circulations. It corresponds to  $\sigma_{GG}^p$  in equation (2-6). A calculation of  $\sigma_{zz}$  involves a knowledge of the exact molecular wave functions of the ground and the excited states and these are seldom known. The two terms are usually of comparable magnitude but of opposite sign; consequently, such calculations have been carried out for small molecules only (23-25).

### 3. Further Extensions of $\sigma$

Saika and Slichter (26) and McConnell (27) found it convenient to subdivide the shielding further. Hence, for a nucleus  $i$ ,

$$\sigma_i = \sigma_i^d + \sigma_i^p + \sigma_i^f \quad (2-9)$$

where  $\sigma_i^d$  and  $\sigma_i^p$  correspond to Ramsey's diamagnetic and paramagnetic terms and  $\sigma_i^f$  is the term arising from distant atoms with anisotropic magnetic susceptibilities.  $\sigma_i^f$  corresponds to  $\sum_{G \neq B} \sigma_{GB}$  in equation (2-6) and will be discussed further in the next section of this chapter.

It is also found that the magnetic environment of a nucleus

is influenced by interatomic currents. This idea was first suggested by Pauling (28), and has led to the calculation of differences in the shielding constants between an aromatic proton and ethylenic proton. This point will be discussed later to explain anomalous effects found in aromatic compounds.

The proton chemical shift has long been assumed to reflect the pi electron density on the particular carbon atom in aromatic molecules. Fraenkel et al (29) and Musher (30) have shown theoretically that

$$\Delta \delta = k \Delta \rho \quad (2-10)$$

where  $\Delta \delta$  is the proton chemical shift relative to benzene,  $\Delta \rho$  is the local "excess" charge on the carbon atom to which the proton is bonded, and k is a constant having a value of approximately 10 ppm per electron. Equation (2-10) has been experimentally demonstrated (29, 31-34), but there appears to be some disagreement over the value of k (33, 35). This equation also implies that chemical shifts and electron charges are additive, as has been shown by Schug and Deck (36) and, as we shall see later, is the basis of the additivity principles that heretofore have been proposed.

## C - ANOMALOUS BEHAVIOUR AND MAGNETIC ANISOTROPY

Since the chemical shift should, in principle, provide a direct measure of local electronic and magnetic environments, it is not unreasonable to expect a relationship between the shift and the acidity of a proton. It turns out that this is a rough correlation only and some protons show anomalous behaviour. For example, aldehydic and aromatic proton resonances occur at lower fields than their acidities would suggest. Moreover, the acidic acetylenic proton resonances occur to higher field than expected and their frequencies lie between those of ethylene and ethane. The interpretation of a chemical shift is often complicated by the fact that the shielding of a nucleus is very sensitive to changes in the molecule as a whole, and the above anomalies have been explained in terms of magnetic anisotropies. This is subdivided into two main effects, which will now be discussed.

### 1. Anisotropy of a Neighbouring Group

The magnetic environment of a nucleus will also depend on the circulation of electrons on neighbouring atoms. These circulations are induced by the applied field and may be either diamagnetic or paramagnetic in nature. One usually evaluates this effect by replacing the currents with magnetic dipoles at the centre of the neighbouring atoms. If the magnitude of the induced currents were independent of orientation, the effect would average to zero over all random orientations of the molecule. However, a local anisotropy in the magnetic susceptibility exists and on averaging over all orient-

ations, there is a secondary field produced at the nucleus due to these distant currents.

The mathematical treatment has been developed by Pople (37) and McConnell (27). For an H-X bond of cylindrical symmetry, McConnell's expression for the contribution to the shielding of the H nucleus,  $\Delta\sigma$ , is

$$\Delta\sigma = \frac{\Delta\chi}{3R^3} (1 - 3 \cos^2\theta) \quad (2-11)$$

where R is the separation between the H nucleus and the point dipole on X;  $\theta$  is the angle between the  $\underline{R}$  vector and the direction of the applied field;  $\Delta\chi$ , the local magnetic anisotropy, is defined by

$$\Delta\chi = \chi_{\parallel} - \chi_{\perp} \quad (2-12)$$

where  $\chi_{\parallel}$  and  $\chi_{\perp}$  are the magnetic susceptibilities parallel to and perpendicular to the H-X bond axis.

The magnetic anisotropy of the triple bond in acetylene has been treated by Pople. Reference to Fig. 2 shows that if the linear acetylene molecule lies perpendicular to the field, paramagnetic currents on the carbon atoms arise from the mixing of the ground state with the  $\sigma - \pi$  excited states.

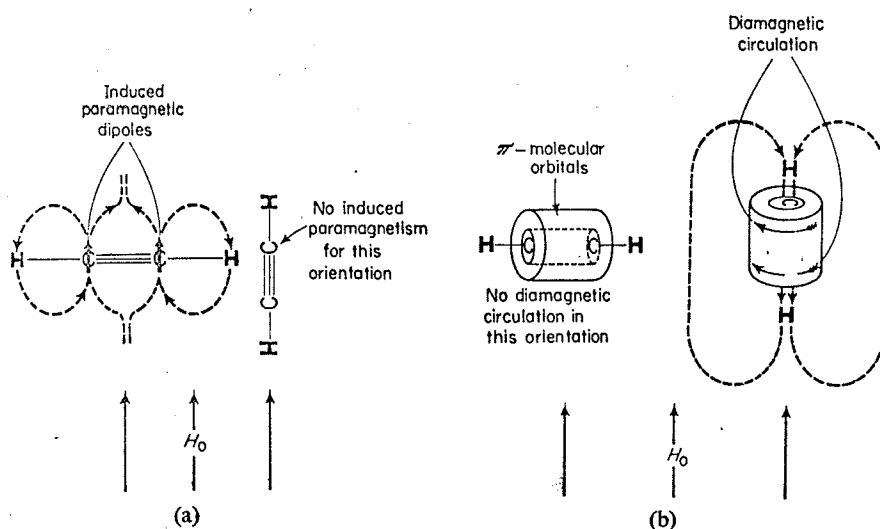


Fig. 2: The shielding of acetylenic protons (a) in terms of paramagnetic currents and (b) in terms of diamagnetic anisotropy.

While the induced or local field is paramagnetic at the carbon atoms, it is diamagnetic at the H atoms, giving rise to increased shielding. If the applied field now lies parallel to the molecular axis of acetylene, only diamagnetic currents, due to the circulation of the pi electrons in the triple bond, are possible. Again, this gives rise to increased shielding at the H atom and the proton resonance in acetylene occurs to higher field than is expected.

The paramagnetic term may work in the opposite direction, as illustrated by the carbonyl group. When the direction of the applied field is in the plane of the trigonal carbon atom, paramagnetic currents are induced about the carbon and oxygen atom and the field at the proton is augmented, corresponding to a deshielding.

The inductive effect of the carbonyl group also reduces the diamagnetic term.

## 2. The Ring Current Effect

This is due to the unusually large magnetic anisotropy of the aromatic ring system (38). This is illustrated for benzene in Fig. 3. The pi electrons behave much like charged particles

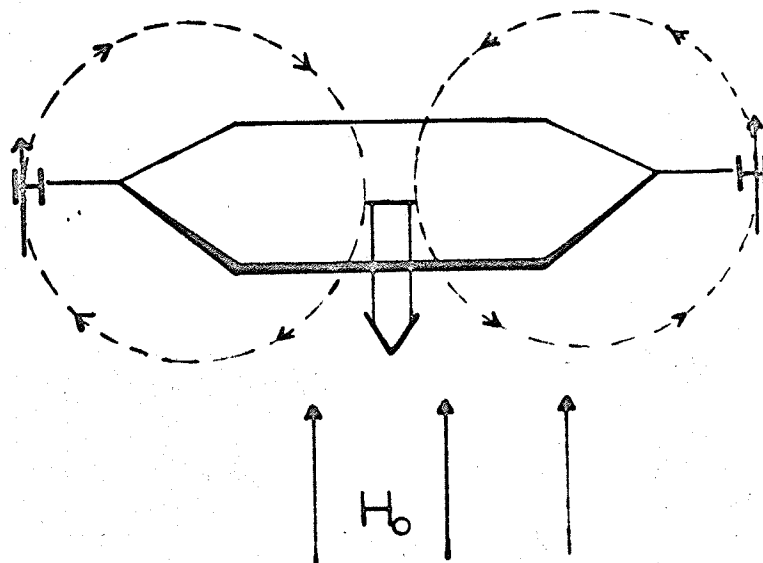


Fig. 3: The deshielding of protons in benzene.

free to move above the plane of the sigma framework in a circle. The direction of the current, according to Lenz's law, is such as to give a diamagnetic moment opposed to the applied field. The magnetic lines of flux, however, at the protons are paramagnetic, and the nucleus is much less shielded. Consequently, aromatic proton resonances occur at lower field than is expected. Several approximate methods have been developed to calculate the ring current effect and the reader is referred to the following sources (39-48).

CHAPTER III

- CORRELATIONS OF THE  $H^1$  CHEMICAL SHIFT IN BENZENES -



A - INTERMOLECULAR EFFECTS

Solvent effects have been shown to be important in aromatic compounds (49). Therefore, these effects must be considered if the data is to be meaningful; they may be minimized by studying all the samples as infinitely dilute solutions in inert solvents. Practical considerations limit the extent to which samples may be diluted and a concentration of 5 mole % or less is often taken as a reasonable approximation to the "isolated molecule" (50).

B - MONSUBSTITUTED BENZENES

Using deuterated derivatives, Spiesecke and Schneider (51) studied the effects of various substituents on the  $C^{13}$  and  $H^1$  chemical shifts in monosubstituted benzenes. The  $C^{13}$  resonance shift was assumed to be a measure of the total electron density on the carbon nucleus. After applying anisotropy corrections, the  $C^{13}$  shift of the carbon attached to the substituent X correlated well with the electronegativities of X. Hence, at this position, magnetic anisotropy and inductive effects of X predominate. The  $C^{13}$  shifts at the ortho position could not be fully explained but again these two effects appeared to be present particularly magnetic anisotropy for the halogen substituents. The resonance effects of X are felt at the para carbon, changing the pi electron density. Here, in the absence of other perturbing effects, the chemical shift may reflect changes in the pi electron densities. The proton chemical shifts exhibit features similar to the  $C^{13}$  shifts; thus, the ortho position is influenced by the magnetic anisotropy and inductive effects of X, the meta position again remains unexplained, and the para proton shifts parallel the para carbon shifts. After a critical examination of the validity of correlating chemical shift data with chemical reactivity parameters, such as Hammett's  $\sigma_p$  and  $\sigma_m$  constants (52) and Taft's  $\sigma_R$  and  $\sigma_I$  constants (53), Spiesecke and Schneider found a rough correlation between the  $C^{13}$  and  $H^1$  shifts at the para position with Hammett's  $\sigma_p$  constant, and no correlation

for the meta shifts.

Bothner-By and Glick (54), in a study of specific medium effects, also found that resonance and inductive effects predominated at the para position, fitting their data to an equation  $H - H_o = -5.0 \sigma_p$ , where  $H_o$  is the extrapolated H for benzene and the H's are extrapolated resonance positions for the para position in the monosubstituted benzenes.

The first work done on monosubstituted benzenes, by Corio and Dailey (55), was an attempt to find the relative electron densities in monosubstituted benzenes from the chemical shift data. Their work is of limited value since solvent effects may well have been important (50 mole % solutions in benzene were used). Nonetheless, they classified the compounds according to their ability to change the electron density by inductive and mesomeric (resonance) effects and concluded that such polarization effects are important in determining the directing influence of a substituent. They also found that the para proton shifts correlated with the Hammett values.

C - DISUBSTITUTED BENZENES

Diehl (56) found that the proton chemical shifts in meta- and para-disubstituted benzenes could be predicted using an additivity relation. In this way, he evaluated characteristic ortho, meta and para constants ( $S_o$ ,  $S_m$  and  $S_p$ ) for eleven substituents. He found, however, that such an additivity relation did not predict the shifts in ortho disubstituted compounds. The constants  $S_o$ ,  $S_m$  and  $S_p$  correlated roughly with Hammett's  $\sigma_p$ . Diehl's work has been extended by Smith (57), evaluating S constants for fifty more substituents and extending the correlations of the S's with  $\sigma_p$ .

Brey and Lawson, in a private communication quoted in Emsley, Feeney and Sutcliffe (58) report that they attempted to predict the chemical shifts of protons in polysubstituted benzenes using a procedure similar to Diehl's. The protons in halosubstituted benzenes and in meta-disubstituted compounds did not conform to the additivity relation.

Diehl's procedure has been refined by Martin and Dailey (59). They were able to predict the chemical shift in para-disubstituted benzenes by the formula

$$\delta = d_o (R_1) + (R_1) d_m (R_4)$$

where  $\delta$  is the chemical shift of the proton ortho to substituent  $R_1$  and meta to substituent  $R_4$ ,  $d_o$  and  $d_m$  are ortho and meta substituent constants and  $\gamma$ 's are polarizabilities. The parameter  $\gamma$  is a measure of the susceptibility of the position ortho to R to

perturbation by substituents para to R.  $\gamma$  decreases as  $d_o$  increases. Reasonable accuracy is obtained in predicting shifts in meta-disubstituted benzenes and shifts meta to the substituents in ortho-disubstituted benzenes; the additivity principle fails for protons next to the substituents in ortho-disubstituted benzenes.

D - THE Q EFFECT

Anomalous behaviour had been noted for protons ortho to halogen substituents in monosubstituted benzenes. The ortho shift did not correlate with para proton shifts or reactivity parameters (51). Diehl (56) also found that, while his  $S_o$  values correlated with  $\sigma_p$ , there were two different correlations: one for the halogens, and another for the remaining substituents studied. Hruska, Hutton and Schaefer (60) have found an empirical correlation between the ortho shifts and a factor Q. Q equals  $P / Ir^3 \text{ ergs}^{-1}$ , where P is the polarizability of the C-X bond, r is the C-X bond length and I is the first ionization potential of atom X. It appears that the shielding of the ortho proton by these substituents is due to an increased paramagnetic term in Ramsey's equation since the correlation with  $1/I$  is almost as good as with  $P / Ir^3$ .

Chapter IV

- THE NATURE OF THE PROBLEM -

### THE NATURE OF THE PROBLEM

Monosubstituted and disubstituted benzenes have been studied in order to investigate the factors affecting the proton chemical shifts in aromatic compounds. The proton chemical shifts of disubstituted benzenes have been predicted, with varying success, by an additivity relation, giving generally poor results when the substituents are halogens. The Q factor has been proposed to correlate the chemical shifts of protons ortho to a halogen.

It is the purpose of this investigation to correlate the proton chemical shifts in tri-, tetra-, and pentasubstituted benzenes, where the substituents are the halogens.



## Chapter V

### - EXPERIMENTAL -

A - MATERIALS

The chemicals used were obtained from the following companies:- (1) Aldrich Chemical Co., Inc.; (2) Pierce Chemical Company; (3) Eastman Organic Chemicals; (4) Matheson, Coleman and Bell; and (5) K & K Laboratories Inc. They were used without further purification, since any lines due to impurities were easily recognized; in any case, spurious lines were found in only two spectra.

The preparation of 1-bromo-3-chloro-5-iodobenzene followed an eight step procedure due to Ault and Kraig (61). The procedure was reduced to two steps by starting with an intermediate compound, 2-chloro-4-bromoaniline, obtained from the Chemicals Procurement Laboratories.

## B - MEASUREMENT OF THE SPECTRA

The samples were prepared as 3 mole % solutions in carbon tetrachloride and cyclohexane. In certain cases, the compound did not dissolve to this extent and the saturated solution was used. Most samples, especially those which gave rise to multiline spectra, were degassed on a vacuum line. A concentration of 3 mole % is considered as a sufficient approximation to the "isolated" molecule. Concentration studies on benzene and 1,3,5-tribromobenzene showed that from 3 mole % downward, there is negligible shift of the resonance frequency due to a concentration effect.

All measurements were performed with a DA-60-I Varian spectrometer using the sideband technique. The use of tetramethylsilane (TMS) as internal reference eliminated any corrections due to differences in bulk diamagnetic susceptibilities. The samples were contained in glass tubes of 4 mm inner diameter and 5 mm outer diameter. The temperature of the sample, as determined by an ethyleneglycol calibration graph, was 28.5°C.

## Chapter VI

### - RESULTS -

TABLE I  
 PROTON CHEMICAL SHIFTS OF POLYHALOSUBSTITUTED  
 BENZENES WITH RESPECT TO BENZENE (PPM)<sup>†</sup>

Compound	Proton	In C <sub>6</sub> H <sub>12</sub>	In CCl <sub>4</sub>
(1) Benzene	—	0.000	0.000
(2) 1,3,5-tribromobenzene	—	-0.310	-0.332
(3) 1,3,5-trichlorobenzene	—	+0.048	+0.014
(4) 1,2,3,4-tetrachlorobenzene	—	+0.049	-0.029
(5) 1,2,3,4-tetrafluorobenzene	—	+0.450	+0.351
(6) 1,2,4,5-tetrabromobenzene	—	-0.557	-0.588
(7) 1,2,4,5-tetrachlorobenzene	—	-0.220	-0.289
(8) 1,2,4,5-tetrafluorobenzene	—	+0.324	+0.207
(9) 1,3,4,5-tetrafluorobenzene	—	+0.618	+0.523
(10) Pentachlorobenzene	—	-0.190	-0.268
(11) Pentafluorobenzene	—	+0.492	+0.373
(12) 1,4-dibromo-2,5-difluorobenzene	—	+0.006	-0.073
(13) 1,3,5-tribromo-2-iodobenzene	—	-0.394	-0.420
(14) 1,2,3-trichlorobenzene	H <sub>4</sub> , H <sub>6</sub>	-0.014	-0.074
	H <sub>5</sub>	+0.266	+0.174
(15) 1-bromo-3,5-dichlorobenzene	H <sub>4</sub>	+0.008	-0.034
	H <sub>2</sub> , H <sub>6</sub>	-0.112	-0.126
(16) 1,3-difluoro-5-iodobenzene	H <sub>2</sub>	+0.563	+0.484
	H <sub>4</sub> , H <sub>6</sub>	+0.047	+0.012
(17) 1,2,4-trichlorobenzene	H <sub>3</sub>	-0.144	-0.190
	H <sub>5</sub>	+0.169	+0.106
	H <sub>6</sub>	-0.012	-0.086
(18) 1-bromo-3-chloro-5-iodobenzene*	H <sub>2</sub>	-0.200	-0.171
	H <sub>4</sub>	-0.200	-0.171
	H <sub>6</sub>	-0.272	-0.283
(19) 1-bromo-2,5-dichlorobenzene	H <sub>3</sub>	-0.016	-0.091
	H <sub>4</sub>	+0.125	+0.051
	H <sub>6</sub>	-0.322	-0.354

TABLE I (Continued)

Compound	Proton	In $C_6H_{12}$	In $CCl_4$
(20) 1-bromo-3,4-dichlorobenzene	H <sub>2</sub>	-0.301	-0.332
	H <sub>5</sub>	+0.048	-0.026
	H <sub>6</sub>	+0.024	-0.026
(21) 1,2-dichloro-4-fluorobenzene	H <sub>3</sub>	+0.128	+0.056
	H <sub>5</sub>	+0.430	+0.340
	H <sub>6</sub>	-0.057	-0.132
(22) 1,2,4-tribromobenzene	H <sub>3</sub>	-0.471	-0.493
	H <sub>5</sub>	+0.063	+0.001
	H <sub>6</sub>	-0.120	-0.186
(23) 2,4-dibromo-1-fluorobenzene	H <sub>3</sub>	-0.401	-0.424
	H <sub>5</sub>	-0.051	-0.158
	H <sub>6</sub>	+0.384	+0.283
(24) 1,2-dichloro-4-iodobenzene	H <sub>3</sub>	-0.487	-0.504
	H <sub>5</sub>	-0.168	-0.214
	H <sub>6</sub>	+0.202	+0.130

† The proton chemical shifts, with a standard deviation of  $\pm 0.005$  ppm, were measured originally with respect to TMS and are given here with respect to benzene.

\* This compound was analyzed in an approximate manner and the chemical shifts are only accurate to  $\pm 0.016$  ppm for protons H<sub>2</sub> and H<sub>4</sub> and to  $\pm 0.008$  ppm for H<sub>6</sub>.

The coupling constants obtained in the analyses of some of the polyhalosubstituted benzenes are given in Appendix I.

The spectra were analyzed according to standard methods as outlined in Appendix II. About half of the spectra consists of either a single peak or a single shift position. The non-trivial spectra represent a wide variety of types: (1) an AB<sub>2</sub> such as

1-bromo-3,5-dichlorobenzene; (2) an ABX such as 1,2-dichloro-4-iodobenzene; (3) an ABXR such as 2,4-dibromo-1-fluorobenzene; (4) an  $AB_2R_2$  such as 1,3-difluoro-5-iodobenzene; (5) a deceptively simple ABX such as 1-bromo-3,4-dichlorobenzene in  $CCl_4$ ; (6) spectra which would be expected to be complex but which are rather simple, such as 1,2,4,5-tetrafluorobenzene, and (7) an ABC such as 1-bromo-3-chloro-5-iodobenzene, which approximates very closely to an  $AB_2$ . Some of these spectra are reproduced on the following pages.

Fig. 4: The complete proton spectrum of a 3 mole% solution of  
1-bromo-3,5-dichlorobenzene in carbon tetrachloride.  
The asterisk denotes a spurious peak.



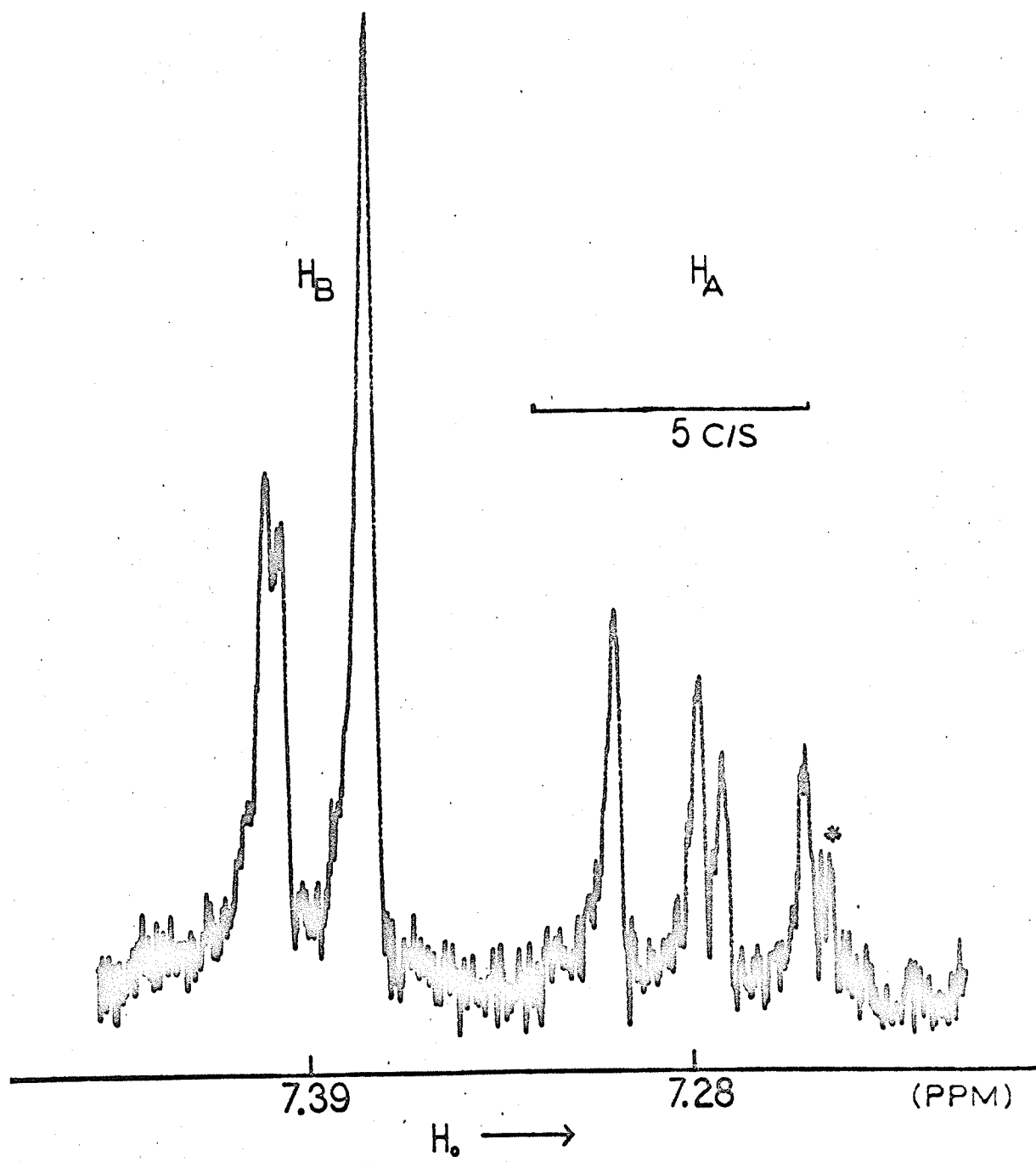


Fig. 5: The complete proton spectrum of a 3 mole% solution of  
1,2-dichloro-4-iodobenzene in carbon tetrachloride.

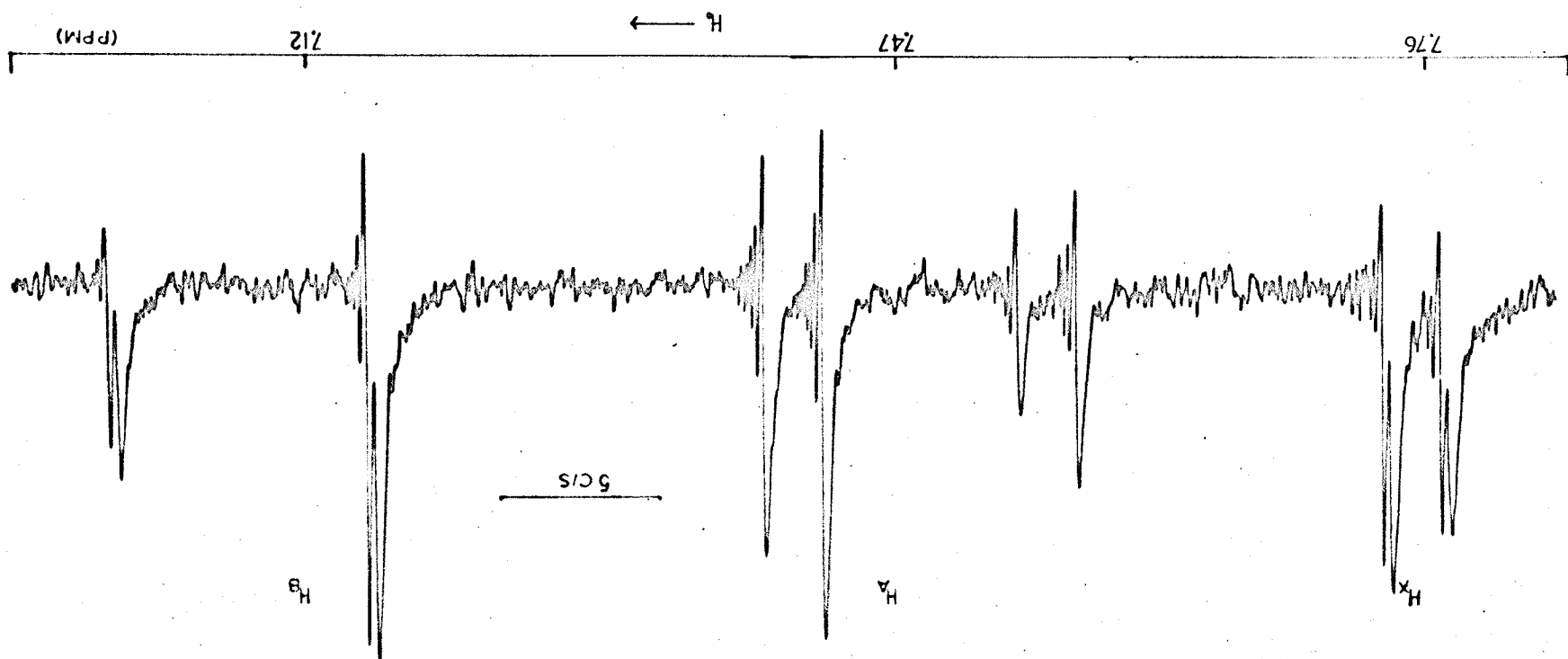
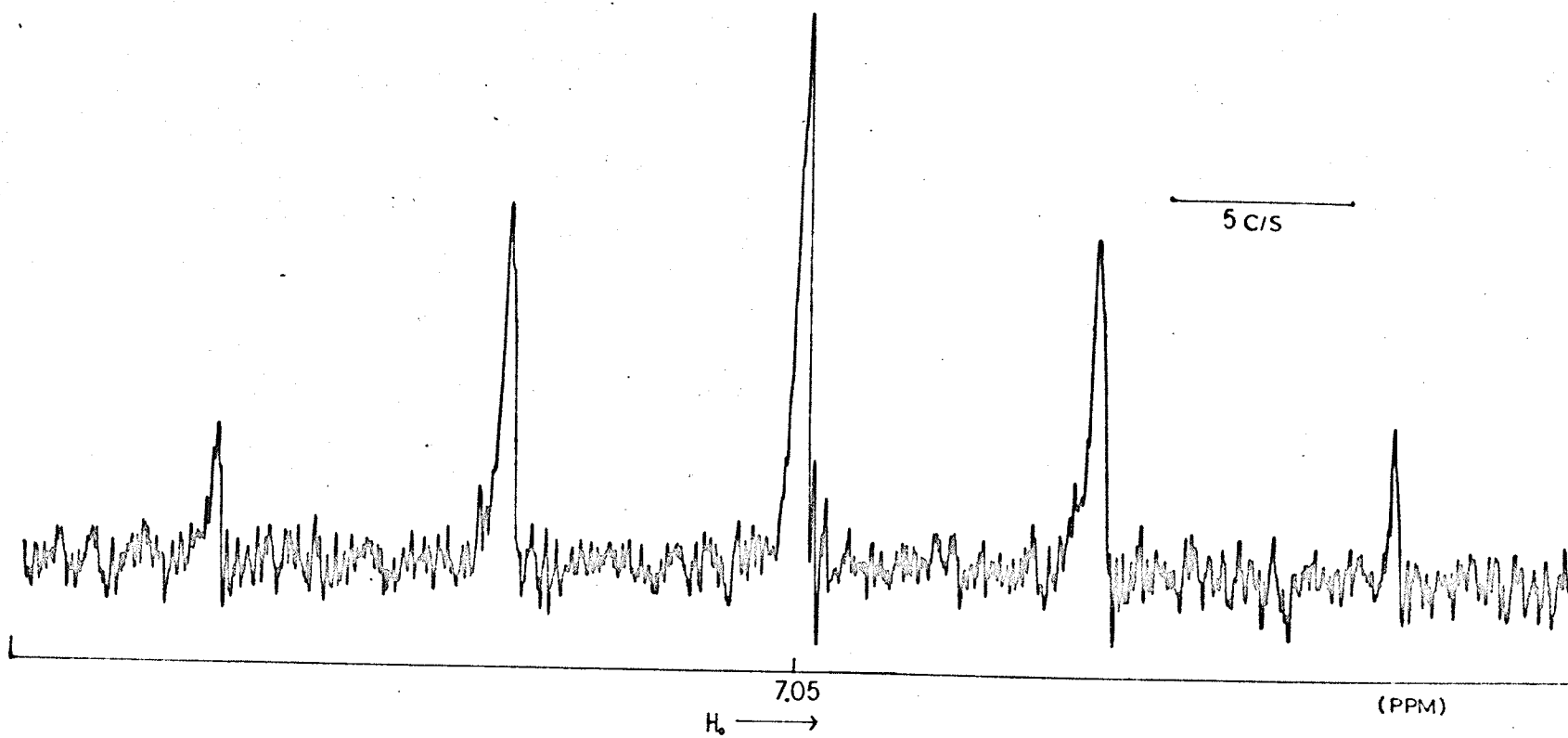


Fig. 6: The complete proton spectrum of a 3 mole% solution of  
1,2,4,5-tetrafluorobenzene in carbon tetrachloride.



## Chapter VII

### - DISCUSSION -

### DISCUSSION

Several factors can affect the chemical shift of aromatic protons. Among them are inductive and mesomeric effects of the substituents, ring currents, electric field effects, magnetic anisotropies of the substituents and solvent effects. It would be highly desirable to predict the chemical shifts using the theoretical equation developed by Ramsey. Such, however, is not possible due to the limitations of molecular quantum mechanics; that is, the ground and excited state wave functions for such complicated molecules are presently beyond contemplation. There remains the possibility of devising an empirical scheme which will prove useful to both the experimentalist and the theoretician. A few means of correlating aromatic proton chemical shifts have been reviewed in Chapter III and serve as a useful starting point in this study.

### A - TESTING THE Q FACTOR

The Q factor was originally proposed to explain the anomalous behavior of protons ortho to a halogen. As such, it might be useful in the present situation since all the substituents are halogens. Figures 7 and 8 are plots of the proton chemical shift versus the sum of the Q's of the ortho substituents when the solvent is cyclohexane and carbon tetrachloride respectively. In both, a clear trend is indicated but the scatter of points is too large for the graph to be useful as a correlation. It appears that the Q effect predominates for most of these compounds but clearly other factors become important enough to give considerable scatter. It is not surprising that the correlation should be so rough since the Q effect was first postulated for molecules with only one substituent. Here, however, there is a minimum of three substituents and the interaction of three perturbations complicates the picture considerably.

It should be possible to improve the plots if the effects of the substituents meta and para to the proton could be eliminated. If it is assumed that the meta and para substituent constants  $d_m$  and  $d_p$  (for carbon tetrachloride as solvent) are accurately known from the work of Martin and Dailey (59), the shift contribution due to substituents in the meta and para positions can be subtracted and then the corrected chemical shifts  $\delta_{\text{corr}}$  plotted against the sum of the Q's of the ortho substituents. The substituent constant,  $d_p$ , for fluorine (F) was calculated by adding 0.04 ppm to the chemical shift of the proton para to fluorine in fluorobenzene, the latter taken from work done by Spiesecke and Schneider (51).



Fig. 7: A plot of the proton chemical shifts (in ppm from benzene) of polyhalosubstituted benzenes in cyclohexane as a function of the sum of the  $Q$ 's of the ortho substituents. The units of  $Q$  are  $10^{-14}$  ergs.

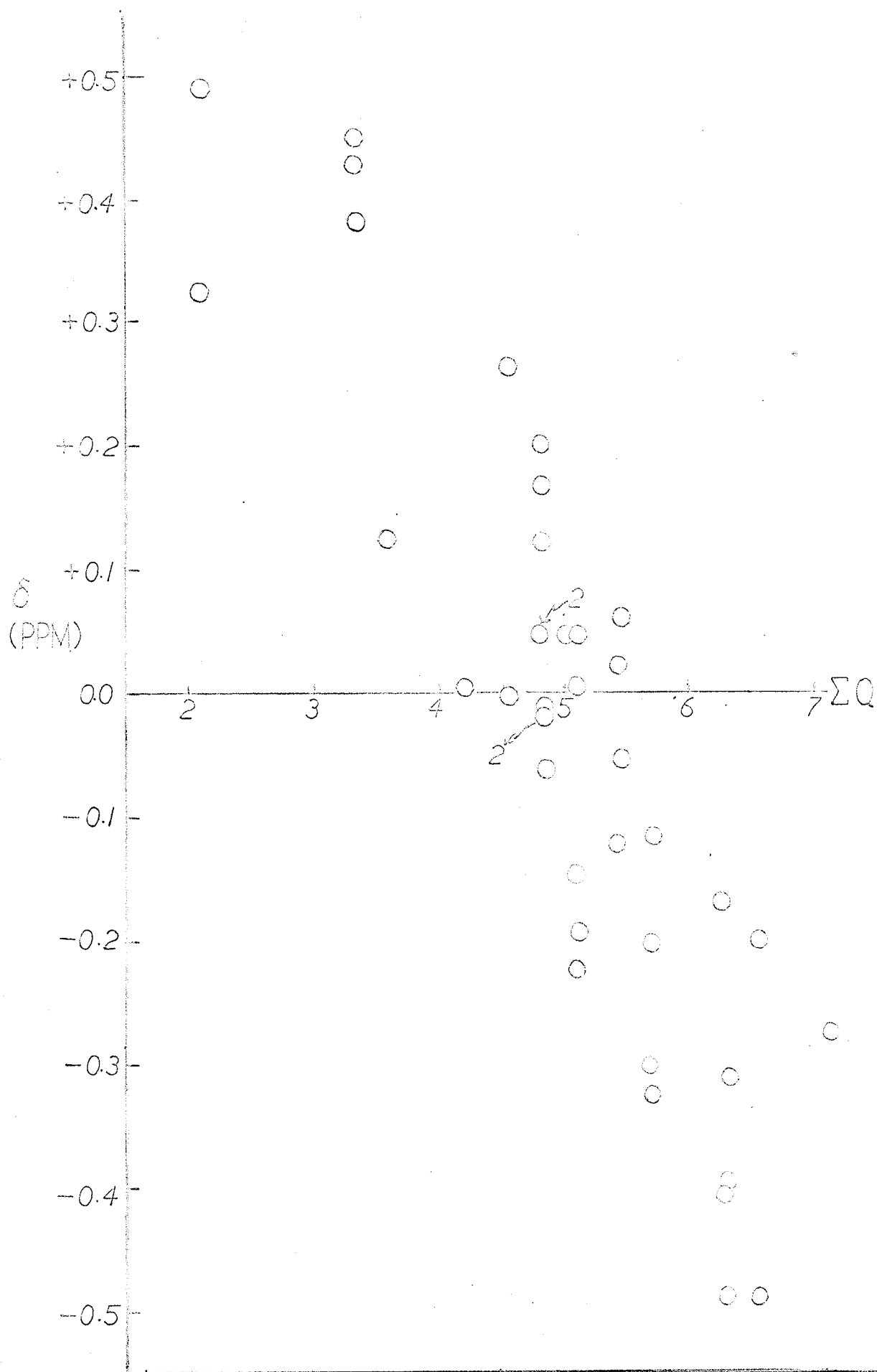
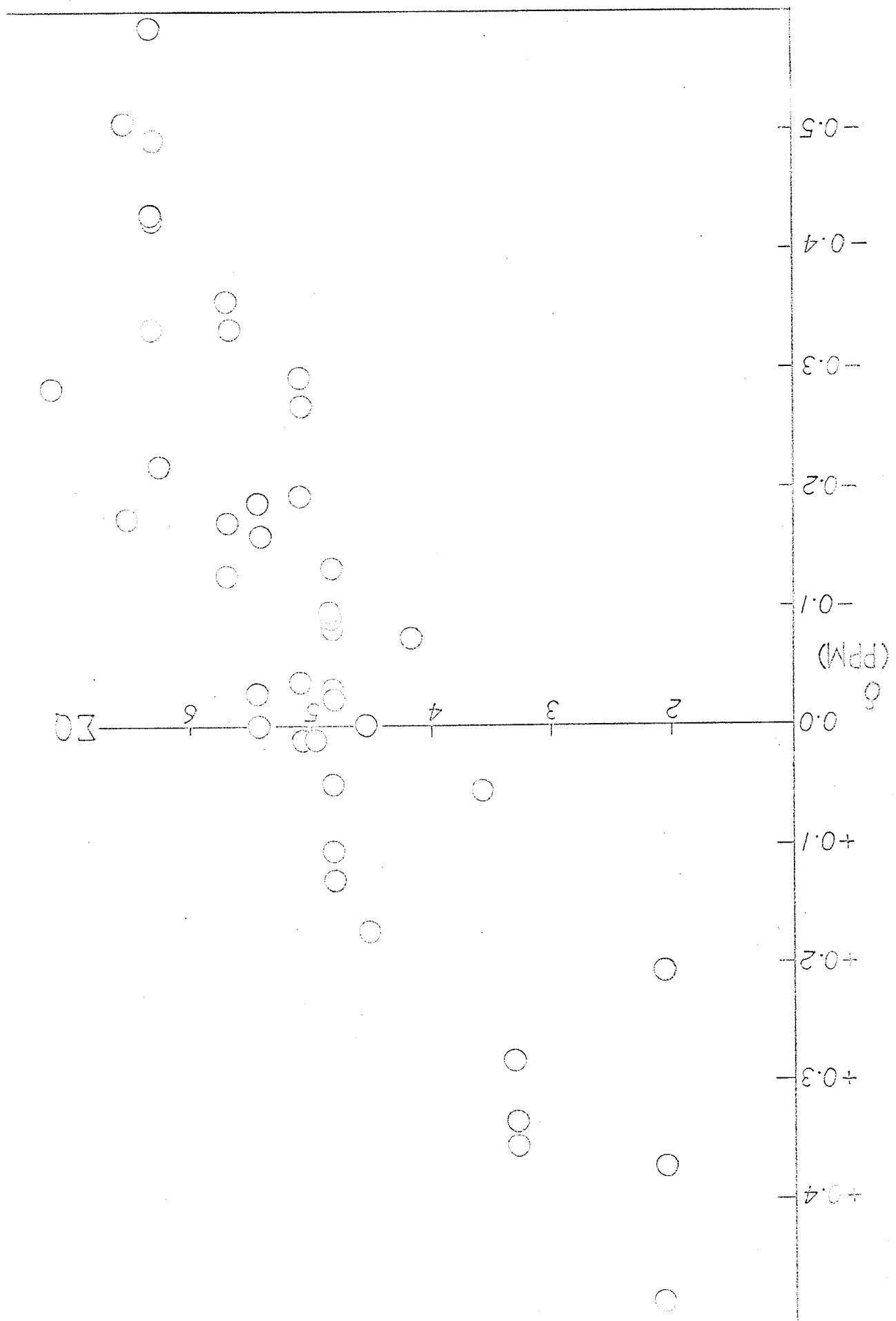


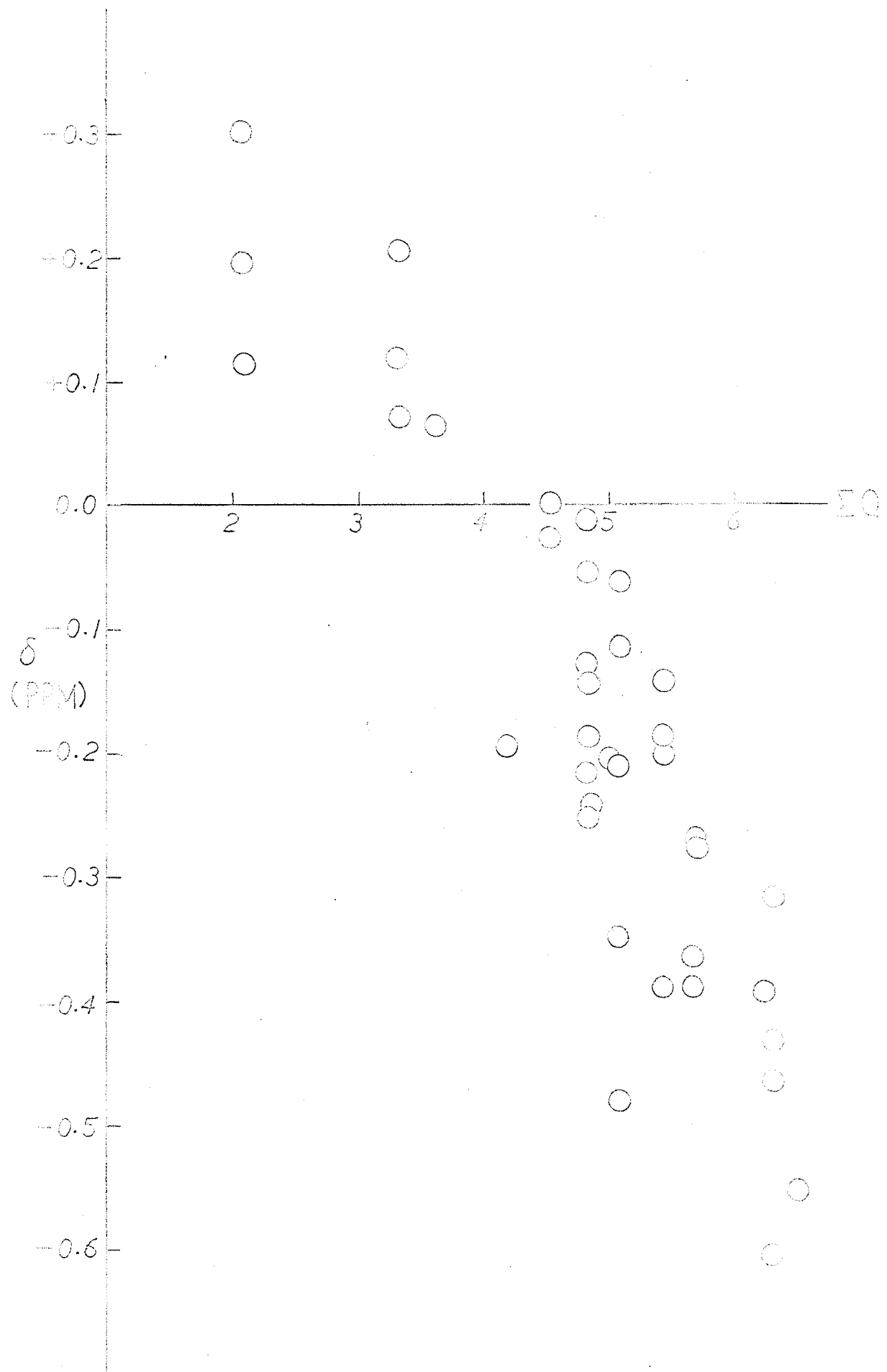
Fig. 8: A plot of the proton chemical shifts (in ppm from benzene) of polyhalosubstituted benzenes in carbon tetrachloride as a function of the sum of the  $Q$ 's of the ortho substituents. The units of  $Q$  are  $10^{-14}$  ergs.



- BIBLIOGRAPHY -

The substituent constant,  $d_m$ , was determined in a similar manner. This was the procedure followed by Martin and Dailey in determining the other  $d_p$  values. Figure 9 shows a plot where the above ideas have been applied to the cyclohexane data. The  $d_p$  values for benzenes in carbon tetrachloride have not been determined and therefore it is not possible to apply this test to the  $CCl_4$  data. The plot of  $\delta_{\text{corr}}$  versus  $\sum Q$  is not, however, improved and this may be accounted for in either of two ways: (1) the contributions to the proton chemical shift from a meta or para substituent may not be additive, as has been assumed; or (2) the substituent constants of Martin and Dailey do not apply to polysubstituted benzenes because the constants  $d_m$  and  $d_p$  were derived from data on disubstituted benzenes. The graph still indicates that the ortho effect is the most important factor.

Fig. 9: A plot of  $\delta_{\text{corr}}$  of polyhalosubstituted benzenes in cyclohexane as a function of  $\sum Q$ . The units of  $Q$  are  $10^{-14}$  ergs.





B - TESTING ADDITIVITY RELATIONSHIPS

Let the substituent constants  $d_o$ ,  $d_m$  and  $d_p$  derived by Martin and Dailey be used to predict the proton chemical shifts of benzenes in cyclohexane solution. Comparison of the results with the experimentally determined values will show if such constants can be applied to benzenes which are more highly substituted than disubstituted benzenes. Table II shows the results obtained and the deviations between the observed values and the predicted chemical shift values.

TABLE II

COMPARISON OF THE EXPERIMENTAL CHEMICAL SHIFTS

WITH THOSE PREDICTED USING  $d_o$ ,  $d_m$  AND  $d_p$  ( $C_6H_{12}$  AS SOLVENT)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviation (ppm)
(1) 1,3,5-tribromobenzene	-	-0.248	-0.310	-0.062
(2) 1,3,5-trichlorobenzene	-	+0.160	+0.048	-0.112
(3) 1,2,3,4-tetrachlorobenzene	-	+0.290	+0.049	-0.241
(4) 1,2,3,4-tetrafluorobenzene	-	+0.648	+0.450	-0.198
(5) 1,2,4,5-tetrabromobenzene	-	-0.050	-0.557	-0.507
(6) 1,2,4,5-tetrachlorobenzene	-	+0.130	-0.220	-0.350
(7) 1,2,4,5-tetrafluorobenzene	-	+0.666	+0.324	-0.342
(8) 1,3,4,5-tetrafluorobenzene	-	+0.851	+0.618	-0.233
(9) Pentachlorobenzene	-	+0.290	-0.190	-0.480
(10) Pentafluorobenzene	-	+0.916	+0.492	-0.324
(11) 1,4-dibromo-2,5-difluorobenzene	-	+0.308	+0.006	-0.302
(12) 1,3,5-tribromo-2-iodobenzene	-	+0.017	-0.394	-0.411
(13) 1,2,3-trichlorobenzene	H <sub>5</sub>	+0.290	+0.266	-0.024
	H <sub>4</sub> , H <sub>6</sub>	+0.225	-0.014	-0.239
(14) 1-bromo-3,5-dichlorobenzene	H <sub>4</sub>	+0.070	+0.008	-0.062
	H <sub>2</sub> , H <sub>6</sub>	+0.001	-0.112	-0.113

TABLE II(Continued)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviation (ppm)
(15) 1,3-difluoro-5-iodobenzene	H <sub>2</sub>	+0.606	+0.563	-0.043
	H <sub>4</sub> , H <sub>6</sub>	+0.165	+0.047	-0.118
(16) 1,2,4-trichlorobenzene	H <sub>3</sub>	+0.065	-0.144	-0.209
	H <sub>5</sub>	+0.225	+0.169	-0.056
	H <sub>6</sub>	+0.130	-0.012	-0.142
(17) 1-bromo-3-chloro-5-iodobenzene	H <sub>2</sub>	-0.089	-0.200	-0.111
	H <sub>4</sub>	-0.293	-0.200	+0.093
	H <sub>6</sub>	-0.362	-0.272	+0.090
(18) 1-bromo-2,5-dichlorobenzene	H <sub>6</sub>	-0.094	-0.322	-0.228
	H <sub>3</sub>	+0.199	-0.016	-0.215
	H <sub>4</sub>	+0.135	+0.125	-0.010
(19) 1-bromo-3,5-dichlorobenzene	H <sub>2</sub>	-0.094	-0.301	-0.207
	H <sub>6</sub>	+0.066	+0.024	-0.042
	H <sub>5</sub>	+0.199	+0.048	-0.151
(20) 1,2-dichloro-4-fluorobenzene	H <sub>6</sub>	+0.130	-0.057	-0.187
	H <sub>3</sub>	+0.333	+0.128	-0.205
	H <sub>5</sub>	+0.493	+0.430	-0.063
(21) 1,2,4-tribromobenzene	H <sub>3</sub>	-0.184	-0.471	-0.287
	H <sub>6</sub>	+0.109	-0.120	-0.229
	H <sub>5</sub>	+0.045	+0.063	+0.018
(22) 2,4-dibromo-1-fluorobenzene	H <sub>3</sub>	-0.253	-0.401	-0.148
	H <sub>5</sub>	-0.024	-0.051	-0.027
	H <sub>6</sub>	+0.536	+0.384	-0.152
(23) 1,2-dichloro-4-iodobenzene	H <sub>3</sub>	-0.298	-0.487	-0.189
	H <sub>5</sub>	-0.138	-0.168	-0.030
	H <sub>6</sub>	+0.330	+0.202	-0.128

The agreement in most cases is very poor (the average deviation being  $+0.178$  ppm) and is perhaps not surprising. Martin and Dailey reported that their substituent constants gave generally poorer results for meta

disubstituted benzenes and failed completely for protons ortho to a substituent in ortho disubstituted benzenes. The benzenes used in this study are of similar structure. It should also be noted that the calculated shift is nearly always on the high field side of the observed shift, giving rise to negative deviations. Martin and Dailey report that, for an extensive series of disubstituted benzenes, the ring proton chemical shifts may be reproduced to an accuracy of about 0.1 ppm assuming their additivity constants.

It would be possible to treat the  $\text{CCl}_4$  data in a similar manner if the  $S_p$  values had been determined. Unfortunately, Smith (57) evaluated only  $S_o$  and  $S_m$  constants (for  $\text{CCl}_4$  as solvent) and nowhere in the literature has work been done on benzenes in carbon tetrachloride which would permit the calculation of  $S_p$  (Chemical shift data on meta dihalosubstituted benzenes in  $\text{CCl}_4$  is required). In view of the poor agreement between the experimentally determined shift values and the predicted values (using  $d_o$ ,  $d_m$  and  $d_p$  of Martin and Dailey) in cyclohexane, it is not unreasonable to suggest that the  $S_o$ ,  $S_m$  and  $S_p$  values originally proposed by Diehl (56) would fail to predict the chemical shift values in carbon tetrachloride.

C - PROPOSING A NEW EMPIRICAL METHOD

A reasonable suggestion as to why the substituent constants do not give good agreement is that there is steric interaction between the halogen substituents and protons. This steric effect can be taken into account by assigning a constant  $\Delta$  to a pair of substituents ortho and meta to the proton whose chemical shift is desired.  $\Delta(X-Y)^*$ , call it an "ortho-meta" constant, then would give the contribution to the proton shift when X is ortho and Y is meta to the proton. X and Y may be either a halogen or hydrogen. In conjunction with  $d_p$  values for the appropriate solvent, the values can be used to predict the chemical shifts of polyhalo-substituted benzenes. Table III gives the "ortho-meta" constants for various combinations of halogens and hydrogen when cyclohexane is the solvent.

TABLE III

"ORTHO-META" CONSTANTS FOR X-Y COMBINATIONSWHEN C<sub>6</sub>H<sub>12</sub> IS THE SOLVENT

<u>X-Y</u>	<u><math>\Delta</math> (PPM)</u>
H-H	0.000
H-F	+0.050
H-Cl	+0.062
H-Br	+0.160
H-I	+0.337
F-H	+0.223

\* See Appendix III for derivation of ortho-meta constants.

TABLE III (Continued)

X-Y	$\Delta$ (PPM)
F-F	+0.142
F-Br	+0.203
Cl-H	-0.043
Cl-Cl	-0.135
Cl-Br	-0.078
Br-H	-0.195
Br-F	-0.207
Br-Cl	-0.287
Br-Br	-0.255
Br-I	-0.222
I-H	-0.405

Using the above  $\Delta$  values and the  $d_p$  values given by Martin and Dailey, the chemical shifts of the polysubstituted benzenes used in this study are calculated and tabulated in Table IV.

TABLE IV

COMPARISON OF THE EXPERIMENTAL CHEMICAL SHIFTS WITH  
THOSE PREDICTED USING  $\Delta$  AND  $d_p$  VALUES ( $C_6H_{12}$  AS SOLVENT)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviation (ppm)
(1) 1,3,5-tribromobenzene	-	-0.320	-0.310	+0.010
(2) 1,3,5-trichlorobenzene	-	+0.070	+0.048	-0.022
(3) 1,2,3,4-tetrachlorobenzene	-	+0.083	+0.049	-0.034
(4) 1,2,3,4-tetrafluorobenzene	-	+0.448	+0.450	+0.002
(5) 1,2,4,5-tetrabromobenzene	-	-0.510	-0.557	-0.047
(6) 1,2,4,5-tetrachlorobenzene	-	-0.270	-0.220	+0.050
(7) 1,2,4,5-tetrafluorobenzene	-	+0.284	+0.324	+0.040
(8) 1,3,4,5-tetrafluorobenzene	-	+0.621	+0.618	-0.003
(9) Pentachlorobenzene	-	-0.114	-0.190	-0.076

TABLE IV (Continued)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviation (ppm)
(10) Pentafluorobenzene	-	+0.540	+0.492	-0.048
(11) 1,4-dibromo-2,5-difluorobenzene	-	-0.004	+0.006	+0.010
(12) 1,3,5-tribromo-2-iodobenzene	-	-0.347	-0.394	-0.047
(13) 1,2,3-trichlorobenzene	H <sub>5</sub>	+0.280	+0.266	-0.014
	H <sub>4</sub> , H <sub>6</sub>	+0.021	-0.014	-0.035
(14) 1,3-difluoro-5-iodobenzene	H <sub>2</sub>	+0.519	+0.563	+0.044
	H <sub>4</sub> , H <sub>6</sub>	+0.074	+0.047	-0.027
(15) 1-bromo-3,5-dichlorobenzene	H <sub>4</sub>	-0.016	+0.008	+0.024
	H <sub>2</sub> , H <sub>6</sub>	-0.082	-0.112	-0.030
(16) 1,2,4-trichlorobenzene	H <sub>3</sub>	-0.178	-0.144	+0.034
	H <sub>5</sub>	+0.175	+0.169	-0.006
	H <sub>6</sub>	-0.073	-0.012	+0.061
(17) 1-bromo-3-chloro-5-iodobenzene	H <sub>2</sub>	-0.165	-0.200	-0.035
	H <sub>4</sub>	-0.378	-0.200	+0.178
	H <sub>6</sub>	-0.444	-0.272	+0.172
(18) 1-bromo-2,5-dichlorobenzene	H <sub>6</sub>	-0.330	-0.322	+0.008
	H <sub>3</sub>	-0.016	-0.016	0.000
	H <sub>4</sub>	+0.089	+0.125	+0.036
(19) 1-bromo-3,4-dichlorobenzene	H <sub>2</sub>	-0.330	-0.301	+0.029
	H <sub>6</sub>	+0.023	+0.024	+0.001
	H <sub>5</sub>	+0.025	+0.048	+0.023
(20) 1,2-dichloro-4-fluorobenzene	H <sub>6</sub>	-0.085	-0.057	+0.028
	H <sub>3</sub>	+0.088	+0.128	+0.040
	H <sub>5</sub>	+0.441	+0.430	-0.011
(21) 1,2,4-tribromobenzene	H <sub>3</sub>	-0.450	-0.471	-0.021
	H <sub>6</sub>	-0.095	-0.120	-0.025
	H <sub>5</sub>	+0.035	+0.063	+0.028
(22) 2,4-dibromo-1-fluorobenzene	H <sub>3</sub>	-0.402	-0.401	+0.001
	H <sub>5</sub>	+0.363	+0.384	+0.021
(23) 1,2-dichloro-4-iodobenzene	H <sub>3</sub>	-0.540	-0.487	+0.053
	H <sub>5</sub>	-0.187	-0.168	+0.019
	H <sub>6</sub>	+0.202	+0.202	0.000

The average deviation is  $+0.034$  ppm, a great improvement over the agreement which was found when the substituent constants of Martin and Dailey were used to calculate the chemical shift. There are, however, two chemical shift values which are not successfully predicted and these are for protons adjacent to the iodine substituent in 1-bromo-3-chloro-5-iodobenzene. Anomalous behaviour has been noted before (59, 62) for iodosubstituted compounds and further investigation is necessary to explain the large deviations found above.

Similarly, the chemical shifts of the polyhalosubstituted benzenes in carbon tetrachloride can be calculated assuming an additivity relationship which incorporates the appropriate "ortho-meta" constants and  $d_p$  values. This time, however, the  $d_p$  values are not available but can be derived from the chemical shift data. The  $d_p$  values and "ortho-meta" constants which apply to the carbon tetrachloride data are tabulated in Table V and Table VI.

TABLE V

$d_p$  VALUES FOR HALOGENS WHEN  $\text{CCl}_4$  IS THE SOLVENT

Halogen	$d_p$ (ppm)
F	+0.166
Cl	+0.075
Br	+0.058
I	+0.040

TABLE VI

"ORTHO-META" CONSTANTS FOR X-Y COMBINATIONS  
WHEN CCL<sub>4</sub> IS THE SOLVENT

X-Y	$\Delta$ (ppm)
H-H	0.000
H-F	+0.040
H-Cl	+0.075
H-Br	+0.128
H-I	+0.275
F-H	+0.203
F-F	+0.115
F-Br	+0.175
Cl-H	-0.032
Cl-Cl	-0.145
Cl-Br	-0.185
Br-H	-0.199
Br-F	-0.225
Br-Cl	-0.342
Br-Br	-0.294
Br-I	-0.285
I-H	-0.330

Using the  $d_p$  values and  $\Delta$  values given in Tables V and VI, it is possible to calculate the chemical shifts of the polyhalosubstituted benzenes in carbon tetrachloride. Table VII shows the results obtained and the comparison with the experimental chemical shift values.



TABLE VII

COMPARISON OF THE EXPERIMENTAL CHEMICAL SHIFTS  
WITH THOSE PREDICTED USING  $\Delta$  AND  $d_p$  VALUES ( $\text{CCl}_4$  AS SOLVENT)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviation (ppm)
(1) 1,3,5-tribromobenzene	-	-0.340	-0.332	+0.008
(2) 1,3,5-trichlorobenzene	-	+0.011	+0.014	-0.003
(3) 1,2,3,4-tetrachlorobenzene	-	+0.005	-0.029	-0.034
(4) 1,2,3,4-tetrafluorobenzene	-	+0.321	+0.351	+0.030
(5) 1,2,4,5-tetrabromobenzene	-	-0.588	-0.588	0.000
(6) 1,2,4,5-tetrafluorobenzene	-	+0.230	+0.207	-0.023
(7) 1,2,4,5-tetrachlorobenzene	-	-0.290	-0.289	+0.001
(8) 1,3,4,5-tetrafluorobenzene	-	+0.484	+0.523	+0.039
(9) Pentachlorobenzene	-	-0.215	-0.268	-0.053
(10) Pentafluorobenzene	-	+0.396	+0.373	-0.023
(11) 1,4-dibromo-2,5-difluorobenzene	-	-0.050	-0.073	-0.023
(12) 1,3,5-tribromo-2-iodobenzene	-	-0.431	-0.420	+0.011
(13) 1,2,3-trichlorobenzene	H <sub>5</sub>	+0.225	+0.174	-0.051
	H <sub>4</sub> , H <sub>6</sub>	-0.070	-0.074	-0.004
(14) 1-bromo-3,5-dichlorobenzene	H <sub>4</sub>	-0.006	-0.034	-0.028
	H <sub>2</sub> , H <sub>6</sub>	-0.156	-0.126	+0.030
(15) 1,3-difluoro-5-iodobenzene	H <sub>2</sub>	+0.446	+0.484	+0.038
	H <sub>4</sub> , H <sub>6</sub>	+0.039	+0.012	-0.027
(16) 1,2,4-trichlorobenzene	H <sub>3</sub>	-0.177	-0.190	-0.013
	H <sub>5</sub>	+0.118	+0.106	-0.012
	H <sub>6</sub>	-0.070	-0.086	-0.016
(17) 1-bromo-3-chloro-5-iodobenzene	H <sub>2</sub>	-0.191	-0.171	+0.020
	H <sub>4</sub>	-0.304	-0.171	+0.133
	H <sub>6</sub>	-0.454	-0.283	+0.171
(18) 1-bromo-2,5-dichlorobenzene	H <sub>3</sub>	-0.110	-0.091	+0.019
	H <sub>4</sub>	+0.101	+0.051	-0.050
	H <sub>6</sub>	-0.374	-0.354	+0.020

TABLE VII (Continued)

Compound	Proton	Calc. Shift (ppm)	Obs. Shift (ppm)	Deviat (ppm)
(19) 1-bromo-3,4-dichlorobenzene	H <sub>2</sub>	-0.344	-0.332	+0.01
	H <sub>5</sub>	-0.017	-0.026	-0.00
	H <sub>6</sub>	-0.049	-0.026	+0.02
(20) 1,2-dichloro-4-fluorobenzene	H <sub>3</sub>	+0.058	+0.056	-0.00
	H <sub>5</sub>	+0.353	+0.340	-0.01
	H <sub>6</sub>	-0.105	-0.132	-0.02
(21) 1,2,4-tribromobenzene	H <sub>3</sub>	-0.493	-0.493	0.00
	H <sub>5</sub>	-0.013	+0.001	+0.01
	H <sub>6</sub>	-0.186	-0.186	0.00
(22) 2,4-dibromo-1-fluorobenzene	H <sub>3</sub>	-0.424	-0.424	0.00
	H <sub>5</sub>	-0.101	-0.158	-0.05
	H <sub>6</sub>	+0.303	+0.283	-0.02
(23) 1,2-dichloro-4-iodobenzene	H <sub>3</sub>	-0.475	-0.504	-0.02
	H <sub>5</sub>	-0.180	-0.214	-0.03
	H <sub>6</sub>	+0.130	+0.130	0.00

The average deviation was found to be  $\pm 0.027$  ppm, indicating that the additivity relationship can be used to predict the chemical shifts in polyhalosubstituted benzenes provided also that suitable "ortho-meta" constants and  $d_p$  values are used. Again, the same two chemical shift values are not predicted satisfactorily. It is believed that in order for an empirical scheme such as this one to be useful, it must predict the chemical shift to within  $\pm 0.075$  ppm. Such requirements are well satisfied by this pairwise additivity scheme.

In this study it has been possible to determine seventeen

of the twenty-five such "ortho-meta" constants which could exist for each solvent. Conceivably, this idea could be extended to include substituents other than the halogens. A brief indication of how the  $\Delta$  values were determined is given in Appendix III.

It can be seen from Tables III and V that, in general, as the size of the ortho substituent in the "ortho-meta" combination increase, the  $\Delta$  value decreases. It can also be noted that as the meta substituent increases the  $\Delta$  value increases slightly. Hence, there is an interplay of these two effects which destroys any trend in the  $\Delta$  values. It is believed, however, that the ortho substituent predominates in the "ortho-meta" constant and that the observed trend ( $\Delta$  decreasing as size of the substituents increases) is best explained by an intramolecular van der Waal's interaction between the proton and the ortho substituent (49, 62a).

Finally, it should be noted that the proposed "ortho-meta" constants can correlate 95% of the chemical shift data for mono- and disubstituted benzenes that has appeared to date (51, 57, 59, 62b). The pertinent data is found in Table IX.

TABLE IX

COMPARISON OF THE EXPERIMENTAL CHEMICAL SHIFTS (FROM OTHER SOURCES) WITH THOSE PREDICTED USING  $\Delta$  AND  $d_p$  VALUES

Compound	Proton	Observed Shift <sup>1</sup>	Calculated Shift (ppm)	Deviation (ppm)	Solvent	Referen
(1) 1,4-dichloro-benzene	-	0.02	0.043	-0.023	2	57
(2) 1,4-dibromo-benzene	-	-0.07	-0.071	0.001	2	57
(3) 1,4-diiodo-benzene	-	-0.12	-0.055	-0.065	2	57
(4) 1-bromo-4-fluorobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.11	-0.159	0.049	2	57
	H <sub>3</sub> ,H <sub>5</sub>	0.38	0.331	0.049	2	57
(5) 1-bromo-4-iodobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.09	-0.124	0.034	2	57
	H <sub>3</sub> ,H <sub>5</sub>	0.10	0.096	0.004	2	57
(6) 1-chloro-4-iodobenzene	H <sub>2</sub> ,H <sub>6</sub>	0.23	0.243	-0.013	2	57
	H <sub>3</sub> ,H <sub>5</sub>	-0.28	-0.255	-0.025	2	57
(7) 1-bromo-2-chlorobenzene	H <sub>3</sub>	-0.277	-0.342	0.065	2	62b
	H <sub>4</sub>	0.243	0.203	0.040	2	62b
	H <sub>5</sub>	0.113	0.133	-0.020	2	62b
	H <sub>6</sub>	-0.127	-0.185	0.058	2	62b
(8) 1-chloro-2-iodobenzene	H <sub>3</sub>	-0.537	- <sup>4</sup>	-	2	62b
	H <sub>4</sub>	0.413	0.350	0.063	2	62b
	H <sub>5</sub>	0.043	0.115	-0.072	2	62b
	H <sub>6</sub>	-0.127	- <sup>4</sup>	-	2	62b
(9) 1-bromo-2-iodobenzene	H <sub>3</sub>	-0.527	- <sup>4</sup>	-	2	62b
	H <sub>4</sub>	0.373	0.333	0.040	2	62b
	H <sub>5</sub>	0.153	0.168	-0.015	2	62b
	H <sub>6</sub>	-0.297	-0.285	-0.012	2	62b
(10) 1,4-dichloro-benzene	-	0.065	0.019	0.046	3	59
(11) 1-bromo-4-chlorobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.092	-0.133	0.041	3	59
	H <sub>3</sub> ,H <sub>5</sub>	0.128	0.117	0.011	3	59
(12) 1-chloro-4-iodobenzene	H <sub>2</sub> ,H <sub>6</sub>	0.258	0.294	-0.036	3	59
	H <sub>3</sub> ,H <sub>5</sub>	-0.286	-0.343	0.057	3	59

TABLE IX (Cont'd)

Compound	Proton	Observed Shift	Calculated Shift (ppm)	Deviation (ppm)	Solvent	Reference
(13) 1,4-dibromobenzene	-	-0.027	-0.035	0.008	3	59
(14) 1,4-diiodobenzene	-	-0.087	-0.068	-0.019	3	59
(15) 1-bromo-4-iodobenzene	H <sub>2</sub> ,H <sub>6</sub>	0.108	0.142	-0.034	3	59
	H <sub>3</sub> ,H <sub>5</sub>	-0.215	-0.245	0.030	3	59
(16) 1,3-dibromobenzene	H <sub>2</sub>	-0.400	-0.390	-0.010	3	59
	H <sub>4</sub> ,H <sub>6</sub>	-0.102	-0.125	0.023	3	59
	H <sub>5</sub>	0.275	0.320	-0.045	3	59
(17) 1,3-diiodobenzene	H <sub>2</sub>	-0.810	-0.810	0.000	3	59
	H <sub>4</sub> ,H <sub>6</sub>	-0.338	-0.335	-0.003	3	59
	H <sub>5</sub>	0.551	0.674	-0.123	3	59
(18) 1,2-dichlorobenzene	H <sub>3</sub> ,H <sub>6</sub>	-0.118	-0.135	0.017	3	59
	H <sub>4</sub> ,H <sub>5</sub>	0.168	0.222	-0.054	3	59
(19) 1,2-dibromobenzene	H <sub>3</sub> ,H <sub>6</sub>	-0.213	-0.255	0.042	3	59
	H <sub>4</sub> ,H <sub>5</sub>	0.297	0.230	0.067	3	59
(20) 1,2-diiodobenzene	H <sub>3</sub> ,H <sub>6</sub>	-0.570	- 4	-	3	59
	H <sub>4</sub> ,H <sub>5</sub>	0.347	0.407	-0.060	3	59
(21) Fluorobenzene	H <sub>2</sub> ,H <sub>6</sub>	0.308	0.223	0.085	3	51
	H <sub>3</sub> ,H <sub>5</sub>	0.023	- 4	-	3	51
	H <sub>4</sub>	0.217	0.250	-0.033	3	51
(22) Chlorobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.020	-0.043	0.023	3	51
	H <sub>3</sub> ,H <sub>5</sub>	0.025	0.062	-0.037	3	51
	H <sub>4</sub>	0.0117	0.160	-0.043	3	51
(23) Bromobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.223	-0.195	-0.028	3	51
	H <sub>3</sub> ,H <sub>5</sub>	0.085	0.160	-0.075	3	51
	H <sub>4</sub>	0.030	0.070	-0.040	3	51
(24) Iodobenzene	H <sub>2</sub> ,H <sub>6</sub>	-0.400	-0.405	0.005	3	51
	H <sub>3</sub> ,H <sub>5</sub>	0.250	0.337	-0.087	3	51
	H <sub>4</sub>	0.033	0.070	-0.037	3	51

1 In ppm relative to benzene

2 Carbon Tetrachloride

3 Cyclohexane

4 Data from which a new  $\Delta$  can be deri

- APPENDIX I -

- COMPILATION OF THE COUPLING CONSTANTS IN  
POLYHALOSUBSTITUTED BENZENES -

TABLE VIII

COUPLING CONSTANTS IN POLYHALOSUBSTITUTED BENZENES (HZ)<sup>†</sup>

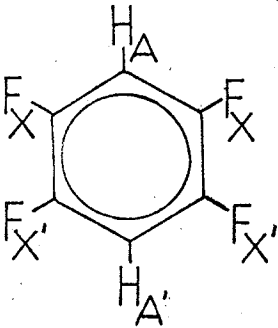
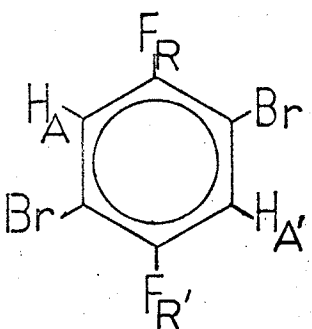
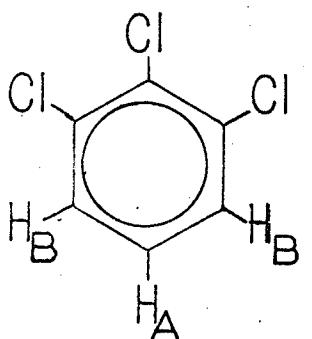
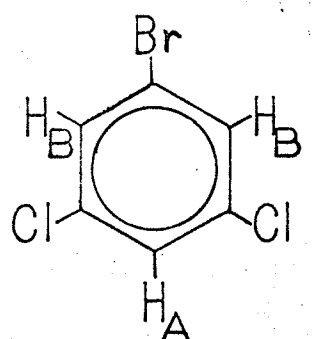
Compound	J	In C <sub>6</sub> H <sub>12</sub>	In CCl <sub>4</sub>	In CH <sub>3</sub> CN
 $J_{AX} + J_{AX'}$		16.84	16.92	17.94
 $J_{AR} + J_{AR'}$		13.12	13.10	13.88
 $J_{AB}$		8.14	8.16	-
 $J_{AB}$		1.84	1.81	-

TABLE VIII (Continued)

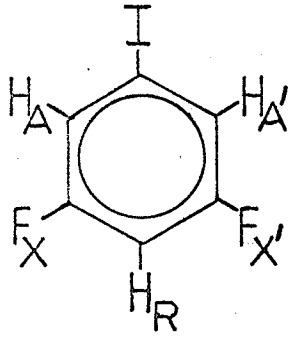
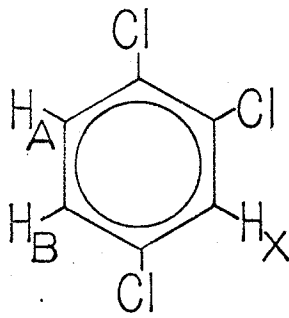
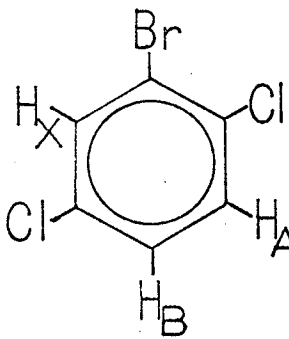
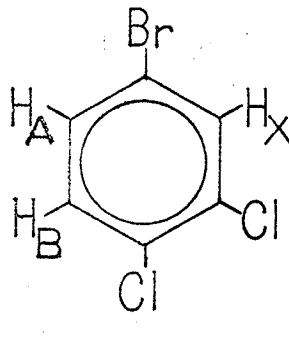
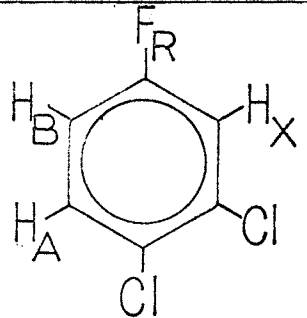
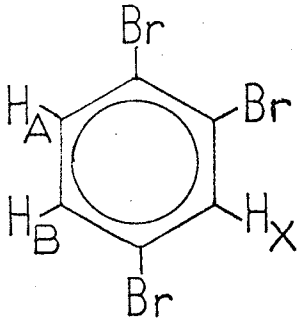
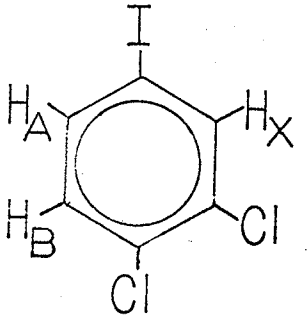
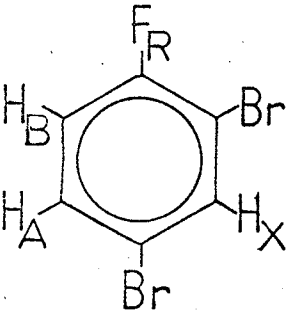
Compound	J	In C <sub>6</sub> H <sub>12</sub>	In CCl <sub>4</sub>	In CH <sub>3</sub> CN
	$J_{AA'}$	-	1.40	1.39
	$J_{AR}$	-	2.31	2.29
	$J_{AX}$	-	7.58	8.00
	$J_{RX}$	-	8.83	9.30
	$J_{AX'}$	-	-1.28	-1.22
	$J_{XX'}$	-	6.23	6.35
	$J_{AB}$	8.57	8.53	-
	$J_{AX}$	0.40	0.30	-
	$J_{BX}$	2.36	2.42	-
	$J_{AB}$	8.55	8.57	-
	$J_{AX}$	0.28	0.28	-
	$J_{BX}$	2.40	2.40	-
	$J_{AB}$	8.53	-	-
	$J_{AX} + J_{BX}$	-	2.56	-



TABLE VIII (Continued)

Compound	J	In $C_6H_{12}$	In $CCl_4$	In $CH_3CN$
	$J_{AB}$	8.83	8.81	-
	$J_{RX}$	7.99	8.08	-
	$J_{AX}$	0.31	0.30	-
	$J_{BX}$	2.94	2.91	-
	$J_{AR}$	5.33	5.44	-
	$J_{BR}$	7.46	7.47	-
	$J_{AB}$	8.46	8.49	-
	$J_{AX}$	0.24	0.22	-
	$J_{BX}$	2.26	2.26	-
	$J_{AB}$	8.37	8.40	-
	$J_{AX}$	2.02	2.06	-
	$J_{BX}$	0.28	0.24	-
	$J_{AB}$	8.70	8.71	-
	$J_{AX}$	2.40	2.45	-
	$J_{BX}$	0.30	0.30	-
	$J_{AR}$	4.23	4.26	-
	$J_{BR}$	7.93	7.94	-
	$J_{RX}$	6.05	6.06	-

† Standard deviations are in all cases less than  $\pm 0.03$  Hz.

- APPENDIX II -

- THE ANALYSIS OF THE NMR SPECTRA -

- APPENDIX II -

In single line spectra, the proton chemical shift corresponds to the frequency of the line position.

The ABX and AB<sub>2</sub> spectra were analyzed according to procedures given in standard texts (2, 4, 6).

The analyses of spectra complicated by fluorine splitting constitutes a future research project. Moreover, the present research is concerned only with the chemical shifts and these are easily recognized from symmetry considerations. The spectrum of 1-bromo-3-chloro-5-iodobenzene (an ABC) was treated approximately as an AB<sub>2</sub>. The spectra of 2,4-dibromo-1-fluorobenzene, 1,2-dichloro-4-fluorobenzene and 3,5-difluoro-1-iodobenzene were analyzed using the concepts of effective Larmor frequency and subspectral analysis (63, 64, 65).

The deceptively simple spectra, and the spectra of 1,2,4,5-tetrafluorobenzene and of 1,4-dibromo-2,5-difluorobenzene, from which only the mean of the coupling constants involved can be obtained, were analyzed by methods in (66, 67, 68).

- APPENDIX III -

- THE DERIVATION OF THE ORTHO-META CONSTANTS -

- APPENDIX III -

One begins by looking at the symmetrical benzenes such as the 1,2,4,5-tetrasubstituted compounds. For example, the  $\Delta(\text{F-F})$  constant is just half the proton chemical shift for the 1,2,4,5-tetrafluorobenzene. Similarly, the  $\Delta(\text{Cl-Cl})$  and  $\Delta(\text{Br-Br})$  values can be determined. If the  $d_p$  values are already known, the  $\Delta(\text{Br-H})$  and  $\Delta(\text{Cl-H})$  values can be calculated from the chemical shift data on 1,3,5-tribromobenzene and 1,3,5-trichlorobenzene. In a similar manner, the  $\Delta(\text{F-H})$ ,  $\Delta(\text{Cl-H})$  and  $\Delta(\text{H-Cl})$  values can be calculated from 1,2,3,4-tetrafluorobenzene, 1,2,3,4-tetrachlorobenzene and 1,2,3-trichlorobenzene. Proceeding to benzenes with two or more different halogen substituents, the other ortho-meta constants can be determined. If the  $d_p$  values are not known, they may be easily determined from the pentasubstituted benzenes or the trisubstituted benzenes, the structure of which allow their evaluation; e.g. once the  $\Delta(\text{F-H})$  is roughly determined, the  $d_p$  for I may be evaluated from 1,3-difluoro-5-iodobenzene. Slight adjustments in the values were necessary to attain self-consistency and to keep within the maximum deviation previously set. The scheme can only be useful as an empirical tool if the maximum deviation in this case were about  $\pm 0.075$  ppm. Between 50 and 75 percent of the data was used in determining the constants and the remainder of the chemical shifts can be used to check for internal consistency.

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