Theoretical studies on the electronic structures and reactivities of some aromatic and heteroaromatic compounds

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A thesis entitled

THEORETICAL STUDIES ON THE ELECTRONIC STRUCTURES AND REACTIVITIES OF SOME AROMATIC AND HETEROAROMATIC COMPOUNDS

submitted by

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Abstract of a thesis entitled "Theoretical Studies on the Electronic Structures and Reactivities of some Aromatic and Heteroaromatic Compounds" submitted by Herbert Frederick Beer, M.A., (Cantab.) (Bede College), a candidate for the degree of Master of Science, 1973.

All valence electron CNDO/2 SCF MO calculations have been performed on some fluoro, chloro and methoxy derivatives of benzene, pyridine and the diazines. The charge distributions and the dipole moments, calculated from them are discussed and compared with the available experimental data. The relative basicities of the derivatives of pyridine and the diazines were investigated and an attempt made to correlate the results with known pK_a values. Localisation energies for the nucleophilic substitution of halogen by methoxide ion were calculated. Relative reactivities were then predicted from these localisation energies and the prediction compared with experimental observations, where these were available.

Acknowledgements

The work described in this thesis was carried out under the supervision of Dr. D.T. Clark, and I wish to record my appreciation of his help and encouragement throughout. I would also like to express my gratitude to Professor W.K.R. Musgrave for the provision of facilities within the Chemistry Department, and the various members of the staff of NUMAC for their help and co-operation.

Thanks are also due to the Governors of the College of the Venerable Bede for their granting of study leave in connection with this work, and finally to Mrs. J. Gill for typing this thesis.

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1969 and December 1972. Except where acknowledged by reference it is the original work of the author and has not been submitted in whole or part for any other degree.

The substance of some of this material has already been presented at the Sixth International Symposium of Fluorine Chemistry.

Contents

Appendices

Summary

A considerable amount of experimental work has been carried out on the reactions and preparations of fluorinated aromatic and heteroaromatic compounds. The object in this work has been to carry out theoretical calculations for the electron distributions in the ground state and the reactivities for some of these compounds. The results of these calculations were then compared with experimental observations where these were known. In the cases where experimental data is not available the theoretical calculations are used to make predictions as to the results that might be expected when the reactions are attempted.

The compounds chosen for study were the monofluoro and perfluoro derivatives of benzene, pyridine, and the three diazines pyridazine, pyrimidine, and pyrazine. Some calculations were carried out for the monomethoxy derivatives of the heteroaromatic compounds mentioned above and also for some of the chloro derivatives of benzene and pyridine. The reactions that were considered were the protonation of the bases pyridine, pyridazine, pyrimidine and pyrazine and some of their halogen and methoxy derivatives and the nucleophilic substitution of halogen by methoxide ion.

The calculations, of the electron distributions and energies of the ground states, involve finding solutions for the Schrödinger wave equation, $\hat{H}\Psi = E\Psi$, for each of the molecules and intermediates considered. The complexities of the molecules and intermediates considered in this work ruled out the possibility of a major non-empirical LCAO MO treatment. The calculations have therefore been carried out employing an approximate treatment in the all valence electron complete neglect of differential overlap (CNDO) SCF MO formalism as developed by

J.A. Pople and coworkers. The programme to perform the calculations has been implemented on the Northumbrian Universities Multiple Access Computor (NUMAC), IBM 360 Model 67.

The relative basicities were deduced from the energy differences between each base and its conjugate acid. The order of energy differences should then give the order of the basicities. That is the base that gives the largest energy difference, on forming its conjugate acid, should be the strongest base, while bases that give smaller energy differences should be weaker ones. A comparison of the energy differences with the pK_a values showed, though, that the correlation for particular bases was not good. However a general trend was observed in that the larger pK_a values tended to be associated with the bigger energy releases on protonation and vice-versa.

In the case of the nucleophilic substitution of halogen by methoxide ion it was assumed that the reaction proceeds via a sigma complex, or Wheland intermediate. It was known that the reactions considered were in general irreversible, under the conditions employed, and therefore subject to kinetic control. The energy of the reactants, the aromatic compound and the methoxide ion, were found and the energy of the intermediate and hence the energy difference. The relative reactivity of two compounds, or of two sites within the same compound, was then determined by which intermediate had the lower energy, compared to the original reactants.

In general quite good agreement was observed between the results of the theoretical calculations and the experimental observations when a similar series of compounds was considered. The relative reactivities of different sites for the same parent compound agreed well with what

has been observed, though in the case of monomethoxyperfluoropyrazine the energy differences, as calculated, were not quite as large as might be expected. When two dissimilar compounds were compared it was not always possible to correlate directly the calculated energy differences with the experimental observations. This is due to a number of causes including the fact that CNDO II LCAO SCF calculations are for isolated molecules in the gas phase at an implied temperature of 0 Kelvin. This means that among other things solvation effects are neglected. Agreement between the relative reactivities of chloro and fluoro compounds may also be affected by the emphasis that the CNDO II treatment places on 'd' orbital contributions in the chloro compounds. It is known from more accurate theoretical treatments that 'd' orbital participation in aliphatic, aromatic and heterocyclic systems is unimportant and is overemphasised in the CNDO II approximation.

The electron distributions calculated corresponded well with those expected from a consideration of the inductive and mesomeric effects of the various atoms. There was also reasonable agreement with the electron densities as determined by ESCA (X-ray photo electron spectroscopy). It is interesting to note that in the case of the basicities the more strongly basic compounds were not necessarily those with the largest electron densities on the nitrogen atom. As previously stated the more basic compounds were those where the energy release on protonation was the greatest and this did not necessarily follow the same order as the electron densities.

From the appropriate density matrices the dipole moments were calculated. It was found that the dipole moments calculated for the fluoro compounds agreed quite well with the results found by experiment.

In the case of the methoxy and the chloro derivatives the agreement was not particularly good. This is probably due in the case of the methoxy derivatives to the fact that the methoxy group may rotate about the C - O bond and this effect was not allowed for in the calculations. In the case of the chloro derivatives the descrepancies are due in part to the inclusion of 'd' orbital contributions. There is also the fact that the calculations were for the isolated molecules and most of the experimental determinations of dipole moments were carried out in solution.

The coordinates of the atoms in the various molecules and the intermediates were calculated from the best available known geometries. Where the geometries were not available then the geometries were assumed by comparison with similar structures. It was assumed that the geometry of the parent ring would remain unchanged for each series based on that particular ring, including the various intermediates formed during the reactions of that series. Although changes in the geometry of the ring system are expected in going from reactant to intermediate, for a closely related series any errors arising from a neglect of these changes are likely to be minimised since we are only attempting to calculate relative energies and hence relative reactivities.

Chapter 1

Introduction

Introduction

The preparation and reactions of the halogen derivatives of benzene, pyridine and the three diazines pyridazine, pyrimidine and pyrazine have been the subject of extensive experimental work in recent years. One of the interesting aspects of this work is the extreme reactivity shown by the perhalogen heteroaromatic compounds in their reactions with various nucleophilic reagents. This is in sharp contrast to the reactivity of the halogen derivatives of benzene.

Thus perfluoropyridine reacts rapidly at 0° C with methoxide ion to give 4-methoxyperfluoropyridine[1]. Perfluorobenzene, however, requires refluxing for several hours in order to obtain the mono-methoxy derivative[2,3]. The reaction of pentachloropyridine with methoxide ion[4], like that of the corresponding fluorine compound, takes place readily at 0°C. There is a difference between the two reactions though since in the case of the pentachloropyridine some 2-methoxy derivative is formed as well as principally 4-methoxy-perchloropyridine[5]. The pentafluoropyridine gives, however, exclusively the 4-methoxy compound in its reaction. From these reactions[4,5] and others it appears that a halogen atom in the 3- position in pyridine is particularly resistant to replacement in nucleophilic substitution reactions. When the diazines are considered as well, the feature that emerges is that halogen atoms in meta positions (see chapter 5), with respect to nitrogen atoms, are less readily displaced in nucleophilic substitutions than halogen atoms in the ortho and para positions.

Perfluorobenzene has been observed to be much less reactive than perfluoropyridine[1], but is itself much more reactive than monofluorobenzene[6,7] when subjected to nucleophilic attack. The presence of groups that are considered to be electron withdrawing, e.g. the nitro group, lead to much greater reactivities. Nitrobenzene is often compared with pyridine and it has been found that perfluoronitrobenzene will react with ammonia at room temperature[8] to give the ortho and para amino products in the ratio 7:3. This high proportion of ortho to para product might seem to suggest that nitrobenzene and pyridine ought not to be compared too closely since with pyridine the para product is usually formed in the greater proportion. It has been suggested[9] though that hydrogen bonding, between the attacking ammonia molecule and the nitro group at some stage of the reaction, is responsible for the large amount of ortho product formed in this reaction. The use of other nucleophiles where hydrogen bonding is less likely gives, in fact, principally the para products[9]. The reactions of 4-nitroperfluoropyridine with ammonia and sodium methoxide[10] are interesting in this respect. With ammonia the products formed are the 4-aminoperfluoropyridine, the 4-nitro, 3-amino -, and the 4-nitro, 2-amino compound in the ratio 27:48:25. With sodium methoxide the corresponding products, (methoxy instead of amino) are formed in the ratio 70:7:23. The perfluoromethyl and perfluroethyl groups, which might also be considered to be electron withdrawing, appear to have the same activating effect on the perfluorobenzene as does the nitro group. The presence of the perfluoro methyl group in perfluorotoluene makes the reaction with alkoxide ion[11] faster than the reaction of perfluorobenzene[7] with the same nucleophiles. Moreover both groups, the perfluoromethyl and the perfluoroethyl, cause

substitution to occur, principally, in the position para to them in the reaction of perfluoro(alkylbenzenes) with alkoxide ions[11,12].

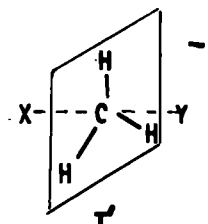
Two methanisms have been established for nucleophilic aromatic substitutions. There is a bimolecular process whereby the attacking species adds on to the original molecule and then the displaced group leaves. This addition-elimination process is sometimes referred to as an $SN2_{aromatic}$ mechanism due to its ressemblence to the aliphatic SN2 mechanism. However unlike the latter, the carbon atom at which substitution takes place remains tetracovalent and hence "relatively" stable intermediates, in some cases isolable[13], called sigma complexes or Wheland intermediates are formed (see figures 1.1a and 1.1b below).

The second suggested mechanism is that of elimination followed by addition via a "benzyne" type of intermediate. There is some evidence that in the case of the monchalobenzenes that nucleophilic substitution in some reactions may proceed simultaneously via a "benzyne" and an $SN2_{aromatic}$ mechanism[14]. Also in the case of some monohalogen derivatives of pyridine there is some evidence[15] that with nucleophiles the substitution may proceed via a "pyridyne" intermediate.

However the perhalogen derivatives of benzene and of the hetero-aromatic compounds considered in this work are believed to react by $SN2_{aromatic}$ mechanisms in nucleophilic substitution reactions with methoxide ion. Also the monohalogen derivatives of benzene, pyridine and pyrazine considered react in part by $SN2_{aromatic}$ mechanisms in their reactions with methoxide ion. Therefore in this thesis the calculations on the nucleophilic substitution of halogen by methoxide ion are carried out on the basis of only an $SN2_{aromatic}$ mechanism being involved.

Figure 1.1a

SN2 mechanism



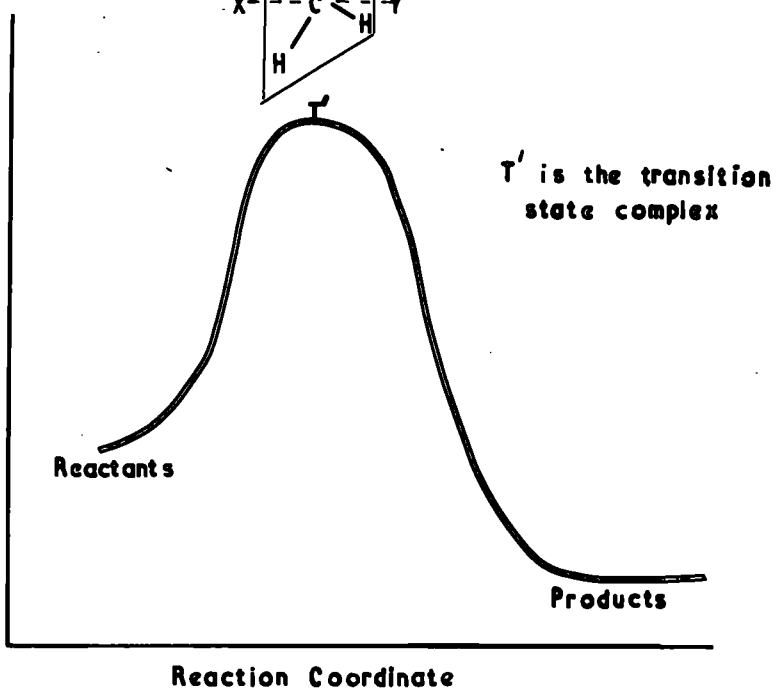


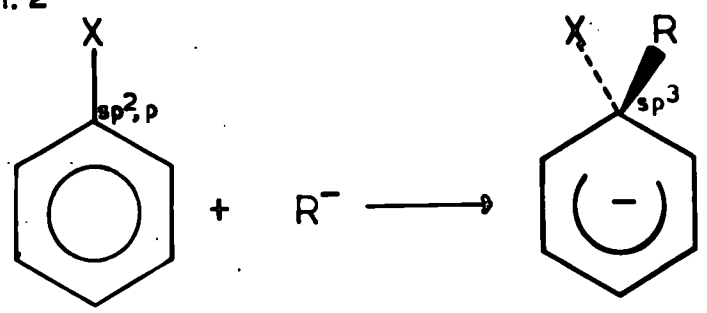
Figure 1.1b

$SN2_{aromatic}$ mechanism

Now in using an $SN2_{aromatic}$ mechanism in studying aromatic substitution reactions it is necessary to choose a good model for the transition state. Two main suggestions have been put forward for this model. In the first it is assumed that the transition state is similar in structure to the original reactants. Comparisons of reactivities and activation energies are then based on the properties of the reactants. This model however does not, in general, give consistent results (see chapter 5).

The second suggestion is to take as the model for the transition state the Wheland intermediate, or sigma complex as it is also known. Wheland[16] assumed that the carbon atom undergoing attack was isolated from the conjugated pi electron system of the molecule by being converted from an sp^2,p state to the sp^3 configuration. Thus;

Figure 1.2

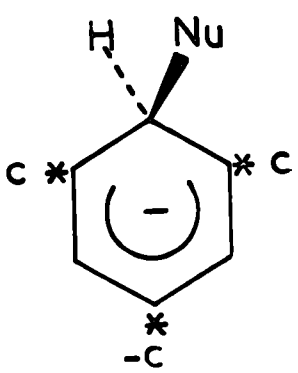


This model can be used[17] provided that the transition state and the Wheland intermediate are similar in structure and therefore similar in energy (see figure 1.1b).

Using the Wheland intermediate as a model, alternant hydrocarbons such as benzene and heterocyclic compounds such as pyridine

and the diazines, whose rings are pi isoelectronic with that of benzene, may be treated by the methods developed by H.C.Longuet-Higgins[18] and others from Hückel theory[19]. Alternant hydrocarbons are conjugated hydrocarbons in which each carbon atom provides a $2p_z$ orbital and one electron to the pi system, and which do not contain odd membered rings. Alternants may be further divided into odd alternants, with an odd number of conjugated atoms and even alternants which have an even number. In simple Huckel theory alternant hydrocarbons have several interesting properties. They have an even electron distribution in the ground state and the energies of the bonding and antibonding orbitals are symetrically disposed about the non-bonding position. The carbon atoms of an alternant may be divided into two sets, usually distinguished as starred and unstarred, such that no two members of the same set are bonded together and that if the number of atoms in each set is not equal then the number of starred atoms is the greater. In the ion formed when the Wheland intermediate is produced it is suggested that the charge of the ion is located on the starred centres (see below) in non-bonding molecular orbitals. It may be shown that the sum of the coefficients, of these non-bonding molecular orbitals on any two starred atoms adjacent to the same unstarred atom is zero. The ratio of the coefficients may thus be found and their values by the normalisation process. In the case of benzene undergoing a nucleophilic attack the results would be as follows:-

Figure 1.3



c is the coefficient of the non-bonding molecular orbital

Now normalisation requires that $\sum_r c_r^2 = 1$ and therefore

$3c^2 = 1$ and $c^2 = \frac{1}{3}$

The probability of finding an electron at the atom r is given by c_r^2 and the total pi electron density at a starred atom is $1+\frac{1}{3}$, or $4/3$, while the pi electron density at the unstarred atoms remains at 1. Pyridine, which is isoelectronic with benzene, forms transition complexes which are also isoelectronic with those of benzene. Therefore for the case of nucleophilic attack on pyridine the pi electron densities will be similar to those of the transition state of benzene, subject to any effects caused by the nitrogen. Now the difference in the pi electronic energy between the isoelectronic pair, pyridine and benzene may be calculated[18] by

$$E_{\pi aza} - E_{\pi ar} = \sum_r d\alpha_r q_r \qquad \ldots \quad 1.1$$

where $E_{\pi aza}$ is the unsaturation energy of pyridine

$E_{\pi ar}$ is the unsaturation energy of benzene

α_r is the coulomb integral for the r^{th} atom in benzene

A commonly accepted way of formulating α_{r_N} is:

$$\alpha_{r_N} = \alpha_{r_C} + h_N\beta$$

and therefore $d\alpha_r = \alpha_{r_N} - \alpha_{r_C} = h_N\beta$

where h_N is the difference in electronegativities of nitrogen and carbon and β is a resonance integral. H.C. Longuet-Higgins has suggested that if $d\alpha_r$ has a value δ at the nitrogen, it is $\delta/3$ for the carbon atoms directly bonded to the nitrogen and zero elsewhere.

When the two transition states, for benzene and pyridine respectively, in nucleophilic substitution are considered then

$$E'_{\pi aza} - E'_{\pi ar} = \sum_r d\alpha_r . q'_r \qquad \ldots \quad 1.2$$

Since q_r will equal 1 on all atoms in benzene and $q'_r = 1 + c_r^2$ in the case of a nucleophilic substitution then subtraction of equation 1.1 from 1.2 gives

$$\Delta E_{\pi aza} - \Delta E_{\pi ar} = \sum_r d\alpha_r . c_r^2 \qquad \ldots \quad 1.3$$

Since $\Delta E_{\pi ar}$ will be constant the reactivity of the different positions of pyridine for nucleophilic substitution may be compared by calculating $\sum_r d\alpha_r . c_r^2$.

Thus for pyridine

Figure 1.4

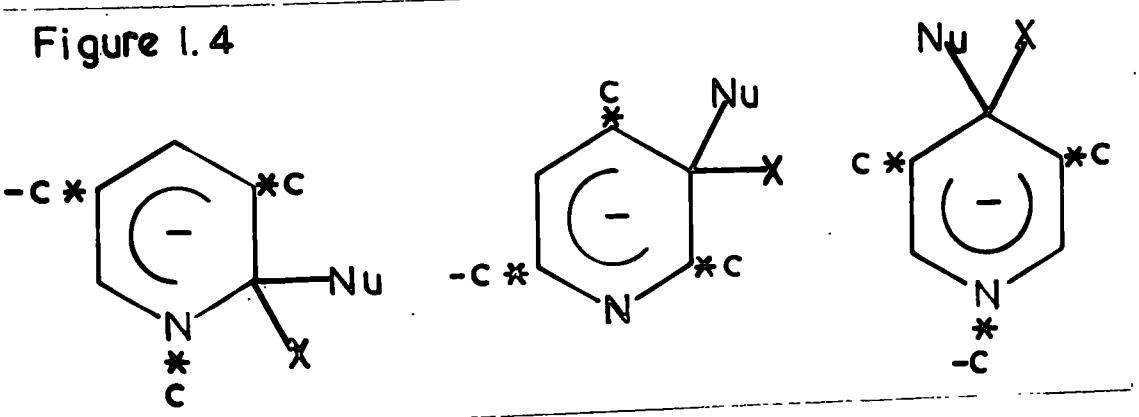


Table 1.1

Substitution at	$d\alpha_r . c_r^2$			$\sum_r d\alpha_r . c_r^2$
	N	C2	C3,4,5,6	
C2	$\delta \times 1/3$	0	0	$\delta/3$
C3	0	$\delta/3 \times 1/3$	$\delta/3 \times 1/3$	$2\delta/9$
C4	$\delta \times 1/3$	0	0	$\delta/3$

Therefore, from table 1.1, in nucleophilic attack positions 2 and 4 for pyridine will be activated more than position 3 and substitution will take place more readily at positions 2 and 4 compared to position 3. This is in general agreement with what is observed but does not explain the difference in reactivity between positions 2 and 4 with different attacking nucleophiles and different leaving groups. The method assumes though in calculating pi electron densities that the charge of the intermediate ion, the Wheland intermediate, resides on the starred atoms and that all the other atoms bear no part of the charge introduced by the attacking group. It also suffers from other major defficiencies in that the Hückel approximation deals only with the pi electrons and ignores the polarisability of the sigma framework and that the parameterisation is somewhat arbitary. No account is taken either of the attacking nucleophile and such a simple theory is incapable of realistic discussions of substitution patterns as a function of the electronic structure of the nucleophile.

In order to overcome some of the difficulties mentioned above, while still retaining the simplicity, other approaches[20,21] have constructed pseudo sigma and pseudo pi orbitals from the orbitals used to bond the attacking and leaving groups to the aromatic nucleus (see chapter 5). Using the pseudo pi orbital, which will include contributions from both the attacking and leaving groups, the pi electron energy of the transition state may be calculated. Using the Hückel approximation this approach has been used by S. Carra, M. Raimondi and M. Simonetta[20] in calculations concerning the nucleophilic attack on various halogen derivatives of benzene and

naphthalene by amines and methoxide ion. They took the activation energy $\Delta E^{\ddagger}$ as been made up as follows

$$\Delta E^{\ddagger} = \Delta E_{\pi} + \Delta E_{\sigma} + \Delta E_{solv} \quad \ldots \quad 1.4$$

where ΔE_{π} is the difference in the pi electron energies of the reactants and the intermediate,

ΔE_{σ} includes differences in sigma electron, nuclear repulsion, zero point and thermal effect energies,

ΔE_{solv} is the difference in solvation energies of the reactants and the intermediate.

The assumption was made that $(\Delta E_{\sigma} + \Delta E_{solv})$ would be constant for a similar series of compounds and therefore the differences in activation energy for two similar compounds undergoing the same reaction might be related to the differences in ΔE_{π} for the two compounds. They found quite good agreement between ΔE_{π} and $\Delta E^{\ddagger}_{experimental}$ for a number of nitrohalobenzenes and naphthalenes for their reactions with piperidine. From this agreement it follows that $(\Delta E_{\sigma} + \Delta E_{solv})$ does remain approximately constant for the different reactions. Therefore the separate terms, ΔE_{σ} and ΔE_{solv}, should also be constant since the probability that these two terms will compensate for changes in each other is small when a number of cases is considered. Some work was also carried out on methoxide substitution of halogen and again reasonable correlation between $\Delta E^{\ddagger}_{experimental}$ and ΔE_{π} was obtained. Again it seems probable that ΔE_{σ} and ΔE_{solv} remain separately constant when a similar series of compounds are compared in similar reactions. When fluorine derivatives were compared with chlorine and bromine derivatives they found that the absolute magnitude of $(\Delta E_{\sigma} + \Delta E_{solv})$ was much

greater for the fluorine derivatives than for the other two series, the difference between the fluoro and chloro derivatives being of the order of 120 kJ mol^{-1}. This difference is not entirely unexpected in view of the large solvation energy of the fluoride ion. It is also interesting to note that this energy difference, 120 kJ mol^{-1}, is very similar to the differences in solvation energy given in table A2.10 calculated using the expression[22]

$$\Delta E_{iso} = -\sum_{ij} \frac{q_i q_j}{2r_{ij}} (1 - 1/D) \qquad \ldots \quad 1.5$$

where q_i and q_j are the charges on atoms i and j respectively,

r_{ij} is the distance between i and j,

D is the dielectric constant of the solvent.

The main disadvantages in using this approach[20] are that arbitary parameters have to be found for the pseudo "atom" of the transition state, the use of the Hückel approximation, and the fact that only the pi electrons were considered. The CNDO II approach[23,24] used in this thesis overcomes some of these problems by considering all valence electrons and by calculating energy differences directly.

The electron distribution in a molecule has often been discussed in terms of the relative inductive and mesomeric effects of the constitutent atoms of the molecule[25,26]. What is calculated in this thesis is the sigma, pi and total charge, on each atom in the molecule, as defined in chapter 2. From these sigma and pi charges the various inductive and mesomeric effects may be deduced. However since the introduction of all valence electron SCF calculations the general usefulness of discussing inductive and mesomeric effects has been much reduced. Therefore this has only been carried out for the nitrogen, fluorine and chlorine atoms in the neutral molecules (see chapter 3).

Chapter 2

Molecular Orbital Theory

Molecular Orbital Theory

Elements of Quantum Mechanics[27]

The Schrödinger equation

$$\hat{H}\Psi = E\Psi \qquad \ldots 2.1$$

provides a theoretical foundation for the solution of virtually all problems in chemistry. At the present time, however, the Schrödinger equation has only been solved exactly for atoms and molecules containing one electron and therefore for larger systems approximate solutions must be used.

For molecules a first approximation is that due to Born and Oppenheimer[28] in which the nuclear and electronic wave functions are considered separable.

$$\Psi = \Psi_e \cdot \Psi_N \qquad \ldots 2.2$$

Using the Born-Oppenheimer approximation the electronic Schrödinger equation

$$\hat{H}_e \Psi_e = E_e \Psi_e \qquad \ldots 2.3$$

is first solved for fixed positions of the N atoms within the molecule. The resulting electronic energies E_e form a potential energy surface $V(\vec{R}_1, \vec{R}_2, \ldots \vec{R}_N)$ where R_A specifies the coordinates of the Ath atom within the molecule. This leads to a Schrödinger equation describing the motion of the nuclei

$$\hat{H}_N \Psi_N = E_N \Psi_N \qquad \ldots 2.4$$

where

$$\hat{H}_N = \sum_A \frac{-\nabla_A^2}{2M_A} + V(\vec{R}_1, \vec{R}_2, \ldots \vec{R}_N) \qquad \ldots 2.5$$

in which $-\nabla_A^2/2M_A$ is the kinetic energy operator for the Ath nucleus. Equation 2.4 may then be solved to yield the approximate total wave function, 2.2, and total energy E(2.1).

In obtaining solutions to equation 2.3 a further basic approximation is made, that of ignoring relativistic effects.

The non-relativistic spin free electronic Hamiltonian, $\hat{H}_e$, is then given, in atomic units, by the expression

$$\hat{H}_e = \sum_{\mu}\left(-\tfrac{1}{2}\nabla_{\mu}^2 - \sum_{A}\frac{Z_A}{r_{A\mu}}\right) + \sum_{\mu>\nu}\sum\frac{1}{r_{\mu\nu}} \qquad \ldots \quad 2.6$$

where $-\frac{1}{2}\nabla_{\mu}^2$ represents the kinetic energy operators of the individual electrons μ,

and $-\sum_{A}\frac{Z_A}{r_{A\mu}}$ are the nuclear-electron attraction potential energy operators, Z_A being the charge on the nucleus A, and $r_{A\mu}$ is the distance between this nucleus and the electron μ,

and $\frac{1}{r_{\mu\nu}}$ are the operators corresponding to the mutual repulsion between two electrons μ and ν.

The solution of equation 2.6 gives the electronic energy, E_e, of the molecule and this with the nuclear repulsion energy, E_{Nr}, gives the total energy of the molecule. The nuclear repulsion energy is given by

$$E_{Nr} = \sum_{A}\sum_{B>A} Z_A Z_B / R_{AB} \qquad \ldots \quad 2.7$$

where Z_A is the core charge of the atom and R_{AB} is the inter-nuclear distance.

The Self Consistent Field Method[29]

a) Non-empirical

The method used, with very few exceptions, for calculating the electronic wave functions of molecules is that of D.R. Hartree[30]

and V. Fock[31]. The wave function is taken as an anti-symmetrised product of spatial and spin functions and for a closed shell the total wave function is defined as

$$\Psi_e = \frac{A}{(2n)!}\left[\psi_1(1)\alpha(1)\psi_1(2)\beta(2).....\psi_n(2n)\beta(2n)\right] \quad \ldots \quad 2.8$$

where A is an anti-symmetriser.

For molecules the spatial functions, $\psi_m(\mu)$, are molecular orbitals which are usually expressed as linear combinations of atomic orbitals χ_i, (L.C.A.O. M.O.)[32]

$$\psi_m(\mu) = \sum_i a_{mi}\chi_i(\mu) \quad \ldots \quad 2.9$$

The coefficients, a_{mi} are determined by the variational principle so as to minimise the expression

$$E_e = \frac{\int \Psi \hat{H}_e \Psi \, d\tau}{\int \Psi \Psi \, d\tau} \quad \ldots \quad 2.10$$

where E_e is the expectation value of the electronic energy associated with the Hamiltonian, $\hat{H}_e$, of the molecule. The set of initial atomic functions, χ_i, is called the basic set. A complete solution of the Hartree-Fock problem requires an infinite basis set but a good approximation can be achieved with a limited number of functions. Molecular orbital theory is simplest to apply and interpret if the basis set is minimal, that is, when it consists of the least number of atomic orbitals (of appropriate symmetry) for the ground state. For typical organic molecules a minimal basis set consists of a 1s orbital for hydrogen, $1s, 2s, 2p_x, 2p_y, 2p_z$ for carbon, nitrogen, etc., and $1s, 2s, 2p_x, 2p_y, 2p_z, 3s, 3p_x, 3p_y, 3p_z$ for chlorine. The simplest type of atomic orbital to use in a minimal basis set, and the one used in CNDO II, involves Slater-type orbitals (STO). These are for hydrogen[24]

$$\chi_{1s} = (s_A^3/\pi)^{\frac{1}{2}} . e^{(-s_A r)}$$

and for atoms lithium to fluorine

$$\chi_{2s} = (s_A^5/96\pi)^{\frac{1}{2}} r.e^{(-s_A r/2)}$$

and

$$\chi_{2p} = (s_A^5/32\pi)^{\frac{1}{2}} r.\cos\theta.e^{(-s_A r/2)}$$

where s_A is the Slater orbital exponent (see table 2.3). An alternative[33] to the use of Slater-type orbitals is to employ gaussian-type functions $\left[\exp(-\alpha r^2)\right]$ to represent the radial part of a given basis function. The disadvantage of gaussian-type orbitals (GTO) is that in the vicinity of the nucleus a linear combination of several GTO's must be used to give a correct radial dependence as opposed to STO's where only a single STO is required.

The variation principle then requires that for each molecular orbital m the coefficients a_{mi} satisfy the following sets of simultaneous equations[29]

$$\sum_i a_{mi}\left(F_{ij} - E_m S_{ij}\right) = 0 \quad \text{for } j \ 1,2,\ldots N \qquad \ldots \ 2.11$$

where N is the number of basis set functions used, and

$$\sum_i \sum_j a_{mi} a_{mj} S_{ij} = 1 \text{ (the normalisation conditions)} \qquad \ldots \ 2.12$$

where S_{ij} is the overlap, equal to $\int \chi_i \chi_j \, d\tau$

The solution of the secular equation[29]

$$\left|F_{ij} - ES_{ij}\right| = 0 \qquad \ldots \ 2.13$$

are the values E_m which satisfy the first set of simultaneous equations, 2.11

For a closed shell system it has been shown that F_{ij} is given by

$$F_{ij} = H^c_{ij} + \sum_k \sum_l P_{kl}\left[(ij|kl) - \tfrac{1}{2}(ik|jl)\right] \qquad \ldots \ 2.14$$

where H^c_{ij} is given by

$$H^c_{ij} = \int \chi_i(\mu) \left(-\tfrac{1}{2}\nabla^2_u - \sum_A \frac{Z_A}{r_{A\mu}} \right) \chi_j(\mu)\, d\tau_\mu \quad \ldots \quad 2.15$$

and P_{kl} is the total electron population in the overlap region between atomic orbitals k and l

$$P_{kl} = 2 \sum_m^{occ} a_{mk} a_{ml} \quad \ldots \quad 2.16$$

and

$$(ij|kl) = \iint \chi_i(\mu)\chi_k(\nu) \frac{1}{r_{\mu\nu}} \chi_j(\mu)\chi_l(\nu)\, d\tau_\mu\, d\tau_\nu \quad \ldots \quad 2.17$$

The solution of the secular equation, 2.13, requires the evaluation of the constituent matrix terms, F_{ij}. The F_{ij}'s are however, functions of the coefficients of the atomic orbitals a_{mi} through P_{kl} (see 2.14) and therefore can only be evaluated by solving the secular equation 2.13. An initial guess has therefore to be made, in the Hartree-Fock method, as to the values of the P_{kl}'s. These values are then used to evaluate the matrix elements F_{ij} and from these to solve the secular determinant. This solution leads to a better approximation to the wave function and this in turn gives a better set of values of P_{kl}. This procedure is then repeated a number of times, each time obtaining an improved set of values for P_{kl}, until there is no difference between the values of successive wave functions. When this condition is satisfied it has been shown that the total electronic energy E_e of a closed shell molecule is given by

$$E_e = \sum_i \sum_j P_{ij} \left\{ H^c_{ij} + \tfrac{1}{2} \sum_k \sum_l P_{kl} \left[(ij|kl) - \tfrac{1}{2}(ik|jl) \right] \right\} \quad \ldots \quad 2.18$$

The main obstacles to the solution of this problem arise from the large number of multicentre integrals (ij|kl) involved (see table 2.1) since in non-empirical calculations all such integrals

are evaluated. For typical molecules of interest to organic chemists the computational effort involved in a non-empirical treatment rapidly becomes unrealistic as a result of the ($\sim n^4$) dependence of the number of two-electron integrals (n is the size of the basis set). Reliable semi-empirical treatments have therefore been developed to alleviate this problem. In the next section a brief outline is given of the semi-empirical method (CNDO II) employed in this study.

b) Semi-empirical All-Valence Electron, Neglect of Diatomic Overlap Method

This method is particularly suitable for simplifying the Hartree-Fock problem due to the simplicity and adequacy of its approximations. These are :

1. Only valence electrons are accounted for specifically.

2. Only atomic orbitals of the same principal quantum number as that of the highest occupied orbital in the isolated atom are included in the basis set.

3. Diatomic differential overlap is neglected, that is if the orbitals χ_i and χ_j are not on the same atoms

$$S_{ij} = \int \chi_i(\mu)\, \chi_j(\mu) d\tau = 0$$

and

$$(ij|kl) = 0$$

unless χ_i and χ_j are atomic orbitals of the atom A and χ_k and χ_l are atomic orbitals of the same atom A, or B.

The first of these approximations permits the inner electrons of an atom to be neglected, treating them as part of a core whose charge is approximately equal to the nuclear charge minus the number of inner electrons. The second approximation considerably reduces the

initial number of integrals to be calculated. The third approximation reduces all three and four centre integrals to zero and also some of the two centre integrals. The matrix elements, F_{ij}, of the secular equation then become :

$$F_{ii} = H^{c}_{ij} + \sum_{B} \sum_{k,l} {}^{B}P_{kl}(ij|kl) - \tfrac{1}{2}\sum_{k,l} {}^{A}P_{kl}(ik|jl) \qquad \ldots \quad 2.19$$

(i and j both on atom A)

$$F_{ij} = H_{ij} - \tfrac{1}{2}\sum_{k}^{A}\sum_{l}^{B} P_{kl}(ik|jl) \qquad \ldots \quad 2.20$$

(i on atom A and j on atom B)

The great advantage of such a method is clearly evident in table 2.1 which shows the number of two electron integrals to be calculated for a non-empirical (minimal basis set) and for a neglect of diatomic differential overlap (NDDO) treatment.

Table 2.1

Number of two electron integrals involved in calculations for propane

Integrals	Hartree-Fock Minimal basis set	NDDO	CNDO
1-centre	368	173	11
2-centre	6652	568	55
3 - 4 centre	31206	0	0
Total	38226	741	66

However even with the approximations discussed above there are still too many integrals for convenient calculations on large molecules. The introduction of further simplifications however is by no means straightforward due to rotational invariance requirements.

Pople et al. have pointed out that though the results for two centre integral evaluation in a non-empirical self consistent field treatment are invariant with respect to an orthogonal transformation of the axes, this is not true in general for an approximate treatment. The integrals in these cases are affected by the choice of coordinates and by the hybridisation of the orbitals. The calculations from an approximate treatment are required to be invariant to these two transformations and this restricts further approximations to either complete neglect of differential overlap or partial neglect of differential overlap methods. Of these methods the CNDO II method of J.A. Pople, D.P. Santry and G.A. Segal[23,24] is used in the calculations in this thesis.

CNDO II Method

J.A. Pople and coworkers in their CNDO method neglected both the one-centre and the two centre integrals involving differential overlap. Writing the electron interaction integrals $(ii|jj)$ as Γ_{AB}, the Hartree-Fock matrix elements, F_{ij}; become

$$F_{ii} = H_{ii} + (P_{AA} - \tfrac{1}{2}P_{ii})\,\Gamma_{AA} + \sum_{B\neq A} P_{BB}\,\Gamma_{AB} \qquad \ldots\ 2.21$$

$$F_{ij} = H_{ij} - \tfrac{1}{2}P_{ij}\,\Gamma_{AB} \qquad (i\neq j) \qquad \ldots\ 2.22$$

where the atomic orbital χ_i is centred on atom A and χ_j on atom B. and P_{ij} are the components of the charge density and bond order matrix

$$P_{ij} = 2\sum_{m}^{occ} a_{mi}a_{mj} \qquad \ldots\ 2.23$$

and P_{AA} is the total charge density on atom A

$$P_{AA} = \sum_{i}^{A} P_{ii} \qquad \ldots\ 2.24$$

The core matrix elements H_{ii} may be separated into two components, the diagonal matrix element of χ_i with respect to the one-electron Hamilton containing only the core of its own atom (U_{ii}), and the interaction (V_{AB}) of an electron in χ_i on atom A with the cores of other atoms B. Thus H_{ii} may be written

$$H_{ii} = U_{ii} - \sum_{B \neq A} V_{AB} \qquad \ldots \quad 2.25$$

and equation 2.18 may be put as

$$F_{ii} = U_{ii} + (P_{AA} - \tfrac{1}{2}P_{ii})\,\Gamma_{AA} + \sum_{B \neq A} (P_{BB}\Gamma_{AB} - V_{AB}) \qquad \ldots \quad 2.26$$

The total energy of a molecule, using the CNDO method may be expressed as the sum of one- and two- atom terms

$$E = \sum_{A} E_A + \sum_{A} \sum_{B} E_{AB} \qquad \ldots \quad 2.27$$

where

$$E_A = \sum_{i}^{A} P_{ii} U_{ii} + \tfrac{1}{2} \sum_{i}^{A} \sum_{j}^{A} (P_{ii}P_{jj} - \tfrac{1}{2}P_{ij}^2)\,\Gamma_{AA} \qquad \ldots \quad 2.28$$

and

$$E_{AB} = \sum_{i}^{A} \sum_{j}^{B} (2P_{ij}H_{ij} - \tfrac{1}{2}P_{ij}^2\,\Gamma_{AB}) + (Z_A Z_B \frac{1}{R_{AB}}$$

$$- P_{AA}V_{AB} - P_{BB}V_{AB} + P_{AA}P_{BB}\Gamma_{AB}) \quad \ldots \quad 2.29$$

where R_{AB} is the distance between the atoms A and B.

Due to the neglect of the one-centre electron interations involving differential overlap between two orbitals the CNDO method does not show quantitatively the effects of Hund's rule. However for calculations on the ground states of closed shell molecules this defect is not too serious.

Evaluation of Integrals in CNDO II

a) One-centre one electron U_{ii}

It may be shown[24] that in general terms U_{ii} are given by

$$U_{ii} = - I_A - (Z_A - 1)\Gamma_{AA} \qquad \ldots \quad 2.30$$

where I_A is the ionisation energy, of the electron, which is obtained from spectroscopic data briefly as follows. For an electronic configuration $(2s)^m (2p)^n$ there will be several states with different energies. What is then done is to assign to the electronic configuration an energy which is a weighted mean of the energies of all the states that arise from the configuration. For the carbon atom for example,

$$E(C,\ 2s^2 2p^2) = \frac{3}{5}.E(C,{}^3P) + \frac{1}{3}.E(C,{}^1D) + \frac{1}{15}.E(C,{}^1S)$$

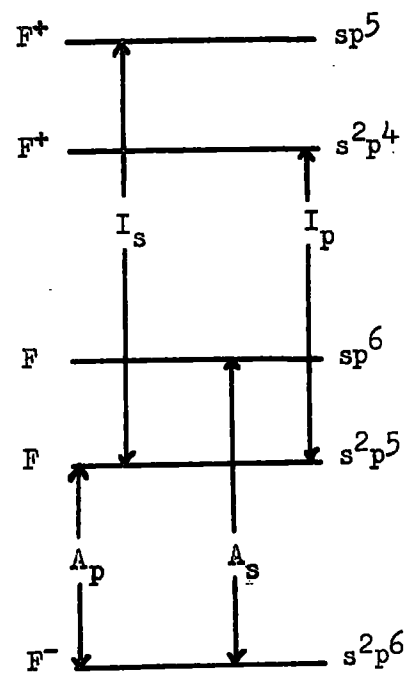
The ionisation energies may then be estimated as shown below,

$$I_s(A, 2s^m 2p^n) = E(A^+, 2s^{m-1} 2p^n) - E(A, 2s^m 2p^n)$$

and $$I_p(A, 2s^m 2p^n) = E(A^+, 2s^m 2p^{n-1}) - E(A, 2s^m 2p^n)$$

This is shown diagrammatically for fluorine in figure 2.1

Figure 2.1



However, since an atomic orbital may either gain or lose an electron, J.A. Pople and G.A. Segal[34] have suggested that a better approximation for U_{ii} would be obtained by using the "orbital electronegativity"[35] instead of the ionisation energy. The orbital electronegativity is given by the average of the ionisation energy and the electron affinity (A). The electron affinity is calculated from spectroscopic data in a like manner to the ionisation energy (see above and figure 2.1). Equation 2.30 then becomes

$$U_{ii} = -\tfrac{1}{2}(I_A + A_A) - (Z_A - \tfrac{1}{2})\Gamma_{AA} \qquad \ldots \quad 2.31$$

The average values of ionisation energy and electron affinity[34,36] are given in table 2.2 for the appropriate atoms in the molecules considered in this thesis.

Table 2.2 $\frac{1}{2}(I + A)$ in electron volts

Atom	H	C	N	O	F	Cl
1s	7.1761	-	-	-	-	-
2s	-	14.051	19.31637	25.39017	32.2724	-
2p	-	5.572	7.275	9.111	11.0881	-
3s	-	-	-	-	-	21.5906
3p	-	-	-	-	-	8.7081
3d	-	-	-	-	-	0.97695

b) <u>One-centre two-electron</u> Γ_{AA}

These are calculated as the electrostatic repulsion energy of two electrons in a Slater s orbital irrespective of the fact that i or j may be p or d orbitals. Thus

$$\Gamma_{AA} = \iint \chi^2_{s_A}(\mu)\, \frac{1}{r_{\mu\nu}}\, \chi^2_{s_A}(\nu)\, d\tau_\mu d\tau_\nu \qquad \ldots \quad 2.32$$

where s_A is the Slater orbital exponent for atom A, the values for which are given in table 2.3

Table 2.3, s_A

Atom	H	C	N	O	F	Cl
s_A	1.2	1.625	1.95	2.275	2.6	2.367

c) Two-centre one-electron (Resonance) H_{ij}

This may be thought of as the energy of an electron occupying the orbital overlap region between the two atomic orbitals χ_i and χ_j and moving in the field of the core and the remaining electrons. In CNDO the resonance integral is regarded as being directly proportional to the overlap integral S_{ij} between the orbitals χ_i and χ_j centred on A and B respectively.

$$H_{ij} = \beta^{o}_{AB} S_{ij} \qquad \ldots \quad 2.33$$

where Slater atomic orbitals are used to calculate S_{ij} and β^{o}_{AB} is a parameter depending on the nature of A and B.

In order that the calculations should be rotationally invarient the parameter β^{o}_{AB} should be characteristic of χ_i and χ_j but independent of their position in space. Pople has suggested that this may be achieved by the averaging of a β^{o} parameter for each atom, thus

$$\beta^{o}_{AB} = \tfrac{1}{2}(\beta^{o}_{A} + \beta^{o}_{B}) \qquad \ldots \quad 2.34$$

The parameters β^{o}_{A} etc. are chosen empirically to reproduce results obtained by experiment or by ab initio calculations[24,36].

Table 2.4 β^{o}

Atom	H	C	N	O	F	Cl
β^{o}	-9	-21	-25	-31	-39	-22.330

d) Two-centre two-electron Γ_{AB}

The most difficult problem in semi-empirical methods of solving the Hartree-Fock problem is the satisfactory calculation of the two-centre two-electron integrals. In the CNDO II method of Pople et al. these are calculated as

$$\Gamma_{AB} = (ii|jj) = \iint \chi^2_{s_A}(\mu) \frac{1}{r_{\mu\nu}} \chi^2_{s_B}(\nu)\, d\tau_\mu\, d\tau_\nu \quad \ldots 2.35$$

where s_A and s_B are the Slater s orbital exponents for atoms A and B (see table 2.3).

The two-centre two-electron integrals represent the interaction between an electron in a valence atomic orbital on atom A with an electron in a valence atomic orbital on atom B.

e) Coulomb Penetration V_{AB}

In CNDO II the effect of the interaction of an electron in χ_i on atom A with the cores of other atoms B, (penetration terms, equation 2.25), are neglected and the coulomb penetration integrals estimated as

$$V_{AB} = Z_B \Gamma_{AB} \quad \ldots 2.36$$

Summary of Approximations used

i) Nuclear repulsion energy E_{Nr}

$$E_{Nr} = \sum_{A} \sum_{B>A} Z_A Z_B \frac{1}{R_{AB}} \quad \ldots \quad 2.7$$

ii) One-centre one-electron U_{ii}

$$U_{ii} = -\tfrac{1}{2}(I_A + A_A) - (Z_A - \tfrac{1}{2})\,\Gamma_{AA} \quad \ldots \quad 2.31$$

iii) One-centre two-electron Γ_{AA}

$$\Gamma_{AA} = \iint \chi^2_{\varsigma_A}(\mu)\,\frac{1}{r_{\mu\nu}}\,\chi^2_{\varsigma_A}(\nu)\,d\tau_\mu\,d\tau_\nu \quad \ldots \quad 2.32$$

iv) Two-centre one-electron (Resonance) H_{ij}

$$H_{ij} = \beta^\circ_{AB} S_{ij} \quad \ldots \quad 2.33$$

$$\beta^\circ_{AB} = \tfrac{1}{2}(\beta^\circ_A + \beta^\circ_B) \quad \ldots \quad 2.34$$

v) Two-centre two-electron Γ_{AB}

$$\Gamma_{AB} = \iint \chi^2_{\varsigma_A}(\mu)\,\frac{1}{r_{\mu\nu}}\,\chi^2_{\varsigma_B}(\nu)\,d\tau_\mu\,d\tau_\nu \quad \ldots \quad 2.35$$

vi) Coulomb penetration V_{AB}

$$V_{AB} = Z_B\,\Gamma_{AB} \quad \ldots \quad 2.36$$

vii) Matrix elements

$$F_{ii} = U_{ii} + (P_{AA} - \tfrac{1}{2}P_{ii})\,\Gamma_{AA} + \sum_{B\neq A} (P_{BB}\Gamma_{AB} - V_{AB}) \quad \ldots \quad 2.26$$

$$F_{ij} = H_{ij} - \tfrac{1}{2}P_{ij}\Gamma_{AB} \quad (i\neq j) \quad \ldots \quad 2.22$$

viii) Total energy

$$E = \sum_A E_A + \sum_{A} \sum_{B>A} E_{AB} \quad \ldots \quad 2.27$$

where

$$E_A = \sum_i^A P_{ii} U_{ii} + \frac{1}{2}\sum_i^A \sum_j^A (P_{ii}P_{jj} - \tfrac{1}{2}P_{ij}^2)\,\Gamma_{AA} \quad \ldots \quad 2.28$$

and

$$E_{AB} = \sum_i^A \sum_j^B (2P_{ij}H_{ij} - \tfrac{1}{2}P_{ij}^2\,\Gamma_{AB}) + (Z_A Z_B \cdot \frac{1}{R_{AB}}$$

$$- P_{AA}V_{AB} - P_{BB}V_{AB} + P_{AA}P_{BB}\,\Gamma_{AB}) \quad \ldots \quad 2.29$$

The calculations were carried out on the Northumbrian Universities Multiple Access Computor (NUMAC), IBM 360 Model 67 using a standard programme (CNINDO) written by P.A. Dobosh in Fortran IV. The running time depends on the number of iterations required and on the number of basis functions which is dependent on the number of valence atomic orbitals in the molecule for which the calculation is being performed. The iterations were repeated until the electronic energy was consistent to 10^{-6}au. up to a total of 20 iterations. Typical running times are of the order of 2 minutes for a molecule such as pyridine and up to 12 minutes for a molecule such as a dimethoxyperfluoropyridazine involving more valence atomic orbitals.

Electron Distribution in Molecules

Charge Density

When the LCAO MO's ψ_m, (equation 2.8) have been determined the charge density may be analysed in terms of the basis functions χ_i.

If there are two electrons in each molecular orbital the total charge density P, is given by:

$$P = 2\sum_{m}^{occ}\psi_m = \sum_{k}\sum_{l} P_{kl}\chi_k\chi_l \qquad \ldots \quad 2.37$$

where P_{kl} is the density matrix as defined in equation 2.16. The diagonal element P_{kk} is the coefficient of the distribution χ_k^2 and measures the electron population of the orbital. The off-diagonal elements P_{kl} are overlap populations related to the overlap region of atomic orbitals k and l.

Net Atomic Charge (Total Charge), Pi Charge, Sigma Charge

In order to assign a specific charge to each atom a Mulliken population analysis is used. The total population q_k for an orbital χ_k is given by

$$q_k = P_{kk} + \sum_{k\neq l} P_{kl}S_{kl} \qquad \ldots \quad 2.38$$

where S_{kl} is the overlap (see equation 2.12 et seq.)

In CNDO II overlap is ignored so that the partitioned bond overlap terms, $\sum_{k\neq l} P_{kl}S_{kl}$, drop out of equation 2.38

which then becomes

$$q_k = P_{kk} \qquad \ldots \quad 2.39$$

The total charge density on an atom A is then given, in CNDO II, by

$$P_{AA} = \sum_{k}^{A} P_{kk} \qquad \text{(see equation 2.24)}$$

and the net charge for the atom A is given by

$$P_{AA} - Z_A \qquad \ldots \quad 2.40$$

where Z_A is the "effective" atomic number, i,e. the atomic number minus the number of "core" electrons, and the sum is over all the atomic orbitals centred on atom A.

Pi Charge

The pi electron charge on an atom is taken as the value of the diagonal element, P_{kk}, of the electron density matrix P_{kl} (equation 2.16), out of the plane of the molecule. The difference between this value of P_{kk} and the number of pi electrons the atom contributes is then taken as the pi charge of the atom.

Sigma Charge

The difference between the net (or total) charge on the atom (equation 2.38) and the pi charge as defined above is taken as the sigma charge.

Ascribing an electron population to a given atom because an orbital is centred on the atom is a simplification since in fact the orbital may be quite diffuse. The analysis should therefore only be regarded as giving a crude idea of the electron distribution in a molecule and the absolute values of the "charges" calculated in this way depend quite markedly on the basis set used. Also ignoring the overlap terms means that the charge on an atom is defined somewhat differently for a CNDO treatment compared with a non-empirical treatment where overlap is specifically taken into account. However despite these limitations the population analysis is conceptually close to qualitative ideas about charge distribution in organic molecules.

Partitioned Bond Overlap Population

Although as stated earlier overlap integrals are neglected in the CNDO II treatment (except in the evaluation of the two-centre one-electron integrals) the density matrix has non-zero off diagonal elements. These on multiplication by the overlap matrix give a partitioned bond overlap matrix, $P_{kl}S_{kl}$, the elements of which

correspond to the off diagonal elements of the charge density bond order matrix for a non-empirical treatment[37]. This partitioned bond overlap matrix may then by used to give information regarding the electron density between atoms in molecules, the electron density or partitioned bond overlap population being given by $\sum_{k \neq l} P_{kl} S_{kl}$.

Chapter 3

Electronic Structures and Dipole Moments of Benzene, Pyridine and the three Diazines and some of their fluoro, chloro and methoxy derivatives.

Electronic Structures

Charge Distributions

The sigma and pi charges for the ring atoms of some of the molecules considered are given in figures 3.1 - 3.3. In table 3.1 are the calculated charges for the atoms in some fluoro and chloro benzene derivatives. These charges are obtained from the diagonal elements of the SCF density matrices (see chapter 2).

Figure 3.1 shows some interesting features and brings out some of the similarities between the charge distributions in all four heterocycles and their perfluoro derivatives. Thus in the perhydro series the nitrogen atoms are overall negative due to sigma electron drift from the ortho carbon atoms and pi electron drift from the ortho and para carbon atoms. For the perfluoro series it is seen that the sigma charge on the nitrogens becomes more positive while the pi charge becomes more negative. In the case of pyridine, perfluoropyridine and perchloropyridine (see below) the calculated charge distributions in conjunction with the charge potential model correlate extremely well with x-ray photo-electron spectroscopic data[38]. It is also noticeable that for perchloropyridine there is little change in the pi charges for the ring atoms as compared to the perhydro compound but the sigma charges are all more positive, due to the electronegativity of the chlorine atoms.

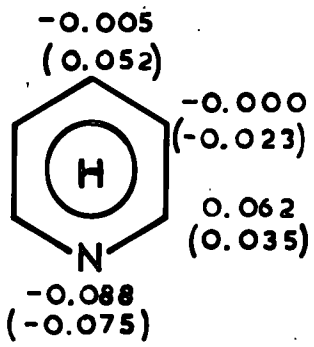
In the perhydro series it is seen that an ortho carbon bears a positive sigma charge while meta and para carbon atoms bear very small negative sigma charges. Atom C2 in pyrimidine is in a special situation lying ortho to two nitrogen atoms thus explaining its relatively large positive sigma charge. As previously stated ortho

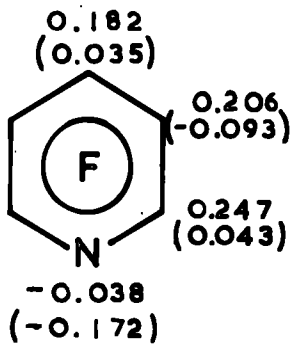
and para carbon atoms donate pi charge to the nitrogen atoms and therefore, as expected, ortho and para carbon atoms bear small positive pi charges. Meta carbon atoms, however, are seen to bear small negative pi charges. In the case of pyridazine and pyrazine the nitrogen atoms do not have such a large effect on the pi charges as in the case of pyridine and pyrimidine. This arises from the fact that in the first two compounds a carbon atom that is ortho (or para in the case of pyridazine) to one nitrogen will be meta to the other nitrogen. The effects of the two nitrogen atoms will oppose each other and the overall effect will be less than in the case of pyridine, with only one nitrogen and pyrimidine where the effects of the two nitrogens will be additive.

In proceeding from the perhydro to the perfluoro series, in the diazines and in pyridine, the ring carbons all bear increased positive sigma charges due to sigma donation to the more electronegative fluorine (see table 3.1 and appendix 3). Now on a ring carbon in perfluorobenzene there is a positive sigma charge of 0.20 and simple addition of this charge to the sigma charges on the carbons in the perhydro series in figure 3.1 gives moderately well the sigma charges on the carbons in the perfluoro series. This suggests that the effect of the nitrogen, or nitrogens, in the perfluoro series is very similar to the effect of nitrogen in the perhydro series as far as the sigma charges on the ring carbons are concerned. When the pi charges are considered it is seen that in pyridazine and pyrazine the pi charges on the ring carbons are smaller than those in pyridine and pyrimidine for both the perhydro and perfluoro series.

Figure 3.1

Sigma and (pi) charges





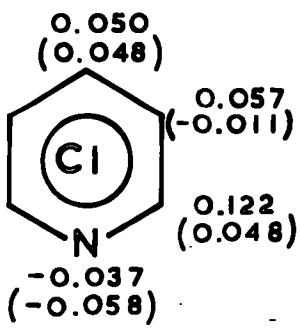


Figure 3.1 cont.

Sigma and
(pi) charges

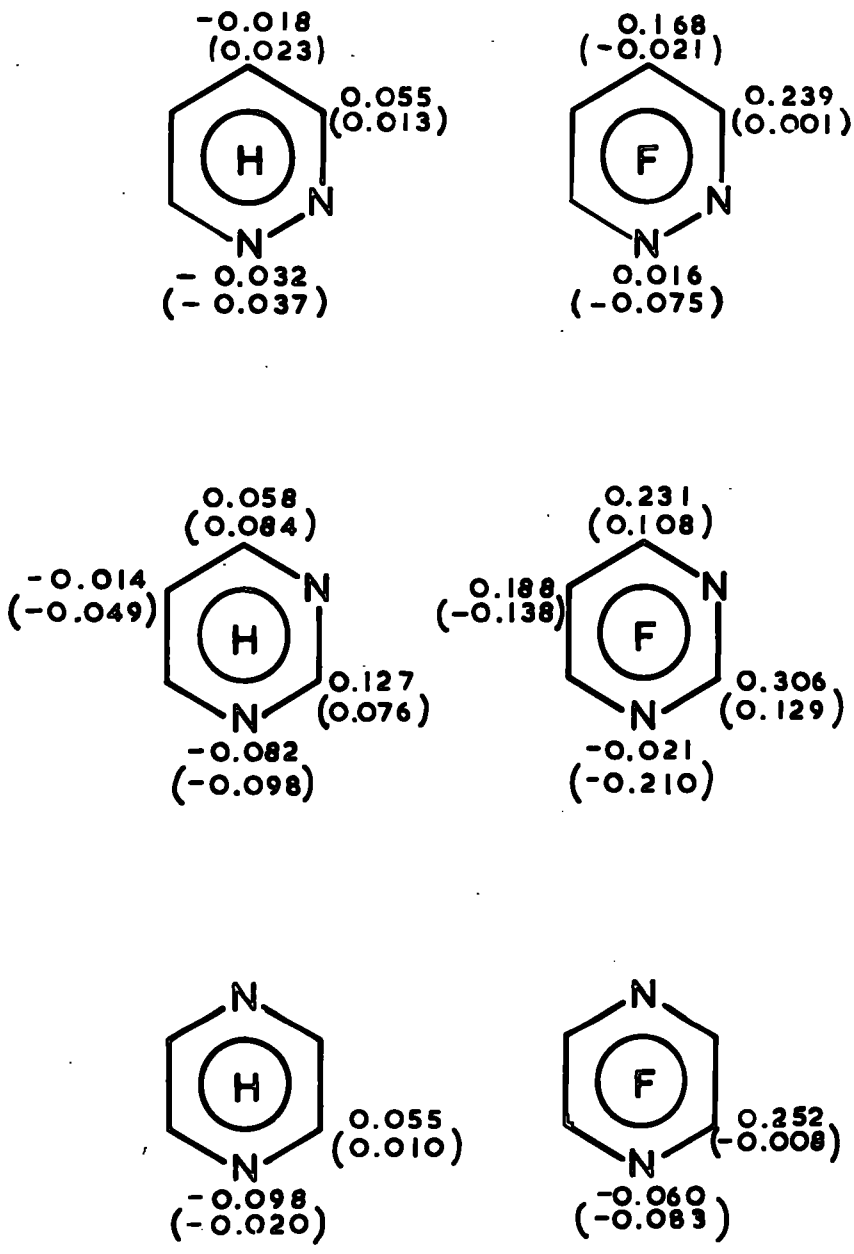


Table 3.1

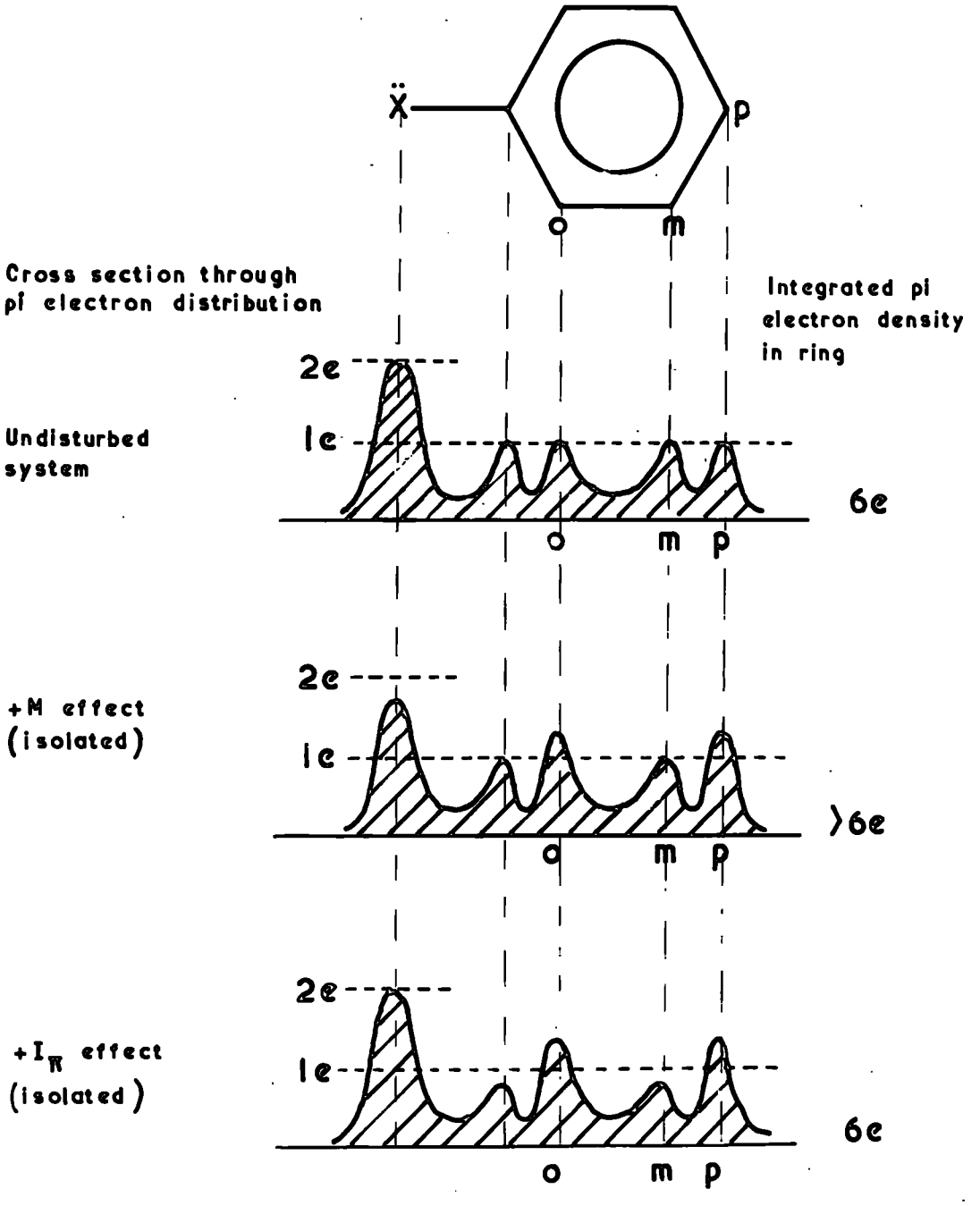
	Total charge	sigma charge	pi charge
	Chlorobenzene		
C1	0.092	0.095	-0.003
C2	0.018	0.007	0.011
C3	0.004	0.007	-0.002
C4	0.010	-0.002	0.012
C5	0.004	0.007	-0.002
C6	0.018	0.007	0.011
H2	0.010		
H3	0.002		
H4	0		
H5	0.002		
H6	0.010		
Cl1	-0.171	-0.198	0.027
	Fluorobenzene		
C1	0.235	0.222	0.034
C2	-0.048	-0.001	-0.047
C3	0.025	0.005	0.020
C4	-0.016	0.012	-0.028
C5	0.025	0.005	0.020
C6	-0.048	-0.001	-0.047
H2	0.017		
H3	0		
H4	-0.001		
H5	0		
H6	0.017		
F1	-0.206	-0.254	0.048
	Perfluorobenzene		
C	0.157	0.202	-0.045
F	-0.157	-0.202	0.045

The electronic charge distribution in molecules has often been discussed[25] in terms of a localised orbital model though since the advent of all valence electron SCF calculations the usefulness of a localised orbital model has been brought into question. Nevertheless from the results in table 3.1 it is possible to investigate the validity of the model, in particular in the case of fluorine and chlorine as substituents. The substituent effects which are considered are the Inductive sigma, I_σ, the Inductive Pi, I_π, and Mesomeric, M, effects.[25,26,39] The I_σ effect of an atom may be inferred from its sigma charge and that of the adjacent atoms and falls off rapidly with distance. The M effect of an atom is inferred from its pi charge and also from the pi charges on alternate atoms moving away from the substituent in the delocalised pi system. The I_π effect is inferred from the pi charge on the adjacent atoms though its effect is transmitted to all the atoms in the delocalised pi electron system. This is shown diagramatically below (figure 3.2), for +M and $+I_\pi$, for the case where a substituent X contributes two electrons to the delocalised system.

Applying these ideas to the results given in table 3.1 enables the inductive and mesomeric effects of the fluorine and chlorine atoms to be deduced. It is seen that the chlorine and fluorine both exert a $-I_\sigma$ effect and that the fluorine shows the larger effect. Also in perfluorobenzene the $-I_\sigma$ effect of the fluorine is smaller than in the monofluorobenzene. This is not altogether unexpected since in perfluorobenzene the fluorine atoms are in a sense all competing with each other for the sigma electrons of the ring carbons. The pi charges on the chlorine and fluorine in the monohalobenzene

Figure 3.2

Pi electron distribution in a delocalised system, showing the results of a +M and a $+I_{\pi}$ effect.



(+M and $+I_{\pi}$ effects greatly exagerated)

show that both these atoms exert a +M effect. As in the case of the I_σ effect the +M effect of the fluorine is less in the perfluoro as compared to the +M effect in the monofluoro compound. In the monohalobenzenes, from the pi charge on the carbon to which the halogen is attached, it is observed that both the fluorine and the chlorine show an I_π effect.

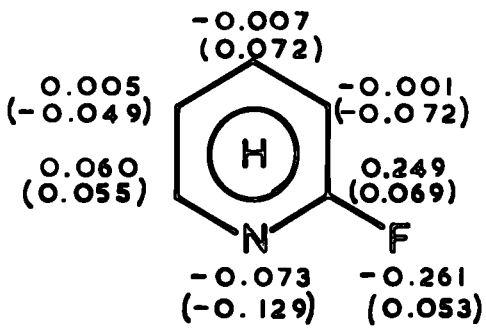
On going from benzene to pyridine the effect of replacing CH by N is such that the potential under which the electrons move is altered but the extent of the delocalised system is unchanged. Therefore for the nitrogen atoms, in the molecules in figure 3.1, only I_σ and I_π effects are considered to take place.[26] Since, for the molecules in figure 3.1, the nitrogens bear negative sigma and pi charges then the nitrogens can be said to be showing $-I_\sigma$ and $-I_\pi$ effects. In the perfluoro compounds the $-I_\sigma$ effect is smaller than in the perhydro compounds, which is similar to the effect noted above for the fluorine in the benzene derivatives discussed. The pi charges on the nitrogens are larger in the perfluoro compounds than in the perhydro compounds and thus it might be said that the $-I_\pi$ effect of the nitrogen is greater in the perfluoro compounds. On the other hand the increased pi charges might be better ascribed to the M effects of the fluorine atoms (see below). Though the elements of the Fock matrix in all valence electron SCF treatments depend on the total electron populations on an atom and therefore although in a planar system there is sigma-pi seperability by symmetry, the two systems, sigma and pi, are mutually interdependent. Therefore any model of substituent effects which tends to separate contributions of sigma and pi systems is unlikely to be wholly adequate.[25]

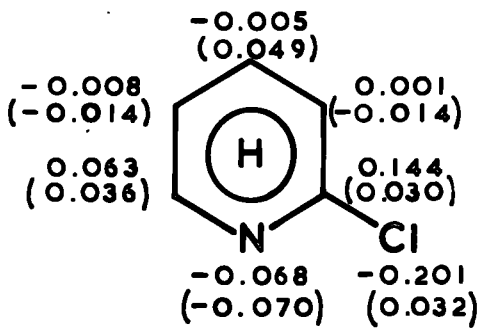
In pyridine and pyrimidine the meta carbon atoms bear negative pi charges, a fact which can be explained again in terms of the nitrogens exerting a $-I_{\pi}$ effect. In the case of the fluorine atoms in the perfluoro compounds shown in figure 3.1, like the fluorine atoms in perfluorobenzene, it is seen that they exert a $-I_{\sigma}$ effect and a +M effect (appendix 3). Furthermore that in all four perfluoro compounds the $-I_{\sigma}$ effect is very similar. Here it is interesting to note that a fluorine, attached to a carbon that is ortho to a nitrogen, although in a sense in competition with the nitrogen for the sigma electrons of the carbon, bears a larger sigma charge than other fluorine atoms. It is not easy to decide if the fluorine atoms exhibit an I_{π} effect and in fact in pyridazine and pyrazine any such effect would overall be self cancelling. In the case of pyridine and pyrimidine however, an I_{π} effect of the fluorines in the perfluoro derivatives would tend to give an additive effect. It was seen that in fluorobenzene that fluorine exerts an I_{π} effect and the assumption that it does so in perfluoropyridine and perfluoropyrimidine affords an explanation of the fact that in these compounds the pi charges on atoms C2, C4 and C6 are more positive than in the perhydro compounds.

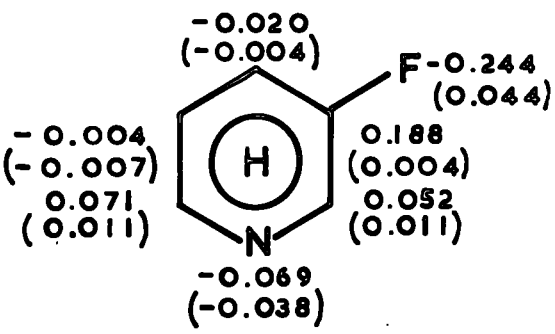
In figure 3.3 the charge distributions, except for the hydrogens, are given for monofluoro and monochloropyridine. For the monochloropyridines it is seen that the sigma and pi charges on all the ring atoms are very similar to those in the perhydro compound (fig. 3.1) except for the carbon to which the chlorine is attached. This does bear an increased positive sigma charge due to sigma donation to the chlorine but there is little effect on its pi charge. In the case of the monofluoropyridines there is more effect, principally on the pi

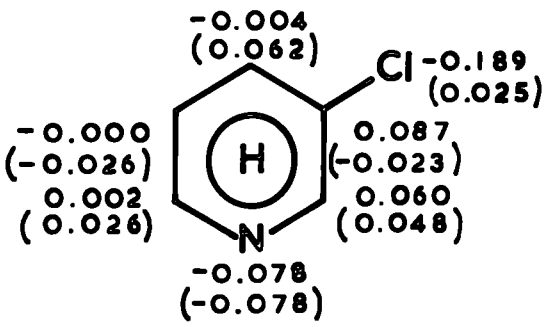
Figure 3.3

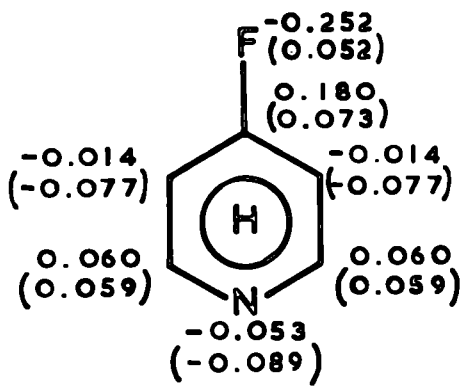
Sigma and (pi) charges











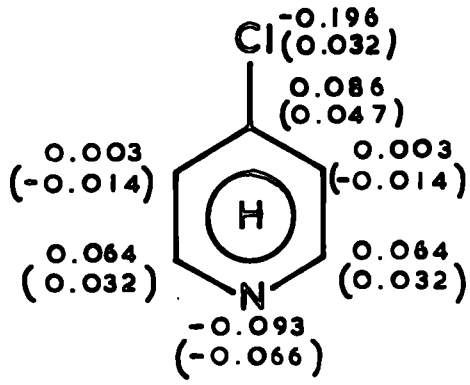
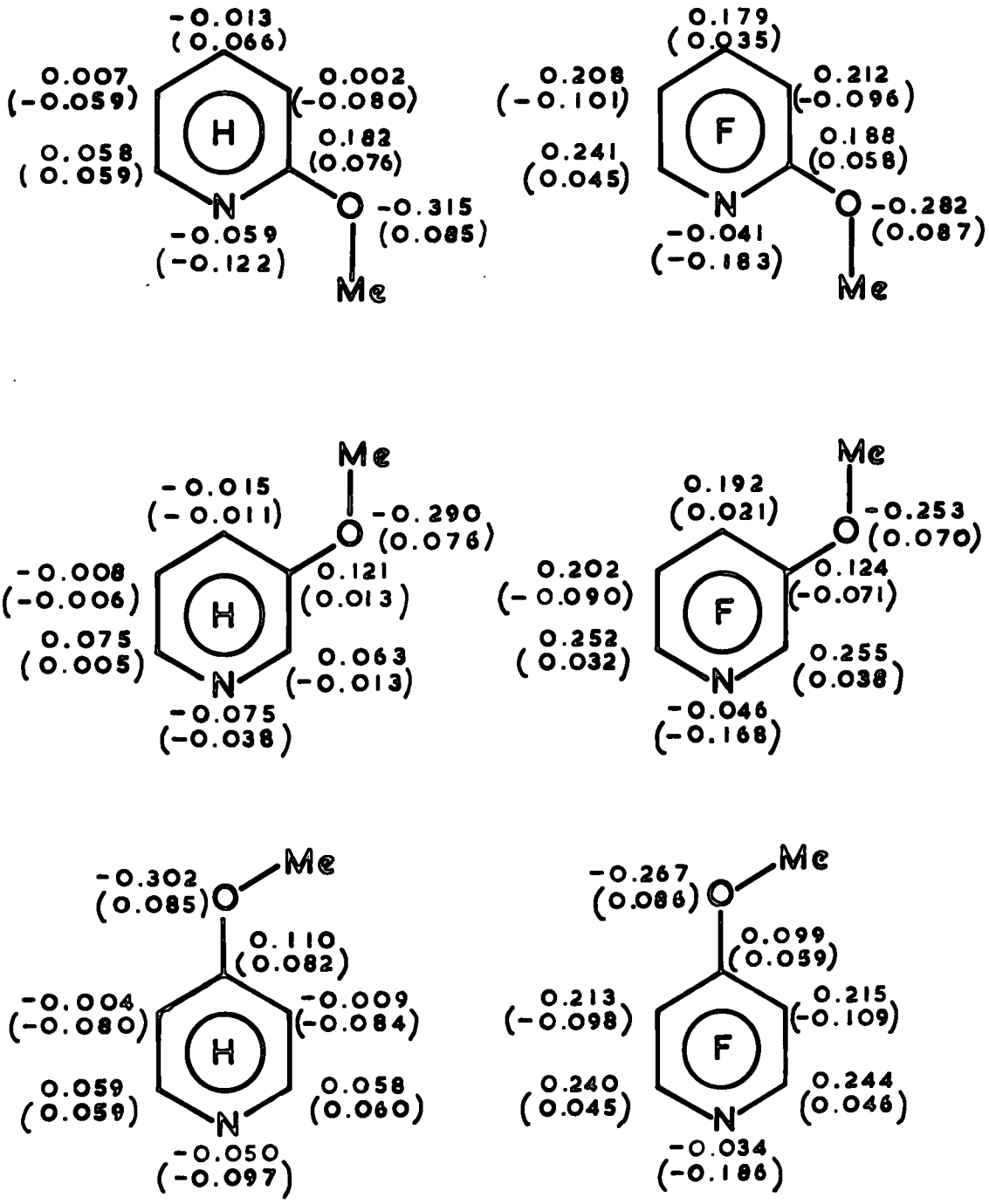


Figure 3.4

Sigma and pi charges



charges. The carbon to which the fluorine is attached, like the case of the chloropyridines, bears a large increased positive sigma charge due to sigma donation to the fluorine. There is also a larger positive pi charge on this carbon which agrees with the idea expressed above that fluorine may show a $+I_{\pi}$ effect. It is also seen that carbon atoms lying ortho and para to the fluorine have more negative pi charges while those meta have more positive pi charges than in the perhydro compound.

In figure 3.4 are the charge distributions for the ring atoms and the oxygen in the monomethoxy derivatives of pyridine and perfluoropyridine. Apart from the smaller sigma charge on the ring carbon attached to the oxygen, the charges in the monomethoxy compounds are very similar to those in the corresponding fluoro compounds, i.e. monofluoro- and perfluoropyridine. Since the electronegativity of oxygen is less than that of fluorine it is not surprising to find a smaller sigma drift from the ring carbon to the oxygen than to fluorine. When the methoxy derivatives of fluorobenzene (table 3.2) and of the perfluoro diazines (tables 3.3, 3.4 and appendix 3) are considered the same effects are observed as for the monomethoxy derivatives of pyridine and perfluoropyridine.

Methoxy Group

In the methoxy compounds there is sigma electron drift from both the carbons attached to the oxygen on to that oxygen. At the same time there is pi electron drift from the oxygen to the ring atoms, principally to those lying ortho and para to the methoxy group.

In the calculations on the methoxy compounds internal rotation of the methoxy group, that is with respect to the $-O-CH_3$ bond, was not considered. However different conformers with respect

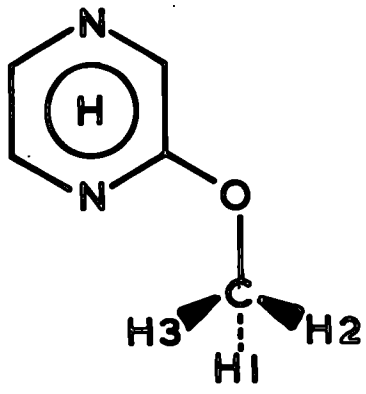
Table 3.2

	Total charge	sigma charge	pi charge
	Methoxybenzene		
C1	0.178	0.135	0.043
C2	-0.050	0.004	-0.054
C3	0.022	0.001	0.021
C4	-0.019	0.016	-0.035
C5	0.022	0.003	0.019
C6	-0.040	0.009	-0.049
H2	0.009		
H3	-0.005		
H4	-0.005		
H5	-0.005		
H6	0.009		
O	-0.218	-0.298	0.080
C	0.127		
H1	-0.009		
H2	-0.010		
H3	-0.008		
	1-methoxyperfluorobenzene		
C1	0.096	0.118	-0.020
C2	0.148	0.210	-0.062
C3	0.154	0.196	-0.042
C4	0.148	0.204	-0.056
C5	0.154	0.195	-0.041
C6	0.159	0.208	-0.049
F2	-0.171	-0.216	0.045
F3	-0.161	-0.205	0.044
F4	-0.160	-0.203	0.043
F5	-0.160	-0.204	0.044
F6	-0.164	-0.208	0.044
O	-0.180	-0.257	0.077
C	0.094		
H1	0.001		
H2	-0.004		
H3	0.044		

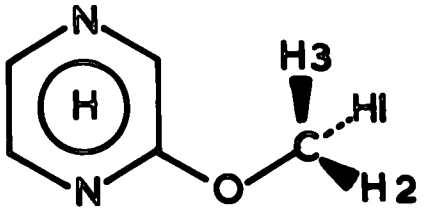
to the ring geometry were investigated. Thus in general two configurations of the methoxy group with respect to the ring were considered and these are referred to as clockwise (K) and anti-clockwise (A) respectively (see figure 3.5 below).

Figure 3.5

2K-methoxypyrazine



2A-methoxypyrazine



An interesting point then arises concerning the methyl hydrogen, H3, in that in some compounds it may bear a noticeably larger positive charge (approximately +0.040) than the other two methyl hydrogens. This effect is absent in the perhydro series and in the perfluoro series where an ortho methoxy group is orientated towards a nitrogen atom (see tables 3.3, 3.4 and appendix 3). Furthermore it is seen that when H3 in the methyl group does bear this larger positive charge then the positive sigma charge on the methyl carbon is reduced, e.g. in 2A-methoxyperfluoropyrazine as shown in table 3.4. The effect on H3 can be explained in terms of

Table 3.3

	Total charge	sigma charge	pi charge
	2K-methoxypyrazine		
N1	-0.162	-0.082	-0.081
N4	-0.091	-0.098	-0.007
C2	0.225	0.173	0.052
C3	0.016	0.059	-0.043
C5	0.041	0.066	-0.025
C6	0.082	0.049	0.033
H3	0.008		
H5	-0.004		
H6	-0.005		
O	-0.221	-0.304	0.083
C	0.131		
H1	-0.007		
H2	-0.007		
H3	-0.005		
	2A-methoxypyrazine		
N1	-0.152	-0.075	-0.077
N4	-0.093	-0.102	0.009
C2	0.224	0.171	0.053
C3	0.005	0.535	-0.049
C5	0.041	0.066	-0.025
C6	0.082	0.050	0.032
H3	0.008		
H5	-0.004		
H6	-0.004		
O	-0.217	-0.300	0.083
C	0.127		
H1	-0.006		
H2	-0.004		
H3	-0.007		

Table 3.4

	Total charge	sigma charge	pi charge
	2K-methoxyperfluoropyrazine		
N1	-0.155	-0.062	-0.093
N4	-0.149	-0.068	-0.082
C2	0.185	0.178	0.007
C3	0.247	0.258	-0.011
C5	0.238	0.255	-0.017
C6	0.239	0.246	-0.007
F3	-0.180	-0.228	0.048
F5	-0.178	-0.226	0.048
F6	-0.179	-0.227	0.048
O	-0.199	-0.281	0.082
C	0.130		
H1	0		
H2	0.001		
H3	-0.001		
	2A-methoxyperfluoropyrazine		
N1	-0.143	-0.055	-0.088
N4	-0.149	-0.070	-0.079
C2	0.185	0.172	0.013
C3	0.235	0.258	-0.023
C5	0.236	0.246	-0.020
C6	0.242	0.246	-0.004
F3	-0.187	-0.236	0.049
F5	-0.177	-0.224	0.047
F6	-0.177	-0.226	0.049
O	-0.199	-0.281	0.082
C	0.096		
H1	0.001		
H2	-0.003		
H3	0.041		

a through space interaction with the fluorine atom attached to the adjacent ring carbon. The fluorine atoms are calculated to be overall negative and the result of this would be to cause sigma electron drift from H3 to the methyl carbon. Thus H3 becomes more positive and the sigma charge on the methyl carbon is reduced, becoming less positive. Calculations, for the two 2-methoxypyrazines, of the distances between the methyl hydrogen, H3, and the nearest ring atom show that this distance is much greater when the methoxy group is in the K orientation than when it is in the A orientation. The partitioned bond overlap populations, $\sum P_{\mu i} S_{\mu i}$, (electron density in orbital overlap region between nuclei) were also calculated for the pyrazine and pyridine methoxy derivatives given in table 3.5. These show that, for the 2-methoxyperfluoropyrazines, there is a significant difference for the K and A orientations and that there is greater bonding in the case of the A orientation. This agrees with the calculated electronic energies, that for the A orientation being lower than that for the K orientation. However the nuclear repulsion energy is larger in the A orientation and is the determining factor that makes the K orientation lower in energy despite the greater bonding that occurs with the A. A similar situation is observed for the methoxy derivatives of pyridine. Although in the case of 2-methoxyperfluoropyrazine it was observed that the nuclear repulsion energy was the factor which determined which orientation of the methoxy group resulted in the lowest energy for the molecule this is not generally true. What is seen, though, is that when Δnuclear repulsion and Δelectronic energy are greater than 5 MJ mol^{-1} the nuclear repulsion energy is the deciding factor. When, however, Δnuclear repulsion and Δelectronic energy are less than 1MJ mol^{-1} then either one may be the deciding factor. From the interatomic

Table 3.5

Inter-atomic distances, partitioned bond overlap populations, and energy differences for some of the methoxy derivatives of Pyridine and Pyrazine, (energy differences in kJ mol^{-1}, distances in ångstroms)

	Pyrazine				
0		Perhydro		Perfluoro	
2K	Inter-atomic distance	N1	2.123030	N1	2.123030
2A	from methyl H3 to :	H3	1.502045	F3	1.441931
2K	$\sum P_{\mu i} S_{\mu i}$		0.0050		0.0047
2A			0.0122		0.0240
	Energy differences, 2A-methoxy - 2K-methoxy				
	ΔNuclear repulsion		942		11807
	ΔElectronic		-907		-11734
	ΔTotal		35		73

column 0 is the position and orientation of the methoxy group

Table 3.5 cont'd.

Pyridine

O			Perhydro		Perfluoro
2K	Inter-atomic distance	N1	2.043184	N1	2.043184
2A	from methyl H3 to :	H3	1.519564	F3	1.438068
2K	$\sum P_{\mu i} S_{\mu i}$		0.0066		0.0065
2A			0.0113		0.0247
	Energy differences,				
	2A-methoxy - 2K-methoxy				
	ΔNuclear repulsion		-25		10262
	ΔElectronic		56		-10191
	ΔTotal		31		71
3K	Inter-atomic distance	H2	1.457593	F2	1.423115
3A	from methyl H3 to :	H4	1.557959	F4	1.494684
3K	$\sum P_{\mu i} S_{\mu i}$		0.0142		0.0259
3A			0.0104		0.0197
	Energy differences,				
	3K-methoxy - 3A-methoxy				
	ΔNuclear repulsion		750		-710
	ΔElectronic		-731		734
	ΔTotal		19		24

distances given in table 3.5 it is observed that in the configuration that gives the lowest energy the distance between the methyl hydrogen, H3, and the nearest ring atom is at a maximum.

As was stated earlier in the chapter the electronic charge distributions have often been discussed, for a localised orbital model,[26] in terms of mesomeric (M) and inductive (I_σ and I_π) effects. In the methoxy compounds shown in figure 3.4 and given in tables 3.2, 3.3 and 3.4 it can be seen that the oxygen, like fluorine, shows +M, $-I_\sigma$ and I_π effects. As was noted earlier there is a smaller I_σ effect by the oxygen on the ring carbon than with the fluorine and the I_σ effect of oxygen is much the same in both the perhydro and perfluoro series. The +M and I_π effects, however, of the oxygen are observed to be larger than those of fluorine in the same positions though the difference is not great.

Dipole Moments

In table 3.6 are given the dipole moments, as calculated, for all the molecules considered in this work and the experimental results where available[15,40].

The dipole moment of a molecule may be regarded as arising from two causes, μ_Q and μ_{hyb}, the total dipole being the simple vector sum of these two[29].

$$\mu_{total} = \mu_Q + \mu_{hyb} \qquad \ldots \ 3.1$$

The term μ_Q arises from the charge distribution within the molecule and may be calculated by means of the expression

$$\mu_Q = 2.5416 \sum_A \Delta P_{AA} R_A \quad \text{debyes} \qquad \ldots \ 3.2$$

where ΔP_{AA} is the net atomic charge on atom A and R_A is the position vector of atom A. The term μ_{hyb} is an atomic polarisation moment due

to the hybridisation of the s and p orbitals on atom A and for a heteroatom includes the moment that arises from the "lone" pair. In the x direction μ_{hyb} may be calculated by;

$$\mu_{hyb} = -14.674 \sum_{A} \frac{P_{2s(A)2px(A)}}{Z'_A} \text{ debyes} \quad \ldots \quad 3.3$$

where Z'_A is the Slater orbital exponent for the 2s and 2p orbitals of atom A. Similar expressions are obtained for the value of μ_{hyb} in the y and z directions.

For second row elements, such as chlorine, μ_{hyb} includes contributions for mixing 3s with 3p, and 3p with 3d orbitals, for example[36];

$$\mu_{sp^z} = -14.674 \sum_{A} \left(\frac{P_{2s(A)2pz(A)}}{Z'_A} + 2.1 \frac{P_{3s(A)3pz(A)}}{Z'_A} \right) \text{debyes} \quad \ldots \quad 3.4$$

and

$$\mu_{pd^x} = -2.5416 \sum_{A} \left(\frac{5376(Z'_A . Z''_A)^{7/2}}{5^{\frac{1}{2}}(Z'_A + Z''_A)^8} \right) \times$$

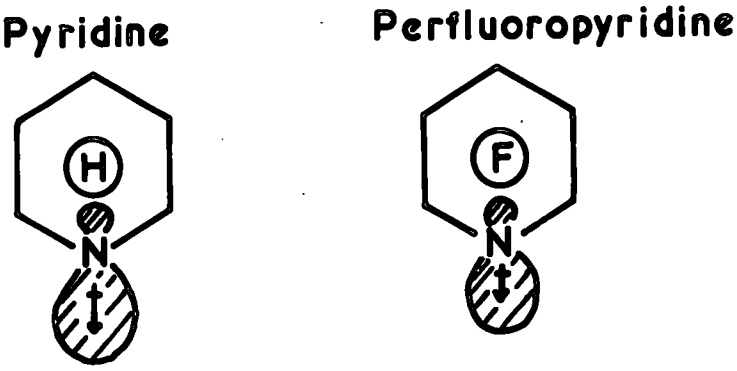
$$\left(P_{3dxz(A)3pz(A)} + P_{3d(x^2 - z^2)(A)3px(A)} + P_{3dxy3py} - \tfrac{1}{2} P_{3dz^2 3px} \right) \text{debyes} \quad \ldots \quad 3.5$$

where Z''_A is the Slater orbital exponent for the d orbital. Similar expressions are obtained for the y and z directions.

Although not many experimental results were available for comparison it is evident from table 3.6 that there is good overall agreement, in the case of the perhydro and fluoro derivatives, between μ_{total} and the experimental results. When the components μ_Q and μ_{hyb} are considered it is seen that, for pyridine, the diazines and their fluoro derivatives, μ_{hyb} is of greater importance than μ_Q. In these compounds the value of μ_{hyb} is largely dependent

on the contribution of the 'lone pair' of the nitrogen and in the case of perfluoropyridine it would appear that the total dipole arises almost entirely from this contribution. Since μ_{hyb} is greater in the perhydro series than in the perfluoro series it may be argued that the centre of charge in the sp^2 orbital of the 'lone pair' must be displaced further from the nitrogen in the perhydro series. Thus for pyridine and perfluoropyridine,

Figure 3.6



These effects may also be seen to a lesser extent in the chloro derivatives of pyridine.

As was stated earlier μ_{total} is the vector sum of μ_Q and μ_{hyb} and it is also evident from table 3.6 that these two, μ_Q and μ_{hyb} are not necessarily orientated in the same direction. It is seen that in the perhydro series μ_Q and μ_{hyb} act in the same direction while in the perfluoro series they act in opposition.

Table 3.6

Dipole moments for some fluoro, chloro and methoxy derivatives of Benzene, Pyridine, Pyridazine, Pyrimidine and Pyrazine. Dipole moments given in Debyes (1 Debye = 10^{-18} esu cm = 3.335640×10^{-30} coulomb metres).

	Exptl[15,40]	μ_Q	μ_{hyb}	μ_{total}
Benzene				
monofluoro	1.60	1.29	0.32	1.61
monochloro	1.73	1.80	0.96	2.75
monomethoxy	1.36	0.60	1.09	1.66
Perfluorobenzene	-	0	0	0
monomethoxy	-	1.48	0.87	1.91
Pyridine	2.20	0.74	1.58	2.32
2-fluoro	-	1.94	1.66	3.53
3-fluoro	-	1.26	1.08	2.01
4-fluoro	-	0.95	1.38	0.43
2-chloro	3.25, 3.22	2.27	0.88	3.09
3-chloro	2.02	1.56	2.35	2.98
4-chloro	0.78	0.93	0.73	1.66
2K-methoxy	1.15	0.61	1.46	2.02
2A-methoxy		1.17	2.64	3.81
3K-methoxy	2.75	0.28	0.60	0.35
3A-methoxy		0.92	2.38	3.28
4K-methoxy	3.00	0.60	1.44	1.93
Perfluoropyridine	-	0.01	1.09	1.08
2K-methoxy	-	1.65	0.96	0.86
2A-methoxy	-	1.47	1.99	2.61
3K-methoxy	-	1.43	0.26	1.56
3A-methoxy	-	1.41	1.81	2.93
4K-methoxy	-	1.55	1.13	2.67
Perchloropyridine	-	0.29	0.76	1.05

Table 3.6 cont'd.

	Exptl	μ_Q	μ_{hyb}	μ_{total}
Pyridazine	4.32, 3.97	1.21	2.86	4.07
Perfluoropyridazine	-	1.00	2.29	1.29
3K-methoxy	-	2.33	1.54	1.05
3A-methoxy	-	1.21	3.20	2.98
4K-methoxy	-	1.49	1.70	2.24
4A-methoxy	-	0.73	2.58	3.27
3K,4K-dimethoxy	-	2.67	0.80	2.75
3K,5K-dimethoxy	-	1.36	1.78	2.24
3K,6K-dimethoxy	-	1.29	2.40	1.12
4K,5K-dimethoxy	-	1.50	2.35	3.77
4K,6K-dimethoxy	-	0.34	2.69	2.82
Pyrimidine	2.0, 2.42	0.67	1.66	2.33
Perfluoropyrimidine	-	0.47	1.13	0.66
2K-methoxy	-	2.01	1.71	1.63
4K-methoxy	-	1.71	0.29	1.73
4A-methoxy	-	1.11	1.85	2.63
5K-methoxy	-	1.02	1.21	2.22
2K,4K-dimethoxy	-	2.05	0.95	1.26
2K,5K-dimethoxy	-	0.79	1.20	0.43
4K,5K-dimethoxy	-	2.23	0.99	3.21
4K,6K-dimethoxy	-	1.15	1.05	2.32
Pyrazine	0	0	0	0
2-fluoro	-	1.34	0.26	1.59
2K-methoxy	-	0.62	1.09	1.71
2A-methoxy	-	0.74	0.99	1.72
Perfluoropyrazine	-	0	0	0
2K-methoxy	-	1.57	0.87	1.87
2A-methoxy	-	1.46	0.96	1.93
2K,3A-dimethoxy	-	1.49	1.38	0.11
2A,5A-dimethoxy	-	0.19	0.12	0.07
2A,6K-dimethoxy	-	0.24	1.87	2.02

This opposition in the perfluoro series is due to the effect that the large negative sigma charges of the fluorines have on the value of u_g and this is also clearly shown in the case of 4-fluoropyridine.

Bearing in mind that the calculations are for the isolated molecules in the gas phase it is possible to suggest values for the dipole moments of the fluoro derivatives where these are not known.

Thus from table 3.6

	Dipoles in Debyes
Perfluorobenzene	0
2-fluoropyridine	3.53
3-fluoropyridine	2.01
4-fluoropyridine	0.43
Perfluoropyridine	1.08
Perfluoropyridazine	1.29
Perfluoropyrimidine	0.66
2-fluoropyrazine	1.59
Perfluoropyrazine	0

Since perfluorobenzene and perfluoropyrazine both possess centres of symmetry they have zero dipole moments.

In the case of the chloro derivatives the agreement is less good[36,41] and so it is with some caution that a value of 1 debye is suggested for the dipole moment of perchloropyridine.

For the methoxy derivatives there seems to be little or no agreement. At the temperatures at which the dipoles have been measured there is free rotation of the methoxy group about the bond linking it with the ring system. It is possible therefore that the lack of agreement is due to this cause, since as already stated the calculations were carried out for only two particular orientations of the

methoxy group. Furthermore the calculations do not take into account any solvation effects. It is also known that CNDO II calculations for dipole moments of oxygen compounds do not agree as well with experimentally determined values as do the calculations for fluoro compounds.

Chapter 4

Basicities and Effects of Protonation on the Electron Distribution for Pyridine, the three Diazines and some of their fluoro, chloro and methoxy derivatives.

Basicities

Acid-Base Theory[42]

The reaction of a base **B** with hydrogen ions (H_3O^+) in dilute aqueous solution is a dynamic equilibrium. The reaction may be written as

$$B + H_3O^+ \rightleftharpoons BH^+ + H_2O \qquad \ldots \quad 4.1$$

and the acidity constant K_a for the base is given by

$$K_a = \frac{a_B \times a_{H_3O^+}}{a_{BH^+}} \qquad \ldots \quad 4.2$$

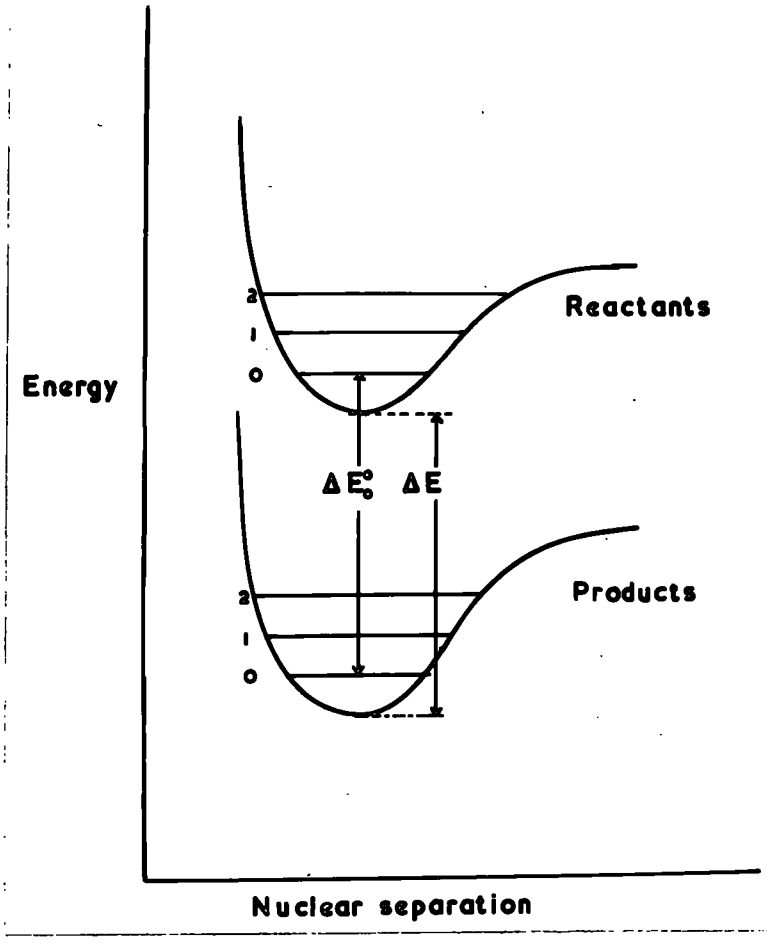
where a_B, $a_{H_3O^+}$, and a_{BH^+} are the activities of the respective molecules and ions and the activity of water is taken as unity.

The equilibrium constant K_{eq} for the forward reaction in 4.1 may be expressed in the form[21]

$$K_{eq} = \frac{f_{BH^+}}{f_B \times f_{H_3O^+}} \cdot e^{-\Delta E_o^o/RT} \qquad \ldots \quad 4.3$$

where f_{BH^+}, f_B, and $f_{H_3O^+}$ are the partition functions of the respective molecules and ions and ΔE_o^o is the difference in internal energy of one mole of the products and one mole of the reactants in their standard states at absolute zero (0 Kelvin). Now ΔE_o^o represents the difference in energy calculated from the lowest (sero point) energy for the products and the reactants, i.e. schematically.

Figure 4.1



Since the zero point energies for the reactants and products will be similar in magnitude and also small compared to ΔE_o^o then their difference will also be small compared to ΔE_o^o. Therefore to a good degree of approximation ΔE, the energy difference between the lowest points of the curves shown in figure 4.1, may be used instead of ΔE_o^o so that

$$\Delta E \simeq \Delta E_o^o \qquad \ldots \quad 4.4$$

The equilibrium constant K_{eq} may therefore be written as

$$K_{eq} = f.e^{-\Delta E/RT} \qquad \ldots \quad 4.5$$

where f is the ratio of the partition functions in 4.3.

It will be seen from 4.1 that

$$K_a = 1/K_{eq} \qquad \ldots \quad 4.6$$

and on taking logarithms of 4.6 that

$$pK_a = -pK_{eq} \qquad \ldots \quad 4.7$$

The calculations carried out give ΔE_g for the gaseous equilibrium whereas the experimental observations of pK_a refer to the equilibrium in aqueous solution. It is therefore convenient to split the term ΔE into two terms[22], ΔE_g and $\Delta E_{solvation(T)}$, this latter term being temperature dependent.

The constant K_{eq} may now be expressed as

$$K_{eq} = f. \exp-(\Delta E_g + \Delta E_{solvation(T)})/RT \quad \ldots 4.8$$

The term $\Delta E_{solvation(T)}$ may itself be expressed as the sum of three terms so that

$$\Delta E_{solvation(T)} = \Delta E_{cav} + \Delta E_{orient} + \Delta E_{inter} \quad \ldots 4.9$$

The term ΔE_{cav} arises from the energy needed to make a cavity for the solute molecule in the solvent and from the fact that the protonated molecule needs a larger cavity than the unprotonated molecule. The term ΔE_{orient} is an energy term due to the orientation of solvent molecules around the reactant and product molecules and ΔE_{inter} is the result of various intermolecular forces (see below). For molecules and ions of similar shapes and sizes the two terms ΔE_{cav} and ΔE_{orient} may be taken as being essentially constant. The term ΔE_{inter} may itself be expressed as the sum of three other terms, ΔE_{disp}, ΔE_{iso}, and ΔE_{aniso} so that ΔE_{inter} may be written as

$$\Delta E_{inter} = \Delta E_{disp} + \Delta E_{iso} + \Delta E_{aniso} \quad \ldots 4.10$$

ΔE_{disp} arises from the dispersion forces and ΔE_{aniso} represents an energy term due to anisotropic interactions between base, conjugate acid and solvent, e.g. hydrogen bonding. The term ΔE_{iso} results

from isotropic charge-dipole and dipole-dipole interactions. For molecules of similar sizes and shapes the term ΔE_{disp} should be approximately constant. The main contribution to ΔE_{aniso} arises from hydrogen bonding and for the closely related series of heterocyclic bases considered this term should also be approximately constant. The main contribution to $\Delta E_{solvation(T)}$ arises from ΔE_{iso} which may be calculated approximately from the expression[22]

$$\Delta E_{iso} = -\sum \frac{q_i q_j}{2r_{ij}} (1 - 1/D) \qquad \ldots \ 1.5$$

where q_i and q_j are the charges on the atoms i and j, r_{ij} is the distance between them and D is the dielectric constant of the solvent. It may be noted that this expression, 1.5, is very similar to the expression for the energy of solvation obtained by M.I. Jano[43].

Calculations carried out using 1.5 show (table A2.10) that for a solvent of dielectric constant 33 (Methanol for example) the term $\Delta E_{solvation(T)}$ does differ on going from pyridine to perchloropyridine. However the difference $\Delta\Delta E_{solvation(T)}$ between BH^+ and $(B + H^+)$ remains approximately the same, being 330.3 and 329.5 kJ mol^{-1} respectively for pyridine and perchloropyridine. There is a bigger difference in the case of perfluoropyridine, $\Delta\Delta E_{solvation(T)}$ is 384.6 kJ mol^{-1} but the energy difference ΔE_g (-1214 kJ mol^{-1}) still remains the dominant factor (see later).

Therefore for a similar series of compounds, such as the heterocycles considered, all the terms considered as contributing to $\Delta E_{solvation(T)}$ may be regarded as being essentially constant. In equation 4.8 K_{eq} may therefore be regarded as being proportional to $e^{-\Delta E_g}$ since for a similar series of compounds f, the ratio of the

partition functions, will also be constant. Taking logarithms of 4.8 then gives

$$\log K_{eq} \propto -\Delta E_g \qquad \ldots \quad 4.12$$

which with 4.7 gives

$$pK_a \propto -\Delta E_g \qquad \ldots \quad 4.13$$

The calculations for the molecules under consideration give a value for E_g with the isolated molecules in the gas phase at absolute zero and at the lowest point of the energy curve as in figure 4.1. The term ΔE_g for the protonation may then be calculated, table 4.1. The base strengths, in terms of pK_a values, are then compared with the relative magnitudes of ΔE_g. Where experimental values for the pK_as are not available the values of ΔE_g may be used to estimate the relative acidities (or basicities) and to suggest possible values for the pK_as.

The values of ΔE_g calculated are observed to be of similar magnitude to the values of proton affinities obtained by ion-cyclotron resonance studies[44]. Considering that the CNDO II calculations have not been specifically parametised to reproduce thermodynamic data, the measured proton affinity (in the gas phase) for pyridine of -941 ± 9 kJ mol^{-1} is in good agreement with the calculated value, table 4.1, of -1361 kJ mol^{-1}. Unfortunately this is the only compound on which calculations were carried out where ion-cyclotron studies had also been performed.

Pyridine Derivatives

The results for some of the pyridine derivatives given in table 4.1 have been plotted and are shown in figure 4.2. It can be seen that there is not an exact correlation between ΔE_g and the pK_a values but that there is a definite trend. Thus as the magnitude

Table 4.1

Energy differences and pKa values for some of the fluoro, chloro and methoxy derivatives of Pyridine, Pyridazine, Pyrimidine and Pyrazine on protonation.

(i) $H^+ + B \rightleftharpoons HB^+$ Base	pK_a [15,40,45]	ΔE_g (kJ mol^{-1})
Pyridine	5.22	-1361
2-fluoropyridine	-0.22	-1334
3-	2.97	-1322
4-	-	-1345
2K-methoxypyridine	3.28	-1354
3K-	4.88	-1360
4K-	6.62	-1388
Perfluoropyridine	(-11)*	-1214
Perchloropyridine	-	-1254
Pyridazine	2.3	-1325
Perfluoropyridazine	-	-1200
Pyrimidine	1.3	-1324
Perfluoropyrimidine	-	-1198
Pyrazine	0.6	-1333
2-fluoropyrazine (4)	-	-1290
(1)	-	-1305
Perfluoropyrazine	(-13)*	-1189
(ii) $HB^+ + H^+ \rightleftharpoons H_2B^{2+}$	pK_{a2}	
1-H-pyridazine	-	-609.5
1-H-perfluoropyridazine	-	-527.3
1-H-pyrimidine	(-6.3)**	-689.0
1-H-perfluoropyrimidine	-	-592.4
1-H-pyrazine	(-5.78)**	-696.0
4-H-2-fluoropyrazine	-	-679.7
1-H-2-fluoropyrazine	-	-664.8
1-H-Perfluoropyrazine	-	-589.4

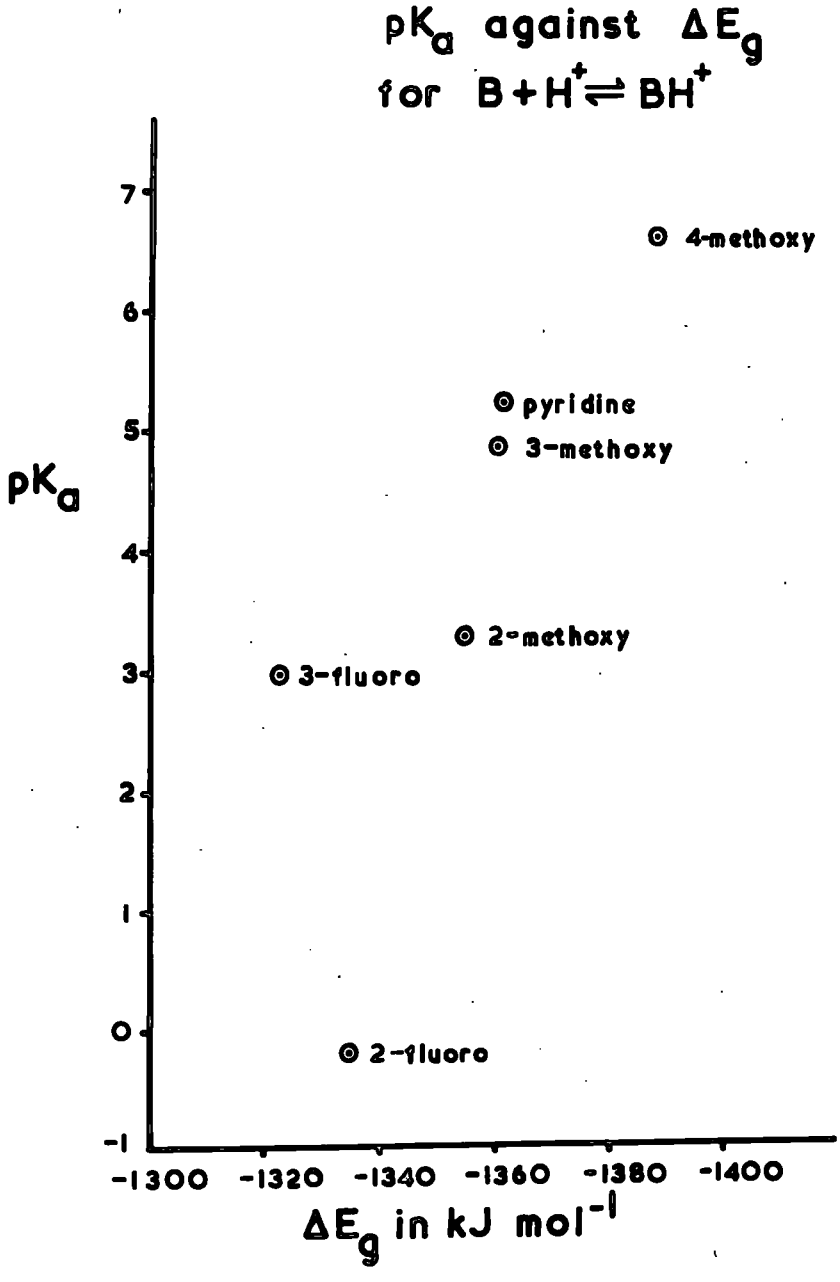
(pKa values for $HB^+ + H_2O \rightleftharpoons B + H_3O^+$)

* ref. 46

** ref. 47, 48.

Figure 4.2

Protonation of some pyridine derivatives



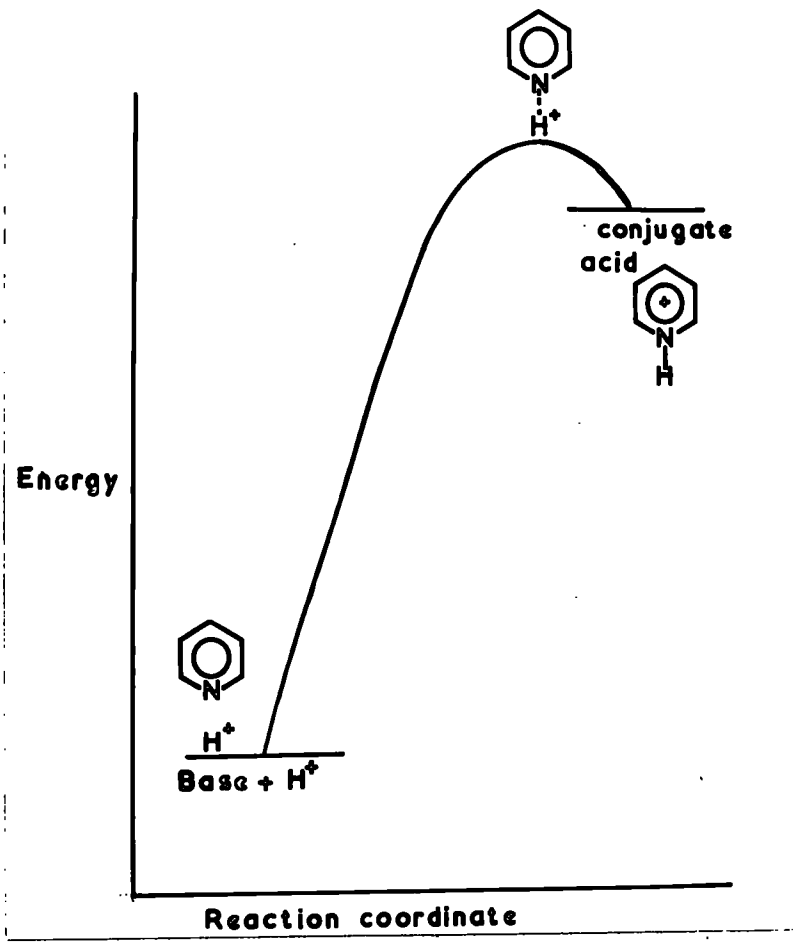
of ΔE_g increases so does the pK_a and the trend fits in the absolute sense that expected from equation 4.13, giving for the stronger bases the greater values of ΔE_g on protonation. It is possible to make an estimate for the pK_a of 4-fluoropyridine from a consideration of the general trend shown in figure 4.2. The value of ΔE_g for this compound is given in table 4.1 as -1345 kJ mol^{-1} and the trend shown in figure 4.2 suggests that the pK_a may lie between 2.5 and 4.5. An extrapolation of the trend in figure 4.2 enables some idea of the pK_as for perchloro and perfluoropyridine to be obtained. The estimates are that the pK_as will be of the order -7 to -14 with perchloropyridine being the stronger base (see also figure 4.10). This is broadly in agreement with experimental observations where it has been noted that perfluoro and perchloropyridine show no basic properties in aqueous acid[1,49,50]. Also observations[45] of the extent of protonation of perfluoropyridine when it is dissolved in strong acid have enabled an estimate of its pK_a to be made as being near -11.

Electronic Charge Distribution in Pyridine Derivatives

As an initial criterion it might have been thought, naively, that the relative basicities of the different molecules would correlate in some manner with the electronic charge on the nitrogen atom before protonation. Examination of the molecules represented in figures 4.4 - 4.6 and of the results in table 4.1 show in fact there is no obvious connection. Thus 3-fluoro and 2-methoxypyridine with pK_a values of 2.97 and 3.28 respectively do not show any correlation with the magnitude of either their sigma or pi charges. When pyridine and 4-methoxypyridine are considered then in fact the molecule with the smaller original sigma charge on the nitrogen is in fact more basic than the other. It was found that for all the molecules represented in figures 4.4 - 4.10 that attempts to correlate the energy, ΔE_g, for protonation with some aspect of the charge on the nitrogen were

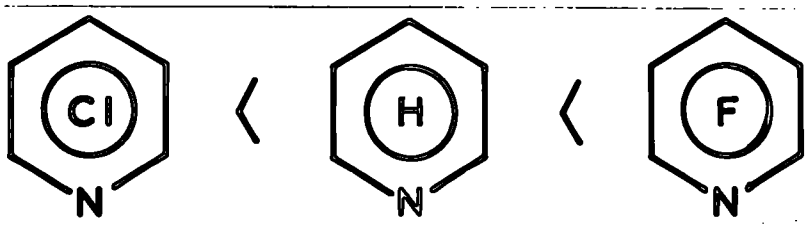
unsuccessful. Now according to the Hammond-Polanyi[17] postulate the reactivity of a compound may be correlated with the energy of the transition state, which the reactants pass through, compared to the energy of the original reactants. A correlation between the original reactants and their reactivity would therefore imply an 'early' transition state. This would mean in the case of protonation that the transition state would 'look' like a proton approaching the original molecule. Since the acid-base equilibra under consideration strongly favour the free base, since all are weak bases, a typical energy profile for the processes involved will be shown in figure 4.3 below.

Figure 4.3

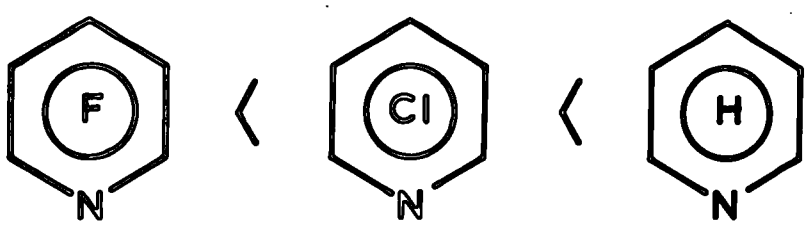


It is evident therefore that the transition state "looks" more like the protonated species than the free base so that a correlation of basicity with electron distribution in the free base would not be expected.

It is interesting to note that the overall charge on the nitrogen becomes more negative in the series shown below.



which should be compared to the calculated order of basicities which is

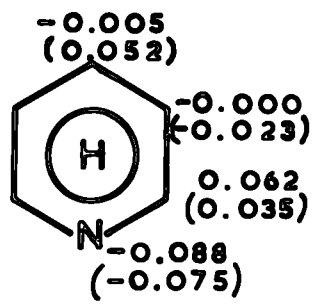


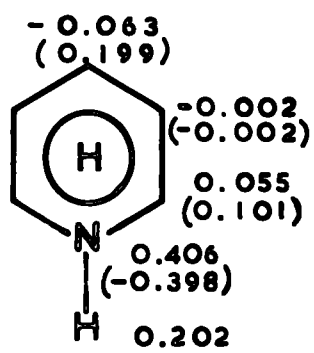
The results for the overall charge on the nitrogen may be compared to the results for the electron densities obtained by x-ray photo electron spectroscopy[38] which are in agreement with the calculated values.

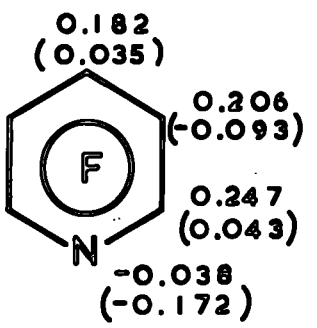
When the protonation of pyridine, perfluoro and perchloro-pyridine are considered (figure 4.4) it is seen that the nitrogen atom bears only a very small overall charge on protonation compared to the moderate negative charge before protonation. This is largely due to sigma electron donation to the proton resulting in the nitrogen bearing a large positive sigma charge. This sigma charge is largely compensated by increased pi electron drift from the ring carbons C2, 4 and 6. It is interesting to note here how small the effects of protonation are at positions 3 and 5, that is positions meta to the nitrogen. The effect on the sigma charges of the ring carbons is also small except at position 4. The carbon atom C4 in

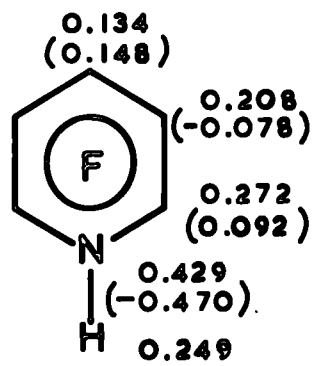
Figure 4.4

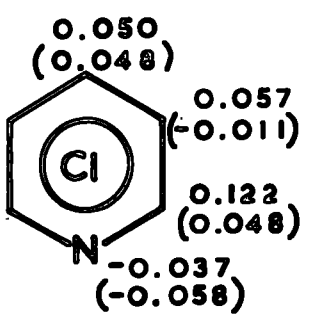
Sigma and (pi) charges

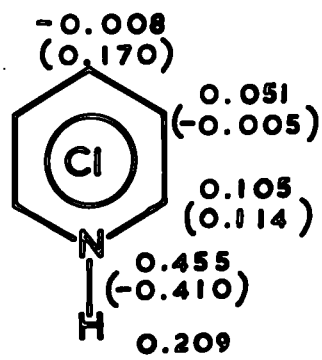










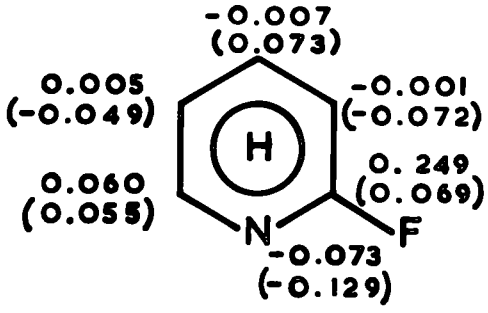


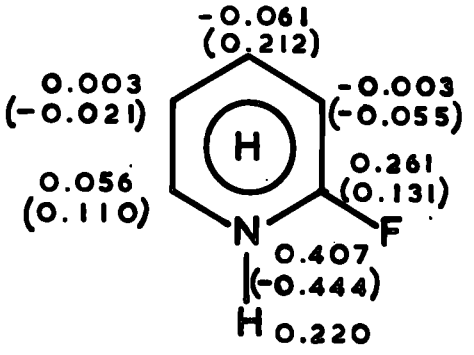
fact seems to be the ring carbon most affected with regard to the pi charges and also as noted to the sigma charge. This latter effect may be thought of as compensation for the pi electron drift to the nitrogen. Thus the pi charge at carbon C4 is more positive on protonation while the sigma charge is more negative.

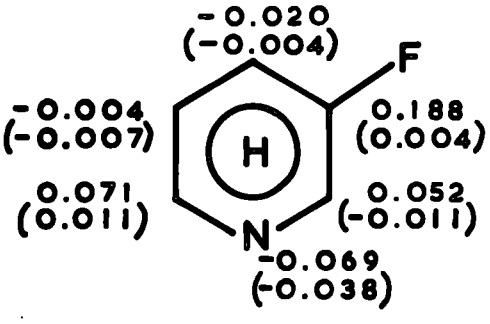
In figures 4.5 and 4.6 are given the sigma and pi charges for the ring atoms in the monofluoro and monomethoxy derivatives of pyridine before and after protonation. The most obvious feature is the great similarity of the charges in the corresponding fluoro and methoxy compounds apart from the sigma charge on the ring carbon to which the fluorine or oxygen is attached. In this case the greater electronegativity of the fluorine gives rise to a larger $-I_{\sigma}$ effect and the sigma charge on the ring carbon is larger than in the case of the corresponding methoxy compound. As in the case of pyridine, perfluoro and perchloropyridine the effects of protonation are observed principally in the changes in the pi charges of the ring carbons C2, 4 and 6 and in the sigma and pi charges of the nitrogen. Again, like the examples referred to, the nitrogen atom only bears a very small net charge on protonation though it bears a large positive sigma charge due to sigma electron donation to the proton. This large sigma charge is again compensated by pi electron drift from the ring carbons C2, 4 and 6, with the principal effect occurring at C4. What is also interesting is how little is the effect on protonation at atoms C3 and 5, the positions meta to the nitrogen. It might be said therefore that substituents at C3 and C5 should have little effect on the protonation of the nitrogen. This is true in that it has little direct effect but C3 and C5 lie in positions ortho and para to atoms C2, 4

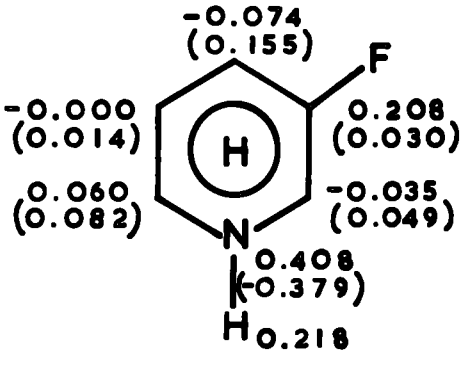
Figure 4.5

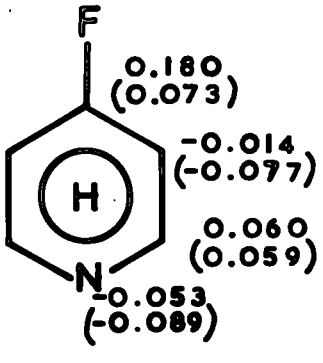
Sigma and (pi) charges











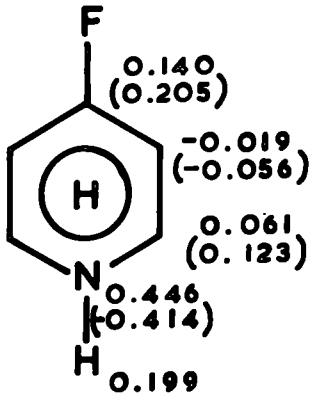
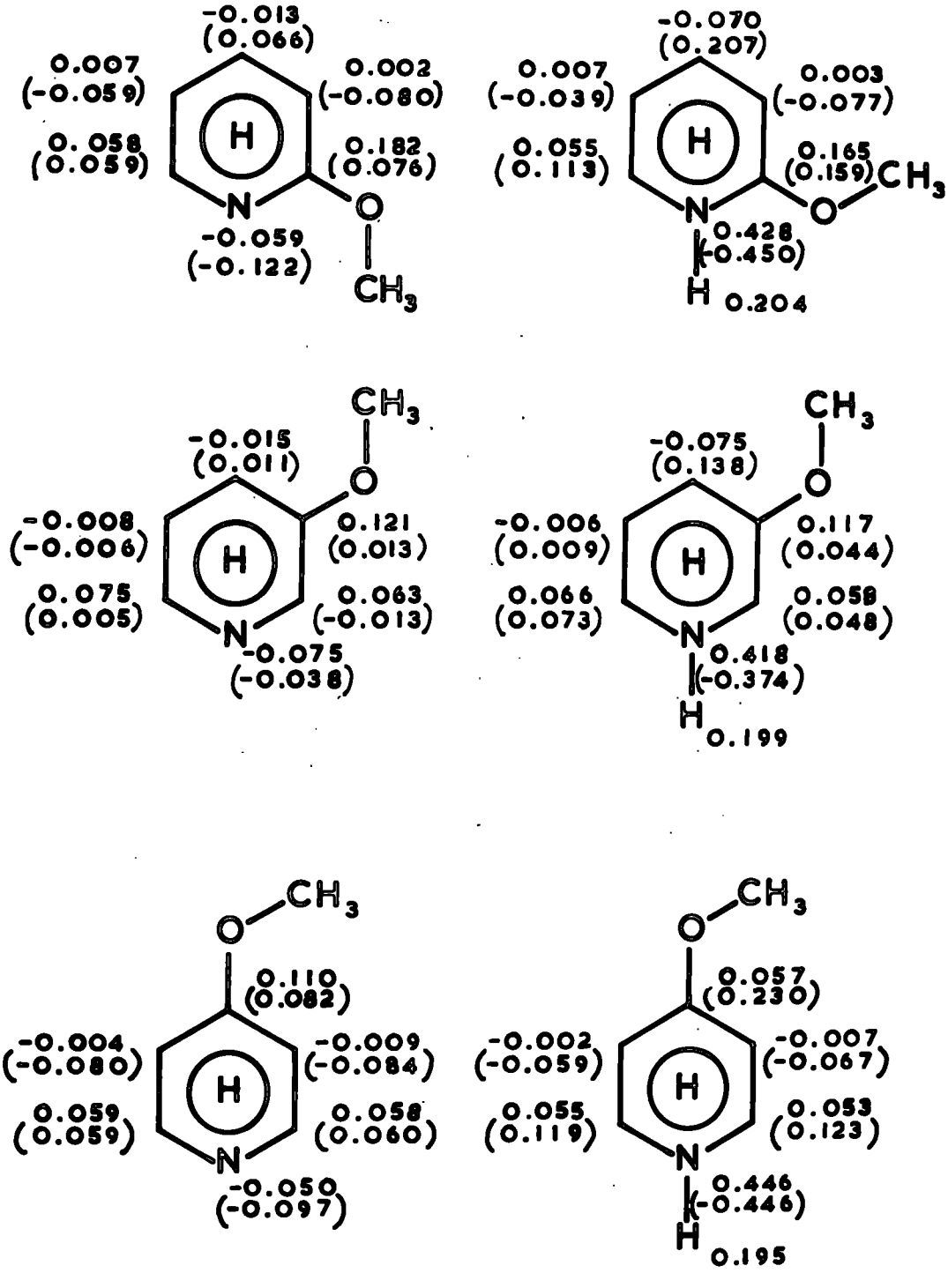


Figure 4.6

Sigma and (pi) charges



and 6. Therefore a substituent at positions C3 and C5 may well have an indirect effect due to the effects they have at positions C2, 4 and 6 which are the positions directly affected on protonation.

Protonation of the Diazines

The compounds represented in figures 4.7 - 4.10 afford examples of heterocycles where there is a possibility of diprotonation taking place. It cannot be assumed that the ΔE_g values of the diazines will correlate with their pK_as in the same way as in the case of pyridine. An examination of the values of ΔE_g given in table 4.1, for the diazines, and the trend shown in figure 4.2 shows, in fact no obvious correlation. It cannot be assumed, that in the diazines, that $\Delta E_{solvation(T)}$ is constant since the various contributing terms, (equations 4.9 and 4.10), may vary with different diazines. Thus due to differences in hydrogen bonding the term ΔE_{aniso} may alter. The term ΔE_{iso}, for which calculations were carried out on the monoprotonated perfluoro diazines, also shows small differences between pyridazine, pyrimidine and pyrazine (see table A2.10). These differences are of the same order as the differences in ΔE_g, given in table 4.1, and should therefore not be ignored. Taking these factors into consideration, it may be said though, that the pK_a and ΔE_g values for pyridazine, pyrimidine and pyrazine do not seriously conflict with the trend observed in figure 4.2. Thus their pK_a values lie between 0.6 and 2.3, that is a change of 1.7 and their values of ΔE_g show a change of only 9 kJ mol^{-1} out of a total of 1333 kJ mol^{-1}.

Suggestions may therefore be made, using the trend shown in figure 4.2, regarding the extent of protonation which might be

Figure 4.7

Sigma and (pi) charges

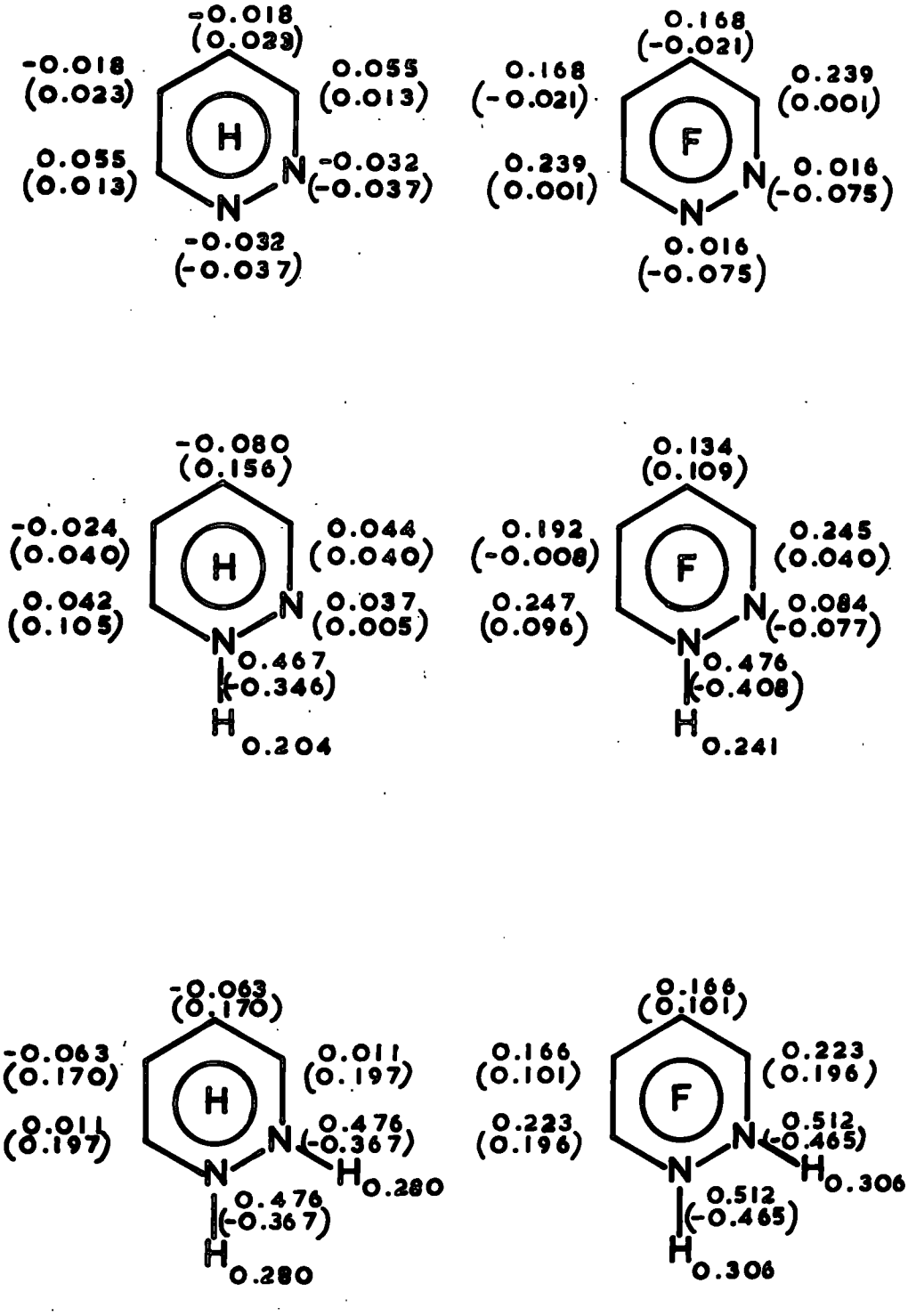


Figure 4.8

Sigma and (pi) charges

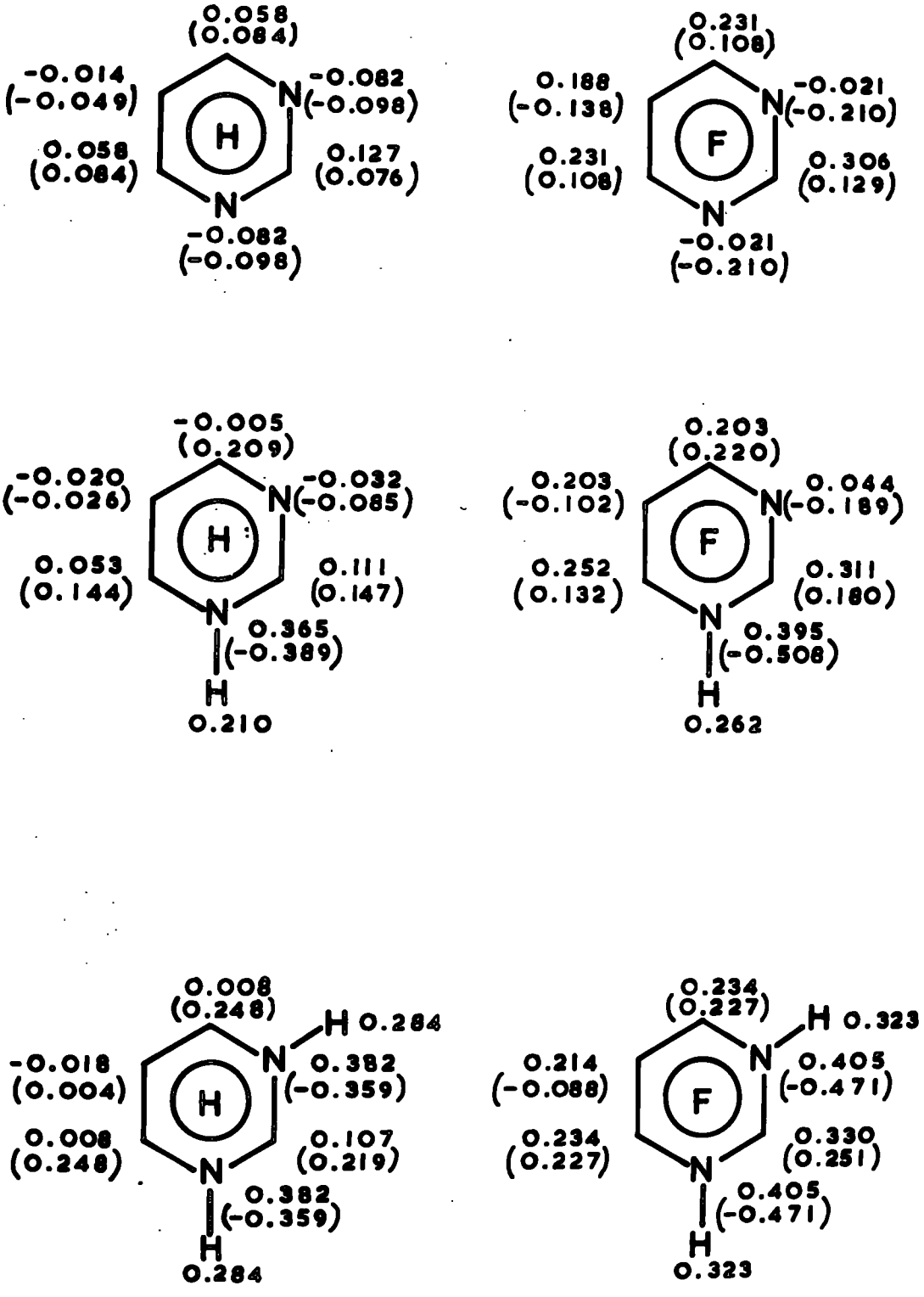


Figure 4.9

Sigma and (pi) charges

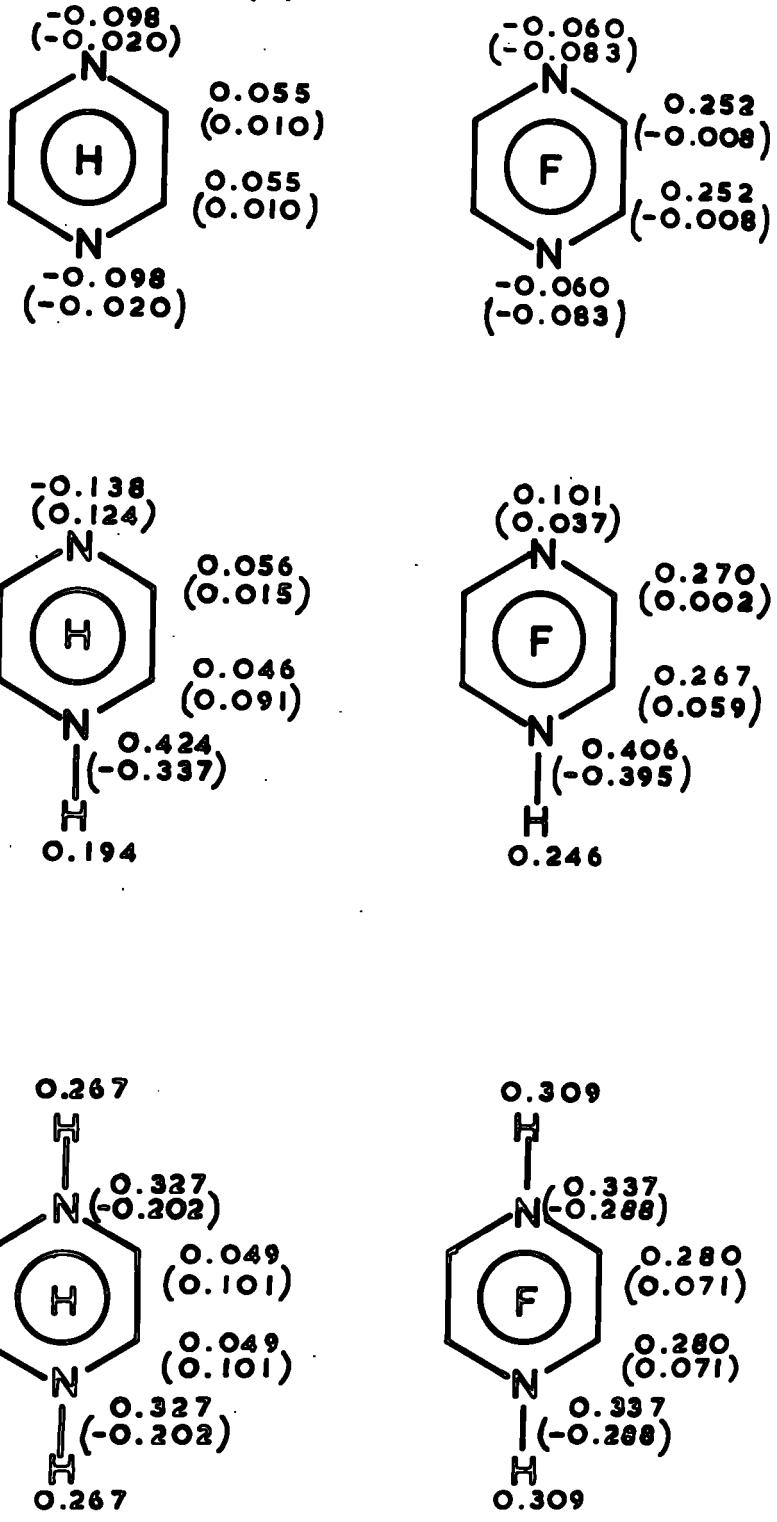
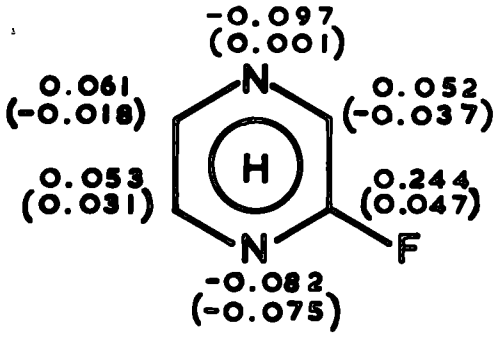
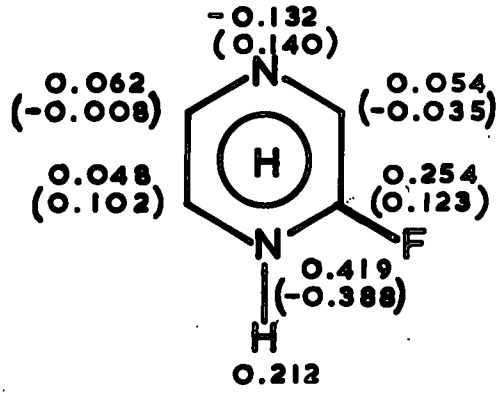
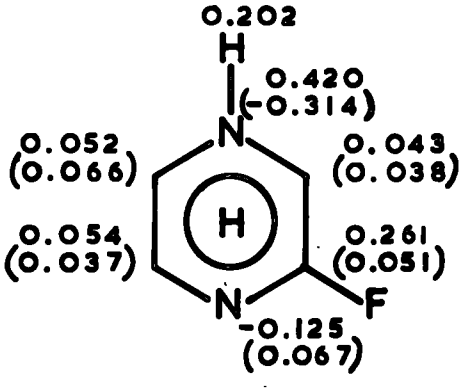


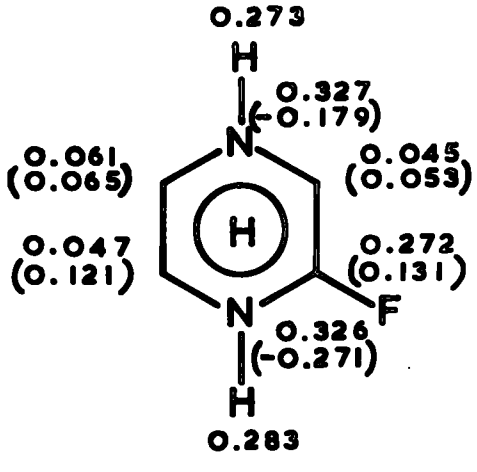
Figure 4.10

Sigma and (pi)charges









expected for the molecules dealt with and, more cautiously, the value of pK_a to be expected. Thus pyridazine, pyrimidine and pyrazine would be expected, with regard to monoprotonation, to be only feebly basic and to have pK_a values between 0 and 3. As already stated this is in moderate agreement with the experimentally determined values. 2-fluoropyrazine would be expected to be less basic than these three and to have a possible pK_a lying between 1 and -3, though this estimate should be treated with caution. It is interesting to note that in 2-fluoropyrazine the nitrogen atom adjacent to the fluorine is predicted to be more readily protonated than the other nitrogen.

When the perfluoro derivatives of the three diazines are considered, the values of ΔE_g in table 4.1 suggest that for monoprotonation they should ressemble perfluoropyridine. Thus they should only by protonated to any appreciable extent in a strongly acid medium and their pK_a values would be expected to be of the order of -7 to -14. This agrees, in general, with the results obtained by Chambers and coworkers[46] for perfluoropyridazine and perfluoropyrazine.

When diprotonation of the three diazines is considered reference to table 4.1 shows that the values of ΔE_g are, in general, approximately half the values for monoprotonation. Therefore it would be expected that diprotonation would be extremely difficult. In view of the trend shown in figure 4.11 (see later) it would, in fact, appear that diprotonation can only take place in extreme acid conditions and that the pK_a values would be large and negative ($\ll -20$). This is somewhat at variance with some reports which give pK_{a2} for pyrazine as -5.78 and for pyrimidine as -6.3. However since double and single charged solvation energy terms become

relatively more important it would not be expected that the same correlation would necessarily apply for both mono and diprotonation. It is not entirely clear, though, that the results reported[47,48] for the pK_{a2}s for pyrazine and pyrimidine refer to the protonation of the monoprotonated species since for perfluoropyrazine it has been suggested[46] that the addition of further acid to the monoprotonated species may lead to the formation of a radical dication rather than to diprotonation.

Charge Distributions in the Protonated Diazines

In figures 4.7 - 4.10 the sigma and pi charges are given for the ring atoms in the various diazine derivatives considered and their conjugate acids.

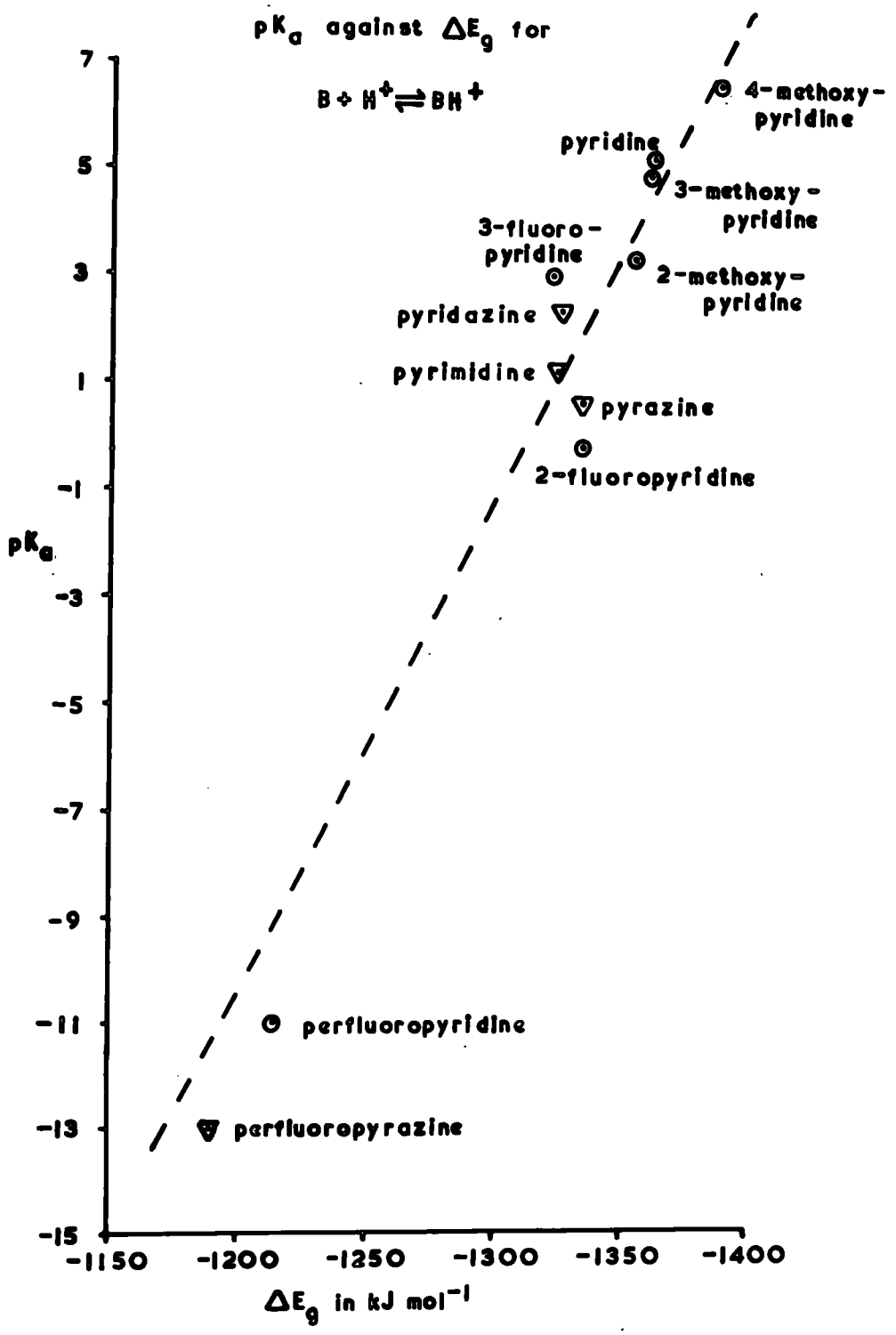
These charge distributions show some interesting features and it is helpful to make comparisons between the various diazines and the corresponding pyridines. Thus like pyridine there is little effect on the sigma charges of the ring carbons when the molecule is protonated except for the carbon atom para to the protonated nitrogen. The atom para to the protonated nitrogen also tends to show the largest positive pi charge. On monoprotonation there is immediately a considerable difference between the two nitrogen atoms in the diazines. The protonated nitrogen bears a large positive sigma charge, due to sigma donation to the proton, and this sigma charge is compensated to some extent in pyridazine and pyrazine derivatives and completely in pyrimidine derivatives by a large negative pi charge. This pi charge arises from pi electron drift from the atoms in positions ortho and para to the protonated nitrogen, the principal drift occurring at the para atom. In the case of perfluoropyridazine the pi electron drift from the ortho nitrogen is very small, while in perfluoropyrazine the pi electron drift from the para nitrogen is very small.

On diprotonation the hydrogens attached to the nitrogens are all more positive, with the hydrogens in the perfluoro series all being more positive than in the corresponding perhydro compounds. Diprotonation does result in the differences between the three diazines becoming more marked. Thus for pyridazine all the carbons are either ortho or para to a protonated nitrogen and the carbon atoms adjacent to the nitrogens bear the largest pi charges. Also the sigma and pi charges on the protonated nitrogens are increased in magnitude compared to the case of monoprotonation. For the pyrimidines one carbon C5 is always in the meta position and there is little effect on its sigma and pi charges either on monoprotonation or on diprotonation. The atom C2 is ortho to both nitrogens and on diprotonation of the perfluoro compound it bears a larger positive pi charge than either C4 or C6 which lie ortho to one nitrogen and para to the other. The nitrogens are interesting since the sigma charge on the protonated nitrogen hardly alters whether the pyrimidine is mono or diprotonated. There is not much change in the pi charge either on the protonated nitrogen and for perfluoropyrimidine the overall charge on the protonated nitrogen is always noticeably negative. In the case of the pyrazines, on protonation the sigma and pi charges on the carbon atoms are similar to those for the carbon atoms ortho to the protonated nitrogen in monoprotonation. The sigma and pi charges on the nitrogen are now less on diprotonation unlike the case of the pyridazines where they were all increased and the case of the pyrimidines where there was little change.

The conclusions that can be drawn from these calculations for the various pyridines, pyridazines, pyrimidines and pyrazines are then as follows.

There is a correlation between pK_a and ΔE_g which appears as a general trend. In figure 4.11 all the pK_a values given in table 4.1 including the estimates for perfluoropyridine and perfluoropyrazine[46], have been plotted. The broken line indicates this general trend and its position is such that all the points plotted lie within two units of pK_a of this line. The position of the lower end of the line was decided to accord with the observation[46] that perfluoropyridazine (ΔE_g -1200 kJ mol^{-1}) is more basic than perfluoropyridine (ΔE_g - 1214 kJ mol^{-1}). The slope of the "trend" line in figure 4.10 may be compared with the value expected from a consideration of equations 4.5 and 4.7[51]. The value obtained from figure 4.10 is ΔpH of 1 for $\Delta\Delta E_g$ of 10 kJ mol^{-1} while equations 4.5 and 4.7 give ΔpH of 1 for approximately $\Delta\Delta E$ of 6 kJ mol^{-1} at 300 K. In view of the approximations that have been made in obtaining the values of ΔE_g and ΔE the agreement is quite reasonable. Furthermore it suggests that though the absolute values of ΔE_g may not correspond to the absolute values of ΔE the differences in energy for the different compounds considered are of the correct order. In order to obtain a better correlation between the calculations and the experimental results there is a need to consider $\Delta E_{solvation(T)}$ since for small differences in ΔE_g the differences in $\Delta E_{solvation(T)}$ are of the same order of magnitude and are not necessarily of the same sign. This is probably more important when considering different series of compounds.

Figure 4.11


pKa against ΔEg for
B + H+ ⇌ BH+
4-methoxy-pyridine
pyridine
3-methoxy-pyridine
3-fluoro-pyridine
2-methoxy-pyridine
pyridazine
pyrimidine
pyrazine
2-fluoropyridine
perfluoropyridine
perfluoropyrazine
pKa
7
5
3
1
-1
-3
-5
-7
-9
-11
-13
-15
-1150
-1200
-1250
-1300
-1350
-1400
ΔEg in kJ mol-1

On protonation it is observed that the positive charge is not located on the nitrogen which for pyridine and the diazines on monoprotonation only bears a very small overall charge. The positive charge is in fact distributed, for the ring atoms, as positive pi charge mainly on the atoms ortho and para to the protonated nitrogen. The hydrogen attached to a nitrogen bears a positive charge of approximately 0.2 electron units and in the perhydro compounds the hydrogens attached to the ring carbons carry, altogether, an appreciable portion of the positive charge (see appendix 3). There does not seem to be any particular ortho and para effects for the positive charge carried by these latter hydrogens.

Chapter 5

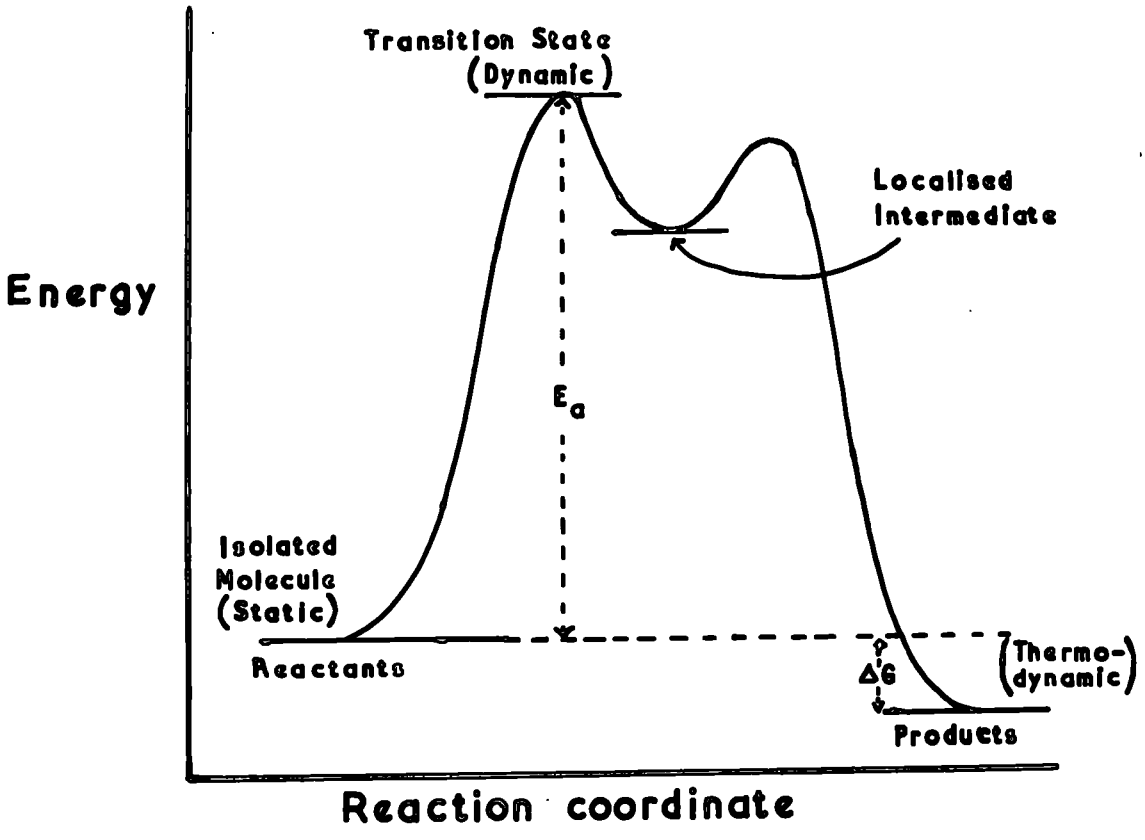
Reaction of some Fluoro, Chloro, and Methoxy Derivatives of Benzene, Pyridine, Pyridazine, Pyrimidine and Pyrazine with Methoxide Ion

Reactivities

Reaction Rate Theory

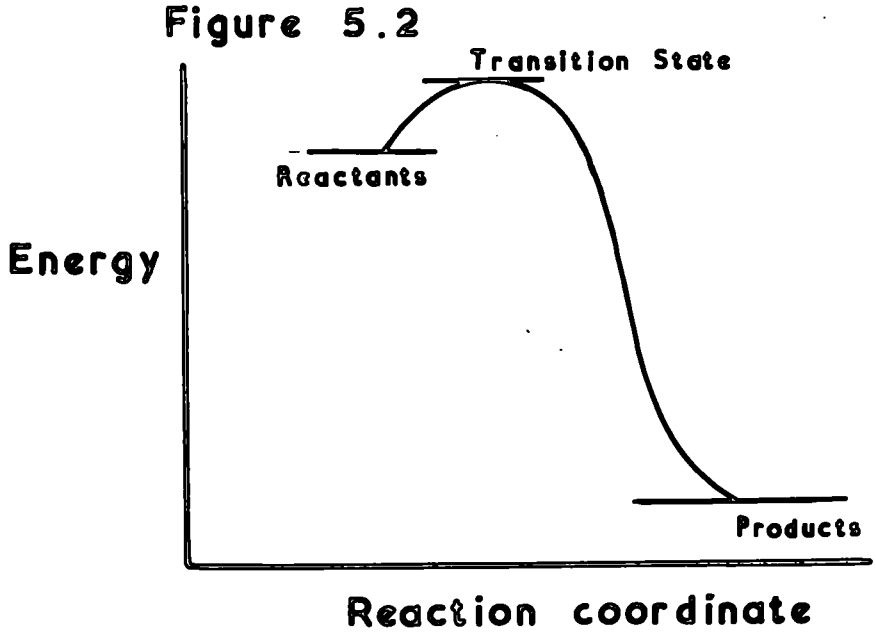
The reactions considered in this chapter are known, in general, to be irreversible under the experimental conditions which have been employed. The products of the reactions are therefore not subject to thermodynamic control but are kinetically or rate controlled. In discussing the relative rates at which molecules, or different sites within the same molecule, react either a static or a dynamic approach may be used. A schematic diagram of a typical reaction profile for which reaction indices might be calculated is shown in figure 5.1.

Figure 5.1



The static, or isolated molecule, approach assumes that the reactivities may be related to the electronic parameters of the original molecule or molecules. Implicit in this approach is the idea that the isolated reactants are a reasonable approximation, (that is "look like") the transition state. According to the Hammond-Polanyi[17,42] hypothesis this will only be the case if the reactants are particularly close in energy to the transition state, as for example in figure 5.2.

Figure 5.2



In nucleophilic aromatic substitutions this, in general, is not the case[52] and the situation is much nearer that indicated in figure 5.1. It might be expected therefore that a more reasonable theoretical model would be to approximate the transition state by means of a localised (Wheland) intermediate. Relative reactivities

can then be discussed in terms of energy differences between reactants and localised intermediates and this corresponds to a dynamic reaction index.

Transition State Theory[42]

In this theory it is assumed that the reactants form an activated complex X^{*}, or transition state, and that this complex then forms the products.

$$\text{Reactants} \rightleftharpoons X^{*} \rightleftharpoons \text{Products}$$

In actual fact more than one activated complex may be involved in the reaction sequence and the rate of the reaction will be determined by that of the slowest step. For the rate determining step, the rate constant is the rate of formation of X^{*} and is given by[21];

$$k_r = (kT/h)f.e^{-\Delta E_o^{\dagger}/RT} \qquad \ldots \ 5.1$$

where k_r is the rate constant, k is Boltzman's constant, h is Plank's constant and $\Delta E_o^{\dagger}$ is the energy of activation when all the substances are in their ground states and f is the ratio of the partition functions of the complex and the reactants. As in chapter 4 $\Delta E_o^{\dagger}$ differs from the potential energy of activation, $\Delta E^{\dagger}$, in the zero point energy difference between the reactants and the transition state complex[53]. Writing $\Delta E_z^{\dagger}$ for this zero point energy difference equation 5.1 may be written;

$$k_r = kT/h.f.e^{-(\Delta E^{\dagger} + \Delta E_z^{\dagger})/RT} \qquad \ldots \ 5.2$$

where $\Delta E^{\dagger}$ is the potential energy of activation.

For the reactions of two molecules, or of two sites within the same molecule, the relative rates for the reactions may be written;

$$k_{r_1}/k_{r_2} = \left[f_1/f_2\right]e^{-\Delta(\Delta E^{\dagger} + \Delta E_z^{\dagger})/RT} \qquad \ldots \ 5.3$$

Now for two similar reacting molecules $\Delta E_z^{\dagger}$ may be presumed to be very similar for both and $\Delta\Delta E_z^{\dagger}$ may therefore be taken as being very small. Therefore equation 5.3 may be put as;

$$k_{r_1}/k_{r_2} = \left[f_1/f_2\right] e^{-\Delta\Delta E^{\dagger}/RT} \quad \ldots 5.4$$

Since for a reaction in solution

$$\Delta H_o^{\dagger} = \Delta E_o^{\dagger} + nRT \quad \ldots 5.5$$

and

$$\Delta H_o^{\dagger} = E_a - RT \quad \ldots 5.6$$

where E_a is the Arrenhius activation energy in

$$k_r = A.e^{-E_a/RT} \quad \ldots 5.7$$

it follows that at the same temperature that

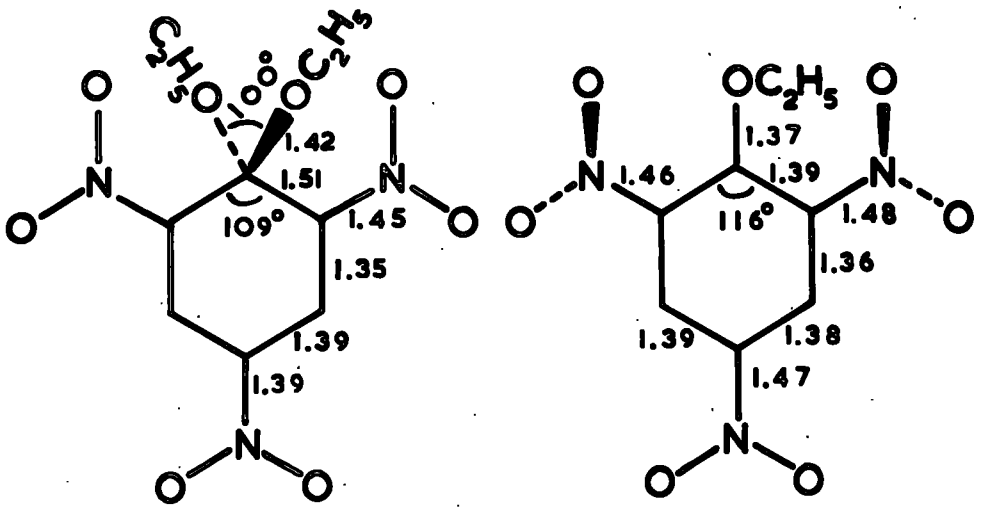
$$\Delta E_a \approx \Delta\Delta E_o^{\dagger} \quad \ldots 5.8$$

Therefore differences in the potential energy of activation may be equated with differences in the Arrenhius energy of activation (see later under benzene and pyridine).

In order to calculate the potential energy surface for a reaction it is necessary to know the geometry of all the species involved. Information regarding the geometry of the transition states is in principle, however, not normally available experimentally for aromatic and heteroaromatic reactions but is theoretically available from direct calculation. Ab initio quantum mechanical treatments of the complex systems involved in nucleophilic aromatic substitutions are, however, not computationally feasible in the forseeable future. The large number of geometic variables make optimisation of geometries, even with semi empirical all valence electron treatments impracticable in terms of computational effort. What is required, therefore, is a good model for the transition state. Now intermediates, known as

sigma complexes or Wheland intermediates, have been isolated[13] for similar reactions to those under consideration (see figure 5.3a). In these intermediates it has been suggested by Wheland[16] that the carbon atom at which substitution occurs has an sp^3 configuration. It is interesting here to observe how the ring geometry changes in trinitrophenetole when it forms the sigma complex with ethoxide ion.

Figures 5.3a[54] and 5.3b[55]



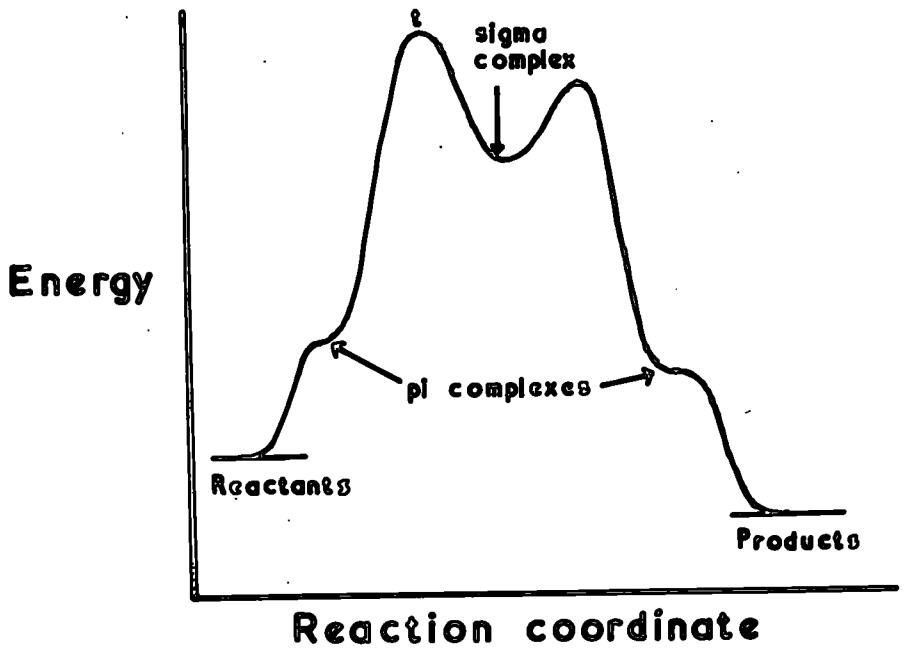
(Distances in ångstroms)

The change for sp^2p to sp^3 configuration for the carbon atom undergoing attack results in a decrease in the pi delocalisation energy of the system.

The general position of the sigma complex on the energy profile is beleived to be as indicated in figure 5.4 below. Pi complexes,

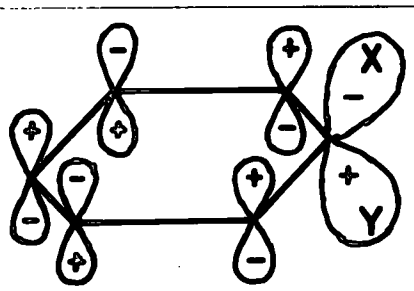
which are known to be formed when aromatic systems are subject to electrophilic attack and which may be formed during nucleophilic attack are represented by small shoulders on the energy diagram.

Figure 5.4



Hammond has suggested[17] that the structure nearest in energy to the transition state will also be closest in structure and this has in fact been shown to be true for bimolecular nucleophilic substitution (SN2) by non-empirical quantum mechanical calculations of cross sections through the potential energy surface[56,57]. Therefore the sigma complex should be a better model for the transition state than either the original reactants or the pi complex.

The sigma complex has in fact been used frequently[52,58,18] when discussing aromatic substitution and will in fact be used in this thesis. However when using it only the change in the localisation energy of the pi electrons is normally considered[18]. This means that the carbon atom at which substitution is taking place is not considered in the calculations and therefore the calculations are unaffected by changes in the attacking species. Also no account is taken of the energy changes in the sigma bond system or in the nuclear repulsion energies. In order to overcome some of these defects other approaches[20,21a,21b] to the problem have been used. These approaches calculate pseudo sigma and pi orbitals from the sigma bonds made by the attacking and leaving groups. Thus if X and Y are the attacking and leaving groups then if for the sigma bonds they make the components are taken out of phase as shown



then their interaction with the pi orbitals of the rest of the system may be calculated. That is a pseudo pi orbital has been constructed and its energy contribution may be calculated. It is therefore possible to calculate a delocalisation pi bond energy for the transition state which includes the attacking species. This still however ignores the contributions of the sigma bond system and the nuclear repulsion energies to the energy of the transition state.

The approach used in this thesis is to calculate the total energy, electronic plus nuclear repulsion for the reactants and the sigma complex respectively. The difference in these energies is then used as a measure of the reactivities of different molecules in the same series and of different sites within the same molecule. An advantage of this approach is that it enables the relative importance of the nuclear repulsion energy compared to the electronic energy in determining reactivities to be seen (tables 5.6 and A2.9). It will also be seen that using this approach that the energy differences as calculated show general agreement with the differences in activation energy as determined experimentally[6,7,59].

Now the calculations are performed for the isolated molecules and the sigma complexes in the gas phase, using conventional geometries based on the original molecules and assuming sp^3 configuration for the carbon atom where substitution is taking place. This is rather a drastic approximation and would be serious if we were attempting to calculate absolute activation energies. However the feature of interest is the interpretation of relative reactivities and hence differences in energy differences.

Solvation Effects

Before comparing the results with experimental observations it is necessary to consider the effects of solvation. In a similar manner to that used in chapter 4, equation 4.8, the term $\Delta\Delta E^{\ddagger}$ in equation 5.4 may be split into two major components and may be expressed as

$$\Delta\Delta E^{\ddagger} = \Delta\Delta E_{g} + \Delta\Delta E_{solvation} \quad \ldots 5.9$$

The term $\Delta\Delta E_{solvation}$ may again be split up in a like manner to that in equations 4.8 and 4.9 and then be written as

$$\Delta\Delta E_{solvation} = \Delta\Delta E_{cav} + \Delta\Delta E_{orient} + \Delta\Delta E_{disp} + \Delta\Delta E_{iso} + \Delta\Delta E_{aniso} \quad \ldots 5.10$$

where the various terms are due to the same causes as those discussed in chapter 4. Once again the terms ΔE_{cav}, ΔE_{orient}, ΔE_{disp} and ΔE_{aniso} are assumed to remain constant within a similar series and their differences in equation 5.10 will be approximately zero. The term $\Delta\Delta E_{iso}$ is calculated from ΔE_{iso} values obtained using the expression 1.5. The results for the perchloropyridine-methoxide sigma complexes (table A2.10) show that for this series $\Delta\Delta E_{iso}$ is small compared to $\Delta\Delta E_{g}$ and therefore $\Delta\Delta E_{iso}$ may be taken as being zero. However when comparing different series it may be necessary to take account of $\Delta\Delta E_{solvation}$ since the various terms in equation 5.10 may not necessarily be very small. Bearing this fact in mind, though, for a similar series of compounds the term $\Delta\Delta E_{solvation}$ in equation 5.9 may be taken as virtually zero. Equation 5.4 may therefore be put as;

$$k_{r_1}/k_{r_2} = \left[f_1/f_2\right] . e^{-\Delta\Delta E_g/RT} \quad \ldots 5.11$$

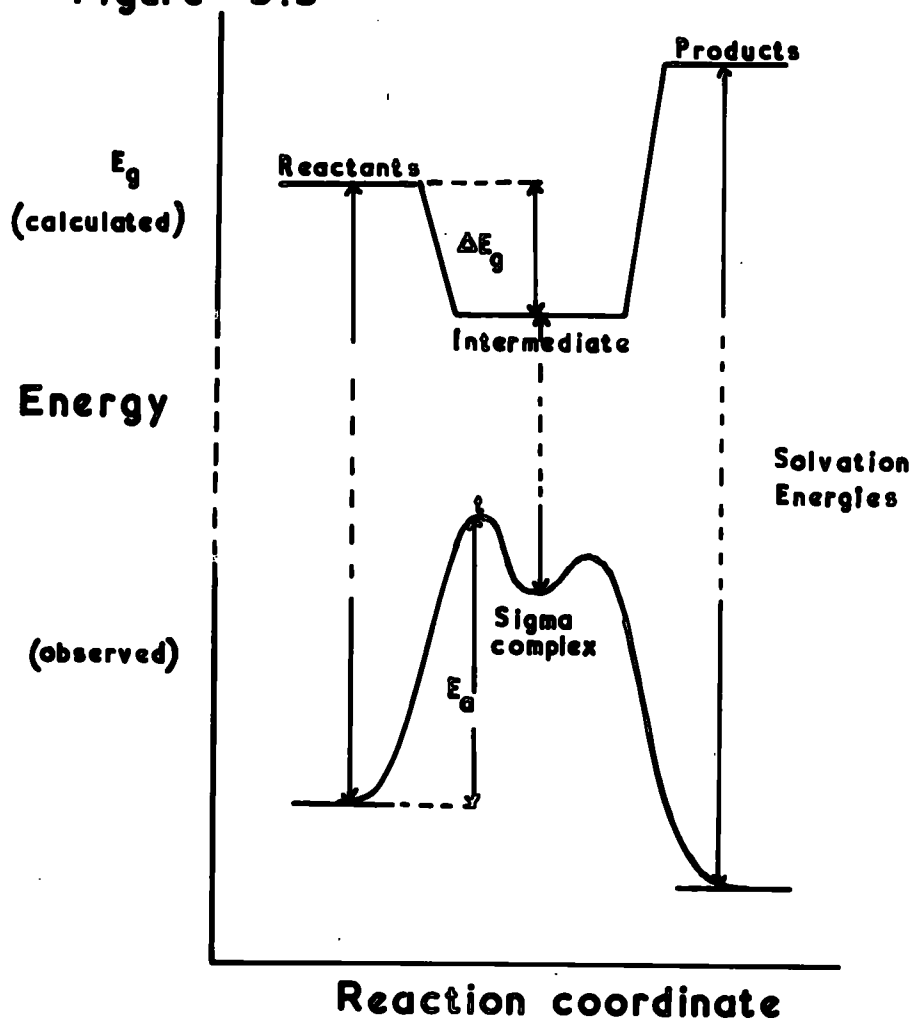
With regard to the term f_1/f_2 the work of J. Burdon and coworkers[6,7] with the fluoro derivatives of benzene and M. Liveris and J. Miller[59]

with the monochloropyridines suggest that this term is of less importance than the term $\Delta\Delta E_g$. Thus for the reactions of perfluorobenzene and monofluorobenzene with methoxide ion[7], at 60°C, the ratio of the preexponential terms is approximately 10^{-2} while the ratio of the exponential terms is approximately e^{-21} or $\sim 10^9$. In the case of the reaction of 4-monochloro and 3-monochloropyridine with methoxide ion at 50°C, the ratio of the preexponential terms is approximately unity while the ratio of the exponential terms is approximately e^{12} or $\sim 10^5$. Therefore there is some justification for using $\Delta\Delta E_g$ as a means of comparing the reactivities of similar series, or of different sites within the same molecule. It may also be used as a means of estimating ΔE_a values (equation 5.8).

Now one effect of ignoring solvation effects is that the potential energy of the reactants is higher than that of the intermediate. Also the energy of the products is higher than both of these. The effect of taking into account the solvation energies is however to invert this situation and to give the observed order in the energies (see figure 5.5 below).

What has been done in this chapter is to express the ΔE_g values of the intermediate and the products relative to the reactants and to take the energies of the reactants as an arbitary zero. Considering what has been said above about solvation energies and illustrated in figure 5.5 when comparing reactivities the intermediate with the largest negative value of ΔE_g will be the most reactive. This is because $\Delta E_{solvation}$ which must be added to each value of ΔE_g will be the same for all members of the series and so its addition will not affect the order of the various ΔE. In the case of the products the most stable thermodynamically will be the one with the smallest value of ΔE_g for similar reasons as those discussed above for the reactivities.

Figure 5.5



Since as discussed earlier the reactions under the conditions employed are irreversible the thermodynamic stability has no effect on the reactivities of the compounds, though it may affect their further reactivities.

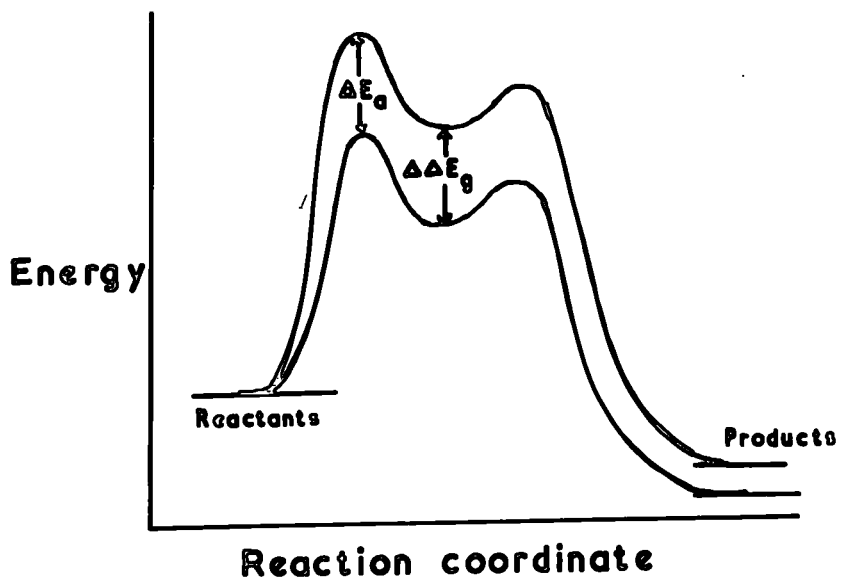
Introduction to discussions of particular compounds

In the following section are tables of ΔE_g for the reaction of the various molecules considered with methoxide ion. These have been calculated from the energy values in tables A2.2, A2.3 and A2.7. For pyridine table 5.4 shows the differences in electronic, nuclear repulsion and total energy for the pyridine derivatives' sigma complexes. Also given are tables showing the electronic charge distributions in the various sigma complexes. Since the distribution of the pi charge in sigma complexes has often been discussed using "resonance" canonicals "pi" charges are also given. There is, though, no longer strict sigma and pi separability in the sigma complexes.

Benzene

Table 5.1(i) indicates that monofluorobenzene is less reactive than perfluorobenzene with $\Delta\Delta E_g$ 135kJ mol^{-1}. This reactivity is in accord with experimental observations[6,7] which also give ΔE_a as 63.5kJ mol^{-1}. This is moderately good agreement considering the approximations involved and the fact that $\Delta\Delta E_g$ refers to the sigma complexes and ΔE_a to the two transition states, see figure 5.6 below

Figure 5.6



That the agreement is not better may be due in part to the possibility that the reaction of monofluorobenzene with methoxide ion may proceed partially via a "benzyne" type intermediate.

Monochlorobenzene, from the values in table 5.1(i), should be more reactive than monofluorobenzene with $\Delta\Delta E_g$ 89.6 kJ mol^{-1}. Now this assumes that $\Delta\Delta E_{solvation}$ may be taken as effectively zero. The calculations for ΔE_{iso} for the chloro and fluoropyridines suggest that this term is likely to have a very similar value for

Table 5.1

Benzene Derivatives

(i) Reactants to intermediate

	P	ΔE_g kJ mol^{-1}	$^{obs}7 E_A$ kJ mol^{-1}
1-fluorobenzene	1	-579.0	157
1-chlorobenzene	1	-668.6	-
Perfluorobenzene	1	-714.3	93.5

(ii) Reactants to products

	O	
1-fluorobenzene	1K	537.1
Perfluorobenzene	1K	560.5

P position of attack

O orientation and position of methoxy group added

both chloro and fluoro compounds of the type being considered (see table A2.10). The other terms that make up $\Delta E_{solvation}$ (see equations 5.10, 4.8 and 4.9) are also likely to have similar values for both series, for example ΔE_{aniso} is unlikely to be different since there is little hydrogen bonding in either the chloro or the fluorobenzenes. Assuming therefore that $\Delta E_{solvation}$ is very similar for both chloro and fluorobenzenes then $\Delta\Delta E_{solvation}$ will be very small and it is then possible to make an estimate for E_a for the reaction of chlorobenzene with methoxide ion as 67 kJ mol^{-1}. However as in the case of monofluorobenzene the reaction may proceed to some extent via a "benzyne" intermediate so this estimate of E_a can only be a tentative one.

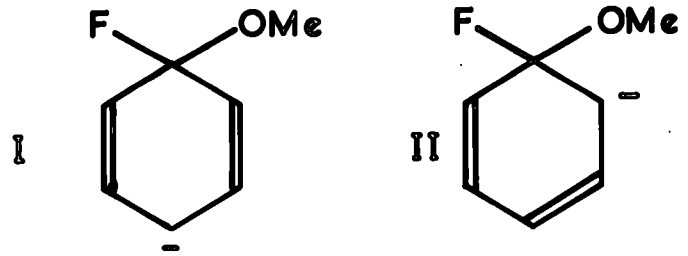
It is evident from table 5.1(ii) that the relative reactivities of fluoro- and perfluorobenzene do not follow the relative energies of the products.

Electronic charge distributions

Table 5.2 gives the electronic charge distributions in the sigma complexes for the chloro and fluorobenzenes dealt with. It can be seen that the negative charge introduced by the methoxide ion is distributed principally on the carbon atoms ortho and para to the position of substitution. It will also be seen that the methoxy group and the halogen that is leaving bear some of the charge and that the chlorine bears a larger charge than the fluorine in the mono-halo derivatives. In the perfluoro compound the non-substituting fluorines bear most of the charge introduced.

The "pi" charges give some justification to the idea, when resonance canonicals are considered, that the para quinoid structure I

is more important that the ortho II, i.e.



However the para "pi" charge is not much larger than the ortho charge and the total para charge is in fact smaller than the total ortho charge in monofluorobenzene.

Table 5.2

Charges on atoms in Wheland intermediates formed by the attack be methoxide ion on fluoro, perfluoro and chlorobenzene

	1-fluoro	1-chloro	perfluoro
C1	0.448	0.369	0.397
C2	-0.241	-0.176	-0.062
C3	0.077	0.061	0.202
C4	-0.208	-0.180	-0.062
C5	0.077	0.061	0.202
C6	-0.241	-0.176	-0.062
H2	-0.039	-0.032	-0.216 F2
H3	-0.073	-0.063	-0.215 F3
H4	-0.067	-0.060	-0.225 F4
H5	-0.073	-0.063	-0.215 F5
H6	-0.039	-0.032	-0.216 F6
F	-0.323 Cl	-0.450 F	-0.287
O	-0.323	-0.290	-0.291
C	0.146	0.141	0.140
H1	-0.018	-0.017	-0.024
H2	-0.052	-0.047	-0.032
H3	-0.052	-0.047	-0.032
"pi" charges on ring atoms			
C1	-	-	-
C2	-0.337	-0.278	-0.357
C3	0.085	0.062	0.038
C4	-0.357	-0.306	-0.390
C5	0.085	0.062	0.038
C6	-0.337	-0.278	-0.357

Pyridine

The results in table 5.3(i) suggest that, for the monofluoropyridines that fluorine at position 4 is more readily replaced than that at position 2 ($\Delta\Delta E_g$ 6.3 kJ mol^{-1}) and that fluorine at position 3 is very difficult to replace compared to that at position 4 ($\Delta\Delta E_g$ 96.3 kJ mol^{-1}). For perfluoropyridine it is seen, again, that fluorine at position 4 should be replaced more readily than that at position 2 ($\Delta\Delta E_g$ 9 kJ mol^{-1}) and that fluorine at position 3 will also be very difficult to replace compared to that at position 4 ($\Delta\Delta E_g$ 128.2 kJ mol^{-1}). Compared to monofluoropyridine, perfluoropyridine should also be more reactive, for substitution at position 4 in each case $\Delta\Delta E_g$ is 133.6 kJ mol^{-1}. The results for perfluoropyridine are in agreement with experimental observations[1,47], it having been observed that fluorine in position 4 is the most readily displaced by methoxide ion. The reaction is also reported to be very rapid at 0°C which suggests for perfluoropyridine that E_a is small. When further substitution takes place in 4-methoxyperfluoropyridine then the value of $\Delta\Delta E_g$ (80 kJ mol^{-1}) suggests that 2,4-dimethoxyperfluoropyridine will be formed in preference to the 3,4-dimethoxy compound. The introduction of the methoxy group in position 4 should also make the derivative less reactive than the original perfluoropyridine with $\Delta\Delta E_g$ 30.3 kJ mol^{-1}. This again agrees with the experimental observations[1,47]. There is also no mention in the experimental reports of fluorine at positions 3 and 5 being replaced in the perfluoro compounds.

The results for the chloropyridines show a similar pattern to those for the fluoro derivatives. In the case of the monochloropyridines there is moderate agreement between the calculated values

Table 5.3

Pyridine Derivatives

(i) Reactants to intermediate	P	ΔE_g kJ mol^{-1}	E_A obs[59] kJ mol^{-1}
2-fluoropyridine	2	-644.6	
3- "	3	-564.6	
4- "	4	-650.9	
2-chloropyridine	2	-729.8	121.5
3-	3	-651.4	137.5
4-	4	-737.1	105.5
Perfluoropyridine	2	-775.5	
	3	-656.3	
	4	-784.5	
4K-methoxyperfluoro-	2	-753.7	
	3	-673.7	
Perchloropyridine	2	-905.6	
	3	-854.7	
	4	-921.4	

(ii) Reactants to products	O	
2-fluoropyridine	2K	509.9
	2A	540.1
3-	3K	539.3
	3A	529.2
4-	4K	531.7
Perfluoropyridine	2K	496.9
	2A	567.3
	3K	565.2
	3A	541.5
	4K	539.0

P position of attack

O orientation and position of methoxy group added

of $\Delta\Delta E_g$ and the values of ΔE_a calculated from experimental data[40]; i.e. taking 4-chloropyridine as the zero

	$\Delta\Delta E_g$ (kJ mol^{-1})	ΔE_a (kJ mol^{-1})
2-chloropyridine	7.3	16
3-chloropyridine	85.7	32
4-chloropyridine	0	0

As was discussed in the case of the monohalobenzenes there is the possibility that the reactions of the monochloropyridines proceed partially via a "pyridyne" type of intermediate. This is more likely to be so for the 3-chloro compound than for the other two[15]. Perchloropyridine, like perfluoropyridine, should according to the results in table 5.3(i) be more reactive than the monochloro derivatives since $\Delta\Delta E_g$ is approximately 190 kJ mol^{-1} for all positions of substitution. The relative reactivities of the three positions, (2, 3 and 4) are predicted to be similar to those in perfluoropyridine. Thus position 4 is the most reactive, then position 2 and least reactive is position 3, the $\Delta\Delta E_g$ values being 15.8 kJ mol^{-1} between positions 2 and 4 and 66.7 kJ mol^{-1} between positions 3 and 4. These figures are interesting because they suggest that compared to the perfluoro compound position 2 is less reactive relative to position 4 and position 3 more reactive relative to position 4 in the perchloro compound. This does conflict somewhat with the experimental results where it has been found that perfluoropyridine gives exclusively the 4- methoxy derivative[1,47] though nucleophiles other than methoxide ion may give some 2- product. Perchloropyridine, on the other hand, with methoxide ion and with other nucleophiles gives some 2- product as well as the 4- product[4,5,60].

Compared with the results for fluorobenzene given in table 5.1 the activating effect of a ring nitrogen in place of a CH group ortho or para to fluorine is clearly evident. This activating influence of the nitrogen is also apparent in going from perfluorobenzene to perfluoropyridine.

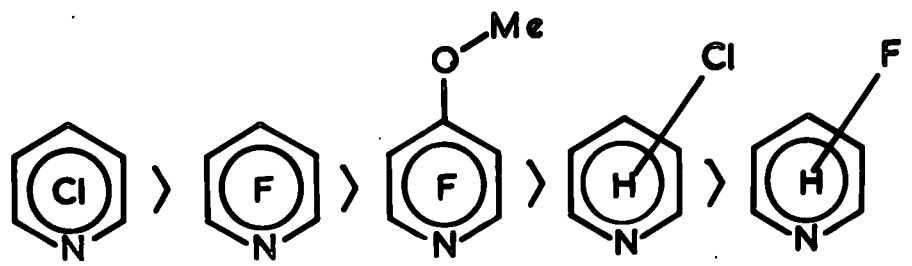
When the results for benzene were discussed use was made of the values of $\Delta\Delta E_g$ and E_a to suggest values of E_a where these were not available from experimental data. If this is done using the values of E_a for the monochloropyridines (table 5.3(i)) and the $\Delta\Delta E_g$ values between this series and the perchloro series then a negative value for E_a would be obtained. This indicates that it is not possible to compare these two series without taking into account solvation energy differences. It may also be noted that the CNDO II SCF MO treatments of molecules involving second row atoms are less adequate than for first row atoms. With the large number of approximations involved it is therefore more realistic to consider relative reactivities of fluoro and chloro substituted compound separately.

A consideration of the electronic charge distributions in tables 5.6 and 5.8 suggest that hydrogen bonding may be different for the two series and this will affect the values of the term ΔE_{aniso} (see equations 5.10, 4.8 and 4.9). In a like manner there is likely to be a difference in the extent of hydrogen bonding in the fluoro and the chloro series. Thus a simple consideration of the ΔE_g values in table 5.3 would suggest that perchloropyridine is more reactive than perfluoropyridine whereas the experimental observations indicate the reverse. When comparing fluoropyridines with pyridines containing other halogens it is interesting to note that when 4-bromoperfluoropyridine reacts with methoxide ion[61] the bromine is not displaced

but substitution takes place at positions 2 and 6.

Section (ii) of table 5.3 shows that were the reactions dealt with above subject to thermodynamic control the reactivities of the monofluoropyridines would be in a different order to that suggested in section (i). In the case of perfluoropyridine the monomethoxy derivative formed, in the greatest amount, would be 2-methoxyperfluoropyridine. This would be quite at varience with the results suggested by section (i) and with the experimental observations[1,47].

The reactivities calculated are summarised below;



Subs. at	4	4	2	4	4	
$\Delta\Delta E_g$	-136.9	(0)	30.8	47.4	133.6	kJ mol^{-1}

Substitution by methoxide ion is predicted to occur preferentially at position 4, then at position 2, while position 3 is most unreactive.

Nuclear Repulsion and Electronic Energies

Table 5.4 shows the relative importance of the nuclear repulsion and electronic energies in determining ΔE_g. It is seen that just to use the electronic energy would mean that position 4 would be the least reactive in the monohalo pyridines. On the other hand this order of reactivities would be reversed in the perhalo pyridines, with position 3 always being intermediate in reactivity between positions 2 and 4. A consideration of just the nuclear repulsion energies would reverse these effects with position 3 being again intermediate in its' reactivity.

Another effect of just using either the nuclear repulsion or electronic energies separately would be that the calculated energy differences, $\Delta\Delta E_g$, would be in the mega joule range which would be far larger than the experimental observations[6,7,59] of ΔE_a. When the sum of the nuclear repulsion and the electronic energies is used then the results obtained are consistent with the experimental observations. Also the energy differences are of the same order as those calculated from experimental data.

Table 5.4

Changes in Nuclear Repulsion, Electronic and Total Energies for the Wheland Intermediate formed by the reaction of Methoxide ion with some of the fluoro and chloro derivatives of Pyridine, taking the 3- position as zero. Energy differences given in MJ mol^{-1}

		Δ Nuclear Repulsion	ΔElectronic	ΔTotal
2-fluoropyridine		2.157	-2.267	-0.110
3-		0	0	0
4-		-1.106	1.008	-0.098
Perfluoropyridine	2	-6.944	6.825	-0.119
	3	0	0	0
	4	1.435	-1.563	-0.128
4K-methoxyperfluoro	2	-14.246	14.166	-0.080
	3	0	0	0
2-chloropyridine		1.945	-2.027	-0.082
3-		0	0	0
4-		-0.853	0.768	-0.085
Perchloropyridine	2	-6.744	6.693	-0.051
	3	0	0	0
	4	1.364	-1.431	-0.067

Electronic Charge Distributions

(Tables 5.5 - 5.9)

These tables show that when substitution occurs at positions 2 or 4 the nitrogen is able to bear a larger portion of the negative charge than when substitution takes place at position 3. The halogen and the methoxy group involved in the substitution bear a moderate portion of the negative charge, the proportion falling in the perhalo compounds compared to the monohalo compounds. The chlorine involved in the substitution is also seen to bear a larger negative charge than a fluorine atom likewise involved. It is also noticeable that the nitrogen in the fluoro series tends to bear a larger negative charge than the nitrogen in the chloro series and that this is more pronounced in the perhalo compounds.

Although the para quinoid structure is often regarded as more important than the ortho structure[52] this does not appear to be so when the charge distribution is considered. Thus substitution occurs more readily at position 4 than at position 2. But when substitution occurs at position 2 the nitrogen bears a slightly larger negative charge than when substitution occurs at position 4, except in the monofluoropyridines. The "pi" charges calculated agree with the charge distributions that would be expected from using resonance canonicals. But even these "pi" charges do not necessarily support the idea that in the para quinoid structure the nitrogen bears a larger charge than in the ortho quinoid structure. The "pi" charges are perhaps most useful when considering the perhalo compounds since as already stated they do agree with the distribution expected whereas this is not easy to see if the total charges on the atoms is considered.

Table 5.5

Charges on atoms in Wheland intermediates formed by the attack of methoxide ion on the three monofluoro-pyridines

	2-fluoro	3-fluoro	4-fluoro
N1	-0.398	-0.110	-0.404
C2	0.514	-0.142	0.148
C3	-0.235	0.426	-0.241
C4	0.074	-0.243	0.455
C5	-0.226	0.049	-0.241
C6	0.158	-0.114	0.148
H2	-	-0.054	-0.090
H3	-0.034	-	-0.037
H4	-0.069	-0.040	-
H5	-0.060	-0.068	-0.037
H6	-0.090	-0.083	-0.090
F	-0.330	-0.324	-0.320
O	-0.327	-0.325	-0.317
C	0.148	0.146	0.145
H1	-0.020	-0.015	-0.015
H2	-0.056	-0.051	-0.051
H3	-0.051	-0.052	-0.051
"pi" charges on ring atoms			
N1	-0.449	0.035	-0.460
C2	-	-0.286	0.104
C3	-0.284	-	-0.313
C4	0.082	-0.341	-
C5	-0.334	0.065	-0.313
C6	0.123	-0.324	0.104

Table 5.6

Charges on atoms in Wheland intermediates formed by the attack of methoxide ion on the three monochloropyridines

	2-chloro	3-chloro	4-chloro
N1	-0.340	-0.123	-0.338
C2	0.438	-0.074	0.149
C3	-0.176	0.346	-0.211
C4	0.065	-0.174	0.362
C5	-0.201	0.033	-0.211
C6	0.151	-0.086	0.149
H2	-	-0.045	-0.082
H3	-0.027	-	-0.029
H4	-0.060	-0.032	-
H5	-0.054	-0.057	-0.029
H6	-0.079	-0.075	-0.082
Cl	-0.454	-0.455	-0.424
O	-0.294	-0.291	-0.291
C	0.143	0.140	0.142
H1	-0.019	-0.016	-0.013
H2	-0.050	-0.046	-0.045
H3	-0.046	-0.046	-0.045
"pi" charges on ring atoms			
N1	-0.403	0.009	-0.402
C2	-	-0.224	0.098
C3	-0.239	-	-0.287
C4	0.071	-0.278	-
C5	-0.298	0.046	-0.287
C6	0.112	-0.274	0.098

Table 5.7

Charges on atoms in the Wheland intermediates formed from perfluoropyridine

	Position of substitution		
	2	3	4
N1	-0.446	-0.184	-0.432
C2	0.487	0.091	0.297
C3	-0.055	0.380	-0.064
C4	0.215	-0.054	0.409
C5	-0.060	0.172	-0.064
C6	0.323	0.052	0.297
F2	-	-0.233	-0.240
F3	-0.216	-	-0.221
F4	-0.217	-0.220	-
F5	-0.228	-0.219	-0.221
F6	-0.237	-0.247	-0.240
F	-0.302	-0.292	-0.286
O	-0.306	-0.295	-0.287
C	0.144	0.139	0.139
H1	-0.024	-0.020	-0.020
H2	-0.039	-0.033	-0.034
H3	-0.038	-0.035	-0.034
"pi" charges on ring atoms			
N1	-0.527	-0.059	-0.517
C2	-	-0.244	0.082
C3	-0.294	-	-0.340
C4	0.042	-0.363	-
C5	-0.363	0.010	-0.340
C6	0.123	-0.328	0.082

Table 5.8

Charges on atoms in the Wheland intermediates formed by the attack of methoxide ion on perchloropyridine

	Position of substitution		
	2	3	4
N1	-0.318	-0.076	-0.318
C2	0.416	0.044	0.240
C3	-0.047	0.334	-0.052
C4	0.188	-0.035	0.359
C5	-0.055	0.160	-0.052
C6	0.252	0.027	0.240
C12	-	-0.235	-0.231
C13	-0.213	-	-0.220
C14	-0.195	-0.225	-
C15	-0.240	-0.196	-0.220
C16	-0.224	-0.269	-0.231
Cl	-0.357	-0.336	-0.324
O	-0.274	-0.263	-0.259
C	0.139	0.137	0.137
H1	-0.016	-0.014	-0.015
H2	-0.029	-0.026	-0.027
H3	-0.030	-0.028	-0.027
"pi" charges on ring atoms			
N1	-0.391	0.033	-0.424
C2	-	-0.190	0.105
C3	-0.201	-	-0.230
C4	0.092	-0.242	-
C5	-0.271	0.079	-0.230
C6	0.127	-0.261	0.105

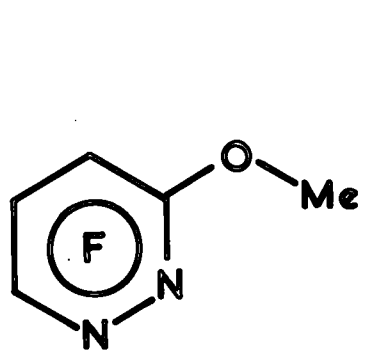
Table 5.9

Charges on atoms in Wheland intermediates formed by the attack of methoxide ion on 4K-methoxyperfluoropyridine

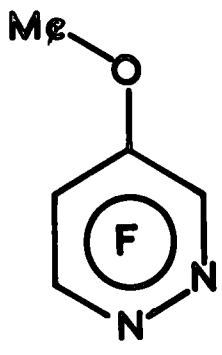
	Position of attack	
	2	3
N1	-0.432	-0.168
C2	0.488	0.079
C3	-0.061	0.383
C4	0.159	-0.112
C5	-0.063	0.182
C6	0.320	0.042
F2	-	-0.236
F3	-0.225	-
F5	-0.232	-0.223
F6	-0.239	-0.250
O	-0.221	-0.214
C	0.102	0.110
H1	-0.024	-0.030
H2	-0.045	-0.050
H3	0.043	0.025
F	-0.306	-0.296
O	-0.308	-0.302
C	0.144	0.138
H1	-0.025	-0.018
H2	-0.042	-0.035
H3	-0.039	-0.035
"pi" charges on ring atoms		
N1	-0.524	-0.041
C2	-	-0.257
C3	-0.316	-
C4	0.058	-0.365
C5	-0.370	0.017
C6	0.129	-0.335

Pyridazine

The results in table 5.10 suggest that for perfluoropyridazine monosubstitution by methoxide ion should occur preferentially at position 4 rather than at position 3 ($\Delta\Delta E_g$ 17.1 kJ mol^{-1}). When further substitution is considered then the orientation of the original methoxy group must be considered as well as its position. Now the calculations in table A2.3 show that, in the original molecule, where the methoxy group is adjacent to the nitrogen the energy is lowest when the methoxy group is orientated as shown in I below. For other positions the energy is lowest when the methoxy group is directed away from the nitrogen as shown in II below.

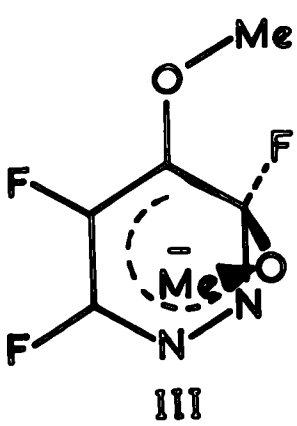


I

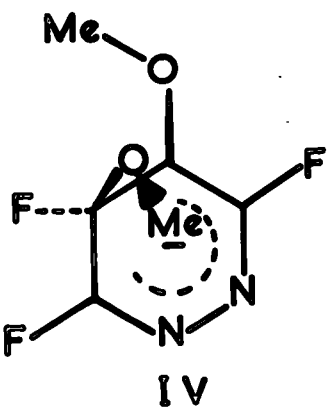


II

In the intermediates, for I the energy is lowest with the same orientation but for II the energy is lowest with the methoxy group orientated towards the position of substitution, e.g.



III



IV

Table 5.10

Pyridazine Derivatives

(i) Reactants to intermediate

	P	ΔE_g kJ mol^{-1}
Perfluoropyridazine	3	-726.0
	4	-743.1
3K-methoxyperfluoro	4	-723.3
	5	-723.5
	6	-704.8
4K-methoxyperfluoro	3	-755.1
	5	-720.3
	6	-549.7
4A-methoxyperfluoro	3*	-735.2
	5	-754.0
	6	-545.6

* The orientation of the methoxy group is 4K in the intermediate since this is the position of lowest energy, see tables A2.3 and A2.7

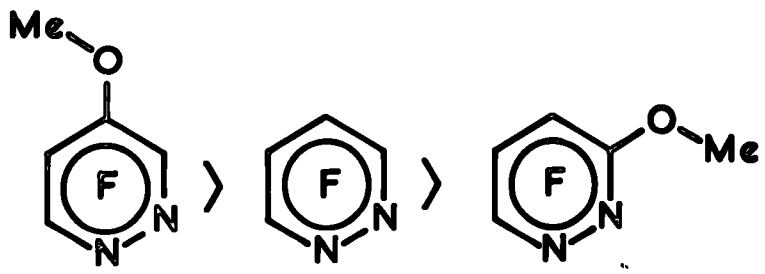
(ii) Reactants to products

	O	
Perfluoropyridazine	3K	496.6
	3A	587.2
	4K	549.9
	4A	530.1
3K-methoxyperfluoro	3K4K	542.9
	3K5K	535.0
	3K6K	589.7
4K-methoxyperfluoro	3K4K	489.5
	4K5K	527.6
	4K6K	589.4

P position of attack

O orientation and position of methoxy group added

Therefore taking this effect into account for 3-methoxyperfluoropyridazine the results show that further substitution should occur at positions 4 and 5 ($\Delta\Delta E_g$ 0.2 kJ mol^{-1}). In the case of 4-methoxyperfluoropyridazine, after allowing for orientation effects the results show that further substitution should occur at position 5. These results, for monosubstitution and disubstitution, agree with the experimental observations[62]. It is seen that the 3-monomethoxy compound is less reactive than the parent compound while the 4-monomethoxy is more reactive. This is summarised briefly below



Subs. at	5	4	4 and 5	
$\Delta\Delta E_g$	-11	(0)	20	kJ mol^{-1}

Position 6 is least reactive especially in the 4-methoxy derivative where $\Delta\Delta E_g$ is 200 kJ mol^{-1} compared to position 5.

Section (ii) of table 5.10 shows the energy difference between the reactants and the products. It can be seen that if the reactions were thermodynamically controlled different results would be obtained that would not agree with the results obtained by experiment[62].

Electronic Charge Distributions

(Tables 5.11 - 5.14)

These show many of the features of the perfluoropyridines with the additional effect of two nitrogens. The two nitrogens are ortho to each other and one of them will always be either ortho or para to the position of substitution and the other will always be in the meta position. It is seen that the nitrogen lying ortho/para bears a large negative charge while the meta nitrogen bears only a small negative charge. Due to the electron withdrawing effect of the fluorines it is not easy to see where the negative charge introduced by the methoxide ion is distributed, the majority of the ring carbons being in fact positive. It is here that the "pi" charges are useful since they agree with the prediction made using simple resonance ideas that the charge is distributed on the atoms lying ortho and para to the position of substitution. As in the case of pyridine the fluorine and the methoxy group involved in the substitution bear a moderate proportion of the charge introduced. It is also noticeable that the carbon atom at which substitution occurs bears a comparatively large positive charge. There does not appear to be any simple connection between the charges on atoms ortho and para to the position of substitution and the position at which substitution takes place. It does seem though that substitution takes place at positions para to a nitrogen in preference to other positions. Compared to perfluoropyridine it is seen that the negative charge on a para nitrogen is less in perfluoropyridazine.

Table 5.11

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with perfluoropyridazine

	Position of substitution	
	3	4
N1	-0.071	-0.341
N2	-0.357	-0.107
C3	0.464	0.095
C4	-0.010	0.386
C5	0.174	-0.073
C6	0.066	0.275
F3	-	-0.239
F4	-0.216	-
F5	-0.220	-0.226
F6	-0.251	-0.245
F	-0.308	-0.288
O	-0.310	-0.288
C	0.143	0.138
H1	-0.021	-0.016
H2	-0.042	-0.035
H3	-0.042	-0.038
"pi" charges on ring atoms		
N1	0.047	-0.491
N2	-0.518	-0.016
C3	-	-0.203
C4	-0.230	-
C5	0.013	-0.366
C6	-0.281	0.086

Table 5.12

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 3K-methoxyperfluoropyridazine

	4	5	6N1
N1	-0.326	-0.092	-0.348
N2	-0.087	-0.322	-0.058
C3	0.026	0.230	0.006
C4	0.390	-0.078	0.181
C5	-0.089	0.379	-0.021
C6	0.280	0.074	0.465
F4	-	-0.228	-0.221
F5	-0.226	-	-0.217
F6	-0.247	-0.242	-
O	-0.229	-0.240	-0.239
C	0.134	0.133	0.133
H1	-0.034	-0.033	-0.036
H2	-0.044	-0.045	-0.046
H3	-0.016	-0.007	-0.017
F	-0.289	-0.288	-0.309
O	-0.294	-0.292	-0.310
C	0.139	0.139	0.143
H1	-0.015	-0.015	-0.021
H2	-0.035	-0.038	-0.043
H3	-0.039	-0.035	-0.043
"pi" charges on ring atoms			
N1	-0.482	0.004	-0.506
N2	-0.000	-0.487	0.062
C3	-0.222	0.091	-0.300
C4	-	-0.373	0.019
C5	-0.375	-	-0.245
C6	0.091	-0.223	-

Table 5.13

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 4K-methoxyperfluoropyridazine

	Position of substitution		
	3	5	6
N1	-0.063	-0.089	-0.348
N2	-0.351	-0.325	-0.064
C3	0.470	0.279	0.055
C4	-0.069	-0.135	0.117
C5	0.178	0.389	-0.010
C6	0.054	0.073	0.463
F3	-	-0.249	-0.257
F5	-0.223	-	-0.220
F6	-0.253	-0.241	-
4K			
O	-0.214	-0.215	-0.222
C	0.109	0.102	0.099
H1	-0.028	-0.036	-0.028
H2	-0.050	-0.056	-0.050
H3	0.030	0.032	0.047
F	-0.313	-0.289	-0.309
O	-0.316	-0.293	-0.311
C	0.143	0.139	0.134
H1	-0.019	-0.015	-0.021
H2	-0.044	-0.038	-0.023
H3	-0.042	-0.036	-0.051
"pi" charges for ring atoms			
N1	0.058	-0.000	-0.513
N2	-0.513	-0.484	0.065
C3	-	0.083	-0.304
C4	-0.234	-0.366	0.023
C5	0.014	-	-0.242
C6	-0.293	-0.221	-

Table 5.14

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 4A-methoxyperfluoropyridazine

	Position of substitution		
	3	5	6
N1	-0.063	-0.088	-0.348
N2	-0.349	-0.325	-0.064
C3	0.473	0.287	0.063
C4	-0.065	-0.137	0.121
C5	0.170	0.386	-0.023
C6	0.054	0.072	0.464
F3	-	-0.249	-0.256
F5	-0.224	-	-0.224
F6	-0.254	-0.242	-
4A			
O	-0.209	-0.217	-0.222
C	0.108	0.113	0.106
H1	-0.031	-0.033	-0.026
H2	-0.048	-0.053	-0.046
H3	0.025	0.019	0.038
F	-0.310	-0.291	-0.311
O	-0.312	-0.296	-0.312
C	0.144	0.139	0.133
H1	-0.021	-0.013	-0.021
H2	-0.044	-0.036	-0.023
H3	-0.043	-0.036	-0.052
"pi" charges on ring atoms			
N1	0.059	0.001	-0.511
N2	-0.513	-0.484	0.062
C3	-	0.090	-0.293
C4	-0.230	-0.370	0.029
C5	0.008	-	-0.257
C6	-0.294	-0.222	-

Pyrimidine

Table 5.4(i) shows that for perfluoropyrimidine substitution should occur preferentially at position 4, position 2 being less reactive, $\Delta\Delta E_g$ 13 kJ mol^{-1}. Position 5 appears to be singularly unreactive, $\Delta\Delta E_g \rangle$ 200 kJ mol^{-1} and this lack of reactivity for position 5 is also observed in the monomethoxyperfluoro derivatives. When the monomethoxyperfluoro derivatives are considered the orientation of the methoxy group has to be allowed for, as in the case of pyridazine. It appears (see table A2.3) that the same "rules" that were applied in the case of perfluoropyridazine may again be used. This being so the results for the monomethoxyperfluoropyrimidine are as given below.

In 2-methoxyperfluoropyrimidine the fluorine at position 4 is most readily replaced, while the fluorine at position 5, as noted above, is very unreactive with $\Delta\Delta E_g \rangle$ 200 kJ mol^{-1}. In the 4-methoxyperfluoro compound the fluorine at position 6 is most readily replaced, while that in position 2 is less readily replaced, $\Delta\Delta E_g$ 13 kJ mol^{-1}, and position 5 again most unreactive, $\Delta\Delta E_g \rangle$ 200 kJ mol^{-1}. When 5-methoxyperfluoropyridazine is considered then again the fluorine at position 4 (6) is more readily replaced and that at position 2 less readily, in fact even less than usual with $\Delta\Delta E_g$ 67 kJ mol^{-1}. The results given above for perfluoropyrimidine and its 4-methoxyperfluoro derivative are in agreement with experimental observations[63]. It has been stated though that the reaction of perfluoropyrimidine with other alkoxide ions may give different orientations for the product[64]. In the cases of the 2- and 5-methoxy-perfluoro derivatives the experimental data is not yet available and the calculations may be used as a prediction of the results.

Table 5.15

Pyrimidine Derivatives

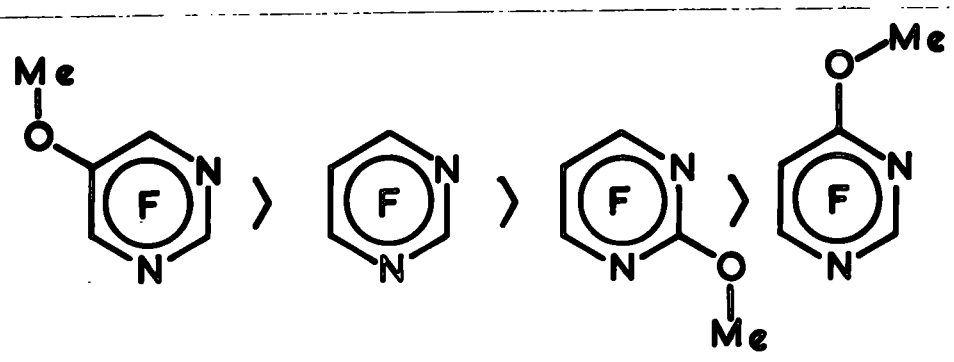
	P	ΔE_g kJ mol^{-1}
(i) Reactants to intermediate		
Perfluoropyrimidine	2	-789.7
	4	-802.7
	5	-578.0
2K-methoxyperfluoro	4	-779.6
	5	-554.8
4K-methoxyperfluoro	2	-765.2
	5	-554.3
	6	-778.2
5K-methoxyperfluoro	2	-768.4
	4	-835.1
(ii) Reactants to products		
	O	
Perfluoropyrimidine	2K	513.5
	4K	500.1
	4A	590.2
	5K	560.5
2K-methoxyperfluoro	2K4K	503.1
	2K5K	562.7
4K-methoxyperfluoro	2K4K	516,5
	4K5K	555.4
	4K6K	593.7
5K-methoxyperfluoro	2K5K	515.9
	4K5K	495.2

P position of attack

O orientation and position of methoxy group added

Section (ii) gives the energy differences between the reactants and the products. It is seen that if the reactions were thermodynamically controlled very similar results are obtained as when kinetic control is assumed (see above). However since the other heterocycles considered only give consistent results if kinetic control is assumed the same assumption will be made for perfluoropyrimidine and its derivatives.

The results obtained are then that substitution occurs most readily at position 4, or the equivalent position 6, and then at position 2 with fluorine at position 5 being very difficult to replace. Substitution is therefore occurring preferentially at carbon atoms ortho and para to the two nitrogens, then at the carbon that is ortho to both nitrogens, with no substitution at the carbon that is meta to the nitrogens (cf pyridine and pyridazine). The introduction of a methoxy group at positions 2 and 4 appears to lower the reactivity (of 4-methoxyperfluoropyridine and 3-methoxyperfluoropyridazine), while at position 5 it increases the reactivity (cf 4-methoxyperfluoropyridazine). This is shown briefly below.



Subs. at	4(6)	4(6)	4(6)	6(4')
$\Delta\Delta E_g$	-33	(0)	23	24 kJ mol^{-1}

Electronic Charge Distribution

(tables 5.16 - 5.19)

In pyrimidine carbon, C2 is ortho to the two nitrogens, carbons C4 and C6 are ortho to one and para to the other nitrogen and carbon C5 is meta to both nitrogens. When substitution occurs at carbons C2, C4 or C6 it is seen that both the nitrogens bear large negative charges. A para nitrogen, with substitution taking place at either C4 or C6, does not bear a larger negative charge than the ortho nitrogen, in fact the reverse is true (cf pyridine and pyridazine). When substitution takes place at C5, meta to the two nitrogens, then the nitrogens bear much smaller negative charges. Apart from this effect there is no obvious relation between the charges on the nitrogens and the most probable position of substitution. The charges on the nitrogens are much the same as those on the nitrogen in perfluoropyridine as compared to those on the nitrogens in perfluoropyridazine, which tend to be smaller.

Simple resonance ideas would suppose that the negative charge introduced is distributed on the atoms ortho and para to the position of substitution. This is more clearly seen when the "pi" charges are considered. It is interesting to note here that substitution at position 5 does not produce much change in the charge on the nitrogens as compared to the original molecule (appendix 3).

When the charges on the ring atoms, other than nitrogen, are considered it is seen that the carbon at which substitution is taking place bears a large positive charge. Also this charge does not change appreciably when the same position of substitution is considered in different derivatives. In fact generally speaking when the same

position of substitution is considered the charges, on the different atoms in the molecules, show only minor changes with each other regardless which derivative is considered. The exception to this is the carbon atom to which a methoxy group is attached in a methoxy derivative becomes less positive than when a fluorine is attached.

Table 5.16

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with perfluoropyrimidine

	Position of substitution		
	2	4	5
N1	-0.424	-0.419	-0.209
N3	-0.424	-0.443	-0.209
C2	0.602	0.444	0.197
C4	0.342	0.502	0.091
C5	-0.103	-0.085	0.357
C6	0.342	0.312	0.091
F2	-	-0.267	-0.273
F4	-0.244	-	-0.243
F5	-0.223	-0.217	-
F6	-0.244	-0.250	-0.243
F	-0.327	-0.307	-0.300
O	-0.325	-0.310	-0.302
C	0.147	0.144	0.138
H1	-0.029	-0.022	-0.020
H2	-0.046	-0.040	-0.037
H3	-0.046	-0.040	-0.037
"pi" charges on ring atoms			
N1	-0.458	-0.477	-0.087
C2	-	0.179	-0.237
N3	-0.458	-0.488	-0.087
C4	0.145	-	-0.258
C5	-0.364	-0.301	-
C6	0.145	0.078	-0.258

Table 5.17

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 2K-methoxyperfluoropyrimidine

	Position of substitution	
	4	5
N1	-0.420	-0.209
N3	-0.437	-0.203
C2	0.350	0.149
C4	0.501	0.091
C5	-0.086	0.358
C6	0.309	0.091
F4	-	-0.244
F5	-0.219	-
F6	-0.252	-0.245
2K		
O	-0.268	-0.264
C	0.135	0.135
H1	-0.032	-0.037
H2	-0.044	-0.048
H3	-0.033	-0.014
F	-0.308	-0.301
O	-0.311	-0.302
C	0.144	0.138
H1	-0.022	-0.020
H2	-0.041	-0.038
H3	-0.041	-0.038
"pi" charges on ring atoms		
N1	-0.477	-0.087
C2	0.178	-0.240
N3	-0.489	-0.087
C4	-	-0.258
C5	-0.303	-
C6	0.080	-0.255

Table 5.18

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 4K-methoxyperfluoropyrimidine

	Position of substitution		
	2	5	6
N1	-0.425	-0.209	-0.445
N3	-0.423	-0.211	-0.419
C2	0.601	0.196	0.441
C4	0.290	0.045	0.262
C5	-0.095	0.367	-0.077
C6	0.340	0.088	0.501
F2	-	-0.275	-0.270
F5	-0.227	-	-0.221
F6	-0.246	-0.244	-
4K			
O	-0.250	-0.228	-0.247
C	0.135	0.133	0.134
H1	-0.028	-0.036	-0.032
H2	-0.042	-0.046	-0.044
H3	0.003	-0.015	-0.005
F	-0.330	-0.303	-0.308
O	-0.327	-0.304	-0.311
C	0.147	0.138	0.144
H1	-0.029	-0.020	-0.022
H2	-0.048	-0.038	-0.041
H3	-0.046	-0.039	-0.041
"pi" charges on ring atoms			
N1	-0.459	-0.087	-0.489
C2	-	-0.234	0.180
N3	-0.460	-0.090	-0.477
C4	0.146	-0.256	0.079
C5	-0.363	-	-0.302
C6	0.144	-0.262	-

Table 5.19

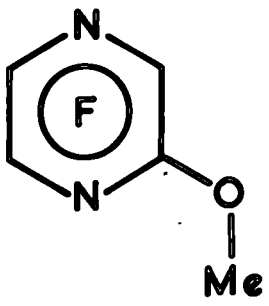
Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 5K-methoxyperfluoropyrimidine

	Position of substitution	
	2	4
N1	-0.426	-0.422
N3	-0.425	-0.447
C2	0.604	0.443
C4	0.345	0.509
C5	-0.156	-0.139
C6	0.352	0.320
F2	-	-0.269
F4	-0.248	-
F6	-0.247	-0.254
5K		
O	-0.219	-0.214
C	0.101	0.110
H1	-0.033	-0.030
H2	-0.051	-0.051
H3	0.340	0.027
F	-0.328	-0.312
O	-0.326	-0.315
C	0.147	0.143
H1	-0.029	-0.020
H2	-0.047	-0.041
H3	-0.046	-0.040
"pi" charges on ring atoms		
N1	-0.459	-0.475
C2	-	0.178
N3	-0.456	-0.489
C4	0.140	-
C5	-0.359	-0.296
C6	0.147	0.244

Pyrazine

The results in table 5.20 (i) suggest that the perfluoro derivative should be more reactive than the monofluoro compound, $\Delta\Delta E_g \sim 100$ kJ mol^{-1}. When further substitution in the perfluoro compound is considered then, as in pyridazine and pyrimidine, the orientation of the methoxy group already present must be taken into account. The calculations, (tables A2.3 and A2.7), show that the orientation referred to as 2K, shown below, gives the lowest energy for both the original compound and the Wheland intermediate.

2K-methoxyperfluoropyrazine



The orientation 2K for the methoxy group then gives position 3 as the most reactive site. However the value of $\Delta\Delta E_g$ for positions 3 and 5 is very small, 1.3 kJ mol^{-1}, and that for positions 3 and 6 only 1.6 kJ mol^{-1}. It would therefore not be surprising to find that as well as 2, 3-dimethoxyperfluoropyrazine some of the 2,5- and 2,6-products might be formed. Experimental evidence[65] does show though that the product is entirely the 2,3- derivative. It is reported further[65] that other groups, e.g. methyl, do give the para 2,5-disubstituted products while alkoxy groups generally give 2,3-disubstituted products.

The results in section (ii) of table 5.20 show that if the reactions were thermodynamically controlled the results would be the same as those predicted from section (i). However the reactions are

Table 5.20

Pyrazine Derivatives

(i) Reactants to intermediates

	P	ΔE_g kJ mol^{-1}
2-fluoropyrazine	2	-663.9
Perfluoropyrazine	2	-760.5
2A-methoxyperfluoro	3	-792.1
	6	-740.7
	5	-736.9
2K-methoxyperfluoro	3	-739.3
	6	-737.7
	5	-738.0

(ii) Reactants to products

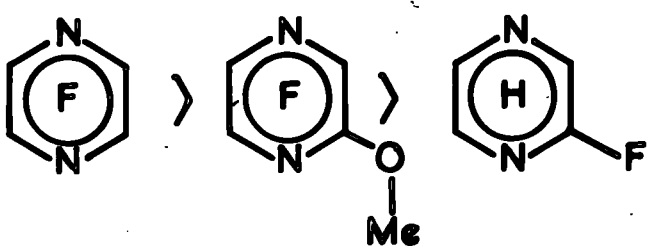
	O	
2-fluoropyrazine	2A	544.8
	2K	509.9
Perfluoropyrazine	2A	573.9
	2K	503.1
2A-methoxyperfluoro	2A6K	576.1
	2A5A	576.3
2K-methoxyperfluoro	2K3A	503.1

P position of attack

O orientation and position of methoxy group added

known to be irreversible under the conditions used and to be consistent kinetic control is assumed as in the case of the other diazines.

The reactivities as calculated are shown briefly below.



Subs. at	2	3	2
$\Delta\Delta E_g$	(0)	21	97 kJ mol^{-1}

It is noticed that as for the other diazines a methoxy group ortho to a nitrogen in the perfluoro series brings about a lowering of the reactivity.

Electronic Charge Distributions in the Intermediates

(tables 5.21 - 5.23)

These show that the nitrogen ortho to the position of substitution bears a large negative charge, while the meta nitrogen bears only a small negative charge. In the perfluoro compound the nitrogens bear slightly larger negative charges than in the monofluoro compound. The carbon atom at which substitution takes place is less positive in the perfluoro compound than in the monofluoro compound. The other carbons are more positive in the perfluoro compound than in the monofluoro and this is largely due to the electron withdrawing characteristics of the fluorine atoms. It is seen that the meta carbon atom bears a more positive charge than the other carbons. The charge

distributions in the monomethoxy Wheland intermediates are very similar to each other and to that for the intermediate formed by perfluoropyrazine. As in the other heterocycles considered the use of the "pi" charges gives similar results to those predicted by the use of resonance cannonicals.

Table 5.21

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 2-fluoropyrazine and perfluoropyrazine, substitution taking place at position 2 in each case

	2-fluoro	perfluoro	
N1	-0.408	-0.431	
N4	-0.105	-0.163	
C2	0.492	0.468	
C3	-0.141	0.093	
C5	-0.141	0.033	
C6	0.139	0.289	
H3	-0.051	-0.232	F3
H5	-0.076	-0.250	F5
H6	-0.085	-0.240	F6
F	-0.326	-0.304	
O	-0.325	-0.307	
C	0.147	0.143	
H1	-0.016	-0.019	
H2	-0.051	-0.039	
H3	-0.054	-0.041	
"pi" charges on ring atoms			
N1	-0.456	-0.527	
C2	-	-	
C3	-0.255	-0.186	
N4	0.057	-0.036	
C5	-0.334	-0.339	
C6	0.125	0.103	

Table 5.22

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 2K-methoxyperfluoropyrazine

	Position of substitution		
	3	5	6
N1	-0.165	-0.162	-0.432
N4	-0.433	-0.432	-0.165
C2	0.045	-0.015	0.239
C3	0.477	0.298	0.042
C5	0.289	0.468	0.091
C6	0.030	0.090	0.465
F3	-	-0.243	-0.254
F5	-0.242	-	-0.234
F6	-0.252	-0.234	-
2K			
O	-0.224	-0.238	-0.240
C	0.134	0.135	0.134
H1	-0.032	-0.037	-0.030
H2	-0.042	-0.048	-0.044
H3	-0.013	-0.017	0.000
F	-0.306	-0.304	-0.306
O	-0.309	-0.308	-0.309
C	0.143	0.143	0.143
H1	-0.018	-0.019	-0.018
H2	-0.043	-0.042	-0.040
H3	-0.039	-0.039	-0.042
"pi" charges on ring atoms			
N1	-0.039	-0.037	-0.529
C2	-0.184	-0.341	0.104
C3	-	0.104	-0.338
N4	-0.529	-0.528	-0.035
C5	0.101	-	-0.189
C6	-0.337	-0.184	-

Table 5.23

Charges on the atoms in the Wheland intermediates formed by the reaction of methoxide ion with 2A-methoxyperfluoropyrazine

	Position of substitution		
	3	5	6
N1	-0.159	-0.156	-0.430
N4	-0.435	-0.432	-0.165
C2	0.042	-0.014	0.239
C3	0.472	0.289	0.030
C5	0.288	0.469	0.090
C6	0.032	0.090	0.466
F3	-	-0.244	-0.256
F5	-0.242	-	-0.234
F6	-0.252	-0.233	-
2A			
O	-0.233	-0.243	-0.242
C	0.107	0.100	0.097
H1	-0.027	-0.036	-0.030
H2	-0.048	-0.055	-0.051
H3	0.032	0.034	0.048
F	-0.309	-0.305	-0.305
O	-0.313	-0.308	-0.305
C	0.142	0.143	0.143
H1	-0.016	-0.019	-0.019
H2	-0.043	-0.041	-0.042
H3	-0.039	-0.039	-0.040
"pi" charges on ring atoms			
N1	-0.040	-0.035	-0.524
C2	-0.179	-0.333	0.110
C3	-	0.097	-0.350
N4	-0.528	-0.526	-0.033
C5	0.100	-	-0.191
C6	-0.336	-0.186	-

Conclusions

The work described in this chapter shows that all valence electron SCF MO CNDO II calculations, using the Wheland intermediate as a model for the transition state, give relative reactivities of a series of compounds or of sites within a molecule that are consistent with experimental data. Furthermore the energy differences between two Wheland intermediates as calculated correspond reasonably closely to the known differences in the activation energies (see benzene and pyridine).

It has been shown that within a closely related series (or for substitution within the same molecule) solvation effects may be ignored (see pyridine). When the series differ as in the case of the perfluoro and perchloropyridines it was found that solvation effects must be considered as the calculated reactivities were not consistent with experimental observations. Another example is the relative reactivities of perfluoropyridine and perfluoropyridazine. The calculations suggest that perfluoropyridine is more reactive than perfluoropyridazine, $\Delta\Delta E_g$ 41 kJ mol^{-1}, but observation[62] indicates that the reactivities are in fact the reverse. The calculations do however give the same order of reactivities, as experiment[1,63], in the case of the perfluoro derivatives of benzene, pyridine and pyrimidine. The calculated order of the reactivities for the perfluoro derivatives considered is as given below.

$\Delta\Delta E_g$ -88 -70 -46 -29 (0) kJ mol^{-1}

Within the perfluoro series some generalisations may be made concerning reactivities. It appears that a fluorine atom that is para to a nitrogen is more readily substituted than an ortho fluorine and that a meta fluorine is very difficult to replace. The introduction of a methoxy group ortho or para to a nitrogen lowers the reactivity, compared to the parent molecule, while a methoxy group meta to a nitrogen increases the reactivity compared to the parent molecule. This latter effect, in the diazines, seems to counteract the effect of a para nitrogen (pyridazine) but not that of an ortho nitrogen (pyrazine).

Some generalisations may also be made concerning the charge distributions in the Wheland intermediates. It is seen that when a nitrogen atom lies ortho or para to the position at which substitution is taking place it bears a larger negative charge than a meta nitrogen. This suggests that the charge on the nitrogen is connected with the energy difference since ortho and para fluorine atoms are more readily replaced than meta fluorines. The connection is not, however, simple since an ortho nitrogen generally bears a larger negative charge than a para nitrogen yet the relative ease of replacement is the converse.

The energy difference therefore agrees with the idea[52] that a para quinoid structure for the intermediate is of lower energy than an ortho quinoid structure. However the charge distributions do not agree with the suggestion that the para quinoid structure is of lower energy because the para nitrogen bears a larger portion of the negative charge introduced.

Although there is not strict sigma and pi electron seperability in the intermediates the "pi" charges are useful in that they show the same principal positions of charge distribution as those predicted by the use of resonance cannonicals.

Appendix 1

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Appendix 2

Tables A2.1 to A2.10

Energies given in atomic units except in tables A2.9 and A2.10, where the energies are given in MJ mol^{-1} and kJ mol^{-1}, respectively.

1 atomic unit (a.u.) = 2.62555 MJ mol^{-1}

Energies labelled as 'calculated from ZE' refer to total energies computed from the electronic energies and the point charge approximation for the nuclear repulsion energies.

Table A2.1

Energies calculated from ZE for Ethane and Monofluoroethane in the staggered and the eclipsed configurations

	au	kJ mol^{-1}
Ethane		
Staggered	-18.8095	
Eclipsed	-18.8061	
Energy difference (e→s)		-9.0 (calc)
		-12.5 ± 1.2 (exptl)
Monofluoroethane		
Staggered	-45.7823	
Eclipsed	-45.7795	
Energy difference (e→s)		-7.4 (calc)

Table A2.2

Energies calculated from ZE for the Fluoride ion and the Methoxide ion

Fluoride ion	-27.3153
Methoxide ion	-27.6514

Table A2.3

Energies calculated from ZE for Benzene, Pyridine, Pyridazine, Pyrimidine, Pyrazine, their fluoro and methoxy derivatives.

	au
Benzene	
1-fluoro	-74.0906
1-methoxy	-74.2221
1-chlorobenzene	-62.5272
Perfluorobenzene	-208.9937
1-methoxy	-209.1163
Pyridine	-50.8713
2-fluoro	-77.8699
3-fluoro	-77.8583
4-fluoro	-77.8629
2K-methoxy	-78.0118
2A-methoxy	-78.0003
3K-methoxy	-77.9890
3A-methoxy	-77.9928
4K-methoxy	-77.9965
Perfluoropyridine	-185.8042
2K-methoxy	-185.9511
2A-methoxy	-185.9242
3K-methoxy	-185.9250
3A-methoxy	-185.9341
4K-methoxy	-185.9350
2-chloropyridine	-66.2976
3-chloropyridine	-66.2965
4-chloropyridine	-66.2961
Perchloropyridine	-128.0029
Pyridazine	-54.6950
Perfluoropyridazine	-162.6397
3K-methoxy	-162.7867
3A-methoxy	-162.7522
4K-methoxy	-162.7663
4A-methoxy	-162.7739
3K,4K-dimethoxy	-162.9160
3K,5K-dimethoxy	-162.9191
3K,6K-dimethoxy	-162.8982
4K,5K-dimethoxy	-162.9014
4K,6K-dimethoxy	-162.8779

Table A2.3 cont'd.

	au
Pyrimidine	-54.6547
Perfluoropyrimidine	-162.6238
2K-methoxy	-162.7665
4K-methoxy	-162.7715
4A-methoxy	-162.7376
5K-methoxy	-162.7488
2K,4K-dimethoxy	-162.9131
2K,5K-dimethoxy	-162.8906
4K,5K-dimethoxy	-162.8984
4K,6K-dimethoxy	-162.8840
Pyrazine	-54.6425
2-fluoro	-81.6360
2K-methoxy	-81.7800
2A-methoxy	-81.7669
Perfluoropyrazine	-162.6003
2K-methoxy	-162.7483
2A-methoxy	-162.7202
2K,3A-dimethoxy	-162.8949
2A,6K-dimethoxy	-162.8393
2A,5A-dimethoxy	-162.8392

Table A2.4

Electronic Energies calculated for Benzene, Pyridine, Pyridazine, Pyrimidine, Pyrazine, their fluoro and methoxy derivatives

	au
Benzene	
1-fluoro	-211.2382
1-methoxy	-253.9647
Perfluorobenzene	-592.1122
1-methoxy	-657.2367
1-chlorobenzene	-194.3610
Pyridine	-155.2002
2-fluoro	-216.8708
3-fluoro	-216.5467
4-fluoro	-216.3724
2K-methoxy	-259.6976
2A-methoxy	-259.6764
3K-methoxy	-259.5289
3A-methoxy	-259.2504
4K-methoxy	-259.1155
Perfluoropyridine	-512.5863
2K-methoxy	-569.0919
2A-methoxy	-573.9735
3K-methoxy	-574.1459
3A-methoxy	-574.4254
4K-methoxy	-574.4863
2-chloropyridine	-199.7986
3-chloropyridine	-199.6060
4-chloropyridine	-199.4702
Perchloropyridine	-421.1683
Pyridazine	-159.9917
Perfluoropyridazine	-438.5334
3K-methoxy	-491.0074
3A-methoxy	-497.5861
4K-methoxy	-496.9335
4A-methoxy	-497.3685
3K,4K-dimethoxy	-554.0764
3K,5K-dimethoxy	-552.5163
3K,6K-dimethoxy	-552.4432
4K,5K-dimethoxy	-560.2607
4K,6K-dimethoxy	-558.6845

Table A2.4 cont'd.

	au
Pyrimidine	-161.3699
Perfluoropyrimidine	-439.3663
2K-methoxy	-492.3063
4K-methoxy	-492.8852
4A-methoxy	-498.5527
5K-methoxy	-497.9442
2K,4K-dimethoxy	-548.5842
2K,5K-dimethoxy	-553.2676
4K,5K-dimethoxy	-556.1209
4K,6K-dimethoxy	-554.7952
Pyrazine	-159.8222
2-fluoro	-221.5701
2K-methoxy	-264.2111
2A-methoxy	-264.5568
Perfluoropyrazine	-435.5868
2K-methoxy	-488.8558
2A-methoxy	-493.3248
2K,3A-dimethoxy	-544.8838
2A,6K-dimethoxy	-553.4347
2A,5A-dimethoxy	-553.4301

Table A2.5

Energies calculated from ZE for Pyridine, Pyridazine, Pyrimidine, Pyrazine and some of their fluoro and methoxy derivatives on protonation

	au
Pyridine	-51.3897
2-fluoro	-78.3781
3-fluoro	-78.3619
4-fluoro	-78.3752
2K-methoxy	-78.5252
2A-methoxy	-78.5275
3K-methoxy	-78.5073
3A-methoxy	-78.5107
4K-methoxy	-78.5250
Perfluoropyridine	-186.2664
Perchloropyridine	-128.4804
Pyridazine	
1-	-55.1989
1,2-	-55.4310
Perfluoropyridazine	
1-	-163.0967
1,2-	-163.2975
Pyrimidine	
1-	-55.1590
1,3-	-55.4214
Perfluoropyrimidine	
1-	-163.0800
1,3-	-163.3037
Pyrazine	
1-	-55.1502
1,4-	-55.4173
2-fluoropyrazine	
4-	-82.1272
1-	-82.1329
1,4-	-82.3861
Perfluoropyrazine	
1-	-163.0531
1,4-	-163.2776

Table A2.6

Electronic Energies calculated for Pyridine, Pyridazine, Pyrimidine, Pyrazine and some of their fluoro and methoxy derivatives on protonation

	au
Pyridine	-163.0605
2-fluoro	-225.9907
3-fluoro	-225.1070
4-fluoro	-224.8395
2K-methoxy	-270.3498
2A-methoxy	-269.4761
3K-methoxy	-268.7886
3A-methoxy	-268.3309
4K-methoxy	-268.1044
Perfluoropyridine	-524.9725
Perchloropyridine	-433.1043
Pyridazine	
1-	-167.9419
1,2-	-175.8481
Perfluoropyridazine	
1-	-449.7611
1,2-	-460.9603
Pyrimidine	
1-	-169.2934
1,3-	-177.1048
Perfluoropyrimidine	
1-	-451.0958
1,3-	-462.7227
Pyrazine	
1-	-167.7406
1,4-	-175.5300
2-fluoropyrazine	
1-	-230.7229
4-	-230.1877
1,4-	-239.2142
Perfluoropyrazine	
1-	-447.3724
1,4-	-459.0414

Table A2.7

Energies calculated from ZE for the Wheland intermediate formed by the reaction of methoxy ion with some of the fluoro and fluoro-methoxy derivatives of Benzene, Pyridine, Pyridazine, Pyrimidine and Pyrazine

	Position of substitution	au
Benzene		
1-fluoro	1	-101.9636
Perfluorobenzene	1	-236.9172
1-chlorobenzene	1	-90.4330
Pyridine		
2-fluoro	2	-105.7668
3-fluoro	3	-105.7248
4-fluoro	4	-105.7622
Perfluoropyridine	2	-213.7510
	3	-213.7056
	4	-213.7544
4K-methoxy	2	-213.8736
	3	-213.8431
2-chloropyridine	2	-94.2270
3-chloropyridine	3	-94.1960
4-chloropyridine	4	-94.2283
Perchloropyridine	2	-155.9992
	3	-155.9798
	4	-156.0052

Table A2.7 cont'd.

	Position of substitution	au
Perfluoropyridazine	3	-190.5676
	4	-190.5741
3K-methoxy	4	-190.7136
	5	-190.7137
	6	-190.7065
4K-methoxy	3	-190.7053
	5	-190.6920
	6	-190.6270
4A-methoxy	3	-190.6924
	5	-190.7125
	6	-190.6331
Perfluoropyrimidine	2	-190.5726
	4	-190.5775
	5	-190.4929
2K-methoxy	4	-190.7115
	5	-190.6269
4K-methoxy	2	-190.7111
	5	-190.6317
	6	-190.7160
5K-methoxy	2	-190.6896
	4	-190.7147
Pyrazine		
2-fluoro	2	-109.5403
Perfluoropyrazine	2	-190.5414
2A-methoxy	3	-190.6733
	6	-190.6537
	5	-190.6523
2K-methoxy	3	-190.6813
	6	-190.6807
	5	-190.6808

Table A2.8

Electronic energies calculated for the Wheland intermediate formed by the reaction of methoxy ion with some of the fluoro and fluoro-methoxy derivatives of Benzene, Pyridine, Pyridazine, Pyrimidine and Pyrazine.

	Position of substitution	au
Benzene		
1-fluoro	1	-348.0918
Perfluorobenzene	1	-783.5381
1-chlorobenzene	1	-329.3316
Pyridine		
2-fluoro	2	-354.9430
3-fluoro	3	-354.0794
4-fluoro	4	-353.6955
Perfluoropyridine	2	-692.4459
	3	-695.0455
	4	-695.6408
4K-methoxy	2	-763.0045
	3	-768.3998
2-chloropyridine	2	-335.9679
3-chloropyridine	3	-335.1960
4-chloropyridine	4	-334.9033
Perchloropyridine	2	-595.5219
	3	-598.0709
	4	-598.6159

Table A2.8 cont'd.

	Position of substitution	au
Perfluoropyridazine	3	-609.1449
	4	-612.5660
3K-methoxy	4	-673.6618
	5	-672.2234
	6	-668.9655
4K-methoxy	3	-678.8589
	5	-679.5451
	6	-675.2350
4A-methoxy	3	-676.5718
	5	-682.8467
	6	-677.0533
Perfluoropyrimidine	2	-608.1632
	4	-611.5373
	5	-613.4813
2K-methoxy	4	-671.8136
	5	-673.7342
4K-methoxy	2	-670.5824
	5	-675.6556
	6	-672.3073
5K-methoxy	2	-674. 546
	4	-681.4256
Pyrazine		
2-fluoro	2	-360.0392
Perfluoropyrazine	2	-606.0176
2A-methoxy	3	-675.1954
	6	-670.9866
	5	-670.9928
2K-methoxy	3	-667.8984
	6	-668.1025
	5	-666.5057

Table A2.9

Nuclear Repulsion, Electronic and Total Energies for the Wheland Intermediates formed by the reaction of methoxide ion with some of the fluoro and chloro derivatives of Pyridine. Energies given in MJ mol^{-1}.

		Nuclear Repulsion	Electronic	Total
2-fluoropyridine		654.2246	-931.9206	-277.6960
3-		652.0674	-929.6532	-277.5858
4-		650.9613	-928.6452	-277.6839
Perfluoropyridine	2	1256.8374	-1818.0513	-561.2137
	3	1263.7820	-1824.8767	-561.0947
	4	1265.2168	-1826.4397	-561.2229
4K-methoxyperfluoro	2	1441.7706	-2003.3065	-561.5359
	3	1456.0163	-2017.4721	-561.4558
2-chloropyridine		634.7028	-882.1005	-247.3977
3-		632.7576	-880.0739	-247.3163
4-		631.9043	-879.3054	-247.4011
Perchloropyridine	2	1153.9888	-1563.5725	-409.5837
	3	1160.7323	-1570.2651	-409.5328
	4	1162.0965	-1571.6960	-409.5995

Table A2.10

$$\Delta E_{iso} = -\sum \frac{q_i q_j}{2r_{ij}} \left(1 - 1/D \right) \quad \text{in methanol}$$

		kJ mol^{-1}
Pyridine		-11.3
Perfluoro pyridine		-200.0
Perchloropyridine		-63.8
1-proto-pyridine		-341.6
1-proto-perfluoropyridine		-584.6
1-proto-perchloropyridine		-393.1
2-methoxyperfluoropyridine		-194.9
3-methoxyperfluoropyridine		-191.8
4-methoxyperfluoropyridine		-161.2
Wheland intermediates		
Perfluoropyridine	subs at 2	-522.8
	3	-501.0
	4	-432.7
Perchloropyridine	2	-376.0
	3	-366.8
	4	-382.8
1-proto-perfluoropyridazine		-559.9
1-proto-perfluoropyrimidine		-574.2
1-proto-perfluoropyrazine		-576.8

Appendix 3

Electron Distributions, Sigma and Pi Charges

(For Benzene Derivatives see chapter 3)

Pyridine

Pyridazine

Pyrimidine

Pyrazine (see also chapter 3)

	Total charge	sigma charge	pi charge
	Pyridine		
N1	-0.163	-0.088	-0.075
C2	0.097	0.062	0.035
C3	-0.023	-0.000	-0.023
C4	0.047	-0.005	0.052
C5	-0.023	-0.000	-0.023
C6	0.097	0.062	0.035
H2	-0.015		
H3	0.001		
H4	-0.005		
H5	0.001		
H6	-0.015		
	N-protonated pyridine		
N1	0.008	0.406	-0.398
C2	0.156	0.055	0.101
C3	-0.004	-0.002	-0.002
C4	0.136	-0.063	0.199
C5	-0.004	-0.002	-0.002
C6	0.156	0.055	0.101
H2	0.066		
H3	0.077		
H4	0.063		
H5	0.077		
H6	0.066		
H1	0.202		

	Total charge	sigma charge	pi charge
	Perfluoropyridine		
N1	-0.210	-0.038	-0.172
C2	0.290	0.247	0.043
C3	0.113	0.206	-0.093
C4	0.217	0.182	0.035
C5	0.113	0.206	-0.093
C6	0.290	0.247	0.043
F2	-0.171	-0.224	0.053
F3	-0.158	-0.197	0.039
F4	-0.154	-0.205	0.051
F5	-0.158	-0.197	0.039
F6	-0.171	-0.224	0.053
	N-protonated perfluoropyridine		
N1	-0.041	0.429	-0.470
C2	0.364	0.272	0.092
C3	0.130	0.208	-0.078
C4	0.282	0.134	0.148
C5	0.130	0.208	-0.078
C6	0.364	0.272	0.092
F2	-0.103	-0.169	0.066
F3	-0.093	-0.137	0.044
F4	-0.085	-0.159	0.074
F5	-0.093	-0.137	0.044
F6	-0.103	-0.169	0.066
H1	0.249		

	Total charge	sigma charge	pi charge
	Perchloropyridine		
N1	-0.095	-0.037	-0.058
C2	0.170	0.122	0.048
C3	0.046	0.057	-0.011
C4	0.098	0.050	0.048
C5	0.046	0.057	-0.011
C6	0.170	0.122	0.048
C12	-0.101	-0.138	0.037
C13	-0.080	-0.112	0.032
C14	-0.074	-0.102	0.038
C15	-0.080	-0.112	0.032
C16	-0.101	-0.138	0.037
	N-protonated perchloropyridine		
N1	0.044	0.455	-0.410
C2	0.218	0.105	0.114
C3	0.046	0.051	-0.005
C4	0.162	-0.008	0.170
C5	0.046	0.051	-0.005
C6	0.218	0.105	0.114
C12	0.013	-0.040	0.052
C13	0.005	-0.030	0.035
C14	0.021	-0.043	0.064
C15	0.005	-0.030	0.035
C16	0.013	-0.040	0.052
H1	0.209		

	Total charge	sigma charge	pi charge
	2-monofluoropyridine		
N1	-0.201	-0.073	-0.129
C2	0.318	0.249	0.069
C3	-0.073	-0.001	-0.072
C4	0.066	-0.007	0.073
C5	-0.044	0.005	-0.049
C6	0.115	0.060	0.055
H3	0.024		
H4	0.002		
H5	0.007		
H6	-0.008		
F2	-0.208	-0.261	0.053
	N-protonated, 2-monofluoropyridine		
N1	-0.043	0.407	-0.444
C2	0.392	0.261	0.131
C3	-0.058	-0.003	-0.055
C4	0.151	-0.061	0.212
C5	-0.018	0.003	-0.021
C6	0.166	0.056	0.110
H3	0.099		
H4	0.070		
H5	0.081		
H6	0.071		
F2	-0.131	-0.198	0.067
H1	0.220		

	Total charge	sigma charge	pi charge
	3-monofluoropyridine		
N1	-0.107	-0.069	-0.038
C2	0.041	0.052	-0.011
C3	0.192	0.188	0.004
C4	-0.024	-0.020	-0.004
C5	-0.011	-0.004	-0.007
C6	0.082	0.071	0.011
H2	0.008		
H4	0.020		
H5	0.008		
H6	-0.010		
F3	-0.200	-0.244	0.044
	N-protonated, 3-monofluoropyridine		
N1	0.029	0.408	-0.379
C2	0.014	-0.035	0.049
C3	0.238	0.208	0.030
C4	0.081	-0.074	0.155
C5	0.014	-0.000	0.014
C6	0.142	0.060	0.082
H2	0.089		
H4	0.086		
H5	0.083		
H6	0.071		
F3	-0.136	-0.186	0.050
H1	0.218		

	Total charge	sigma charge	pi charge
	4-monofluoropyridine		
N1	-0.142	-0.053	-0.089
C2	0.119	0.060	0.059
C3	-0.090	-0.014	-0.077
C4	0.253	0.180	0.073
C5	-0.090	-0.014	-0.077
C6	0.119	0.060	0.059
H2	-0.010		
H3	0.025		
H5	0.025		
H6	-0.010		
F4	-0.200	-0.252	0.052
	N-protonated, 4-monofluoropyridine		
N1	0.032	0.446	-0.414
C2	0.184	0.061	0.123
C3	-0.075	-0.019	-0.056
C4	0.345	0.140	0.205
C5	-0.075	-0.019	-0.056
C6	0.184	0.061	0.123
H2	0.069		
H3	0.100		
H5	0.100		
H6	0.069		
F4	-0.131	-0.207	0.076
H1	0.199		

	Total charge	sigma charge	pi charge
	2-chloropyridine		
N1	-0.138	-0.068	-0.070
C2	0.174	0.144	0.030
C3	-0.013	0.001	-0.014
C4	0.044	-0.005	0.049
C5	-0.022	-0.008	-0.014
C6	0.099	0.063	0.036
H3	0.018		
H4	0.004		
H5	0.008		
H6	-0.006		
Cl2	-0.170	-0.201	0.032
	3-chloropyridine		
N1	-0.156	-0.078	-0.078
C2	0.108	0.060	0.048
C3	0.065	0.087	-0.023
C4	0.057	-0.004	0.062
C5	-0.026	-0.000	-0.026
C6	0.101	0.055	0.047
H2	0.001		
H4	0.011		
H5	0.009		
H6	-0.008		
Cl3	-0.164	-0.189	0.025
	4-chloropyridine		
N1	-0.159	-0.093	-0.066
C2	0.096	0.064	0.032
C3	-0.012	0.003	-0.014
C4	0.133	0.086	0.047
C5	-0.012	0.003	-0.014
C6	0.096	0.064	0.032
H2	-0.007		
H3	0.017		
H5	0.017		
H6	-0.007		
Cl4	-0.164	-0.196	0.032

	Total charge	sigma charge	pi charge
	2K-methoxypyridine		
N1	-0.181	-0.059	-0.122
C2	0.258	0.182	0.076
C3	-0.078	0.002	-0.080
C4	0.053	-0.013	0.066
C5	-0.052	0.007	-0.059
C6	0.116	0.058	0.059
H3	0.016		
H4	-0.001		
H5	0.003		
H6	-0.016		
O	-0.230	-0.315	0.085
C	0.132		
H1	-0.008		
H2	-0.010		
H3	-0.002		
	N-protonated, 2K-methoxypyridine		
N1	-0.064	0.389	-0.453
C2	0.321	0.174	0.147
C3	-0.054	0.008	-0.062
C4	0.145	-0.061	0.206
C5	-0.022	0.007	-0.029
C6	0.159	0.055	0.105
H3	0.086		
H4	0.061		
H5	0.073		
H6	0.060		
O	-0.164	-0.272	0.108
C	0.119		
H1	0.030		
H2	0.053		
H3	-0.021		
H1	0.216		

	Total charge	sigma charge	pi charge
	2A-methoxypyridine		
N1	-0.171	-0.052	-0.118
C2	0.257	0.181	0.076
C3	-0.088	-0.004	-0.084
C4	0.052	-0.015	0.067
C5	-0.053	0.006	-0.059
C6	0.116	0.059	0.057
H3	0.016		
H4	-0.002		
H5	-0.003		
H6	-0.014		
O	-0.222	-0.307	0.085
C	0.127		
H1	-0.008		
H2	-0.006		
H3	-0.009		
	N-protonated, 2A-methoxypyridine		
N1	-0.022	0.428	-0.450
C2	0.323	0.165	0.159
C3	-0.075	0.003	-0.077
C4	0.137	-0.070	0.207
C5	-0.032	0.007	-0.039
C6	0.167	0.055	0.113
H3	0.081		
H4	0.060		
H5	0.074		
H6	0.062		
O	-0.180	-0.288	0.108
C	0.123		
H1	0.030		
H2	0.043		
H3	0.005		
H1	0.204		

	Total charge	sigma charge	pi charge
	3K-methoxypyridine		
N1	-0.113	-0.078	-0.035
C2	0.039	0.058	-0.019
C3	0.134	0.121	0.013
C4	-0.016	-0.009	-0.007
C5	-0.014	-0.007	-0.007
C6	0.079	0.075	0.005
H2	0.001		
H4	0.012		
H5	0.004		
H6	-0.015		
O	-0.216	-0.292	0.076
C	0.127		
H1	-0.008		
H2	-0.008		
H3	-0.007		
	N-protonated, 3K-methoxypyridine		
N1	0.043	0.417	-0.374
C2	0.089	0.050	0.039
C3	0.162	0.120	0.043
C4	0.077	-0.071	0.147
C5	0.002	-0.005	0.007
C6	0.141	0.065	0.076
H2	0.078		
H4	0.075		
H5	0.077		
H6	0.063		
O	-0.169	-0.252	0.083
C	0.121		
H1	0.022		
H2	0.038		
H3	-0.014		
H1	0.197		

	Total charge	sigma charge	pi charge
	3A-methoxypyridine		
N1	-0.112	-0.075	-0.038
C2	0.050	0.063	-0.013
C3	0.134	0.121	0.013
C4	-0.026	-0.015	-0.011
C5	-0.014	-0.008	-0.006
C6	0.079	0.075	0.005
H2	-0.001		
H4	0.012		
H5	0.003		
H6	-0.014		
O	-0.214	-0.290	0.076
C	0.127		
H1	-0.008		
H2	-0.007		
H3	-0.010		
	N-protonated, 3A-methoxypyridine		
N1	0.044	0.418	-0.374
C2	0.105	0.058	0.048
C3	0.161	0.117	0.044
C4	0.063	-0.075	0.138
C5	0.003	-0.006	0.009
C6	0.139	0.066	0.073
H2	0.075		
H4	0.072		
H5	0.075		
H6	0.063		
O	-0.173	-0.256	0.083
C	0.122		
H1	0.022		
H2	0.035		
H3	-0.006		
H1	0.199		

	Total charge	sigma charge	pi charge
	4-methoxypyridine		
N1	-0.147	-0.050	-0.097
C2	0.118	0.058	0.060
C3	-0.093	-0.009	-0.084
C4	0.192	0.110	0.082
C5	-0.083	-0.004	-0.080
C6	0.118	0.059	0.059
H2	-0.016		
H3	0.016		
H5	0.017		
H6	-0.015		
O	-0.217	-0.302	0.085
C	0.128		
H1	-0.006		
H2	-0.006		
H3	-0.007		
	N-protonated, 4-methoxypyridine		
N1	-0.000	0.446	-0.446
C2	0.176	0.053	0.123
C3	-0.074	-0.007	-0.067
C4	0.287	0.057	0.230
C5	-0.061	-0.002	-0.059
C6	0.174	0.055	0.119
H2	0.061		
H3	0.084		
H5	0.086		
H6	0.062		
O	-0.169	-0.289	0.121
C	0.121		
H1	0.025		
H2	0.038		
H3	-0.003		
H1	0.195		

	Total charge	sigma charge	pi charge
	2K-methoxyperfluoropyridine		
N1	-0.224	-0.041	-0.183
C2	0.230	0.188	0.058
C3	0.116	0.212	-0.096
C4	0.214	0.179	0.035
C5	0.107	0.208	-0.101
C6	0.286	0.241	0.045
F3	-0.167	-0.206	0.039
F4	-0.159	-0.210	0.051
F5	-0.163	-0.201	0.038
F6	-0.178	-0.230	0.052
O	-0.195	-0.282	0.087
C	0.128		
H1	0.001		
H2	0.002		
H3	0.002		
	2A-methoxyperfluoropyridine		
N1	-0.212	-0.035	-0.178
C2	0.229	0.167	0.062
C3	0.107	0.214	-0.107
C4	0.217	0.180	0.037
C5	0.107	0.210	-0.103
C6	0.288	0.242	0.046
F3	-0.174	-0.214	0.040
F4	-0.160	-0.211	0.051
F5	-0.163	-0.201	0.038
F6	-0.176	-0.229	0.053
O	-0.200	-0.286	0.086
C	0.097		
H1	0.001		
H2	-0.004		
H3	0.043		

	Total charge	sigma charge	pi charge
	3K-methoxyperfluoropyridine		
N1	-0.214	-0.047	-0.167
C2	0.284	0.258	0.026
C3	0.053	0.121	-0.068
C4	0.220	0.190	0.030
C5	0.111	0.200	-0.089
C6	0.283	0.251	0.032
F2	-0.187	-0.240	0.053
F4	-0.162	-0.213	0.051
F5	-0.163	-0.202	0.039
F6	-0.176	-0.227	0.051
O	-0.181	-0.251	0.070
C	0.092		
H1	0.001		
H2	-0.005		
H3	0.043		
	3A-methoxyperfluoropyridine		
N1	-0.214	-0.046	-0.168
C2	0.293	0.255	0.038
C3	0.053	0.124	-0.071
C4	0.212	0.192	0.021
C5	0.112	0.202	-0.090
C6	0.284	0.252	0.032
F2	-0.179	-0.231	0.052
F4	-0.169	-0.220	0.051
F5	-0.164	-0.203	0.039
F6	-0.176	-0.228	0.052
O	-0.183	-0.253	0.070
C	0.102		
H1	0.001		
H2	-0.003		
H3	0.033		

	Total charge	sigma charge	pi charge
	4K-methoxyperfluoropyridine		
N1	-0.220	-0.034	-0.186
C2	0.289	0.244	0.046
C3	0.106	0.215	-0.109
C4	0.157	0.099	0.059
C5	0.115	0.213	-0.098
C6	0.285	0.240	0.045
F2	-0.178	-0.231	0.053
F3	-0.175	-0.214	0.039
F5	-0.167	-0.206	0.039
F6	-0.176	-0.229	0.053
O	-0.181	-0.267	0.086
C	0.100		
H1	0.004		
H2	-0.001		
H3	0.040		

	Total charge	sigma charge	pi charge
	Pyridazine		
N1	-0.068	-0.032	-0.037
N2	-0.068	-0.032	-0.037
C3	0.069	0.055	0.013
C4	0.005	-0.018	0.023
C5	0.005	-0.018	0.023
C6	0.069	0.055	0.013
H3	-0.011		
H4	-0.005		
H5	0.005		
H6	-0.011		
	Perfluoropyridazine		
N1	-0.059	0.016	-0.075
N2	-0.059	0.016	-0.075
C3	0.240	0.239	0.001
C4	0.147	0.168	-0.021
C5	0.147	0.168	-0.021
C6	0.240	0.239	0.001
F3	-0.176	-0.224	0.048
F4	-0.152	-0.199	0.047
F5	-0.152	-0.199	0.047
F6	-0.176	-0.224	0.048

	Total charge	sigma charge	pi charge
	N-monoprotonated pyridazine		
N1	0.121	0.467	-0.346
N2	0.041	0.037	0.005
C3	0.084	0.044	0.040
C4	0.076	-0.080	0.156
C5	0.016	-0.024	0.040
C6	0.147	0.042	0.105
H3	0.007		
H4	0.079		
H5	0.084		
H6	0.071		
H1	0.204		
	N-monoprotonated perfluoropyridazine		
N1	0.068	0.476	-0.408
N2	0.007	0.084	-0.077
C3	0.285	0.245	0.040
C4	0.243	0.134	0.109
C5	0.184	0.192	-0.008
C6	0.343	0.247	0.096
F3	-0.101	-0.159	0.058
F4	-0.082	-0.152	0.070
F5	-0.086	-0.139	0.053
F6	-0.100	-0.167	0.067
H1	0.241		

	Total charge	sigma charge	pi charge
	N-diprotonated pyridazine		
N1	0.109	0.476	-0.367
N2	0.109	0.476	-0.367
C3	0.207	0.011	0.197
C4	0.107	-0.063	0.170
C5	0.107	-0.063	0.170
C6	0.207	0.011	0.197
H3	0.147		
H4	0.150		
H5	0.150		
H6	0.147		
H1	0.280		
H2	0.280		
	N-diprotonated perfluoropyridazine		
N1	0.047	0.512	-0.465
N2	0.047	0.512	-0.465
C3	0.419	0.223	0.196
C4	0.267	0.166	0.101
C5	0.267	0.166	0.101
C6	0.419	0.223	0.196
F3	-0.022	-0.113	0.091
F4	-0.017	-0.094	0.077
F5	-0.017	-0.094	0.077
F6	-0.022	-0.113	0.091
H1	0.306		
H2	0.306		

	Total charge	sigma charge	pi charge
	3K-methoxyperfluoropyridazine		
N1	-0.065	0.005	-0.070
N2	-0.067	0.019	-0.086
C3	0.180	0.166	0.014
C4	0.149	0.174	-0.025
C5	0.143	0.165	-0.022
C6	0.234	0.242	-0.008
F4	-0.161	-0.207	0.046
F5	-0.157	-0.203	0.046
F6	-0.182	-0.229	0.047
O	-0.205	-0.285	0.080
C	0.130		
H1	0.000		
H2	0.001		
H3	-0.001		
	3A-methoxyperfluoropyridazine		
N1	-0.061	0.006	-0.067
N2	-0.058	0.024	-0.082
C3	0.180	0.159	0.021
C4	0.138	0.176	-0.038
C5	0.145	0.174	-0.019
C6	0.233	0.244	-0.011
F4	-0.169	-0.217	0.048
F5	-0.158	-0.205	0.047
F6	-0.181	-0.228	0.047
O	-0.200	-0.281	0.081
C	0.090		
H1	0.000		
H2	-0.005		
H3	0.045		

	Total charge	sigma charge	pi charge
4K-methoxyperfluoropyridazine			
N1	-0.067	0.022	-0.089
N2	-0.062	0.007	-0.069
C3	0.233	0.248	-0.015
C4	0.084	0.083	0.001
C5	0.148	0.177	-0.029
C6	0.239	0.234	0.005
F3	-0.191	-0.239	0.048
F5	-0.161	-0.207	0.046
F6	-0.181	-0.229	0.048
O	-0.181	-0.260	0.079
C	0.097		
H1	0.003		
H2	-0.003		
H3	0.042		
4A-methoxyperfluoropyridazine			
N1	-0.083	0.013	-0.096
N2	-0.078	-0.001	-0.077
C3	0.247	0.250	-0.004
C4	0.098	0.090	0.008
C5	0.150	0.183	-0.033
C6	0.244	0.238	0.006
F3	-0.184	-0.231	0.048
F5	-0.170	-0.216	0.046
F6	-0.182	-0.230	0.048
O	-0.180	-0.259	0.080
C	0.104		
H1	0.003		
H2	-0.001		
H3	0.033		

		Total charge	sigma charge	pi charge
	3K, 4K-dimethoxyperfluoropyridazine			
N1		-0.091	0.001	-0.092
N2		-0.089	-0.000	-0.087
C3		0.182	0.183	-0.001
C4		0.103	0.099	0.004
C5		0.158	0.180	-0.023
C6		0.239	0.240	-0.001
F5		-0.167	-0.212	0.046
F6		-0.185	-0.232	0.047
	3K			
O		-0.209	-0.291	0.081
C		0.119		
H1		-0.002		
H2		-0.004		
H3		-0.002		
	4K			
O		-0.185	-0.264	0.078
C		0.094		
H1		-0.001		
H2		-0.007		
H3		0.048		

		Total charge	sigma charge	pi charge
	3K, 5K-dimethoxyperfluoropyridazine			
N1		-0.068	-0.003	-0.065
N2		-0.074	0.024	-0.098
C3		0.180	0.163	0.017
C4		0.141	0.183	-0.042
C5		0.081	0.082	-0.001
C6		0.237	0.249	-0.012
F4		-0.176	-0.221	0.045
F6		-0.190	-0.237	0.047
	3K			
O		-0.209	-0.289	0.080
C		0.131		
H1		-0.002		
H2		-0.002		
H3		-0.001		
	5K			
O		-0.182	-0.261	0.079
C		0.104		
H1		0.001		
H2		-0.003		
H3		0.032		

	Total charge	sigma charge	pi charge
3K, 6K-dimethoxyperfluoropyridazine			
N1	-0.064	0.012	-0.076
N2	-0.069	0.008	-0.077
C3	0.174	0.172	0.003
C4	0.147	0.170	-0.023
C5	0.135	0.173	-0.038
C6	0.176	0.164	0.012
F4	-0.166	-0.212	0.046
F5	-0.166	-0.213	0.047
3K			
O	-0.208	-0.287	0.079
C	0.131		
H1	-0.002		
H2	-0.002		
H3	-0.001		
6K			
O	-0.204	-0.283	0.079
C	0.091		
H1	-0.002		
H2	-0.008		
H3	0.045		

	Total charge	sigma charge	pi charge
4K,5K-dimethoxyperfluoropyridazine			
N1	-0.069	0.013	-0.082
N2	-0.069	0.127	-0.082
C3	0.234	0.244	-0.010
C4	0.077	0.095	-0.018
C5	0.086	0.093	-0.007
C6	0.242	0.242	-0.000
F3	-0.195	-0.243	0.048
F6	-0.195	-0.243	0.048
4K			
O	-0.194	-0.272	0.078
C	0.091		
H1	0.001		
H2	-0.007		
H3	0.042		
5K			
O	-0.185	-0.263	0.078
C	0.102		
H1	0.000		
H2	-0.004		
H3	0.036		

		Total charge	sigma charge	pi charge
	4K,6K-dimethoxyperfluoropyridazine			
N1		-0.066	0.029	-0.095
N2		-0.064	-0.003	-0.061
C3		0.226	0.252	-0.026
C4		0.082	0.080	0.002
C5		0.140	0.185	-0.045
C6		0.180	0.155	0.025
F3		-0.195	-0.242	0.047
F5		-0.195	-0.242	0.047
	4K			
O		-0.186	-0.265	0.079
C		0.098		
H1		0.001		
H2		-0.005		
H3		0.042		
	6K			
O		-0.230	-0.311	0.081
C		0.090		
H1		-0.002		
H2		-0.008		
H3		0.046		

	Total charge	sigma charge	pi charge
	Pyrimidine		
N1	-0.180	-0.082	-0.098
N3	-0.180	-0.082	-0.098
C2	0.203	0.127	0.076
C4	0.142	0.058	0.084
C5	-0.062	-0.014	-0.049
C6	0.142	0.058	0.084
H2	-0.031		
H4	-0.022		
H5	0.012		
H6	-0.022		
	Perfluoropyrimidine		
N1	-0.231	-0.021	-0.210
N3	-0.231	-0.021	-0.210
C2	0.435	0.306	0.129
C4	0.339	0.231	0.108
C5	0.050	0.188	-0.138
C6	0.339	0.231	0.108
F2	-0.195	-0.255	0.060
F4	-0.176	-0.235	0.059
F5	-0.155	-0.190	0.035
F6	-0.176	-0.235	0.059

	Total charge	sigma charge	pi charge
	N-monoprotonated pyrimidine		
N1	0.024	0.365	-0.389
N3	-0.117	-0.032	-0.085
C2	0.258	0.111	0.147
C4	0.204	-0.005	0.209
C5	-0.046	-0.020	-0.026
C6	0.197	0.053	0.144
H2	0.057		
H4	0.059		
H5	0.091		
H6	0.063		
H1	0.210		
	N-monoprotonated perfluoropyrimidine		
N1	-0.112	0.395	-0.508
N3	-0.145	0.044	-0.189
C2	0.491	0.311	0.180
C4	0.423	0.203	0.220
C5	0.101	0.203	-0.102
C6	0.384	0.252	0.132
F2	-0.115	-0.189	0.074
F4	-0.104	-0.185	0.081
F5	-0.088	-0.128	0.040
F6	-0.098	-0.169	0.071
H1	0.262		

	Total charge	sigma charge	pi charge
	N-diprotonated pyrimidine		
N1	0.023	0.382	-0.359
N3	0.023	0.382	-0.359
C2	0.325	0.107	0.219
C4	0.256	0.008	0.248
C5	-0.014	-0.018	0.004
C6	0.256	0.008	0.248
H2	0.134		
H4	0.132		
H5	0.162		
H6	0.132		
H1	0.284		
H3	0.284		
	N-diprotonated perfluoropyrimidine		
N1	-0.066	0.405	-0.471
N3	-0.066	0.405	-0.471
C2	0.580	0.330	0.251
C4	0.461	0.234	0.227
C5	0.126	0.214	-0.088
C6	0.461	0.234	0.227
F2	-0.046	-0.138	0.092
F4	-0.035	-0.129	0.094
F5	-0.026	-0.071	0.045
F6	-0.035	-0.129	0.094
H1	0.323		
H3	0.323		

	Total charge	sigma charge	pi charge
	2K-methoxyperfluoropyrimidine		
N1	-0.243	-0.025	-0.218
N3	-0.230	-0.017	-0.213
C2	0.376	0.238	0.138
C4	0.335	0.227	0.108
C5	0.045	0.190	-0.145
C6	0.333	0.224	0.109
F4	-0.182	-0.240	0.058
F5	-0.160	-0.194	0.034
F6	-0.183	-0.241	0.058
O	-0.222	-0.317	0.095
C	0.130		
H1	0.000		
H2	0.001		
H3	0.002		

	Total charge	sigma charge	pi charge
	4K-methoxyperfluoropyrimidine		
N1	-0.238	-0.019	-0.219
N3	-0.243	-0.025	-0.219
C2	0.432	0.302	0.131
C4	0.277	0.158	0.119
C5	0.054	0.195	-0.141
C6	0.335	0.228	0.107
F2	-0.202	-0.261	0.059
F5	-0.164	-0.198	0.034
F6	-0.182	-0.240	0.058
O	-0.205	-0.299	0.094
C	0.130		
H1	0.001		
H2	0.002		
H3	0.003		
	4A-methoxyperfluoropyrimidine		
N1	-0.245	-0.021	-0.224
N3	-0.237	-0.021	-0.215
C2	0.431	0.299	0.131
C4	0.278	0.150	0.129
C5	0.051	0.202	-0.152
C6	0.339	0.228	0.111
F2	-0.199	-0.258	0.059
F5	-0.173	-0.209	0.036
F6	-0.183	-0.241	0.058
O	-0.203	-0.296	0.093
C	0.091		
H1	0.002		
H2	-0.004		
H3	0.051		

	Total charge	sigma charge	pi charge
	5K-methoxyperfluoropyrimidine		
N1	-0.235	-0.028	-0.207
N3	-0.236	-0.028	-0.208
C2	0.430	0.309	0.121
C4	0.334	0.240	0.094
C5	-0.012	0.105	-0.117
C6	0.343	0.239	0.104
F2	-0.200	-0.259	0.059
F4	-0.190	-0.248	0.058
F6	-0.184	-0.242	0.058
O	-0.180	-0.244	0.064
C	0.097		
H1	0.000		
H2	-0.005		
H3	0.037		

	Total charge	sigma charge	pi charge
2K,4K-dimethoxyperfluoropyrimidine			
N1	-0.250	-0.035	-0.226
N3	-0.241	-0.021	-0.220
C2	0.373	0.234	0.139
C4	0.274	0.156	0.118
C5	0.050	0.198	-0.148
C6	0.330	0.223	0.107
F5	-0.169	-0.202	0.033
F6	-0.188	-0.246	0.058
2K			
O	-0.228	-0.322	0.094
C	0.130		
H1	-0.003		
H2	-0.003		
H3	0.001		
4K			
O	-0.208	-0.301	0.093
C	0.130		
H1	-0.001		
H2	0.000		
H3	0.002		

	Total charge	sigma charge	pi charge
2K,5K-dimethoxyperfluoropyrimidine			
N1	-0.247	-0.033	-0.214
N3	-0.235	-0.025	-0.210
C2	0.372	0.243	0.130
C4	0.330	0.235	0.094
C5	-0.016	0.109	-0.125
C6	0.338	0.233	0.105
F4	-0.195	-0.253	0.058
F6	-0.191	-0.249	0.058
2K			
O	-0.225	-0.318	0.093
C	0.130		
H1	-0.002		
H2	-0.002		
H3	0.001		
5K			
O	-0.183	-0.246	0.063
C	0.098		
H1	-0.002		
H2	-0.007		
H3	0.037		

		Total charge	sigma charge	pi charge
	4K,5K-dimethoxyperfluoropyrimidine			
N1		-0.240	-0.026	-0.214
N3		-0.245	-0.031	-0.214
C2		0.427	0.305	0.123
C4		0.274	0.170	0.104
C5		-0.007	0.114	-0.121
C6		0.340	0.237	0.103
F2		-0.206	-0.264	0.058
F6		-0.189	-0.247	0.058
	4K			
O		-0.216	-0.310	0.094
C		0.121		
H1		0.000		
H2		-0.002		
H3		0.003		
	5K			
O		-0.185	-0.248	0.063
C		0.095		
H1		-0.004		
H2		-0.008		
H3		0.043		

		Total charge	sigma charge	pi charge
	4K,6K-dimethoxyperfluoropyrimidine			
N1		-0.237	-0.006	-0.222
N3		-0.251	-0.022	-0.229
C2		0.430	0.297	0.133
C4		0.276	0.157	0.119
C5		0.047	0.204	-0.157
C6		0.274	0.150	0.124
F2		-0.207	-0.266	0.059
F5		-0.180	-0.216	0.036
	4K			
O		-0.210	-0.303	0.093
C		0.130		
H1		-0.001		
H2		-0.001		
H3		0.002		
	6K			
O		-0.207	-0.301	0.094
C		0.091		
H1		0.000		
H2		-0.007		
H3		0.051		

	Total charge	sigma charge	pi charge
	Pyrazine		
N1,N4	-0.118	-0.098	-0.020
C2,3,5,6	0.065	0.055	0.010
H2,3,5,6	-0.006		
	Perfluoropyrazine		
N1,N4	-0.143	-0.060	-0.083
C2,3,5,6	0.244	0.252	-0.008
F2,3,5,6	-0.172	-0.221	0.049
	N-monoprotonated pyrazine		
N1	0.087	0.424	-0.337
N4	-0.014	-0.138	0.124
C2,6	0.137	0.046	0.091
C3,4	0.071	0.056	0.015
H2,6	0.079		
H3,5	0.080		
H1	0.194		
	N-monoprotonated perfluoropyrazine		
N1	0.011	0.406	-0.395
N4	-0.063	-0.100	0.037
C2,6	0.326	0.267	0.059
C3,5	0.272	0.270	0.002
F2,6	-0.096	-0.160	0.064
F3,5	-0.099	-0.153	0.054
H1	0.246		
	N-diprotonated pyrazine		
N1,4	0.125	0.327	-0.202
C2,3,5,6	0.150	0.049	0.101
H2,3,5,6	0.155		
H1,4	0.267		
	N-diprotonated perfluoropyrazine		
N1,4	0.049	0.337	-0.288
C2,3,5,6	0.351	0.280	0.071
F2,3,5,6	-0.030	-0.103	0.073
H1,4	0.309		

	Total charge	sigma charge	pi charge
	2-fluoropyrazine		
N1	-0.157	-0.082	-0.075
N4	-0.096	-0.097	0.001
C2	0.291	0.244	0.047
C3	0.015	0.052	-0.037
C5	0.043	0.061	-0.018
C6	0.084	0.053	0.031
H3	0.016		
H5	0.002		
H6	0.002		
F2	-0.200	-0.251	0.051
	N1-monoprotonated,2-fluoropyrazine		
N1	0.031	0.419	-0.388
N4	0.008	-0.132	0.140
C2	0.377	0.254	0.123
C3	0.019	0.054	-0.035
C5	0.054	0.062	-0.008
C6	0.150	0.048	0.102
H3	0.102		
H5	0.086		
H6	0.084		
F2	-0.122	-0.188	0.066
H1	0.212		
	N4-monoprotonated,2-fluoropyrazine		
N1	-0.058	-0.125	0.067
N4	0.106	0.420	-0.314
C2	0.312	0.261	0.051
C3	0.081	0.043	0.038
C5	0.118	0.052	0.066
C6	0.091	0.054	0.037
H3	0.100		
H5	0.085		
H6	0.088		
F2	-0.125	-0.181	0.056
H4	0.202		

	Total charge	sigma charge	pi charge
	N,N-diprotonated,2-fluoropyrazine		
N1	0.055	0.326	-0.271
N4	0.148	0.327	-0.179
C2	0.404	0.272	0.131
C3	0.098	0.045	0.053
C5	0.126	0.061	0.065
C6	0.168	0.047	0.121
H3	0.175		
H5	0.159		
H6	0.160		
F2	-0.049	-0.127	0.078
H1	0.283		
H4	0.273		

		Total charge	sigma charge	pi charge
2K,3A-dimethoxyperfluoropyrazine				
N1		-0.159	-0.067	-0.092
N4		-0.159	-0.067	-0.092
C2		0.190	0.187	0.003
C3		0.190	0.187	0.003
C5		0.234	0.250	-0.016
C6		0.234	0.250	-0.016
F5		-0.184	-0.231	0.047
F6		-0.184	-0.231	0.047
	2K			
O		-0.250	-0.332	0.082
C		0.130		
H1		-0.002		
H2		-0.002		
H3		-0.002		
	3A			
O		-0.250	-0.332	0.082
C		0.130		
H1		-0.002		
H2		-0.002		
H3		-0.002		

		Total charge	sigma charge	pi charge
2A,5A-dimethoxyperfluoropyrazine				
N1		-0.148	-0.064	-0.085
N4		-0.148	-0.064	-0.085
C2		0.179	0.180	0.001
C3		0.233	0.252	-0.019
C5		0.179	0.180	0.001
C6		0.233	0.252	-0.019
F3		-0.191	-0.240	0.049
F6		-0.191	-0.240	0.049
	2A			
O		-0.203	-0.283	0.080
C		0.096		
H1		-0.001		
H2		-0.006		
H3		0.041		
	5A			
O		-0.203	-0.283	0.080
C		0.096		
H1		-0.001		
H2		-0.006		
H3		0.041		

		Total charge	sigma charge	pi charge
2A,6K-dimethoxyperfluoropyrazine				
N1		-0.142	-0.049	-0.093
N4		-0.155	-0.079	-0.076
C2		0.184	0.118	0.016
C3		0.228	0.262	-0.034
C5		0.228	0.262	-0.034
C6		0.184	0.118	0.016
F3		-0.192	-0.240	0.048
F5		-0.192	-0.240	0.048
	2A			
O		-0.202	-0.284	0.082
C		0.096		
H1		-0.001		
H2		-0.006		
H3		0.041		
	6K			
O		-0.202	-0.284	0.082
C		0.096		
H1		-0.001		
H2		-0.006		
H3		0.041		

Appendix 4

Coordinates of Atoms in Molecules

These have been calculated from the appropriate parameters as given in "Tables of Interatomic Distances and Configurations in Molecules and Ions", Chem. Soc. Special Publications, Editor L.E. Sutton, 1958 and Supplement 1965, except in the case of Pyridine and Pyrazine. In these compounds the values are those of E. Clementi, given in Chem. Reviews (1968) 68, 341 and J C P (1967) 46, 4731, 4737. In all the compounds and derivatives the C-F bond length was taken as 1.3315 Å, the C-Cl bond length as 1.7 Å and the N-H bond length as 1.0 Å.

Where the geometry of the parent ring was not available the geometry was estimated from that of the most suitable derivatives for which information was available. The calculations were carried out on NUMAC using simple APL programmes and the units are ångstroms.

(1 Å = 100 pico metres = 10^{-10} metres)

Benzene

	x	y	z
C1	0	1.397	0
C2	1.209837	0.6985	0
C3	1.209837	-0.6985	0
C4	0	-1.397	0
C5	-1.209837	-0.6985	0
C6	-1.209837	0.6985	0
H1	0	2.481	0
H2	2.148609	1.2405	0
H3	2.148609	-1.2405	0
H4	0	-2.481	0
H5	-2.148609	-1.2405	0
H6	-2.148609	1.2405	0
F1	0	2.7285	0
F2	2.36295	1.36425	0
F3	2.36295	-1.36425	0
F4	0	-2.7285	0
F5	-2.36295	-1.36425	0
F6	-2.36295	1.36425	0
Cl1	0	3.097	0

Pyridine

	x	y	z
N1	0	-0.7031745	0
C2	1.156413	0	0
C3	1.200734	1.381148	0
C4	0	2.101199	0
C5	-1.200734	1.381148	0
C6	-1.156413	0	0
H2	2.08672	-0.5447188	0
H3	2.149483	1.89542	0
H4	0	3.179169	0
H5	-2.149483	1.89542	0
H6	-2.08672	-0.5447188	0
F2	2.278972	-0.7160676	0
F3	2.37783	2.003512	0
F4	0	3.432699	0
F5	-2.37783	2.003512	0
F6	-2.278972	-0.7160676	0
C12	2.6254	-0.8569	0
C13	2.6937	2.195	0
C14	0	3.8012	0
C15	-2.6937	2.195	0
C16	-2.654	-0.8569	0
H1 at N1	0	-1.703174	0

Pyridazine

	x	y	z
N1	-0.66	-1.163966	0
N2	0.66	-1.163966	0
C3	1.323915	0	0
C4	0.7	1.251816	0
C5	-0.7	1.251816	0
C6	-1.323915	0	0
H3	2.407465	-0.03121264	0
H4	1.269611	2.174095	0
H5	-1.269611	2.174095	0
H6	-2.407465	-0.03121264	0
F3	2.654863	-0.03833915	0
F4	1.399666	2.384671	0
F5	-1.399666	2.384671	0
F6	-2.654863	-0.3833915	0
H1 at N1	-1.162266	-2.02868	0
H2 at N2	1.162266	-2.02868	0

Pyrimidine

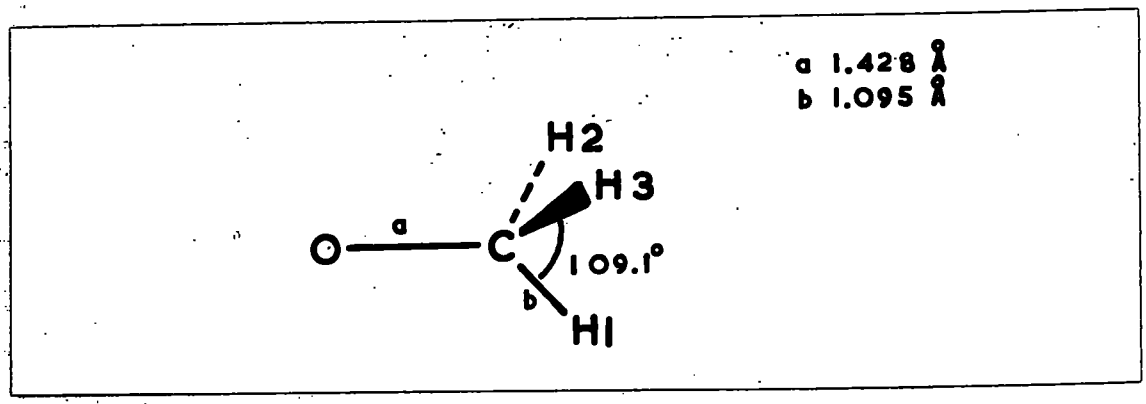
	x	y	z
N1	-1.186408	0	0
N3	1.186408	0	0
C2	0	-0.5786499	0
C4	1.161826	1.339796	0
C5	0	2.065785	0
C6	-1.161826	1.339796	0
H2	0	-1.66265	0
H4	2.105291	1.873583	0
H5	0	3.149785	0
H6	-2.105291	1.873583	0
F2	0	-1.91015	0
F4	2.320705	1.995458	0
F5	0	3.397285	0
F6	-2.320705	1.995458	0
H1 at F1	-2.039048	-0.5224986	0
H3 at N3	2.039048	-0.5224986	0

Pyrazine

	x	y	z
N1	0	-1.370072	0
N4	0	1.370072	0
C2	1.169204	-0.6950354	0
C3	1.169204	0.6950354	0
C5	-1.169204	0.6950354	0
C6	-1.169204	-0.6950354	0
H2	2.113223	-1.240064	0
H3	2.113223	1.240064	0
H5	-2.113223	1.240064	0
H6	-2.113223	-1.240064	0
F2	2.318815	-1.366814	0
F3	2.318815	1.366814	0
F5	-2.318815	1.366814	0
F6	-2.318815	-1.366814	0
H1 at N1	0	-2.370072	0
H4 at N4	0	2.370072	0

Methoxy ion

The coordinates of the atoms are calculated from the appropriate parameters for methanol.



Methoxy group

The ring carbon-oxygen bond length is that for carbon-oxygen in dimethyl ether and the ring carbon-oxygen-methyl carbon angle is likewise taken from dimethyl ether. The dimensions of the methyl group are again as those in methanol. From these dimensions the coordinates of the atoms were calculated.