SYNTHESIS AND ^{19}F NUCLEAR MAGNETIC RESONANCE STUDIES OF SUBSTITUTED FLUOROMETHYLNAPHTHALENES

BY

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ABSTRACT

A series of twenty-two substituted fluoromethylnaphthalenes has been synthesised and their ^{19}F n.m.r. and ^{1}H n.m.r. substituent chemical shifts and coupling constants measured. An analysis of the substituent effect on these n.m.r. parameters has been carried out in terms of a dual substituent parameter equation using a multiple linear regression treatment:

$$\Delta\phi = \sigma_I\rho_I + \sigma_R\rho_R$$

The dual substituent parameter equation describes the effect of a substituent in terms of two independent parameters, σ_I and σ_R, which correspond to the polar inductive and polar resonance effects respectively. Various substituent constant scales are investigated and their degree of correspondence to the dual substituent model for these data assessed.

Moderately good correlations of the data with the dual substituent parameter model are observed for coupling constants and ^{1}H n.m.r. substituted chemical shifts; good correlations are shown with $\Delta\phi$ values for 4-substituted-1-fluoromethylnaphthalenes in particular; correlations for 3-substituted derivatives are far less good.

The signs and magnitudes of the reaction constants, ρ_I and ρ_R, for ^{19}F substituent chemical shifts are interpreted in terms of current theories of screening of a fluorine nucleus in aromatic molecules and the ^{19}F n.m.r. response to substituent effects in aromatic systems. The sign of these coefficients are surprising. Both are large positive

quantities indicating that electron withdrawal by a substituent results in screening of the fluorine nucleus. Explanations of these observations are proposed in terms of fluorine hyperconjugation and the p-π mechanism. The magnitudes of the ρ values are compared with those for substituted-fluorobenzenes, substituted-fluoronaphthalenes and substituted-benzyl fluorides.

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CHAPTER 1

INTRODUCTION

Linear Free Energy Relationships

(i) The Hammett Equation

Several empirical relationships have been suggested in an attempt to correlate quantitatively substituent effects on reaction rates and mechanisms. The rate or equilibrium constant of a reaction of a molecule may be influenced by structural modifications, through the medium of polar, steric, or resonance effects.

If one accepts that most molecular properties are related to the electronic nature of the species, in terms of distribution and magnitude, then ideally it should be possible to describe the observed phenomena in precise quantum mechanical terms. Because the present state of understanding of both the phenomena and quantum mechanics does not permit such a complete and definitive explanation, attempts to correlate observed phenomena have been in terms of empirical relationships, hopefully of a predictive nature. Extension and refinement of the detailed form of these empirical relationships have led to a clearer understanding of the implications and interpretation of the parameters, in terms of the physical properties of the system.

Many of these correlations take the form of linear relationships

involving the logarithms of rates or equilibrium constants. One of the earliest, put forward by Hammett[1] in 1937, described the influence of meta- and para-substituents on the side-chain reactions of benzene derivatives. As the standard reaction series Hammett took the ionisation of the meta- and para-substituted benzoic acids in water, as there were considerable accurate data available concerning this series. The equation is of the form:-

$$\log(k/k_o) = \sigma\rho \qquad \text{for rate data}$$

$$\log(K/K_o) = \sigma\rho \qquad \text{for equilibrium data}$$

In these equations k_o and K_o refer to the parent compound, k and K to the substituted derivative. For the defining substituted benzoic acid series, ρ, the reaction constant is equal to unity.

The substituent constant or 'sigma-value', initially defined as

$$\sigma = \log(K/K_o)$$

for the standard reaction series, measures the polar effect of the substituent relative to hydrogen, and so represents the ability of a substituent to attract or repel electrons by inductive and resonance effects. If the substituent has an effect of overall electron donation then the σ-value is negative; if the overall effect is one of electron attraction the σ-value is positive. Any given substituent has different σ-values for meta- and para-positions, for example, the Hammett σ-value for p-OCH_3 is -0.268 and for m-OCH_3 is +0.115. Originally Hammett stated that σ-values were independent of the nature of the reaction;

this is however never more than approximately true, but analysis of deviations from this ideal situation has led to the development of more detailed and more comprehensive linear correlations, and through these to a clearer understanding of the effects operating.

In the Hammett equation the quantity ρ is the reaction constant or "rho-value" and this represents the susceptibility of a reaction series to substituent effects. Reactions aided by electron withdrawal from the phenyl ring have positive ρ-values; conversely, reactions aided by electron donation have negative ρ-values. The ρ-value is obtained from a plot of log (k/k_o) against σ; knowledge of σ-values for substituents, and rate or equilibrium data for reaction series with the substituents as members enables ρ-values to be calculated for these series. Correspondingly, knowledge of ρ-values and reactivity data enables σ-values to be calculated. σ-Values are known for about a hundred substituents, ρ-values for about four hundred reaction series. From these, rate or ionisation data are calculable for about forty thousand different compounds.

The dependence of the reaction rate or equilibrium constant upon the solvent system or temperature, for example, is reflected in ρ.

Limitations and Applications of Linear Free Energy Relationships

A linear free energy relationship can be expected only under one of three circumstances. Each reaction series must exhibit one of the following types of behaviour:-

(a) ΔH° is constant throughout the series

(b) ΔS° is constant

(c) ΔH° is linearly related to ΔS°.

Bolton, Fleming and Hall[2] repeated the pK_a measurements of the benzoic acid series at different temperatures and calculated $\Delta G°$, $\Delta H°$ and $\Delta S°$ for these compounds. Relative plots of these thermodynamic parameters gave linear relationships:

$$\Delta H° \quad \text{vs} \quad \Delta S° \qquad r = 0.9992$$

$$\Delta G° \quad \text{vs} \quad \Delta H° \qquad r = 0.9984$$

where r is the correlation coefficient, and is essentially a ratio which expresses the extent to which changes in one variable are accompanied by or are dependent upon changes in a second variable. The more linear the relationship the closer r is to 1.00. From these precise measurements the authors concluded that the linear free energy relationship observed in the ionisation of the benzoic acid series was a consequence of $\Delta H°$ being linearly related to $\Delta S°$.

In general terms, the expression $\log(k/k_o)$ is proportional to the difference in the free energies of reaction of the substituted derivative and the parent compound if the K's are equilibrium constants, or to the difference in the free energies of activation if the k's are rate constants. It is not immediately apparent that such a linear free energy relationship should hold and that one of the three conditions be satisfied, particularly when it is realised that entropy, kinetic energy, and potential energy changes all contribute to the free energy change. It appears that most of the reactions which closely follow the Hammett relationship do not involve any appreciable relative entropy change.

The acknowledgement that systems where neither the kinetic energy nor the entropy remains constant are not correlated in terms of the Hammett equation and that the equation itself may therefore be considered in terms of potential energy differences between appropriate energy states, leads to an equation of the form:-

$$\log(K/K_o) = \Delta E(\text{final}) - \Delta E(\text{initial})$$

where ΔE terms are themselves energy differences between corresponding potential energies of the parent compound and the substituted derivative

$$\Delta E = E - E_o$$

It was based on this assumption that Ehrenson[3] carried out a quantum mechanical perturbation formulation of the problem which he subsequently applied to the justification of the separation of the inductive and resonance contributions to the σ-constant. Assuming that the total Hamiltonian could be conceived as the sum of one electron operators, he considered the effect of both the substituent and the reaction centre on each molecular orbital of the parent hydrocarbon, benzene. He obtained the result that the total change in potential energy was partly dependent on the perturbation due to the substituent, and this was multiplied by a term describing a part dependence on the parent reaction substituent, or, the total potential energy change between the two states (ground state and transition state, say, for kinetic data) was given by an expression in which a substituent function was multiplied by a reaction function. This intrinsically is

the form of the original Hammett equation.

This result was obtained without specifying the symmetry types involved. The only assumption made was that the total Hamiltonian was the sum of one electron operators. If orbital types were to be specified, then this would lead to a division into summations over σ- and π-type orbitals. This possibility of this separation would be expected only if pi and sigma electron perturbations were distinctly different and if interactions between the two were small.

Throughout linear free energy studies ortho-substituents have produced 'anomalous' results. The reason for lack of correlation of ortho-substituted compounds is justifiable in the light of the previous observations and interpretations. The restriction of the validity of the equation to meta- and para-substituted benzenes, and the exclusion of ortho-substituents, leads to the conclusion that steric and other proximity phenomena play a large part in the effects peculiar to ortho-substituents. This observation has implications which have led to several important concepts relating to the nature of substituent effects. It has led to the postulation of primary steric effects of several kinds, including steric hindrance to solvation, or to the approach of the reagent, and proximity effects such as intramolecular hydrogen bonding or other intramolecular interactions. Attempts have been made to separate steric effects from polar and other effects. Many reactions have been studied in this context, but very limited success has attended these attempts to obtain a general separation of effects of ortho-substituents. Shorter[4] has expressed the opinion that "...the complexity of the influence of ortho-substituents on reactivity may make the search for a

single generally applicable scale of σ_o-values quite fruitless..." and this view is subsequently reiterated by Charton.[5]

The unsatisfactory nature of the correlation of ortho-substituted systems does also have bearing on the success of that shown in the case of the meta and para-substituted series.

(ii) Extension of the Hammett Equation to the Correlations of N.M.R. Chemical Shift Data

In addition to equilibrium constant and rate constant linear free energy correlations, there have been reported many correlations with a variety of physical properties for various substrates; notably among these, chemical shifts in nuclear magnetic resonance.

The phenomenon of nuclear magnetic resonance is a consequence of the nuclear properties of the atomic species within the molecule. Most nuclei possess a magnetic moment, and when such a nucleus is placed in a magnetic field, it takes up one of a number of quantised orientations with respect to that field. Each orientation corresponds to an energy level, the lowest being that in which the nuclear magnetic moment is most closely aligned with the field. Nuclear magnetic resonance spectroscopy comprises the induction of transitions between such energy levels by means of fluctuating magnetic fields of the appropriate frequency.

Although its volume is small, a magnetic nucleus gives rise to a finite spatial distribution of positive charge. If, in addition, the nucleus has spin angular momentum, then this phenomenon, which may be thought of as the spinning of the nucleus, will cause the positive charge distribution to rotate and give rise to the

equivalent of a current flowing in a circular path. This produces a magnetic field which is nearly parallel to the axis of spin, and thus the nucleus possesses a magnetic moment, μ.

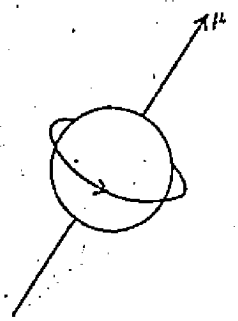


Fig. 1. The magnetic moment, μ, resulting from the rotation of the positive charge distribution of a nucleus.

The quantum mechanical expression for the angular momentum is given by:-

$$I(I+1)h/2\pi$$

where I is the spin quantum number (or spin operator). If I is not equal to zero, then the nucleus has spin angular momentum and under appropriate conditions will exhibit nuclear magnetic resonance phenomena. Species with I = 0 include ^{12}C, ^{16}O, ^{24}Mg, ^{28}Si; species with I = 1/2 include ^{1}H, ^{19}F, ^{31}P, ^{13}C and ^{15}N. Of all these, by far the most important from the point of view of general applicability and well resolved spectra is ^{1}H, but ^{19}F and ^{31}P are now considered routine

nuclei for n.m.r. study.

In an applied magnetic field a proton (I = 1/2) will assume one of two possible orientations with respect to the direction of the applied magnetic field. (In general, the number of possible orientations is given by (2I+1)). The orientations correspond to energy levels of $\pm \mu H_o$, where μ is the magnetic moment of the species and H_o is the strength of the applied field. The transition of a proton from one orientation to the other and thus from one energy level to another may be effected by the absorption or emission of a discrete amount of energy, such that:-

$$E = h\nu = 2\mu H_o$$

where ν is the frequency of the electromagnetic radiation absorbed or emitted, and is the precessional frequency (Larmor frequency) of the nucleus. Unless the axis of the nuclear magnet is oriented exactly parallel or antiparallel with the applied magnetic field, since the nucleus is spinning, its rotational axis draws out a circle perpendicular to the applied field, or the nucleus is said to precess. The nuclear transition corresponds to a change in the angle that the axis of the nuclear magnet makes with the applied magnetic field. This change can be brought about by applying electromagnetic radiation whose magnetic vector component rotates in a plane perpendicular to the main magnetic field. When the frequency of the radiation is equal to that of the precessing nucleus then emission or absorption of energy occurs and the condition of resonance is achieved. For protons in a magnetic field of

1.40 Tesla the frequency of this energy is in the radio-frequency region - about 60 MHz. For fluorine nuclei in the same magnetic field the frequency of the electromagnetic radiation required is about 56.5 MHz.

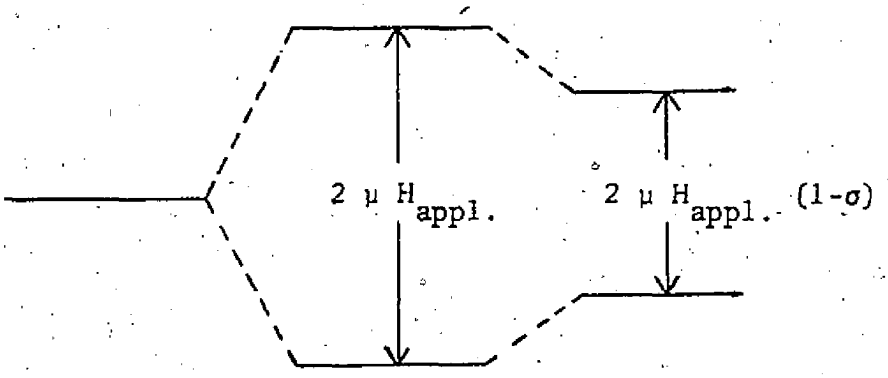
It is possible to induce a nuclear transition in one of two ways; either by maintaining a constant value of the applied magnetic field, and varying the frequency of the rotating magnetic field, or by maintaining the frequency of the rotating field and varying the strength of the applied field over a small range. This latter is the more common procedure.

The fact that nuclear magnetic resonance spectroscopy is such a valuable technique is due in large part to the fact that n.m.r. frequencies are to a small degree dependent on the molecular environment of the nucleus. The surrounding electrons shield the nucleus, and so the effective magnetic field is not the same as that applied. If any atom or molecule is placed in a magnetic field it acquires a diamagnetic moment by virtue of the induced orbital motions of its electrons. These moving electrons constitute effective currents within the molecule and thereby produce a secondary magnetic field which also acts on the nuclei present. The induced currents are proportional to the applied field for diamagnetic molecules. As a result, the local magnetic field at the position of the nucleus is given by

$$H_{local} = H_{appl.}(1-\sigma)$$

where σ is a non-dimensional constant, independent of $H_{appl.}$ and dependent upon the electronic environment. This constant σ is known as the shielding or screening constant, because the local field is usually

less than the applied. The effect of the screening constant brings the energy levels closer together, and so the energy of the transition is smaller and resonance occurs at lower frequency. If resonance is achieved at a fixed frequency by varying the applied field, then a larger field must be applied.



Thus, examination of n.m.r. spectra of a nuclear species in various chemical environments, either in the same molecule or a different molecule, indicates that the shielding constant has different values, and so resonance occurs in a different part of the spectrum for each chemically distinct position. The displacement of a signal corresponding to different chemical environments due to variations in shielding constants is known as a chemical shift and is expressed as a displacement from the resonance signal of a standard reference compound. The chemical shift for the proton is defined:-

$$\delta = \frac{H-H_r}{H_r} \times 10^6$$

where H is the resonance field of the sample

H_r is the resonance field of the reference signal.

It also follows:-

$$\delta = \sigma - \sigma_r$$

The shielding that a proton experiences is a combination of at least three types of electronic circulations: local diamagnetic effects, diamagnetic and paramagnetic effects from neighbouring atoms, and effects from interatomic currents.

A quantitative theory of the atomic contributions to the chemical shifts observed in fluorine magnetic resonance was developed by Saika and Slichter.[6] Saika and Slichter suggested that the principal cause of chemical shifts observed in fluorine containing compounds is paramagnetic in origin. Using simple valence bond wave functions they calculated the paramagnetic contribution to shielding. This should correspond to the difference between a purely ionic bond and a purely covalent bond. This is substantiated by the observation that the fluorine nuclei in F_2 are less shielded than in other fluorine compounds. The more ionic the bond, the more the paramagnetic contribution is reduced, and so this would lead to an approximately linear dependence on the electronegativity of the neighbouring atom or group. In a series of binary fluorides XF_x the ^{19}F shielding increases in a linear fashion as the electronegativity of X decreases.[7]

Many of the attempts at explaining the variations of fluorine shielding constants in molecules have centred on aromatic systems, and almost always on substituted benzenes. The fluorine chemical screening constant is a sensitive means of reflecting the changes in the electronic structure of a substituted aromatic compound. The changes are large at the ortho- and para-positions and less so at the meta-

positions. If a fluorine nucleus is disposed para-to a substituent then the observed chemical shift depends to a large extent on the π-electron distributing effect of the substituent. Substituents such as $-NH_2$ and -OH which result in an increase in π-electron density at the para-carbon atom give rise to an increased shielding of the fluorine atom; correspondingly the converse is observed with π-electron withdrawing substituents. For fluorine, this has been expressed:-

$$^{19}F = K_{^{19}F} \Delta\rho_c$$

where $K_{^{19}F}$ is a constant and $\Delta\rho_c$ is the change in π-electron density at the para-carbon atom. Similarly this trend is observed in ^{13}C and ^{1}H nuclear magnetic shielding. Substituent proton chemical shifts in the para-position are believed to arise, to a large extent, from changes in the π-electron density at the para-carbon atom brought about by the introduction of a substituent.

Studies concerning ^{19}F nuclear magnetic shielding parameters have followed two main approaches. They have either been concerned with describing in detail the connection between a nuclear magnetic resonance shielding constant which it is thought reflects electron density, and the Hammett σ-constant parameter derived from rate or equilibrium constants; or the calculation of shielding parameters from quantum mechanical or electron density models and their subsequent comparison with experimentally observed values.

The effect of substituents on ^{19}F nuclear magnetic shielding in substituted fluorobenzenes is very large and can be accurately measured.

A comparison of the ^{19}F nuclear magnetic shielding in fluorobenzene with that in a substituted fluorobenzene is used to define a ϕ-parameter. $\Delta\phi$ is the ^{19}F magnetic shielding parameter and is defined :

$$\Delta\phi = \left(\frac{H-H_r}{H_r}\right) \times 10^6$$

where H is the applied field for the ^{19}F resonance in the substituted fluorobenzene, and H_r is the applied magnetic field for the ^{19}F resonance in fluorobenzene itself.*

Gutowsky et al.[8] in 1952 reported that an empirical correlation of chemical shift values for meta- and para-substituents with the corresponding Hammett substituent σ-constant revealed systematic differences which were attributed to the dependence of the σ-values on the nature of the electronic interactions of the substituent. These

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* Considerable confusion has arisen in the measurement and recording of ^{19}F substituent chemical shifts for substituted fluorobenzenes as a result of various conventions used by different authors.[7-12] Originally substituent chemical shifts in this series were defined according to

$$\delta = \frac{(H_r-H)}{H_r} \times 10^5$$

where H_r referred to fluorobenzene itself and H to the substituted derivative. Latterly[16,45], the convention has been widely adopted where

$$\Delta\phi = \frac{(H-H_r)}{H_r} \times 10^6$$

The correlation reported by Taft[14] shown on page 17 uses the former convention. This same correlation is reported by Pople, Schneider and Bernstein[141] as

$$\delta_m = -(5.83)\ \sigma_I + (0.0)\ \sigma_R$$

$$\delta_p = -(5.83)\ \sigma_I - (18.80)\ \sigma_R$$

Thus the coefficients are opposite in sign and differ by one order of magnitude. For this reason care should be taken to verify the convention used for the δ or $\Delta\phi$ parameters.

workers reported a general correlation between ϕ- and Hammett σ-parameters, but noted that meta-substituents followed a trend differing from that of the para-substituents. Interpretation of the data by separate solutions demonstrated a fundamental difference in the particular effects operative at the meta- and para-positions.

(iii) Dual Substituent Parameter Relationship

Throughout linear free energy relationship studies workers invariably noticed this intrinsic difference in the nature of the electronic effects transmitted from meta- and para-positions. This was qualitatively explained in terms of the inductive effect only operating from the meta-position; the inductive and resonance effects both operate from the para-position.

With data obtained from aliphatic series, Taft[9-12] defined a parameter σ_I, the inductive parameter, which enabled him to separate quantitatively the Hammett σ-value into independent inductive and resonance contributions according to the equation:-

$$\sigma = \sigma_I + \sigma_R$$

σ_I is the inductive contribution and may be regarded asa measure of the electronic effect of the substituent relative to the hydrogen atom resulting from its power to attract or repel electrons through space and through the sigma bonds of the benzene system. The resonance contribution, σ_R, may be regarded as a measure of the electronic effect resulting from resonance interactions of the substituent with the π-orbital of the benzene system.

Roberts and Moreland[13] obtained pure inductive values of σ_I from a study carried out on an aliphatic series. These workers determined the reactivities of a series of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and their esters:-

Transmission of electrical effects through this system is not possible by resonance involving conjugated unsaturation and so σ-values obtained from these studies are pure inductive parameters.

Taft[9,14] similarly used aliphatic reactivities in the determination of σ_I. Following the observation by Ingold[15] that the system would lend itself to the isolation of this effect, Taft studied the acid and base catalyzed hydrolyses of aliphatic esters:-

$$XCH_2COOEt + H_2O \xrightarrow[k_{H^+}]{k_{OH^-}} XCH_2COOH + EtOH$$

The transition states for these closely related reactions have similar steric requirements, but carry opposite charges. Aromatic σ^*-values are obtained from the equation:-

$$\sigma^* = [\log(k/k_o)_{OH^-} - \log(k/k_o)_{H^+}]/2.48$$

The rate constants k refer to reactions of RCOOR' and k_o to reactions of CH_3COOR' as standard. The OH^- and H^+ refer to base and acid hydrolysis, carried out for the same ester R', solvent and temperature. The ρ value of 2.48 puts the σ^* values on approximately the same scale as Hammett σ-values. It was found that the σ' values of Roberts and Moreland[13] for substituents-X were proportional to σ^* for $-CH_2X$. The value for the ratio σ'/σ^* was +0.45 and so a new scale of inductive substituent constants (σ_I values) was therefore defined as $\sigma_I = 0.45\ \sigma^*$. With a value for the inductive parameter, it was then possible to calculate the resonance parameter contribution to the total Hammett σ-value.

Taft[14] re-evaluated the ^{19}F shielding parameters reported by Gutowsky et al.[8] for substituted fluorobenzenes in these terms. Taft found that correlation of nuclear magnetic shielding effects follows an equation of the general form:-

$$\delta^F = \alpha\ \sigma_I + \beta\ \sigma_R$$

The empirical constants α and β may be regarded as the susceptibilities of the nuclear magnetic shielding to the inductive and resonance interactions of the substituents, respectively. Specifically,

for meta-substituted derivatives:-

$$\delta^F_m = (0.58)\sigma_I + (0.0)\sigma_R$$

for para-substituted derivatives:-

$$\delta^F_p = (0.58)\sigma_I + (1.88)\sigma_R.$$

(see Footnote page 14).

The Hammett sigma values follow equations of a similar form:-

$$\sigma_{meta} = 1.00\ \sigma_I + 0.33\ \sigma_R$$

$$\sigma_{para} = 1.00\ \sigma_I + 1.00\ \sigma_R$$

If indeed δ^F-values and σ-values are related to σ_I and σ_R values, then one would reasonably expect that it would be by different functions. The form of the equations, however, lends considerable support to the thesis that both δ^F and σ are determined by the same basic properties of the substituents, implying that the electronic effect of a meta- and a para-substituent on the free energy of a benzene derivative follows the above equation.

One of the most recent linear free energy relationship studies reported is a refinement of the dual substituent parameter treatment (as this separation of the inductive and resonance contributions to σ-constants has come to be called) and further improvement of σ-values. The article entitled "A Generalized Treatment of Substituent Effects in the Benzene Series. A Statistical Analysis of the Dual Substituent Parameter Equation" is by Ehrenson, Brownlee and Taft.[16] It comprises a rigorous and extensive statistical analysis of existing data, which lends support to many of the earlier concepts concerning linear free energy relationships, but also extends the interpretation of the data. The authors state, "...(1) structural considerations discriminate between at least four practical classes of pi-delocalization behavior, each of which has "limited generality"; (2) the blend of polar and pi-

delocalization effect contributions to the observed effect of a substituent is widely variable among different reaction or data sets (the contributions may be opposite as well as alike in direction), depending upon structural considerations and the nature of the measurement; (3) solvent may play an important role in determination of the observed blend of effects...". The discrimination of at least four practical classes of pi-delocalisation effects and also four classes of substituent constants described above will be discussed at length later.

(iv) Linear Free Energy Relationship Studies in the Naphthalene Series

Wells, Ehrenson and Taft[17] extended the basic dual substituent parameter equation:-

$$\log(K/K_o)_i = \sigma_I \rho_I^i + \sigma_R^o \rho_R^i$$

(the index i indicates the position of the substituent) to the naphthalene system with two objectives in mind. Firstly, in order to test the validity of σ_I and σ_R; if these parameters are characteristic of the substituent then they should be independent of reaction or position of substitution and should be applicable to aromatic systems other than benzene. Secondly, the naphthalene system allows the investigation of the transmission of effects from more than two aromatic positions, which is a limitation in benzene series. The dual substituent parameter equation was examined using data from the study of the acidity of naphthoic acids,[18,19] the saponification of ethyl naphthoates,[20] and of

methyl naphthoates;[21] the acidity of naphthyl ammonium cations;[22] the acidity of naphthols;[23] of pyridinium, of quinolinium and isoquinolinium cations.[24] The analysis was also extended to ^{19}F n.m.r. shielding effects[25] involving all positions of naphthalene which are not subject to serious steric effects. The σ_I and σ_R parameters were fitted independently to the naphthalene system, and the ratio σ_R/σ_I was defined as the blending factor λ. The blending factor would be characteristic of the different positional relations and reactions.

In the naphthalene series the $\sigma_I\rho_I$ term has been attributed to the field and π-inductive effects especially for substituents in the second ring. The π-inductive effect where the reaction site is insulated from conjugation with the aromatic system and also where conjugation is possible has been estimated, but shows little correspondence to the observed relative pattern of σ_I in the naphthalene series. A third effect may also be expected to operate in substituted naphthalenes. If substitution is in the 4, 5 or 8-position of the naphthalene system, the peri-hydrogen exerts a twisting effect on those systems for which a coplanar conformation with the ring is required. This would tend to decrease the conjugative effect of substituents in these positions.

A large proportion of the studies which attempt to derive and define correlations between nuclear magnetic resonance shielding parameters and substituent constants has been made on aromatic systems; at first this was mainly on substituted benzenes. Of late, attention has been turned towards the naphthalene system in order to test the general validity of the concepts. The article by Wells et al.[17] reviews general substituent effect correlations in naphthalene derivatives,

including the correlation of ^{19}F n.m.r. chemical shifts. The ^{19}F n.m.r. shielding values showed a good fit with the dual substituent parameter equation, also showing two different polar or inductive parameter mechanisms. The reaction constants ρ_I are strongly reaction and position dependent; in contrast ρ_R values appear to display essentially identical patterns in both n.m.r. and reactivity data.

The study[17] confirmed that the additive blends of polar and pi-delocalisation effects as described in the dual substituent parameter equation with the substituent parameters defined in previous studies are applicable to the naphthalene system, and are in fact essential for the rationalisation and correlation of observed reactivities and chemical shifts.

Dewar et al.,[25] whilst acknowledging the separation necessary for the successful correlation of substituent effects with ^{19}F n.m.r. chemical shifts, have adopted a slightly different approach. Essentially they combine the direct field effect of a substituent in its simplest form that does not include resonance effects, with a second term which makes allowance for these effects. They suggest the expression:-

$$\sigma_{ij} = \frac{F}{r_{ij}} + Mq_{ij}$$

where F/r_{ij} describes the change in electrostatic energy calculated for a point charge. The second term describes the effect on σ of a change in pi-electron density at j by a substituent at i conjugating with the delocalised aromatic system.

This equation has been applied to 3'- and 4'-substituted-4-

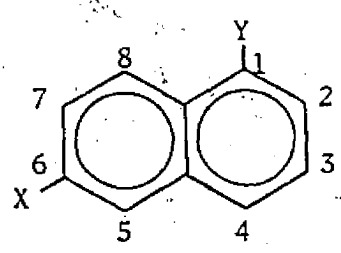
fluorobiphenyls;[26] 3''-substituted-4-fluoroterphenyls;[26] and to substituted 1- and 2-fluoronaphthalenes.[17] This slightly intuitive approach has been criticised[27] in that, by its nature, it tacitly assumes that ^{19}F n.m.r. chemical shifts are determined by the electrostatic potential energy at the fluorine atom caused by a polar substituent plus a term proportional to the pi-electron density. If a similar expression is derived from theoretical considerations, then the shielding constant is proportional to both the electric field component along the bond to the fluorine atom, and also to the square of the electric field at fluorine.[28-30]

The proponents[25] of this treatment of structure-reactivity correlations refute the concepts of Taft's approach, and yet in essence make similar considerations and rationalise the experimental observations in similar terms. Adcock and Dewar[25] have demonstrated a good linear correlation between the substituent effect on the chemical shift (S.C.S.) of the substituted fluoronaphthalene and the pK_a of the correspondingly substituted naphthoic acid (in which the F of the fluoronaphthalene is replaced by -COOH):-

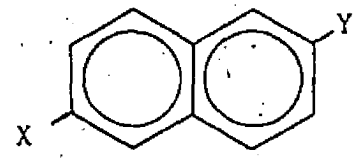
$$S.C.S. = a(pK_a) + b$$

However, the relative sensitivity of the ^{19}F chemical shift to the effect of the substituent, compared with the sensitivity of the pK_a value to the effect of the same substituent, is very dependent on the position of the substituent and the functional group. Thus when the functional group is in the 1-position and the substituent at the

6-position (I) a in the above equation is -3.1. When the functional group is at the 2-position and the substituent is at the 6-position (II), a is -12.0.



Y = F,COOH
X = substituent
(I)



Y = F, COOH
X = substituent
(II)

Adcock and Dewar[25] suggest that the ^{19}F chemical shift is dependent on the field along the line of the C-F bond, i.e., there is an anisotropic response of fluorine to an applied field. On the other hand, the stabilisation of the carboxylate ion (presumably the important factor in the substituent effect on the acid dissociation) exhibits no such directional dependence on the field. It is to be noted that in (II) the substituent dipole is in line with the C-F bond, and is thus more favourably positioned than in (I) to exert the maximum effect on the ^{19}F n.m.r. shift.

Theoretical Considerations of Chemical Shift - Substituent Parameter Correlations

(i). Quantum Mechanical Calculation of Shielding Parameters

There have been many attempts to calculate the nuclear magnetic shielding constants of fluorine nuclei.[28-35] These calculations have only been applied to very small molecules if at the same time the author has made any claim to mathematical rigour. Treatments applied to larger molecules are therefore based on principles more exhaustively investigated for small molecules, e.g. F_2, HF and LiF.

One of the earliest attempts reported was that by Ramsey[31] who derived a shielding tensor ($\sigma_{N_{zz}}$) using second-order perturbation theory, summed over all electrons (K) and all unoccupied unperturbed molecular orbitals ψ_n. The operator L_{zK} is the z component of the orbital angular momentum of electron K, and r_{NK} is the distance from the nucleus N to the electron K. The first term summed over ground state wave functions is known as the diamagnetic term, and the second summed over the unoccupied wave functions is known as the paramagnetic term.

$$\sigma_{N_{zz}} = \frac{e^2}{2mc^2} \sum_K \left\langle \psi_{OK} \left| \frac{x_K^2 + y_K^2}{r_{NK}^3} \right| \psi_{OK} \right\rangle - \frac{e^2\hbar^2}{2m^2c^2} \sum_K \left\{ \sum_{n\neq 0} \left[\frac{1}{E_n - E_o}\right] \times \right.$$

$$\left\langle \psi_{OK} \left| L_{zK} \right| \psi_{nK} \right\rangle \left\langle \psi_{nK} \left| L_{zK}\, r_{NK}^{-3} \right| \psi_{OK} \right\rangle + \left\langle \psi_{OK} \left| L_{zK}\, r_{NK}^{-3} \right| \psi_{nK} \right\rangle$$

$$\left. \left\langle \psi_{nK} \left| L_{zK} \right| \psi_{OK} \right\rangle \right\}$$

For an atom in an s state the second term of this equation is zero; for example, the shielding of fluorine in the free fluoride is purely a consequence of the diamagnetic behaviour of the electrons. One might therefore predict a correlation between the shielding constant and the ionic character of the bond in diatomic fluorides. As mentioned previously, Gutowsky and Hoffman[7] showed that a very good correlation of this kind does exist in this series, with one notable exception, that of ClF. This exception has been rationalised in terms of the paramagnetic term in Ramsey's equation being large and positive due to a dominant term in the sum over unoccupied unperturbed molecular orbitals which involves a $\pi^* \rightarrow \sigma^*$ transition between orbitals now closely separated in energy.

To solve Ramsey's equation and hence calculate the shielding constant requires a good set of wave functions. The first term, the summation over ground state wave functions ψ_{0K} may be evaluated, but the second term involves a summation over unoccupied wavefunctions and is therefore very difficult for all but the simplest systems with few electrons. For these reasons several approaches have been adopted based in the first instance on Ramsey's treatment, but incorporating modifying assumptions which make shielding constants amenable to calculation.

Karplus and Pople[32] assumed that wave functions could be expressed as linear combinations of atomic orbitals; all two-centre integrals were neglected. The modified equation for the shielding of the nucleus N was:-

$$\sigma_{N_{zz}} = \frac{e^2}{3mc^2} \sum_K P_{KK} \left\langle r^{-1} \right\rangle_K \frac{-2e^2\hbar^2}{m^2c^2} \left\langle r^{-3} \right\rangle_{2P_N} \sum_i^{occ} \sum_j^{unocc} (E_j - E_i)^{-1}$$

$$(C_{ixN}C_{jyN} - C_{iyN}C_{jxN}) \times \sum_B (C_{ixB}C_{jyB} - C_{iyB}C_{jxB})$$

Where P_{KK} is the population of atomic orbital K, and C_{ixN} and C_{jxN} are coefficients of the $2p_x$ atomic orbital centre on N, in respectively occupied and unoccupied orbitals. This equation still requires a knowledge of the unoccupied molecular orbitals and so is commonly modified further by the use of the average energy approximation so that the equation becomes:-

$$\sigma_{N_{zz}} = \frac{e^2}{3mc^2} \sum_K P_{KK} \left\langle r^{-1} \right\rangle_K \frac{-e^2\hbar^2}{2m^2c^2} \Delta E \left\langle r^{-3} \right\rangle_{2P_N} \sum_B (Q_{NB})_{zz}$$

where $(Q_{NB})_{zz}$ depends only on ground state wave functions.

(ii) Electron Density - Substituent Parameter Correlations

It is possible to calculate the shielding constant for the fluorine nucleus (σ_F) using the modified Karplus-Pople equation. It is still desirable to reduce this equation to a simpler expression relating σ_F to changes in π-electron density in planar conjugated systems, and so the equation is summed over two atoms, the fluorine atom and the carbon atom to which it is attached. This gives rise to a relation between the change in the paramagnetic component of the shielding constant, $\Delta\sigma^p$, the change in the π-density on fluorine, ΔP_F, and the change in the π-bond order, ΔP_{CF}, between the two atoms.

$$\Delta\sigma_F^P = -\frac{36.008}{\Delta E}(A - 0.3308\ P_F)^3(B + C\Delta P_F + D\Delta P_{CF})$$

A, B, C and D are constants depending on the σ-electron distribution, C only is negative. The diamagnetic contribution to the total shielding is usually zero and so $\Delta\sigma_F \simeq \Delta\sigma_F^P$.

Assuming that only electrons in atomic orbitals centred on fluorine are of any significance in this context, Karplus and Das[33] derived an equation relating change in ionic character ΔI, and π-density, ΔP_F, to the chemical shift:-

$$\delta = 765\ \Delta I + 777\Delta P_F$$

Prosser and Goodman[34] derived a similar expression, the differences being due to their including electrons in atomic orbitals centred on both fluorine and the attached carbon atom, and assuming ΔI = 0:-

$$\delta = \frac{488}{\Delta E}[11.9\Delta P_F + 0.1\Delta P_C + 3.9\Delta P_{CF}]$$

where ΔP_C and ΔP_{CF} are changes in the π-density on carbon and the C-F π-bond order respectively. Dailey and Wu[35] produced a similar equation in which the coefficient λ is the ionic character of the bond:-

$$\delta = 627.1\Delta P_F - 155.1\Delta P_{CF} + 574.9\Delta\lambda$$

All the previous equations are derived in the first instance from Ramsey's equation. Their differences are due to the slightly different

nature of the simplifying assumptions made, and yet all appear to be striving towards a linear relationship between π-electron densities and the chemical shifts of fluorine nuclei.

At this point it is probably appropriate to mention that as with all the different aspects of the implications, the extensions, and the theoretical concepts pertaining to the subject of fluorine chemical shifts, all sources of information are interrelated. The flow of evidence and support is multi-directional, which is at the same time both the weakness and the strength of the study. To attempt to shed a little light onto this rather nebulous statement, consider the Hückel method of determining π-densities. One might argue that if the Hückel method is used to determined π-densities, then Coulomb and resonance integrals should be determined by reproducing some property directly proportional to π-densities, for instance the chemical shift itself. It would be possible to determine a set of relative Coulomb and resonance integrals to produce the correct para fluorine shifts, say in the Prosser and Goodman equation, and subsequently to determine the π-densities at meta- and ortho-positions using these values. The weakness of this method would be the inadequacy of the Hückel method in deriving correct π-electron distributions in molecules with constant values of the substituent parameters. Attempted correlations are adequate within the context of their own implicit limitations.

"...But as yet not one of the calculations has used a method for calculating the π-charge distribution which has any claim to mathematical rigour..."[27]

To illustrate the nature of many such contemporary studies, their

limitations and their applications, two of the most recently reported will be described. The first is a study by Paleta, Skála and Kuthan,[36] in which these workers attempted to estimate π- and σ-electronic structure of some fluorinated hydrocarbons, namely a number of fluorobenzenes and perfluoronaphthalenes, by means of simple M.O. methods. The π-structure was calculated by means of a simple H.M.O. method and the σ-electronic structure was calculated using the Del Re method. This study was an attempt to verify the conclusions drawn by Karplus and Das,[33] and Prosser and Goodman[34] that the fluorine chemical shift depends mainly on the π-electron density on fluorine and on the bond order of the corresponding π-bond. Correlations were attempted between chemical shifts and π-charges alone, and between chemical shifts and the total π- and σ-charges. A better correlation was obtained with π-electron charges alone. When the total charges were used, the correlation field split into three groups according to the number of ortho interactions with fluorine atoms in the individual derivatives. No single treatment was adequate to describe all cases considered, but if the structure types were acknowledged then rationalisation of their behaviour was possible.

Brownlee and Taft[37] calculated charge densities using a CNDO/2 method for ten meta- and para-substituted fluorobenzenes, trans-substituted fluoroethylenes, and substituted fluoroacetylenes, for mono-derivatives of these and for 4-substituted [2.2.2]-bicycloocty1-1-fluorides. Brownlee and Taft make the somewhat familiar observation that none of the existing formulations of ^{19}F nuclear magnetic resonance shift in terms of charge density and bond order gives satisfactory

calculation of experimental results using CNDO/2 results; their conclusions are therefore empirical in nature. Like Paleta et al.,[36] Brownlee and Taft concluded that π-orbital charge density of the fluorine probe reflected the π-electron effect prevailing at the bonded carbon atom. The substituent effect on the fluorine σ-orbital charge density of para-substituted fluorobenzenes and 4-substituted [2.2.2]-bicyclo-octyl-1-fluorides corresponded well to the polar effect scale, σ_I. Neither the π-electron density at the carbon bonded to the fluorine nor the fluorine σ-orbital charge density appeared to be related to the electron densities at any of the intervening carbon atoms and the authors suggested that the effects observed are a consequence of a direct dipolar substituent-polar fluorine interaction.

The dominant effect of the meta-substituent on the fluorine orbital densities is on the σ-charge density; the π-effect from the same position was too small to even identify its direction correctly. Brownlee and Taft stated that the close correspondence between empirical correlations and conclusions from CNDO/2 calculations strongly suggests that the fluorine nuclear magnetic resonance shift may be directly related, at least approximately, to the sum of the separate effects on the σ- and π-charge densities of the fluorine orbitals. Their results indicate that the fluorine nuclear magnetic resonance shifts are more highly dependent upon charge density in the fluorine $2p_z(\pi)$ orbital than that in the $2p_y(\sigma)$ orbital, a conclusion also reached by Dewar and Kelemen[38] from studies of fluorine n.m.r. shifts of aryl polyfluorides. One might predict that a consequence of this different dependence would be lack of correlation of ^{19}F n.m.r. shifts for para XC_6H_4F and the

substituent effect on the total charge density of fluorine (in fact this is found to be the case, which reiterates the findings of Paleta et al.[36]). The fluorine shifts of the 4-substituted [2.2.2]-bicyclooctyl-1-fluorides are in a qualitative σ_I order but the direction of the shifts is opposite to that in the fluorobenzene system. It was suggested that geometrical considerations probably are the dominant factor in influencing experimental ^{19}F n.m.r. shifts in this system.

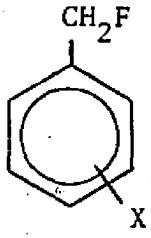
The present state of knowledge concerning the factors affecting fluorine chemical shifts does not adequately describe many experimental observations. Many of the discrepancies arise from the unavailability of reliable values for parameters used in theoretical treatments of the problem. However, in spite of the fact that the corresponding parameters for proton chemical shifts have been determined with far greater certainty in a recent study by Emsley, Lindon and Salman[39] of several 1-substituted naphthalenes these authors stated that no one simple model was capable of predicting substituent chemical shift values in these naphthalenes.

Benzyl Fluorides and Fluoromethylnaphthalenes

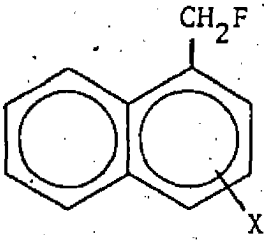
The foregoing description of the present state of knowledge of linear free energy correlations and ^{19}F nuclear magnetic resonance shifts constitutes the context for the current study, the ^{19}F n.m.r. chemical shifts of substituted fluoromethylnaphthalenes.

Fluoromethylnaphthalenes are not previously known. Their benzene analogues, the benzyl fluorides, were first synthesised in 1928 by the Ingolds.[40] They have been reported in the literature several times since then[41-46] and have been studied in both the context of reactivity

in terms of kinetic studies[41-44], and in the context of correlations between substituent effects and ^{19}F n.m.r. chemical shifts.[45,46] In these latter n.m.r. studies of substituted benzyl fluorides



benzyl fluorides

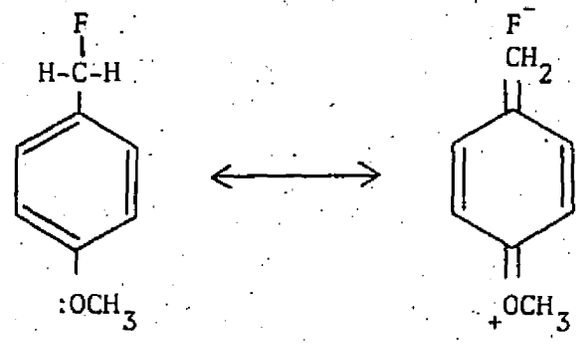


fluoromethylnaphthalenes

Bĕguin[45] and Yokoyama et al.[46] described a poor correlation between proton magnetic resonance chemical shifts and substituent parameters; good correlations were observed with ^{19}F n.m.r. chemical shifts. Bĕguin[45] reported that the introduction of an electron-donating substituent into the benzyl fluorides induced a fluorine n.m.r. signal at lower field than in the unsubstituted derivative. This is in contrast to the effect observed in fluorobenzenes when introduction of an electron-donating substituent results in increased shielding at the fluorine atom and hence in an upfield shift. The substituent effect in the fluorobenzenes is in the expected direction, i.e., an increase in the electron density results in increased shielding. Substituent effects in 2-phenylethylfluorides are similar to those in benzyl fluorides,[48] electron-donating substituents deshield the fluorine. In the benzyl fluorides this observed inversion of the effect has been rationalised in terms of hyperconjugation.[16,45]

Bĕguin carried out Hückel M.O. calculations of π-charge density and bond orders for fluorobenzenes and benzyl fluorides, and showed that conjugation diminished in passing from fluorobenzene to para-methoxy fluorobenzene; the bond order decreased accordingly. The π-charge on

the fluorine atom was augmented. Similar calculations in the benzyl fluoride system allowed for the incorporation of two electrons from the $-CH_2F$ group into the π-system if one assumed fluorine hyperconjugation:-

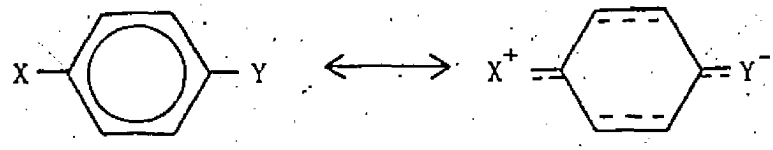


The effects are in the π-bond orders and π-charges which arise from the interaction of the π-electron cloud of the benzene system with the σ-electrons of the C-H and C-F bonds of $-CH_2F$. The calculation showed that hyperconjugation augments in passing from benzyl fluoride to <u>para</u>-methoxybenzyl fluoride. The π-bond order increases correspondingly, as does the π-charge. In the fluorobenzene system, as mentioned, the reverse is observed.

Bĕguin concluded that there is an important intrinsic difference in the n.m.r. of the proton and the fluorine atom. For the proton the factor which essentially determines the chemical shift is associated with the electron density on the proton; for fluorine the chemical shift is associated above all with the electronic structure of the chemical bonds in the vicinity of the fluorine, and not solely with the magnitude of the electron density on the fluorine, a concept that we have considered earlier in some detail. The variation of bond order best allows one to interpret the influence of a substituent on the chemical shift. An electron-donating substituent induces a decrease in double-bond character between Ph- and -F in the fluorobenzenes, which gives a displacement towards high field in the fluorine n.m.r., but

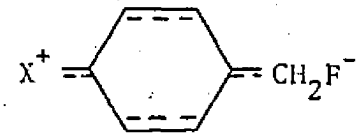
induces an increase in double-bond character between Ph- and $-CH_2F$ in the benzyl fluorides, which gives a displacement towards low field in the fluorine n.m.r.

Ehrenson, Brownlee and Taft[16] discussed the ^{19}F n.m.r. phenomena of this series in considerable detail in connection with their analysis of the dual substituent parameter equation. Their subsequent observation is that there are at least four classes of pi-delocalisation behaviour, each with limited generality. The ^{19}F n.m.r. studies of the benzyl fluorides were included by these authors in the BA class, correlated by $\sigma_{R(BA)}$. The ionisation of benzoic acids in water at 25°C plus several analogous reactions, such as ionisation and saponification of benzoic acids, naphthoic acids,[47] cinnamic acids and phenylpropriolic acids, defined the $\sigma_{R(BA)}$ parameters for this class. The fluorine n.m.r. shifts of benzyl fluorides were introduced as an additional data series of the BA type. In this analysis[16] this data set was rationalised as a structural analogue of the defining reaction series, all being of the type:-

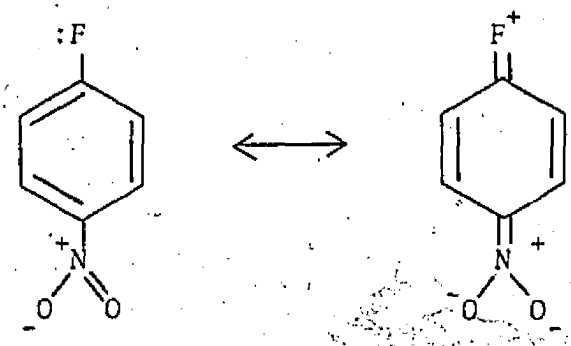


where Y is a weak to moderate pi-acceptor group. Examples of such Y groups include carboxylic acid and derivative groups, SO_2NHR, $Se(OH)_2$, $As(OH)_2$, $As(OH)_2O^-$, $COC_6H_4F(p)$, SF_5, $C_6H_4F(p)$, $SC_6H_4F(p)$ and CH_2F. The groups apparently all possess weak pi-electron acceptor

orbitals. "...The CH_2F can presumably act as a weak acceptor through the contribution of the hyperconjugative form"[16]:-



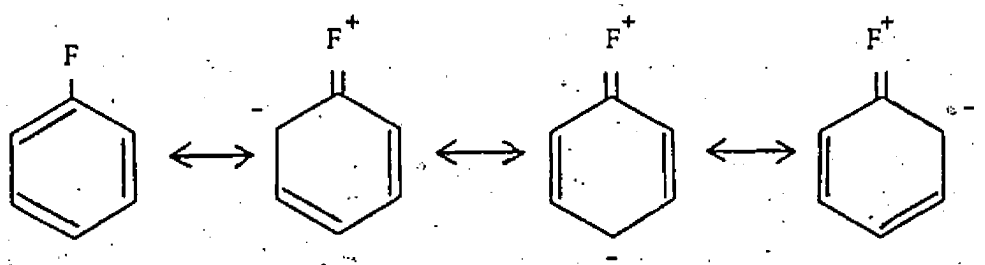
In this study the fluorobenzenes are found to fall into the σ_R^o series "...for which neither +R nor -R substituent effects from the para-position are enhanced or retarded by quinoidal-type resonance effects..."[16] The most obvious reaction series of this type is that in which a methylene group is interposed between side-chain reaction centre and the benzene ring (a notable exception being the ^{19}F n.m.r chemical shifts of benzyl fluorides). The ^{19}F n.m.r. shielding effects of para-substituted fluorobenzenes appear to be well correlated by σ_R^o values and in fact were used prominently in defining the scale. This is contrary to that which one might expect, however. Although fluorine is the weakest π-electron donor of the first row elements capable of donating an electron pair, it has a significant σ_R value. Para-quinoidal type resonance structures would be expected to contribute, e.g., in p-fluoro-nitrobenzene:-



and give rise to enhanced resonance effects. Thus, $\sigma^{-}_{R(A)}$ rather than σ^{o}_{R} behaviour would be anticipated. Such resonance effects are of minor importance in this series for reasons not yet understood.

It would therefore seem that the existence and nature of resonance stabilisation in the benzyl fluorides and fluorobenzenes is quite different. It is also of interest to note that of all the ^{19}F n.m.r. studies included in these two categories, only two, the benzyl fluorides and the aryl sulphur pentafluorides, both $\sigma_{R(BA)}$ type, have positive ρ-values; all others are negative. It is worth noting that the ρ-value from a single substituent parameter analysis for ^{19}F n.m.r. shifts of substituted fluorobenzenes in methanol is -14.99 and in cyclohexane -13.30, whereas for the benzyl fluorides in carbon tetrachloride it is +11.28, opposite in sign, but of the same order of magnitude.

The concept of conjugation of fluorine has been objected to. The classical resonance picture as applied to the fluorobenzenes in order to explain the ortho-para directive effects and the use of resonance contributors such as:-

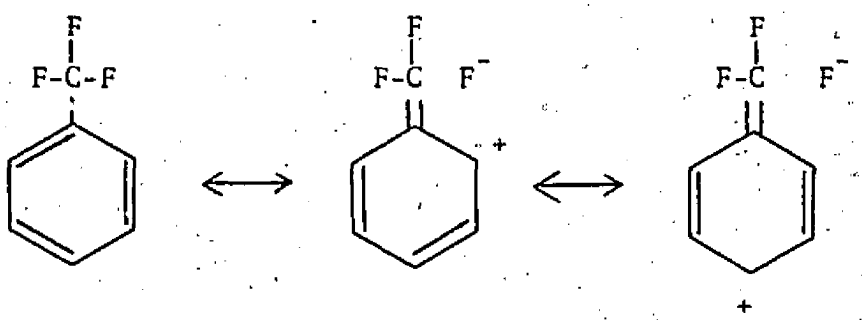


has been questioned and considered inadequate, particularly when explaining the marked preference for para-substitution over ortho-. The σ_R value, which is a semi-quantitative measure of electron donation or withdrawal by resonance is large and negative for fluorine. The conclusion that this indicates a strong electron donation by resonance

has been criticised as misleading. The shortness of the C-F bond and the correspondence of size of the orbitals containing p- and π-electrons means that p-π interaction is at a maximum. The powerful inductive effect of the fluorine is felt more strongly at the ortho-position but falls off in effect very rapidly with distance. The conventional resonance picture above is misleading in as much as fluorine will never carry a positive charge. The large electronegativity of fluorine results in the withdrawal of electrons from the sigma framework and accumulation of electron density on fluorine. This accumulation of charge is only partly fed back to the π-system by resonance.

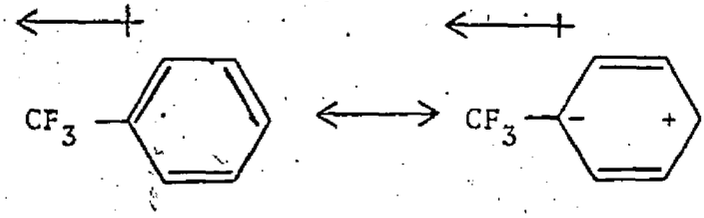
Murrell[48] has proposed that fluorine is different from other halogens and does not return electrons to the π-system by resonance at all, but rather, strongly repels the π-electrons. The high electron density accumulated by the inductive effect of the fluorine has a strong repulsive effect on the π-electron density and concentrates the charge density in the para-position.

Fluoride ion hyperconjugation, or no-bond resonance first conceived by Roberts,[49] was invoked to rationalise the observation of a significant +R(-M) resonance effect for a $-CF_3$ group, which cannot be accounted for by classical resonance interactions.



Alternative mechanisms to fluoride ion hyperconjugation have been proposed, namely the π-inductive mechanism, and the p-π mechanism.

Holtz[50] interprets the reactivity behaviour of the trifluoromethyl group by means of an inductive model, the so-called π-inductive effect. This describes the strong electron-withdrawing effect of the trifluoromethyl group as a dipole external to the benzene ring polarising the π-system, and in so doing, enhancing the delocalisation of negative charge.



Sheppard[51,52] proposed a rationalisation of the observations in terms of a fluorine p-π interaction. This was that the interaction of the p-electrons of the fluorine atoms with the π-system of the aromatic ring causes significant return of electron density to the ring. This return is more effective to the meta-position than the para-, so the para-position appears to be more strongly deactivated. The mode of overlap is shown below; the fluorine is within the minimum distance necessary for such interaction to occur.

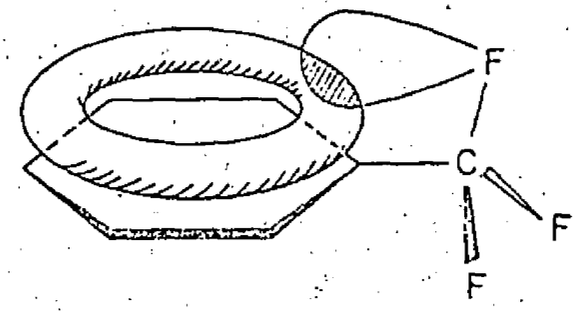
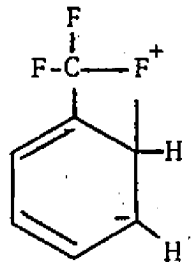


Figure 2. Diagram showing orbital overlap in benzotrifluoride.

This overlap may be represented:-



Molecular orbital calculations support the feasibility of the feed-back through the π-system. The net charge density in benzotrifluoride is calculated to alternate so that the ortho- and para-positions appear more deficient in charge density than the meta-position.

Reactivity of Benzyl Fluorides

Alkyl fluorides are considerably less reactive than their analogous chlorides. For the methyl, benzyl, diphenylmethyl and triphenylmethyl halides substitution reactions are possible and the rate determining steps for the two established mechanisms are as follows:-

$$Ph_3C\text{-}X \longrightarrow [Ph_3C^{\delta+} \cdots X^{\delta-}] \longrightarrow Ph_3C^{+} + X^{-} \quad S_N1$$

$$H_2O + MeX \longrightarrow [H_2O^{\delta+} \cdots Me \cdots X^{\delta-}] \rightarrow H_2O\text{-}Me^{+} + X^{-} \quad S_N2$$

The fluorine-chlorine reactivity ratio increases (becomes nearer to unity) for the hydrolytic reactions in the series triphenylmethyl → diphenylmethyl → benzyl[42] → methyl (3° → 2° → 1°), i.e. as the transition state increases in S_N2 character. That alkyl fluorides are much less reactive than the corresponding chlorides has been shown in the following

cases: solvolysis in aqueous ethanol of the cyclohexyl, 1-methylbutyl, 2-methylbutyl, pentyl and t-pentyl halides,[53] the reactions of the 3-methylbutyl halides with methanolic sodium methoxide and with excess piperidine,[54] reaction of methylhalogenoacetates and halogenoacetate ions with sodium thiosulphate in water,[54] the solvolysis of the benzyl halides and substituted benzyl halides in aqueous ethanol, and their reactions with ethanolic sodium ethoxide and with sodium iodide in acetone.[55,56] It has also been shown that methyl fluoride and trifluoromethyl fluoride are much less reactive towards sodium atoms in the gas phase than the corresponding chlorides.[57,58]

When Arrhenius parameters are determined for reactions in hydroxylic solvents, they show that the lower reactivity of alkyl fluorides than of alkyl chlorides is a consequence of an increased energy of activation and a decreased entropy of activation (e.g. methyl halides with water or OH^-).[59,60] The increase in solvation on formation of the transition state is much greater for the fluoride than for the chloride (because of the very high solvation of the incipient fluoride ion) with a consequent reduction in entropy of activation for the fluoride. The energy of activation for the fluoride reaction is reduced below what it would be without this solvation, and may even be reduced below that for the chloride reaction. It is probable that in non-hydroxylic solvents or in the absence of solvent, the fluoride reactions would have very high energies of activation because of the very high bond strength of C-F bonds, and this is confirmed by the results with sodium atoms.[57,58]

The high solvation energy of the incipient fluoride ion in hydroxylic solvents is due to hydrogen bonding,[61] and since a solvated

proton should be able to hydrogen-bond to an incipient fluoride ion more efficiently than a molecule of water or alcohol, these reactions would be expected to show acid catalysis in appropriate circumstances. This has in fact been shown for the solvolysis of benzyl fluoride in aqueous acetone,[42] for the solvolysis of benzyl fluoride in formic acid,[43] of benzyl fluoride and substituted benzyl fluorides,[56] cyclohexyl, 1-methylbutyl, 2-methylbutyl, 1-pentyl and t-pentyl fluorides[53] in aqueous ethanol. The reactions of the corresponding chlorides do not show acid catalysis and this is due to the inability of chlorine to form strong hydrogen-bonds.

Swain and Spalding[42] have shown that for the acid catalysed hydrolysis of benzyl fluoride in 10% aqueous acetone the log of the rate constant is proportional to the Hammett acidity function, H^{o} (and not $[H^{+}]$) and they favour an A1 mechanism:-

$$PhCH_2F + H_3O^+ \underset{\text{fast}}{\rightleftharpoons} PhCH_2\overset{+}{F}H + H_2O$$

$$PhCH_2\overset{+}{F}H \xrightarrow{\text{slow}} PhCH_2^+ + HF$$

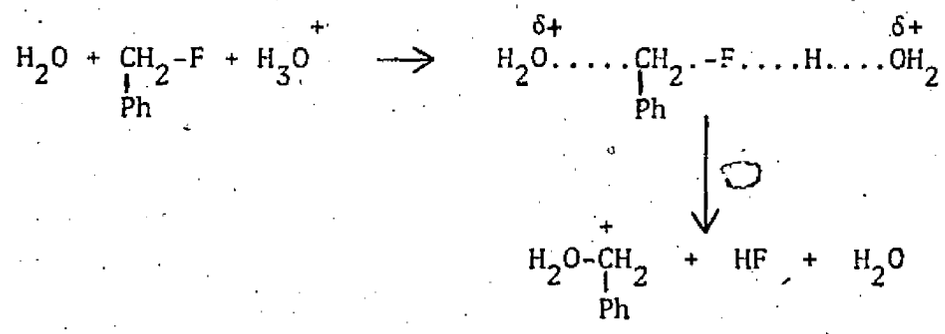
and for the hydrolysis of methyl fluoride they expect an A2 mechanism:-

$$CH_3F + \overset{+}{H_3O} \underset{\text{fast}}{\rightleftharpoons} CH_3\overset{+}{F}H + H_2O$$

$$H_2O + CH_3\overset{+}{F}\text{-}H \xrightarrow{\text{slow}} H_2\overset{+}{O}\text{-}CH_3 + HF$$

Parker[62] disagrees with the A1 mechanism for hydrolysis of benzyl fluorides and suggests that a water molecule would be involved as a

nucleophile in the rate determining step for the reactions of both of these primary halides (even though the transition state for the benzyl fluoride reaction may well be more S_N1 in character than S_N2, with extremely long F-R-Y bonds in the transition state). He suggests that $PhCH_2\overset{+}{F}\text{-}H$ containing divalent fluorine is doubtful and he proposes the following alternative mechanism:-



The only well-established cases where saturated alkyl fluorides appear to be more reactive than the chlorides are in Friedel-Crafts alkylation reactions. Fluorides have been shown to be more reactive than chlorides in the reactions of butyl, benzyl, and substituted benzyl halides with benzene,[41,63] and the cyclohexyl halides with toluene.[61] This means that either the rate-determining step does not involve appreciable C-X bond stretching, or that if it does, the extra energy necessary to stretch the C-F bond is more than balanced by a greater gain of energy for the fluoride than the chloride from some other process. Parker[63] suggests that the latter explanation is more likely and that the gain of energy probably arises from the coordination to aluminum chloride or other Lewis acid (electrophilic catalysis). In order to explain fluorine to chlorine ratios greater than one, it is necessary to assume that the greater gain of energy from

the formation of an Al-F bond than for an Al-Cl bond, more than compensates the greater consumption of energy in the breaking of an R-F bond, rather than an R-Cl bond. Bernstein, Roth and Miller[41] reported that "...the benzyl fluorides underwent Friedel-Crafts type reaction with aromatic hydrocarbons, in many cases with great ease. They underwent typical halide replacement-type reactions, but at much slower rates than the corresponding chlorides..." (Details of the reactions of benzyl fluoride were first reported by Ingold[40] in 1928). In the solvolysis of a series of substituted benzyl chlorides there appears to be a transition from a S_N2 to S_N1 type mechanism. Such behaviour is not exhibited in the formolysis of benzyl fluorides, all of which appear to solvolyse by the S_N1 mechanism. The Grignard reagent could not be prepared from benzyl fluoride. Attempts to prepare it under vigorous conditions always led to the formation of dibenzyl.

The relative rates of solvolysis of the substituted benzyl fluorides have been reported by Miller and Bernstein.[56] Bēguin and Meary-Tertian[44] observed a similar order:

$$p\text{-}OCH_3 \rangle\ p\text{-}CH_3 \rangle\ p\text{-}F \rangle\ m\text{-}CH_3 \rangle\ H \rangle\ m\text{-}OCH_3 \rangle\ p\text{-}Cl \rangle$$
$$p\text{-}Br \rangle\ m\text{-}F \rangle\ m\text{-}Cl \rangle\ m\text{-}CN \rangle\ p\text{-}CN \rangle\ m\text{-}NO_2 \rangle\ p\text{-}NO_2$$

for the effect of substitution in increasing the reactivity of the side-chain in the formolysis of benzyl fluorides. The rate of formolysis was proportional to σ^+ from which they deduced that the acid-catalyzed solvolysis occurred by a mechanism having a transition state approaching the benzyl cation. In general, electron-donating groups which conjugate

with the reaction centre lead to rapid solvolyses consistent with the intermediate formation of a benzyl cation. Thus the reaction consists initially of the departure of the fluoride ion, rendered more facile by means of the acid catalysis. Béguin and Meary-Tertian[44] reported a ρ-value of -6.20 for this reaction. This large negative value is consistent with a highly positive transition state, i.e. S_N1. One of the conclusions from the work of Ehrenson, Brownlee and Taft[16] in which they analysed statistically a number of reactivity studies in naphthalene systems,[64-66] was that resonance interactions between an electron-withdrawing group in the 1-position and an electron-donating group in the 4-position are greater than in the benzene series. In valence bond theory terms this observation may be readily rationalised by considering the relative number of discrete resonance canonicals contributing to the total hybrid, three for benzene derivatives of this type, five for 1,4-disubstituted naphthalenes.

Objectives of the Present Project

The aim of this work is to synthesise a series of substituted fluoromethylnaphthalenes and to measure their fluorine n.m.r. chemical shifts. Several aspects of the structure - ^{19}F n.m.r. correlations of these compounds are of considerable interest. The data reported for the analogous benzyl fluorides have raised many questions regarding the electronic distribution in these molecules, and in particular the nature of the ^{19}F n.m.r. response to this distribution. The explanation of the observed trend in the benzyl fluorides, opposite to that in the substituted fluorobenzenes, in terms of the π-electron density prevailing at the carbon bonded to the fluorine,[45] is entirely empirical

in nature. The present state of knowledge of the factors contributing to the screening constant of the fluorine nucleus is quite contrary to this assumption; the major factor is thought to be the paramagnetic term which is a reflection of the electron density and its distribution at the fluorine atom itself. For these reasons it is of interest to see if the sign of the substituent effect on the ^{19}F n.m.r. chemical shift is opposite to that in the fluoronaphthalenes. Proton chemical shifts of benzyl fluorides did not correlate well with substituent parameters, neither did the coupling constant J_{CH_2-F}.[45] Measurement of these parameters in the case of the fluoromethylnaphthalenes may or may not follow this pattern. Not only is this study of significance in the context of interpretation and understanding of the ^{19}F n.m.r. phenomenon but it is also of interest from the point of view of rationalisation by invoking the concept of fluorine hyperconjugation as Bĕguin[45] did for the benzyl fluorides. Several alternative structural concepts have been proposed, and the data gleaned from the present study must be analysed in terms of these. Moreover, if resonance effects are an important component of the total substituent effects as Bĕguin[45] claims to have found in the case of the benzyl fluorides, then this should be even more important in the fluoromethylnaphthalenes as long as the peri-hydrogen does not exert a twisting and hence resonance-inhibiting effect on either substituent.

CHAPTER 2

EXPERIMENTAL

Introduction

Infrared spectra were determined on a Perkin-Elmer model 337 spectrometer calibrated with polystyrene. Nuclear magnetic resonance spectra were determined on a Perkin-Elmer R 12 A, on a Varian HA-60-IL or on a Varian HA-100-IL spectrometer using tetramethylsilane as internal standard for ^{1}H spectra and CCl_3F as external standard for ^{19}F spectra. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-7 instrument. Microanalyses were by Dr. A.D. Campbell, University of Otago, Dunedin, New Zealand and by Dr. D. McGillivray, University of Victoria, Victoria, B.C., Canada. Melting points are uncorrected.

The nomenclature used to describe the various compounds synthesised in this study is not strictly based on I.U.P.A.C. rules.[68] In several cases the alphabetical order of substituent groups has been disregarded in order that in every case the substituent whose ultimate synthetic fate is the 1-fluoromethyl substituent should be designated as occupying the 1-position of the naphthalene nucleus. The justification for this departure from the established rules is based on clarity and readability. Many of the synthetic transformations are essentially

similar and this approach allows comparisons to be drawn readily and for the entire synthetic pathways to be followed with ease. In most cases this approach has involved a reordering of substituent groups. In several instances the departure from systematic nomenclature is more radical. In these cases the systematic name is included in parenthesis following the name used in this study.

All synthetic routes to the substituted fluoromethylnaphthalenes involved the exchange of bromide ion by fluoride ion by means of the reaction between the bromomethylnaphthalene and anhydrous potassium fluoride in N-methyl-2-pyrrolidone. Bromomethyl derivatives were obtained by one of three methods: bromination of the carbinol with phosphorus tribromide, cleavage of the ether with anhydrous hydrogen bromide in dry benzene, or by bromination of the methylnaphthalene with N-bromo-succinimide in carbon tetrachloride.

Details of all synthetic procedures are given below. A diagrammatic scheme of these transformations plus a key for purposes of nomenclature are included at pages 131-149 following the description of experimental details. In order to avoid needless repetition, reactions where the same reagents and similar reaction conditions are used are described in detail only once; thereafter they are merely described in more general terms. Discussions which follow refer to this specific method and describe essential details and any variations made to the general method.

All previously unknown compounds, except the fluoromethylnaphthalenes, were characterised by melting point or boiling point, by elemental analysis and by accurate mass measurement. The fluoromethylnaphthalenes

could not be characterised by their boiling points. Even on moderate warming these compounds showed a tendency towards polymerisation. Polymerisation of the benzyl fluorides was reported by Delpuech and Béguin,[43] by the Ingolds,[40] and by Bernstein, Roth and Miller[41]; this polymerisation is an acid catalysed Friedel-Crafts type reaction. In the earlier preparations all the glassware was rinsed with an ethereal solution of quinoline and then dried. In later preparations one drop of N,N-diisopropylethylamine, a very strong but sterically hindered base, was added prior to the isolation of the fluoromethylnaphthalene to prevent the polymerisation from occurring. This latter base was preferable as it did not interfere with the n.m.r. spectra. All peaks in the spectrum of N,N-diisopropylethylamine appear at high field, viz. τ 8-9 p.p.m. Another advantage is that it is considerably more volatile than quinoline and so it could be removed from the sample by prolonged exposure to a high vacuum. In spite of the precaution of adding the base stabiliser several samples did undergo the polymerisation reaction. Addition of this trace amount of stabilising amine precluded elemental analysis and boiling point or melting point as a means of characterisation. Accurate masses were determined, and the very characteristic ^{1}H and ^{19}F n.m.r. spectra served to confirm the identity of the products. N.m.r. heteronuclear decoupling experiments were also carried out on the fluoromethylnaphthalenes as additional confirmation.

Preparation of the Compounds

1-Acetyl-4-methylnaphthalene (2)

Considerable difficulty was encountered in the synthesis of 1-acetyl-4-methylnaphthalene (2). This was due to the starting material 1-methylnaphthalene (1) containing substantial amounts of 2-methylnaphthalene. Jacobs et al.[69] reported that the isomeric chloro-acetylnaphthalenes were readily separated by fractional crystallisation of their picrates and so analogous separation of the methyl-acetylnaphthalenes was attempted. Separation was successful but only a very small quantity of the required 1,4-isomer was obtained. The main fraction isolated consisted of the 2,6-isomer, and as the ratio of 1,4-isomer to 2,6-isomer was substantially greater than the ratio of 1- to 2-methylnaphthalene in the starting material, it was concluded that migration of the methyl group from the 1- to the 2-position had occurred under the influence of the $AlCl_3$, the 2-isomer predominating as the thermodynamically more stable product. Acetylation of pure 1-methylnaphthalene (1) using an efficient ice-bath resulted in a 70% yield of pure product after distillation.

1-Methylnaphthalene (Aldrich) (67.0 g; 0.48 mol), dry CH_2Cl_2 (340 cm^3) and finely ground anhydrous $AlCl_3$ (76 g; 0.57 mol) were placed in a 1 ℓ 3-necked flask fitted with a water-cooled double-surface reflux-condenser and drying tube, a mechanical stirrer, and a 100 cm^3 equilibrating dropping funnel. The flask was immersed in an ice-bath and acetyl chloride (38 cm^3; 39.3 g; 0.48 mol) was added from the dropping funnel over 45 min. After the addition was complete the ice-bath was removed and the mixture allowed to reach room temperature; vigorous stirring

was continued for 4 h. Stirring was discontinued and the reaction mixture was refluxed on a water bath for 2 1/2 h, allowed to cool for 15 min and then poured onto a mixture of concentrated HCl (30 cm^3) and ice (200 g). The heavy oil layer was separated from the aqueous layer and washed with water (2 x 200 cm^3), with 3 N NaOH solution (2 x 200 cm^3) and again with water (2 x 200 cm^3). The oil was dried with anhydrous $MgSO_4$, filtered, and the solvent removed. The resulting brown liquid was distilled at 115-120° at 0.2 mm (lit.[70] b.p. 175°/15 mm) to give a 71.4% yield of 1-acetyl-4-methylnaphthalene; i.r. (film) 3075 (aromatic C-H), 2930, 2875 (aliphatic C-H), 1680 (aromatic C=O), 1590 (naphthalene ring), 830, 760 cm^{-1} (1,4-disubstituted naphthalene, C-H out-of-plane bending); n.m.r. (CCl_4) τ 2.0-3.0 (m, 6, $C_{10}\underline{H}_6$), 7.45 (s, 3, $COCH_{\underline{3}}$), 7.5 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 184 (25, M_r ($^{12}C_{13}$ $^{1}H_{12}$ $^{16}O_1$) = 184), 170 (41), 169 (100), 141 (90), 115 (72).

4-Methyl-1-naphthoic acid (3)

1-Acetyl-4-methylnaphthalene (40.66 g; 0.22 mol) was refluxed for 4 1/2 h with a hypochlorite solution prepared by dissolving NaOH (100 g; 2.5 mol) in water (135 cm^3) and ice (550 g), and bubbling Cl_2 into this solution until the increase in weight was 71 g (1 mol). After heating under reflux with the ketone (2) the solution was allowed to cool and $NaHSO_3$ (60 g) added in order to destroy excess hypochlorite. Concentrated HCl (75 cm^3) was added to the solution, whereupon a heavy cream precipitate separated. This was filtered, washed and recrystallised from 95% EtOH to give a yield of 37.4 g (91%) of a white solid; m.p. 175-175.5° (lit.[70] m.p. 175°); i.r. (nujol) 3150 (bonded OH), 1680

(aromatic carboxylic acid C=O), 835, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.8-2.8 (m, 6, $C_{10}\underline{H}_6$), 7.25 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 186 (100, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_2$) = 186), 169 (63), 142 (19), 141 (31), 139 (43), 115 (90).

Most of the 4-substituted-1-naphthoic acids were prepared by the sodium hypochlorite oxidation of the corresponding acetylnaphthalene. This reaction proved to be far more troublesome than was suggested by the trivial accounts in the literature. After a long series of abortive attempts two factors emerged as being critical reaction conditions. The method of preparation of the hypochlorite solution is critical; the solution must be maintained at 0-10° and the amount of chlorine passed is carefully controlled. The hypochlorite solution was eventually prepared according to the method of Newman and Holmes.[71] The hypochlorite solution was refluxed with the ketone until there was no residual ketone present as a separate phase. The period of reflux necessary to effect the oxidation was considerably longer, and the reaction temperature higher than those recommended in the literature.

4-Methyl-1-naphthylcarbinol (4)

A suspension of $LiAlH_4$ (Koch-Light) (0.7 g; 0.18 mol) in anhydrous ether (50 cm^3) was placed in a 1 ℓ 3-necked flask fitted with double-surface reflux condenser and drying tube, a 250 cm^3 equilibrating dropping funnel and a magnetic stirrer; the apparatus was maintained under an atmosphere of nitrogen. The suspension was stirred for 10 min and then a suspension of 4-methyl-1-naphthoic acid (4.57 g; 0.025 mol) in

anhydrous ether (100 cm^3) was added from the dropping funnel at such a rate that boiling of the solvent was maintained. The naphthoic acid was added over 45 min, the mixture was stirred at room temperature for 30 min, under reflux for 3 h and again at room temperature for 14 h. The reaction mixture was cooled in an ice-bath and 10% H_2SO_4 (100 cm^3) was added very gradually. The aqueous and ethereal layers were separated and the ether extract washed with water (2 x 150 cm^3), with 10% Na_2CO_3 solution (2 x 200 cm^3), and again with water (2 x 200 cm^3). The solution was dried with anhydrous $MgSO_4$ and evaporated to a white solid residue. The residue was recrystallised from 60-70° petroleum ether to white needles m.p. 76-77° (lit.[72] m.p. 77°). The yield of recrystallised solid was 3.48 g (82.5%); i.r. (melt) 3350 (hydrogen bonded OH), 2975, 2900 (aliphatic C-H), 1595 (naphthalene ring), 1075 (primary alcohol), 835, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.9-3.0 (m, 6, $C_{10}\underline{H}_6$), 5.1 (s, 2, $C\underline{H}_2$), 7.35 (s, 3, $C\underline{H}_3$), 8.15 p.p.m. (s, 1, $O\underline{H}$). The peak at τ 8.15 p.p.m. disappeared when the sample was shaken with a few drops of D_2O; mass spectrum (70 eV) (relative intensity) 172 (30, M_r ($^{12}C_{12}$ $^{1}H_{12}$ $^{16}O_1$) = 172), 171 (40), 154 (60), 128 (100). The general procedure followed in this preparation is that described by Fieser and Fieser,[73] the proportion of hydride to carboxylic acid is the same as that recommended by Nystrom and Brown,[74] and the heating and stirring periods are those recommended by Bergmann and Szmuszkovicz[75] for the reduction of naphthoic acids.

1-Bromomethyl-4-methylnaphthalene (5)

Bromination of the naphthylcarbinols was effected by warming the carbinol with PBr_3 in benzene with a trace of pyridine at 55-60° for 6 h using the method of Bergmann and Szmuszkovicz.[75] All bromomethylnaphthalenes prepared were strong lachrymators and so they were prepared and handled in a fume hood. Many showed a slight tendency toward hydrolysis in moist air and were therefore stored in a desiccator in a refrigerator.

1-Bromomethyl-4-methylnaphthalene was prepared by dissolving 4-methyl-1-naphthylcarbinol (10.3 g; 0.06 mol) in dry benzene (100 cm^3) to which was added PBr_3 (19.5 g; 0.072 mol) and two drops of pyridine. The solution was stirred and heated at 50-55° for 6 h; the reaction mixture was then poured onto ice (100 g) and the organic and aqueous layers were separated. The aqueous layer was extracted with benzene and the benzene solutions combined, washed with water (2 x 150 cm^3), with 15% Na_2CO_3 solution (3 x 200 cm^3) and again with water (2 x 150 cm^3). The benzene solution was dried with anhydrous $MgSO_4$, filtered and the benzene removed on a rotary evaporator. The dark green solid which was obtained was recrystallised three times from 35-45° petroleum ether to white crystalline needles (11.8 g; 84% yield) which melted at 77-79° (lit.[76] m.p. 80°); i.r. (nujol) 3080, 3045 (aromatic C-H), 1595 (naphthalene ring), 832, 758 (1,4-disubstituted naphthalene ring), 550, 530 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.7-2.0 (m, 6, $C_{10}\underline{H}_6$), 5.12, (s, 2, $C\underline{H}_2Br$), 7.32 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity), 236 (23, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{81}Br_1$) = 236), 234 (24, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{79}Br_1$) = 234), 155 (100), 153 (52), 152 (46), 141 (40), 115 (40).

Preparation of Sulphonate Esters of 4-Substituted-1-naphthylcarbinols

At first the p-toluenesulphonate esters of the carbinols appeared to be suitable precursors to the fluoromethylnaphthalenes, "...Oxygen bonded groups, such as sulphonate esters that are good leaving groups, are easily replaced by potassium fluoride in polar solvent...".[79] Preparation of the sulphonate esters with pyridine as solvent and base was unsuccessful; sulphonation with powdered caustic potash, diethyl ether and p-toluenesulphonyl chloride resulted in the formation of a crystalline sulphonate ester, but this rapidly transformed into an oil on standing. Examples in the literature confirmed this behaviour as general for esters of this type and so synthesis of these compounds was abandoned. In spite of their tendency to hydrolyse, the bromomethylnaphthalenes proved to be far more suitable as precursors to the fluoromethyl compounds.

1-Fluoromethyl-4-methylnaphthalene (6)

The fluoromethylnaphthalenes were prepared by fluoride-bromide exchange of the corresponding bromomethylnaphthalene. The exchange was carried out in a dipolar aprotic solvent, N-methylpyrrolidone, with anhydrous KF (under these conditions this is a source of "strongly nucleophilic, weakly solvated and well dissociated fluoride ion"[77]). This method of fluoride-bromide exchange is that described by Delpuech and Beguin.[43]

1-Bromomethyl-4-methylnaphthalene (7.25 g; 0.031 mol) was dissolved in N-methylpyrrolidone (25 cm^3) which had been dried with anhydrous $MgSO_4$, filtered and distilled at 202-204° at atmospheric pressure. Anhydrous KF (B.D.H.) (18.0 g; 0.31 mol) which had been dried in an oven

at 140° overnight was suspended in pyrrolidone (100 cm^3) in a 250 cm^3 3-necked flask fitted with a heating mantle, magnetic stirrer, 25 cm^3 equilibrating dropping funnel, reflux condenser with drying tube. The suspension was stirred at 100° for 15 min, the bromomethylnaphthalene solution was then added from the dropping funnel over 15 min. The reaction temperature was raised to 150° and maintained at this temperature for 3 h. The dark brown reaction mixture was allowed to cool, taken up in CH_2Cl_2 (200 cm^3) and washed with water (100 cm^3). The brown CH_2Cl_2 solution was washed thoroughly with saturated NH_4Cl solution (6 x 200 cm^3) in order to extract as much of the pyrrolidone as possible. It was then dried with anhydrous $MgSO_4$, the solid was filtered off and the CH_2Cl_2 removed on a rotary evaporator. The brown residue weighing 11.3 g was analysed by n.m.r. This indicated the presence of large amounts of pyrrolidone plus naphthalene compounds, over 90% of which was fluoromethylnaphthalene. The relative quantity of fluoromethyl compound in the mixture could be estimated by comparing the integration of the readily distinguishable methylene doublet due to the $-CH_2F$ function (J_{H-F} = 48 Hz) with that of the methylene of the bromomethylnaphthalene and/or naphthylcarbinol. The relative amount of fluoromethylnaphthalene in the reaction mixture was estimated in this manner for all fluoromethylnaphthalenes prepared.

Thin layer chromatography of the brown residue revealed that the fluoromethylnaphthalene could readily be separated from the bromomethylnaphthalene, naphthylcarbinol and pyrrolidone using silica gel as the stationary phase and eluting with 35-45° petroleum ether. A chromatographic column was prepared using 250 g silica gel (Baker "Analysed") slurried with 34-45° petroleum ether. A small layer of fine sand was introduced onto the silica gel and the reaction mixture was adsorbed

onto the sand layer. The column was eluted with petroleum ether and the fractions collected evaporated to dryness, weighed and analysed by n.m.r. spectroscopy. All glassware used in the chromatographic isolation of 4-methyl-1-fluoromethylnaphthalene was rinsed with an ethereal soluton of quinoline and dried. Thirteen fractions of 150 cm^3 each were collected and it was found that fractions 3-11 contained fluoromethylnaphthalene, 1.4 g in all which represented a 54% yield; i.r. (film) 3075, 3045 (aromatic C-H), 2975, 2925 (alkyl C-H), 1595 (naphthalene ring), 1060 (aliphatic C-F), 825, 758 cm^{-1} (1,4-disubstituted naphthalene ring); n.m.r. (CCl_4) τ 1.85-3.0 (m, 6, $C_{10}\underline{H}_6$), 4.32 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 7.34 p.p.m. (d, 3, $C\underline{H}_3$, J = 2 Hz); mass spectrum (70 eV) m/e (relative intensity) 174.074 (14, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{19}F_1$) = 174.085) 173 (100), 172 (25), 159 (80), 141 (36), 115 (8).

1-Acetyl-4-chloronaphthalene (8)

1-Chloronaphthalene (Baker) (71.0 g; 0.44 mol) was redistilled under vacuum at 30 mm and 146-147°, and dissolved with anhydrous $AlCl_3$ (70.0 g; 0.5 mol) in CH_2Cl_2 (500 cm^3) in a 1 ℓ 3-necked flask. Acetyl chloride (Baker) (25 cm^3; 0.46 mol) was added over 45 min. The mixture was stirred at room temperature for 4 h and at reflux for 2 h. Decomposition with conc. HCl (20 cm^3) and ice (200 g), followed by washing, drying and evaporation of solvent gave a brown-yellow oil. This was distilled under vacuum at 0.2 mm and 140-146° to give 64.1 g of a pale straw viscous liquid; this represented a 72% yield. (lit.[69] 140-146°/1.5 mm, [78] 155-165°/3-4 mm); i.r. (film) 3050, 3010 (aromatic C-H), 2910 (aliphatic C-H), 1680 (aromatic C=O), 1560, 1510 (naphthalene ring) 830, 765 cm^{-1} (1,4-disubstituted naphthalene);

n.m.r. (CCl_4) τ 1.7-2.85 (m,6,$C_{10}\underline{H}_6$), 7.5 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 206 (3, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{37}Cl_1$) = 206), 204 (10, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{35}Cl_1$) = 204), 189 (33), 164 (26), 163 (49), 162 (100), 127 (61).

4-Chloro-1-naphthoic Acid (9)

The NaOCl solution was prepared using NaOH (145.5 g; 3.63 mol), 200 cm^3 of water, 834 g of ice and Cl_2 gas (104.0g; 2.6 mol). The ketone (8) (67.64 g; 0.33 mol) was added and the solution warmed at 55° for 1 h. No reaction appeared to be taking place and so the temperature was gradually increased to 80°. This temperature was maintained for 6 h during which time the two separate phases disappeared. $NaHSO_3$ (34 g) in water (132 cm^3) was added to destroy excess hypochlorite. Conc. HCl was added to precipitate the carboxylic acid. The pale cream solid (25.53 g; 38.5% yield) was recrystallised three times from 95% EtOH to a constant melting point of 222-224° (lit.[69] m.p. 223-224°); i.r. (nujol) 3100 (hydrogen bonded OH), 1690 (C=O stretch aromatic carboxylic acid), 925 (OH out of plane deformation), 838, 788 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$]. τ 1.5-2.5 p.p.m. (m, $C_{10}\underline{H}_6$); mass spectrum (70 eV) m/e (relative intensity) 208 (35, M_r ($^{12}C_{11}$ $^{1}H_7$ $^{16}O_2$ $^{37}Cl_1$) = 208), 207 (40 ($^{12}C_{11}$ $^{1}H_6$ $^{16}O_2$ $^{37}Cl_1$) = 207), 206 (100, M_r ($^{12}C_{11}$ $^{1}H_7$ $^{16}O_2$ $^{35}Cl_1$) = 206), 191 (74), 189 (70), 163 (65), 161 (60).

4-Chloro-1-naphthylcarbinol (10)

The carbinol (10) was prepared from 4-chloro-1-naphthoic acid by reduction with $LiAlH_4$ in anhydrous ether. Carboxylic acid (20.5 g; 0.1 mol) on reduction with $LiAlH_4$ (2.85 g; 0.075 mol) suspended in

anhydrous ether (200 cm^3) gave a yield of 14.22 g (74% yield) of colourless needles after crystallisation from 35-45° petroleum ether. The crystals melted at 73-74.5°; i.r. (melt) 3300 (hydrogen bonded OH), 3090 (aromatic C-H), 2925, 2875 (aliphatic C-H), 1270, 1072 (primary alcohol), 830, 755 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.7-3.0 (m, 6, $C_{10}\underline{H}_6$), 5.21 (s, 2, $C\underline{H}_2$), 7.01 p.p.m. (s, 1, $O\underline{H}$). The broad singlet at τ 7.01 disappeared on addition of two drops of D_2O; mass spectrum (70 eV) m/e (relative intensity) 194 (26, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{37}Cl_1$) = 194), 192.041 (92; M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{35}Cl_1$) = 192.034), 177 (6), 175 (23), 163 (52), 157 (60), 141 (3), 128 (100), 115 (8).

Anal. Calcd. for $C_{11}H_9OCl$: C, 68.59; H, 4.71. Found: C, 68.61; H, 4.70.

1-Bromomethyl-4-chloronaphthalene (11)

The alcohol (10) (12.8 g; 0.0655 mol) was dissolved in dry benzene (100 cm^3) by gentle warming. Pyridine (2 drops) was added, followed by PBr_3 (19.0 g; 0.07 mol). After a period of 6 h at 55° followed by work-up of the reaction residue, a yield of 12.66 g (74.5%) was obtained. Recrystallisation from 60-75° petroleum ether gave colourless needles which melted at 100-101°; i.r. (nujol) 3050 (aromatic C-H), 1030 (aromatic C-Cl), 830, 763 (1,4-di substituted naphthalene), 550, 530 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.5-2.6 (m, 6, $C_{10}\underline{H}_6$), 5.17 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 257.953 (3, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{81}Br_1$ $^{37}Cl_1$) = 257.945), 256 (9, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{81}Br_1$ $^{35}Cl_1$), 254 (8), 177 (35), 175 (100), 141 (25), 115 (5).

Anal. Calcd. for $C_{11}H_8BrCl$: C, 51.70; H, 3.17. Found: C, 51.44; H, 3.08.

4-Chloro-1-fluoromethylnaphthalene (12)

Anhydrous KF (25 g; 0.43 mol) was dissolved and suspended in pyrrolidone (120 cm^3). 4-Chloro-1-bromomethylnaphthalene (11 g; 0.043 mol) dissolved in pyrrolidone (30 cm^3) was added and the mixture heated at 145-150° for 5 h. The residue was worked up and an n.m.r. of the brown, oily liquid showed a 94% conversion from bromide to fluoride. Chromatography on silica gel gave 5.0 g of 4-chloro-1-fluoromethylnaphthalene (59.5% yield); i.r. (film) 3080, 3060 (aromatic C-H), 2975, 2920 (aliphatic C-H), 1060 (aliphatic C-F), 825, 750 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.5-3.0 (m, 6, $C_{10}\underline{H}_6$), 4.38 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 196.023 (22, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{37}Cl_1$ $^{19}F_1$) = 196.028), 195 (15), 194 (67, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{35}Cl_1$ $^{19}F_1$) = 194), 193 (68), 160 (12), 159 (100), 141 (5), 115 (2).

1-Acetyl-4-fluoronaphthalene (14)

Acetylation of 1-fluoronaphthalene (13) (25 g; 0.17 mol) with acetyl chloride (20 g; 0.255 mol) and anhydrous $AlCl_3$ (40 g; 0.3 mol) in CH_2Cl_2 (250 cm^3) gave a quantitative yield of 1-acetyl-4-fluoronaphthalene (b.p. 100-115°/0.001 mm, lit.[69] b.p. 138-140°/4.5 mm). This preparation differed slightly from the other acetylation reactions inasmuch as the $AlCl_3$ was added to the solution of acetyl chloride and 1-fluoronaphthalene from a dry Erlenmeyer by means of a piece of wide-bore rubber tubing; i.r. (film) 3100, 3020 (aromatic C-H), 2935 (aliphatic

C-H), 1680 (aromatic C=O), 1185 (aromatic C-F), 835, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.8-3.2 (m, 6, $C_{10}\underline{H}_6$), 7.44 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 188 (7, M_r, ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{19}F_1$) = 188), 187 (49), 173 (100), 145 (65), 125 (21), 43 (14).

4-Fluoro-1-naphthoic Acid (15)

The ketone (14) was oxidised with a solution of NaOCl by warming at 80° for 3 1/2 h. The 4-fluoronaphthoic acid was obtained in 60% yield. The white amorphous solid was recrystallised from 95% EtOH and melted at 219-222° (lit.[69] m.p. 224.5-225°); i.r. (nujol) 3100 (hydrogen bonded OH), 1700 (C=O aromatic carboxylic acid), 1170 (aromatic C-F), 840, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.5-3.0 p.p.m. (m, $C_{10}\underline{H}_6$); mass spectrum (70 eV) m/e (relative intensity) 190 (100, M_r ($^{12}C_{11}$ $^{1}H_7$ $^{16}O_2$ $^{19}F_1$) = 190), 173 (99), 145 (91), 144 (66), 125 (81).

4-Fluoro-1-naphthylcarbinol (16)

4-Fluoro-1-naphthylcarbinol was prepared from 4-fluoro-1-naphthoic acid by $LiAlH_4$ reduction in 55.5% yield. The white solid was recrystallised from 95-110° petroleum ether to long white needle-shaped crystals which melted at 74-75°; i.r. (nujol) 3300 (hydrogen bonded OH), 1170 (aromatic C-F), 825, 752 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.8-3.4 (m, 6, $C_{10}\underline{H}_6$), 5.21 (s, 2, $C\underline{H}_2$), 7.01 p.p.m. (s, 1, O$\underline{H}$). The singlet at τ 7.01 disappeared on addition of D_2O; mass spectrum (70 eV) m/e (relative intensity) 176.056 (100, M_r

($^{12}C_{11}$ $^{1}H_{9}$ $^{16}O_{1}$ $^{19}F_{1}$) = 176.065), 175 (25), 159 (51), 146 (12), 145 (51), 141 (5), 115 (3).

Anal. Calcd. for $C_{11}H_9OF$: C, 74.97; H, 5.15. Found: C, 75.14; H, 5.26.

1-Bromomethyl-4-fluoronaphthalene (17)

The carbinol (16) was brominated with PBr_3 in benzene to give 1-bromomethyl-4-fluoronaphthalene in quantitative yield. The pale yellow solid residue was recrystallised from 60-65° petroleum ether to long, colourless needles which melted at 68.5-69.5°; i.r. (nujol) 3075 (aromatic C-H), 1160 (aromatic C-F), 550 cm^{-1} (aliphatic C-Br); n.m.r. [$(CD_3)_2CO$] τ 1.7-3.2 (m, 6, $C_{10}\underline{H}_6$), 5.15 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 239.978 (5, M_r ($^{12}C_{11}$ $^{1}H_{8}$ $^{19}F_{1}$ $^{81}Br_{1}$) = 239.978), 238 (5), 160 (18), 159 (100), 157 (14), 141 (2), 139 (6), 133 (18), 115 (1).

Anal. Calcd. for $C_{11}H_8FBr$: C, 55.21; H, 3.37. Found: C, 55.51; H, 3.32.

4-Fluoro-1-fluoromethylnaphthalene (18)

Fluoride-bromide exchange was carried out on 1-bromomethyl-4-fluoronaphthalene with anhydrous KF in the dipolar aprotic solvent, N-methylpyrrolidone. The dark brown reaction mixture was washed thoroughly with a saturated solution of NH_4Cl in water. The n.m.r. spectrum of the residue indicated a 85% bromide to fluoride conversion. This residue was chromatographed on silica gel using 33-38° petroleum ether as eluent. A 71% yield of 4-fluoro-1-fluoromethylnaphthalene, a clear, viscous liquid, was obtained; i.r. (film) 3080 (aromatic C-H),

2980, 2910 (aliphatic C-H), 1170 (aromatic C-F), 1058 (aliphatic C-F), 830, 770 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.7-3.2 (m, 6, $C_{10}\underline{H}_6$), 4.35 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 178.052 (100, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{19}F_2$) = 178.060), 177 (95), 159 (35), 157 (30), 151 (35).

1-Acetyl-4-bromonaphthalene (20)

A Friedel-Crafts acetylation was carried out on 1-bromonaphthalene. Addition of anhydrous $AlCl_3$ was made, by means of a piece of wide bore tubing attached to a dry Erlenmeyer flask, to a solution of 1-bromonaphthalene and acetyl chloride in CH_2Cl_2 at 0-2°. The resulting suspension was stirred at 0-2° for 75 h and at 15-16° for 6 h. Washing and vacuum distillation of the reaction mixture gave a 87% yield of 1-acetyl-4-bromonaphthalene (b.p. 125-138°/0.2-0.25 mm, lit.[69] b.p. 165-175°/2-4 mm); i.r. (film) 3100, 3025 (aromatic C-H), 1680 (aromatic C=O), 1040 (aromatic C-Br), 830, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.2-2.7 (m, 6, $C_{10}\underline{H}_6$), 7.49 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 250 (5, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{81}Br_1$) = 250), 248 (6, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{79}Br_1$) = 248), 235 (7), 233 (9), 208 (59), 206 (61), 170 (25), 155 (45), 125 (100).

4-Bromo-1-naphthoic Acid (21)

1-Acetyl-4-bromonaphthalene was readily oxidised to 4-bromo-1-naphthoic acid with NaOCl. The yield of carboxylic acid obtained was 94%. Recrystallisation from 95% EtOH gave a white solid, m.p. 217?5-220° (lit.[69] m.p. 217-219°); i.r. (nujol) 3100 (hydrogen bonded OH),

1700 (aromatic carboxylic acid C=O), 1042 (aromatic C-Br), 838, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.75-2.5 p.p.m. (m, $C_{10}\underline{H}_6$); mass spectrum (70 eV) m/e (relative intensity) 252 (63, M_r ($^{12}C_{11}$ $^{1}H_7$ $^{16}O_2$ $^{81}Br_1$) = 252), 251 (29), 250 (66, M_r ($^{12}C_{11}$ $^{1}H_7$ $^{16}O_2$ $^{79}Br_1$) = 250), 249 (35), 234 (98), 233(22), 232 (100).

4-Bromo-1-naphthylcarbinol (22)

4-Bromo-1-naphthoic acid was reduced in 25% yield to 4-bromo-1-naphthylcarbinol with $LiAlH_4$ in anhydrous diethyl ether. The low yield was probably a result of the sparing solubility of the carboxylic acid in this solvent and to the low reaction temperature (i.e. the boiling point of ether). A far more suitable solvent for this reaction would have been the higher boiling alicyclic ether, tetrahydrofuran. The white solid carbinol (22) was recrystallised from 95-110° petroleum ether to long, colourless needles, m.p. 98-100° (lit.[80] b.p. 162-4°/12 mm); i.r. (melt) 3350 (hydrogen bonded OH), 3080 (aromatic C-H), 2990, 2880 (aliphatic C-H), 1375, 1070 (primary alcohol), 1010 (aromatic C-Br), 830, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.7-3.1 (m, 6, $C_{10}\underline{H}_6$), 5.3 (s, 2, $C\underline{H}_2OH$), 6.63 p.p.m. (s, 1, $CH_2O\underline{H}$). The singlet at τ 6.63 disappeared on shaking the CCl_4 solution with two drops of D_2O; mass spectrum (70 eV) m/e (relative intensity) 238 (15, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{81}Br_1$) = 238), 236 (16, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{79}Br_1$) = 236), 221 (3), 219 (3), 157 (23), 141 (2), 139 (18), 128 (100), 115 (2).

4-Bromo-1-bromomethylnaphthalene (23)

The bromomethylnaphthalene (23) was prepared from the carbinol with PBr_3 in benzene. The reaction mixture was washed with water and

dilute base, and evaporated to a pale yellow residue. Recrystallisation from 60-75° petroleum ether three times gave a 84.6% yield of pale yellow needles which melted at 102-104° (lit.[80,81] m.p. 103-4°); i.r. (nujol) 3040 (aromatic C-H), 1020 (aromatic C-Br), 820, 750 (1,4-disubstituted naphthalene), 530 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.6-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.28 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 302 (6, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{81}Br_2$) = 302), 300 (12, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{81}Br_1$ $^{79}Br_1$) = 300), 298 (6, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{79}Br_2$) = 298), 222 (26), 221 (100), 220 (27), 219 (100), 149 (10), 141 (25), 140 (40), 139 (40), 115 (5).

4-Bromo-1-fluoromethylnaphthalene (24)

A 38.5% yield of 4-bromo-1-fluoromethylnaphthalene was obtained from the reaction of the bromide with anhydrous KF; i.r. (film) 3080, 3025 (aromatic C-H), 2950, 2885 (aliphatic C-H), 1475 (CH_2 C-H deformation), 1063 (aliphatic C-F), 825, 755 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.6-2.9 (m, 6, $C_{10}\underline{H}_6$), 4.35 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 240 (8, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{19}F_1$ $^{81}Br_1$) = 240), 237.973 (9, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{19}F_1$ $^{79}Br_1$) = 237.973), 159 (24), 141 (2), 115 (5), 99 (100), 98 (75).

1-Methyl-4-nitronaphthalene (25)

1-Methyl-4-nitronaphthalene was prepared by the method of Thompson.[82] 1-Methylnaphthalene (Aldrich) (20 g; 0.14 mol) was cooled in an ice-salt bath and conc. HNO_3 (65 cm^3; d = 1.42) was added dropwise, with continuous stirring and cooling over 1 h. Water

($100\ cm^3$) was added and the reaction mixture extracted with benzene; this extract was washed with 10% NaOH solution ($2 \times 200\ cm^3$) to remove excess acid, and with water ($2 \times 100\ cm^3$). The organic extract was dried with anhydrous $MgSO_4$, filtered, evaporated, and the residue recrystallised from 65-70° petroleum ether. By recrystallising the 1-methyl-4-nitronaphthalene at 50° and decanting the yellow solution from an orange oil which separated at the bottom of the flask, the 1,4-isomer was separated from the 1,5-isomer which was also produced in the reaction. Pure 1-methyl-4-nitronaphthalene (4 g; 15.2% yield) was obtained, m.p. 69-71° (lit.[82,83] m.p. 71-72°); i.r. (nujol) 3050 (aromatic C-H), 1510, 1355, 1340 (aromatic NO_2), 828, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.4-2.9 (m, 6, $C_{10}\underline{H}_6$), 7.25 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 187 (13, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{16}O_2\ ^{14}N_1$) = 187), 186 (96), 170 (30), 159 (22), 157 (19), 141 (79), 115 (100).

4-Nitro-1-bromomethylnaphthalene (26)

Several authors[84,85] describe the free radical bromination of alkyl naphthalenes using molecular bromine and a source of ultraviolet light. However, the low yields and condition of the reaction products obtained discouraged the use of this method of bromination. The reports concerning N-bromosuccinimide[86,87] were far more encouraging. The method adopted was the one described by Chapman and Williams.[87]

The N-bromosuccinimide used (Koch-Light) was vigorously purified in order to remove all traces of molecular bromine. It was recrystallised from hot glacial acetic acid (1 kg/1 ℓ) and then left exposed to a high vacuum over phosphorous pentoxide for 36 h.

The ratio of methylnaphthalene to bromosuccinimide used was 1 to 1.1. 1-Methyl-4-nitronaphthalene (24 g; 0.13 mol) was dissolved in CCl_4 (250 cm^3) and stirred for 15 min. N-Bromosuccinimide (24 g; 0.134 mol) was added and this mixture was stirred at the boiling point of the solvent for 28 h. The mixture was cooled in an ice-bath and the solid succinimide filtered off. The solvent was removed and i.r. and n.m.r. spectra run on the residue. These revealed that the reaction had proceeded such that only 20% of the residue was 1-bromomethyl-4-nitronaphthalene. A crude recrystallisation of the residue gave two fractions, the second of which (9.0 g) was approximately 30% bromomethyl compound. This was chromatographed on 250 g silica gel using 33-36° petroleum ether as eluent. The first six fractions collected contained 1-methyl-4-nitronaphthalene, the next five a mixture of bromide and hydrocarbon and the next five pure 1-bromomethyl-4-nitronaphthalene (2.17 g; 6.3% yield). Recrystallisation three times from 45-60° petroleum ether gave thin, yellow, needle-shaped crystals which melted at 93-94.5°; i.r. (melt) 3120 (aromatic C-H), 2875 (aliphatic C-H), 1510, 1355, 1340 (aromatic NO_2), 830, 770 (1,4-disubstituted naphthalene), 565, 530 cm^{-1} (aliphatic C-Br); n.m.r. ($CDCl_3$) τ 1.3-2.6 (m, 6, $C_{10}H_6$), 5.12 p.p.m. (s, 2, CH_2Br); mass spectrum (70 eV) m/e (relative intensity) 267 (18, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{14}N_1$ $^{16}O_2$ $^{81}Br_1$) = 267), 264.983 (20, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{14}N_1$ $^{16}O_2$ $^{79}Br_1$) = 264.982), 187 (18), 186 (100), 156 (14), 141 (8), 140 (25), 139 (37), 128 (34), 115 (6).

1-Fluoromethyl-4-nitronaphthalene (27)

The fluoromethylnaphthalene (27) was prepared from the corresponding bromo compound (26) using anhydrous KF as the fluorinating reagent. The reaction temperature was 125-130° and was maintained for 4 1/2 h. The conversion of bromide to fluoride was approximately 50%. Chromatography of the residue on silica gel gave a 32% yield of the fluoromethyl compound (27) overall. The pale yellow solid crystals, in the presence of a trace of quinoline, melted at 64-66°; i.r. (nujol) 3040 (aromatic C-H), 1510, 1375, 1350 (aromatic NO_2), 1062 (aliphatic C-F), 820, 770 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.0-2.85 (m, 6, $C_{10}\underline{H}_6$), 4.17 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 205.058 (100, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{16}O_2$ $^{14}N_1$ $^{19}F_1$) = 205.055), 170 (58), 159 (50), 146 (40), 141 (3), 133 (90), 115 (7).

1-Naphthylcarbinol (29)

1-Naphthoic acid (28) (Eastman) was reduced with $LiAlH_4$ in anhydrous diethyl ether in 57% yield. The alcohol was recrystallised from 60-75° petroleum ether to long white needles, m.p. 61.5-62.5° (lit.[88] m.p. 59.5-60°); i.r. (nujol) 3400, 3325 (bonded OH), 802, 792, 775 cm^{-1} (1-substituted naphthalene); n.m.r. (CCl_4) τ 2.0-2.95 (m, 7, $C_{10}\underline{H}_7$), 5.2 (s, 2, $C\underline{H}_2$), 3.3 p.p.m. (s, 1, O$\underline{H}$). The broad singlet at τ 3.3 disappeared when the solution was shaken with D_2O; mass spectrum (70 eV) m/e (relative intensity) 158 (58, M_r ($^{12}C_{11}$ $^{1}H_{10}$ $^{16}O_1$) = 158), 141 (16), 139 (5), 129 (100), 115 (13).

1-Bromomethylnaphthalene (30)

1-Naphthylcarbinol was brominated with PBr_3 in dry benzene with two drops of pyridine added. The yield obtained of the bromide (30) was 91%, and the white solid after recrystallisation three times from 60-75° petroleum ether, melted at 54.5-56° (lit.[85,86,89,90] m.p. 56.0°); i.r. (nujol) 3050 (aromatic C-H), 800, 778 (1-substituted naphthalene), 575, 515 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.8-3.33 (m, 7, $C_{10}\underline{H}_7$), 5.17 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 222 (10, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{81}Br_1$) = 222), 220 (11), 142 (40), 141 (100), 140 (35), 139 (90), 115 (30).

1-Fluoromethylnaphthalene (31)

1-Bromomethylnaphthalene was stirred and heated at 145-150° for 4 1/2 h and at 170° for 1 h with anhydrous KF in N-methylpyrrolidone. The proportion of bromide which underwent exchange with fluoride was 63% and the overall yield of 1-fluoromethylnaphthalene, following chromatography of the reaction residue, was 56%; i.r. (film) 3120, 3080 (C-H aromatic), 2975, 2920 (aliphatic C-H), 1060 (aliphatic C-F), 800, 785 cm^{-1} (1-substituted naphthalene); n.m.r. (CCl_4) τ 1.9-3.0 (m, 6, $C_{10}\underline{H}_6$), 4.38 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 160.069 (100, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{19}F_1$) = 160.068), 159 (92), 141 (9), 139 (2), 133 (39), 115 (7).

2-Naphthylcarbinol (33)

2-Naphthoic acid (32) (Eastman) was reduced with $LiAlH_4$ to give a 65% yield of 2-naphthylcarbinol. The pale-cream solid residue was recrystallised from 40-50° petroleum ether to white leaflets, m.p. 79.5-

80.5° (lit.[91] m.p. 80-80.5°); i.r. (nujol) 3275 (hydrogen bonded OH), 3070 (aromatic C-H), 850, 805, 735 cm^{-1} (2-substituted naphthalene); n.m.r. (CCl_4) τ 2.1-2.8 (m, 7, $C_{10}\underline{H}_7$), 5.35 (s, 2, $C\underline{H}_2OH$), 7.52 p.p.m. (s, 1, O$\underline{H}$). The broad singlet at τ 7.52 p.p.m. disappeared on addition of D_2O; mass spectrum (70 eV) m/e (relative intensity) 158 (63, M_r ($^{12}C_{11}$ $^{1}H_{10}$ $^{16}O_1$) = 158), 141 (17), 129 (100), 128 (31), 127 (23), 115 (9).

2-Bromomethylnaphthalene (34)

The carbinol (33) was converted to the bromide (34) in 98% yield with PBr_3 in benzene. The off-white solid residue was recrystallised from 60-75° petroleum ether twice to give a white solid which melted at 53-54° (lit.[87] m.p. 54°); i.r. (nujol) 3070 (aromatic C-H), 860, 850, 830, 765, 750 (2-substituted naphthalene), 585 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 2.2-2.8 (m, 7, $C_{10}\underline{H}_7$), 5.55 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 222 (11, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{81}Br_1$) = 222), 220 (12), 185 (9), 142 (3), 141 (100), 139 (17), 115 (23).

2-Fluoromethylnaphthalene (35)

2-Fluoromethylnaphthalene was prepared from 2-bromomethylnaphthalene in the manner previously described for other fluorinations. The n.m.r. spectrum of the crude brown residue indicated that 85% exchange from bromide to fluoride had taken place. The residue was chromatographed on silica gel and the yield of 2-fluoromethylnaphthalene obtained was 40.5% of the theoretical amount. The white solid melted at 59.5-61.5°; i.r. (nujol) 3040 (aromatic C-H), 1065 (aliphatic C-F), 869, 825, 750 cm^{-1}

(2-substituted naphthalene); n.m.r. (CCl_4) τ 2.2-2.8 (m, 7; $C_{10}\underline{H}_7$), 4.65 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 160.069 (100, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{19}F_1$)= 160.069), 159 (94), 141 (8), 139 (12), 133 (28), 115 (5).

4-Acetyl-1-bromomethylnaphthalene (36) and 4-Bromoacetyl-1-bromomethylnaphthalene (37)

1-Acetyl-4-methylnaphthalene (93 g; 0.5 mol) was dissolved in CCl_4 (1250 cm^3) in a 2 ℓ flask fitted with heating mantle, magnetic stirrer and double-surface reflux condenser. N-Bromosuccinimide (133.5 g; 0.75 mol), recrystallised from glacial acetic acid and exposed to a high vacuum over P_2O_5 for 30 h, was added and the suspension stirred under reflux for 48 h. Initially the solution was light straw coloured, but soon assumed a bright orange colour. Over the next 24 h succinimide accumulated at the surface of the CCl_4. After 40 h the solution turned black and remained so until the end of the reaction.

The reaction mixture was allowed to cool and was then washed three times with water (3 x 200 cm^3). The organic solution was dried with anhydrous $MgSO_4$, filtered, and evaporated. Analysis of the dark brown residue (157.37 g) by n.m.r. showed that the reaction mixture contained some unreacted 1-acetyl-4-methylnaphthalene, but was comprised mainly of 4-bromoacetyl-1-bromomethylnaphthalene (37) and 4-acetyl-1-bromomethylnaphthalene in a ratio of approximately 1 to 1.8.

A chromatographic column was prepared using 1400 g silica gel and 40-50° petroleum ether. The reaction mixture was introduced onto the top of this column and the components of the mixture were eluted with

petroleum ether. The first 8 fractions collected in 7200 cm^3 petroleum ether contained mainly 1-acetyl-4-methylnaphthalene and weighed 2.59 g. The next two (fractions 9 and 10) collected in 2 ℓ were pure 4-bromoacetyl-1-bromomethylnaphthalene (37.43 g). The next 25 fractions contained both bromomethylnaphthalenes, (36) and (37) (48.99 g in 12 ℓ 10% benzene in petroleum ether). The final 3 fractions, 27-29, contained 32.76 g of 4-acetyl-1-bromomethylnaphthalene. Fraction 29 was recrystallised from 60-75° petroleum ether to give fine white platelets of 4-acetyl-1-bromomethylnaphthalene (36) which melted at 83-84°; i.r. (melt) 3100, 3045 (aromatic C-H), 2975, 2950 (aliphatic C-H), 1685 (aromatic ketone C=O), 830, 820, 780, 760 (1,4-disubstituted naphthalene), 552 cm^{-1} (aliphatic C-Br); n.m.r. ($CDCl_3$) τ 1.25-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.2 (s, 2, $C\underline{H}_2Br$), 7.39 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 263.998 (24, M_r ($^{12}C_{13}\ ^{1}H_{11}\ ^{16}O_1\ ^{81}Br_1$) = 263.997), 262 (25), 184 (27), 183 (100), 168 (24), 155 (60), 141 (11), 140 (59), 139 (50), 115 (5).

Anal. Calcd. for $C_{13}H_{11}OBr$: C, 59.35; H, 4.21. Found: C, 59.10; H, 4.12.

Fraction 10 was recrystallised in a similar manner to give pale-straw coloured needles of 4-bromoacetyl-1-bromomethylnaphthalene (37) which melted at 118.5-119.5°; i.r. (melt) 3100, 3075, 3040 (aromatic C-H), 2930, 2900 (aliphatic C-H), 1795 (aromatic α-halo ketone, C=O), 820, 760 (1,4-disubstituted naphthalene), 595, 555 cm^{-1} (aliphatic C-Br); n.m.r. ($CDCl_3$) τ 1.3-2.82 (m, 6, $C_{10}\underline{H}_6$), 5.15 (s, 2, $C\underline{H}_2Br$), 5.55 p.p.m. (s, 2, $COC\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 344 (6, M_r ($^{12}C_{13}\ ^{1}H_{10}\ ^{16}O_1\ ^{81}Br_2$) = 344), 341.912 (11, M_r ($^{12}C_{13}\ ^{1}H_{10}\ ^{16}O_1$

$^{81}Br_1$ $^{79}Br_1$) = 341.910), 340 (6), 265 (98), 263 (100), 238 (48), 236 (50), 184 (32), 153 (30), 141 (4), 139 (97), 115 (3).

Anal. Calcd. for $C_{13}H_{10}OBr_2$: C, 45.64; H, 3.15. Found: C, 45.85; H, 2.99.

4-Acetyl-1-fluoromethylnaphthalene (38)

The bromide (36) was stirred at 170° for 5 h with anhydrous KF. Following work-up with saturated NH_4Cl solution the reaction residue was examined by n.m.r. spectroscopy. This revealed that 50% of the bromide had undergone conversion to fluoride. The residue was chromatographed on silica gel using 39-41° petroleum ether as eluent. The yield of 4-acetyl-1-fluoromethylnaphthalene, which was a white solid, was 33%.

Traces of 1-acetyl-4-methylnaphthalene were detected in the first few fractions eluted from the chromatographic column. Substituted methylnaphthalene was detected as a minor product of many other fluorination reactions. At first it was thought that the methyl compound had originated as a trace impurity in the corresponding bromomethylnaphthalene precursor. In several cases the methylnaphthalene was the immediate precursor to the bromomethylnaphthalene and so the methyl compound could have been introduced into the reaction this way. This possibility applies in this case, but careful scrutiny of the n.m.r. spectrum of the 4-acetyl-1-bromomethylnaphthalene (36) precluded this explanation. Unequivocal evidence for the formation of methyl compound from fluoromethyl was afforded in the case of p-nitrobenzyl fluoride (106) (see page 126). This compound was prepared from the bromide in the usual way. Substantial amounts of p-nitrotoluene were detected

following chromatography of the reaction residue. The i.r. spectrum of the p-nitrotoluene produced in the reaction was identical to that of an authentic sample of p-nitrotoluene. The bromide (107) was prepared from p-nitrobenzoic acid (103) via the corresponding alcohol (104). No methyl compound could be detected in any of the precursors and so the toluene must have been formed in the final fluorination reaction.

It was found that the amount of methyl compound formed as a side-product could be minimised by carrying out the reaction at a moderate temperature, say 140-160°. The use of higher temperatures was attended by increased amounts of side-product. Presumably the energy of activation of the side-reaction is greater than that of the fluoride exchange; i.r. (film) 3100, 3060, 3020 (aromatic C-H), 2980, 2925 (aliphatic C-H), 1680 (aromatic ketone C=O), 1058 (aliphatic C-F), 835, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.2-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.38 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 7.45 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 202.087 (55, M_r ($^{12}C_{13}\ ^{1}H_{11}\ ^{16}O_1\ ^{19}F_1$) = 202.080), 188 (18), 187 (100), 169 (24), 159 (65), 141 (11), 139 (20), 133 (34), 115 (10).

4-Fluoroacetyl-1-fluoromethylnaphthalene (39)

4-Fluoroacetyl-1-fluoromethylnaphthalene (39) was prepared from the corresponding dibromo compound in the usual way; the % conversion from bromide to fluoride estimated from the n.m.r. of the crude reaction product was 30%. The residue was chromatographed on silica gel and gave a yield of 27% of 4-fluoroacetyl-1-fluoromethylnaphthalene,

which was a clear liquid; i.r. (film) 3090, 3075 (aromatic C-H), 2975, 2945, 2860 (aliphatic C-H), 1705 (α-halo aromatic C=O), 1060, 1050 (aliphatic C-F), 835, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.2-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.25 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 4.75 p.p.m. (d, 2, $COC\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 220.063 (16, M_r ($^{12}C_{13}$ $^{1}H_{10}$ $^{16}O_1$ $^{19}F_2$) = 220.070), 203 (21), 187 (100), 169 (28), 159 (60), 141 (18), 139 (25), 133 (45), 115 (17).

1-Acetyl-4-methoxymethylnaphthalene (40)

4-Acetyl-1-bromomethylnaphthalene (39.25 g; 0.15 mol) was dissolved in MeOH (400 cm^3) and added gradually over 3 h to a NaOMe solution (4.6 g of Na (0.2 g atom) in 2.2 dm^3 of methanol) in a 3-necked 3 ℓ flask. The flask was fitted with heating mantle, double-surface reflux condenser, magnetic stirrer and dropping funnel. This solution was stirred at room temperature for 3 h and then under reflux for 14 h. The colour of the solution changed very little throughout the reaction, remaining amber-coloured. The methanol was removed on a rotary evaporator, and the residue taken up in ether. The ethereal solution was washed with water (2 x 200 cm^3) with dilute HCl (3 x 200 cm^3) and with 10% $NaHCO_3$ solution (3 x 200 cm^3) and water (4 x 150 cm^3). The ethereal solution was dried with anhydrous $MgSO_4$, filtered and evaporated to an amber coloured viscous liquid residue which weighed 32.3 g, corresponding to a quantitative yield of the methyl ether; i.r. (film) 3125, 3085, 3060 (aromatic C-H), 2945, 2900, 2825 (aliphatic C-H), 1680 (aromatic C=O), 1120, 1100 ($-CH_2-O-CH_2-$), 835, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.2-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.3 (s, 2, $C\underline{H}_2$), 6.69 (s, 3, $CH_2OC\underline{H}_3$), 7.45 p.p.m. (s, 3, $COC\underline{H}_3$);

mass spectrum (70 eV) m/e (relative intensity) 214.101 (91; M_r ($^{12}C_{14}$ $^{1}H_{14}$ $^{16}O_2$) = 214.099), 199 (100), 171 (60), 155 (20), 141 (15), 139 (49), 115 (8).

4-Methoxymethyl-1-naphthoic Acid (41)

1-Acetyl-4-methoxymethylnaphthalene (40) (27.0 g; 0.13 mol) was refluxed with a NaOCl solution for 10 h. The hypochlorite solution was prepared by bubbling Cl_2 (40.6 g; 0.57 mol) into a solution of NaOH (55 g; 1.27 mol) in water (70 cm^3) and ice (330 g). The reaction mixture was allowed to cool and $NaHSO_3$ solution was added to destroy excess hypochlorite. Concentrated HCl (20 cm^3) was added very slowly. The solution effervesced and a pale cream solid separated. This was filtered, washed with water and was recrystallised twice from 95% ethanol. The white powdery solid melted at 136-7° and weighed 17.62 g (62% yield); i.r. (nujol) 3200-2150 (bonded OH carboxylic acid), 1690 (aromatic carboxylic acid C=O), 1120 ($-CH_2-O-CH_2-$), 955, 920 (carboxylic acid OH), 840, 772 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.9-2.7 (m, 6, $C_{10}\underline{H}_6$), 5.1 (s, 2, $C\underline{H}_2$), 6.6 p.p.m. (s, 3, $CH_2OC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 216.080 (100, M_r ($^{12}C_{13}$ $^{1}H_{12}$ $^{16}O_3$) = 216.078), 199 (6), 186 (30), 185 (51), 183 (29), 171 (80), 156 (38), 141 (24), 139 (40), 128 (50), 115 (20).

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.20; H, 5.59. Found: C, 72.04; H, 5.33.

4-Methoxymethyl-1-naphthylcarbinol (42)

The carboxylic acid (41) was reduced in 90% yield to 4-methoxymethyl-

1-naphthylcarbinol by $LiAlH_4$ in anhydrous diethyl ether. The pale yellow viscous liquid residue quickly solidified and was recrystallised three times from 60-75° petroleum ether to long white crystalline needles, m.p. 70.5-71.5°; i.r. (melt) 3475 (bonded OH), 3100, 3050 (aromatic C-H), 2950, 2825 (aliphatic C-H), 1120, 1100 ($-CH_2-O-CH_2-$), 840, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 2.05-3.0 (m, 6, $C_{10}\underline{H}_6$), 5.38 (s, 2, $C\underline{H}_2OH$), 5.45 (s, 2, $C\underline{H}_2OCH_3$), 6.45 (s, 1, $O\underline{H}$), 6.8 p.p.m. (s, 3, $CH_2OC\underline{H}_3$). The broad singlet at τ 6.45 disappeared when the solution was shaken with D_2O; mass spectrum (70 eV) m/e (relative intensity) 202.101 (76, M_r ($^{12}C_{13}\ ^{1}H_{14}\ ^{16}O_2$) = 202.099), 172 (35), 171 (100), 143 (35), 141 (54), 128 (52), 115 (23).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.14; H, 6.97. Found: C, 77.44; H, 6.94.

1,4-Bisbromomethylnaphthalene (43) and 1-Bromomethyl-4-methoxymethyl-naphthalene (44)

4-Methoxymethyl-1-naphthylcarbinol was dissolved in benzene with a trace of pyridine added. PBr_3 was added and the reaction mixture refluxed on a water bath for 5 h. The pale yellow mixture was poured onto ice and was worked up with water and dilute base. The white solid residue was examined by n.m.r. and showed that both 1,4-bisbromomethylnaphthalene and 1-bromomethyl-4-methoxymethylnaphthalene were present in the ratio 4 to 3, methoxymethyl to bisbromomethyl. These compounds were readily separated by recrystallisation from 60-75° petroleum ether. This preparation procedure was repeated but the time was reduced to 90 min. Under these conditions an 80% yield of pure

1-bromomethyl-4-methoxymethylnaphthalene was obtained after two recrystallisations from petroleum ether. 1,4-Bisbromomethylnaphthalene (43) melted at 111-112°; i.r. (nujol) 3100, 3075 (aromatic C-H), 843, 768 (1,4-disubstituted naphthalene), 522 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.85-2.6 (m, 6, $C_{10}\underline{H}_6$), 5.1 p.p.m. (s, 4, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 315.916 (4, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{81}Br_2$) = 315.911), 314 (10), 312 (5), 235 (57), 233 (58), 154 (100), 141 (2), 115 (5).

Anal. Calcd. for $C_{12}H_{10}Br_2$: C, 45.90; H, 3.21. Found: C, 45.89; H, 3.14.

The 1-bromomethyl-4-methoxymethylnaphthalene (44) melted at 59-61°; i.r. (nujol) 3080, 3060 (aromatic C-H), 1120, 1100 ($-CH_2-O-CH_2-$), 845, 780 (1,4-disubstituted naphthalene), 542 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.85-2.7 (m, 6, $C_{10}\underline{H}_6$), 5.2 (s, 2, $C\underline{H}_2Br$), 5.25 (s, 2, $C\underline{H}_2OCH_3$), 6.7 p.p.m. (s, 3, $CH_2OC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 266.012 (10, M_r ($^{12}C_{13}$ $^{1}H_{13}$ $^{16}O_1$ $^{81}Br_1$) = 266.013), 264 (11), 186 (16), 185 (100), 155 (23), 154 (38), 153 (36), 141 (17), 115 (10).

Anal. Calcd. for $C_{13}H_{13}OBr$: C, 58.5; H, 4.84. Found: C, 58.23; H, 4.72.

1,4-Bisfluoromethylnaphthalene (45)

1,4-Bisfluoromethylnaphthalene was prepared from the corresponding dibromide (43) in 30% yield by fluoride-bromide exchange using anhydrous KF as the reagent. The clear liquid product rapidly solidified; i.r. (nujol) 3040 (aromatic C-H), 1065 (aliphatic C-F), 840, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 2.05-2.8

(m, 6, $C_{10}\underline{H}_6$), 4.59 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 192 (28, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{19}F_2$) = 192), 159.056 (100, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{19}F_1$) = 159.055), 141 (7), 133 (20), 123 (24), 115 (5).

1-Fluoromethyl-4-methoxymethylnaphthalene (46)

1-Bromomethyl-4-methoxymethylnaphthalene was heated at 140° for 4 h with anhydrous KF in N-methylpyrrolidone. The residue was worked up in the usual way and chromatographed on silica gel. The first three fractions eluted with 39-41° petroleum ether contained 1,4-difluoromethylnaphthalene. 10% Benzene in petroleum ether eluted the 1-fluoromethyl-4-methoxymethylnaphthalene. This was a viscous liquid and was obtained in 29% yield; i.r. (film) 3095, 3080 (aromatic C-H), 2995, 2945, 2905 (aliphatic C-H), 1120, 1100 ($-CH_2-O-CH_2$), 1058 (aliphatic C-F), 840, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.8-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.39 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 5.3 (s, 2, $C\underline{H}_2OCH_3$), 6.7 p.p.m. (s, 3, $CH_2O\underline{CH}_3$); mass spectrum (70 eV) m/e (relative intensity) 204.096 (81, M_r ($^{12}C_{13}$ $^{1}H_{13}$ $^{16}O_1$ $^{19}F_1$) = 204.095), 173 (71), 172 (35), 171 (100), 159 (21), 141 (30), 129 (18), 115 (7).

4-Cyano-1-naphthylcarbinol (47) (4-Hydroxymethyl-1-naphthonitrile)

The preparation of this compound involved the exchange of bromide by cyanide on the aromatic nucleus. The method used is that described by Newman and Boden[92] inasmuch as the solvent used was N-methylpyrrolidone. The ratio of reactants and the work-up procedure was that of Friedman and Shechter.[93]

Powdered CuCN (8.05 g; 0.09 mol), which had been dried over $CaSO_4$ under high vacuum for 22 h, was suspended in N-methylpyrrolidone and warmed with stirring in a 250 cm^3 flask. The flask was fitted with reflux condenser, magnetic stirrer and heating mantle. 4-Bromo-1-naphthylcarbinol (9.2 g; 0.04 mol) was added and the dark brown-green suspension which resulted was heated under reflux with stirring for 6 h. The reaction mixture was allowed to cool and was then poured into a solution of hydrated $FeCl_3$ (20 g) in concentrated HCl acid (5 cm^3) and water (30 cm^3). The resulting dark green suspension was stirred at 50-60° for 20 min. The reaction mixture was then diluted with water (250 cm^3) and left to stand overnight. The mixture was extracted with benzene three times and the benzene extract washed with a solution of concentrated HCl in water; 3:1 (2 x 200 cm^3). The benzene extract was then washed with 10% NaOH solution (2 x 250 cm^3) and with water (2 x 100 cm^3). The benzene solution was dried with anhydrous $MgSO_4$, filtered, and evaporated to a pale yellow residue which weighed 4.5 g; a 64% yield. The solid was recrystallised from 60-75° petroleum ether to give a white solid which melted at 110-112°; i.r. (nujol) 3350 (bonded OH), 2225 (aromatic nitrile C≡N), 835, 758 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.65-2.5 (m, 6, $C_{10}\underline{H}_6$), 4.95 (d, 2, $C\underline{H}_2$, J = 6 Hz), 7.8 p.p.m. (t, 1, O$\underline{H}$, J = 6 Hz). On addition of D_2O the doublet at τ 4.95 p.p.m. collapsed to a singlet, and the triplet at τ 7.8 p.p.m. disappeared altogether; mass spectrum (70 eV) m/e (relative intensity) 183.068 (74, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{14}\underline{N}_1$) = 183.068), 182 (18), 155 (23), 154 (100), 129 (19), 128 (28), 127 (35), 115 (4).

Anal. Calcd. for $C_{12}H_9ON$: C, 78.47; H, 4.95; N, 7.65. Found: C, 78.63; H, 4.89; N, 7.84.

1-Bromomethyl-4-cyanonaphthalene (48) (4-Bromomethyl-1-naphthonitrile)

4- Cyano-1-naphthylcarbinol was brominated with PBr_3 in benzene in 77% yield. The white solid residue was recrystallised three times from 60-75° petroleum ether, m.p. 131-132.5°; i.r. (nujol) 3075, 3010 (aromatic C-H), 2230 (aromatic nitrile C≡N), 840, 760 (1,4-disubstituted naphthalene), 560 cm^{-1} (aliphatic C-Br); n.m.r. ($CDCl_3$) τ 1.66-2.55 (m, 6, $C_{10}\underline{H}_6$), 5.19 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 247 (9, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{81}Br_1$) = 247), 244.978 (10, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{79}Br_1$) = 244.984), 221 (3), 219 (3), 167 (46), 166 (100), 141 (1), 140 (53), 115 (1).

Anal. Calcd. for $C_{12}H_8NBr$: C, 58.55; H, 3.28; N, 5.69. Found: C, 58.51; H, 3.24; N, 5.65.

1-Fluoromethyl-4-cyanonaphthalene (49) (4-Fluoromethyl-1-naphthonitrile)

The fluoromethyl compound (49) was prepared from the corresponding bromide (48) in 42% yield. 1-Fluoromethyl-4-cyanonaphthalene was a white solid which melted at 93.5-95.5°; i.r. (nujol) 3050 (aromatic C-H), 2230 (aromatic C≡N), 1070 (aliphatic C-F), 850, 750 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.55-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.18 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48 Hz); mass spectrum (70 eV) m/e (relative intensity) 185.0585 (100, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{19}F_1$) = 185.0581), 184 (81), 159 (30), 158 (16), 141 (5), 133 (5), 115 (1).

4-Methoxymethyl-1-naphthoylchloride (50)

4-Methoxymethyl-1-naphthoic acid (2.16 g; 0.01 mol) was stirred with $SOCl_2$ (10 g) at room temperature for 3 h. At first the reaction mixture was a pale cream suspension; after about 1 h the suspension was

a pale mauve colour. This was stirred at 50-60° for 2 h and at room temperature for a further 15 h. The excess $SOCl_2$ was removed by distillation initially at atmospheric pressure, and subsequently at reduced pressure. A yellow-green oily residue resulted which weighed 2.31 g (98.5%); i.r. (film) 3100, 3005 (aromatic C-H), 2960, 2850 (aliphatic C-H), 1765 (aryl acid chloride C=O), 1130 ($-CH_2-O-CH_2-$), 810, 775 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 0.9-2.7 (m, 6, $C_{10}\underline{H}_6$), 5.04 (s, 2, $\underline{CH}_2OCH_3$), 6.06 p.p.m. (s, 3, $CH_2O\underline{CH}_3$); mass spectrum (70 eV) m/e (relative intensity) 236 (15, M_r ($^{12}C_{13}\,^{1}H_{11}\,^{16}O_2\,^{37}Cl_1$)= 236), 234.046 (44, M_r ($^{12}C_{13}\,^{1}H_{11}\,^{16}O_2\,^{35}Cl_1$) = 234.048), 203 (28), 199 (100), 141 (7), 139 (32), 115 (3).

4-Carbamoyl-1-naphthylcarbinol (51) (4-Hydroxymethyl-1-naphthamide)

4-Cyano-1-naphthylcarbinol (1.37 g; 0.0075 mol) was dissolved in 95% ethanol (10 cm^3) and 6 N NaOH (2 cm^3) in a 50 cm^3, 3-necked flask fitted with reflux condenser, thermometer, magnetic stirrer and hot water bath.

Initially the solution was immersed in ice and cooled to 10-15°. Hydrogen peroxide (30%) (10 cm^3) was added and the solution effervesced slightly. Heat was applied very slowly and bubbles of oxygen were given off gradually. The reaction mixture was stirred at 55-60° for 4 h. The ethanol was removed on a rotary evaporator and the residue allowed to cool when a white solid precipitated out. This was filtered off from the solution and washed with ice-cold water. The white solid residue was recrystallised twice from warm water. The yield of 4-carbamoyl-1-naphthylcarbinol was quantitative. The solid melted at

146-147°. This method for the preparation of an amide from a nitrile is given in Organic Syntheses[94]; i.r. (nujol) 3300, 3200 (bonded OH, bonded NH), 1675 (amide C=O), 835, 779 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 1.45-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.92 (s, 2, $C\underline{H}_2OH$), 6.31 p.p.m. (s, 3, $CH_2\underline{O}H$ and $CONH\underline{H}_2$); mass spectrum (70 eV) m/e (relative intensity) 201.068 (100, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{16}O_2$ $^{14}N_1$) = 201.079), 185 (27), 172 (43), 155 (23), 141 (2), 139 (23), 129 (90), 115 (9).

Anal. Calcd. for $C_{12}H_{11}O_2N$: C, 71.63; H, 5.50; N, 6.96. Found: C, 71.48; H, 5.53; N, 6.80.

1-Bromomethyl-4-carbamoylnaphthalene (52) (4-Bromomethyl-1-naphthamide)

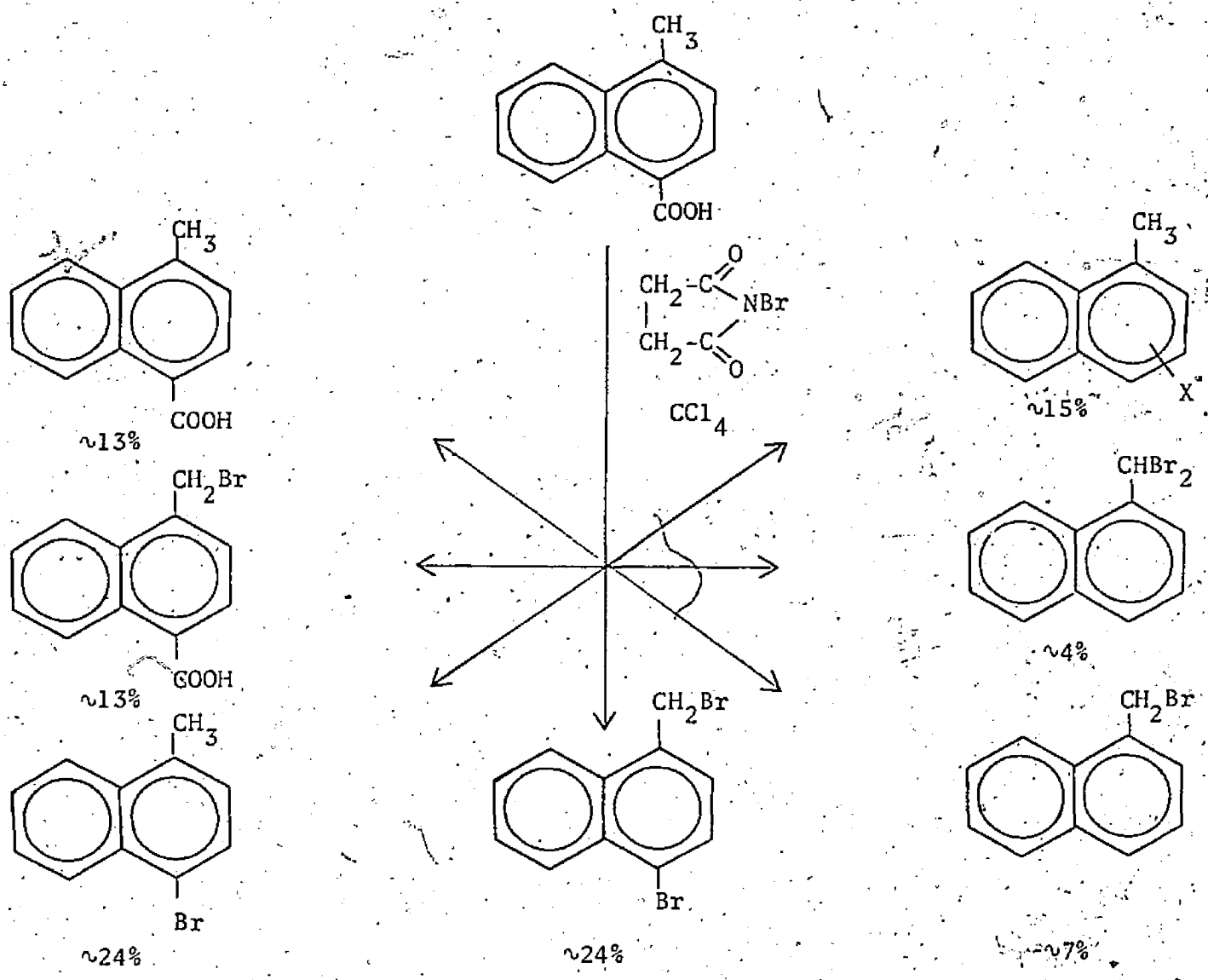
The bromomethylnaphthalene (52) was prepared from the corresponding carbinol (51) in quantitative yield using PBr_3 in benzene as the reagent. The white solid residue was recrystallised twice from a 10% benzene/100-110° petroleum ether mixture to a fine white solid which melted at 198.5-199°; i.r. (nujol) 3350 (bonded NH), 1650 (amide C=O), 835, 755, 742 (1,4-disubstituted naphthalene), 560 cm^{-1} (aliphatic C-Br); n.m.r. (D_2O) τ 1.5-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.95 (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 265 (11, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_1$ $^{14}N_1$ $^{81}Br_1$) = 265), 262.990 (12, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_1$ $^{14}N_1$ $^{79}Br_1$) = 262.994), 184 (100), 156 (50), 141 (13), 140 (38), 139 (52), 115 (12).

Anal. Calcd. for $C_{12}H_{10}ONBr$: C, 52.56; H, 3.26; N, 5.11. Found: C, 52.86; H, 3.46; N, 5.14.

1-Bromomethyl-4-carboxynaphthalene (53) (4-Bromomethyl-1-naphthoic Acid)

Two other possible synthetic routes to the naphthoic acid (53) were attempted before the adoption of the method described here, but without success. These were:-

(a) 4-Methyl-1-naphthoic acid (3) was dissolved in CCl_4 with warming and stirring. N-Bromosuccinimide in slight molar excess was added and the suspension stirred at the boiling point of the solvent for 36 h. Succinimide collected at the surface of the solvent throughout. The reaction mixture was cooled and the succinimide filtered off. The organic solution was washed with water and evaporated. N.m.r. spectroscopic investigation of the product indicated several compounds were present in the solid residue. In order to investigate the nature of this solid further, acid components were esterified by reacting a suspension of the solid residue in diethyl ether with an ethereal solution of CH_2N_2 (for the preparation of CH_2N_2 see page 87). The liquid residue which resulted after work-up was chromatographed on silica gel. The different fractions collected (20 in all) were analysed by i.r., n.m.r. and mass spectrometry, and by vapour phase chromatography using authentic compounds as references wherever available and appropriate. From this investigation an estimate of the major products of the bromination was made. This was:-



1-Bromomethyl-4-carboxynaphthalene was present, but only in limited amounts. For this reason this procedure was abandoned and an alternative attempted:-

(b) 1-Acetyl-4-bromomethylnaphthalene was stirred under reflux for 10 h with NaOCl solution. The solution was cooled, $NaHSO_3$ solution was added, and then concentrated HCl. A white solid precipitated; the solution was filtered and the solid washed with water and recrystallised from 95% ethanol. The white solid which melted at 318-319° was examined by n.m.r., i.r. and mass spectrometry. The i.r. spectrum

confirmed the solid as a carboxylic acid, however, the n.m.r. showed a very symmetrical and previously unobserved pattern in the aromatic region. Due to the symmetrical nature of the n.m.r. absorption, the Varian catalogue spectrum of 1,4-dinitronaphthalene[95] was consulted. The pattern was identical, the shifts being different (for a further discussion of these spectra see page 207). The molecular ion peak in the mass spectrum had an m/e value of 216; the molecular weight of 1,4-dinaphthoic acid is 216. The identity of the product was confirmed by the reported[72] melting point of this compound as 320°.

(c) 1-Bromomethyl-4-carboxynaphthalene was finally prepared from 4-methoxymethyl-1-naphthoic acid. The carboxylic acid (41) (2.16 g; 0.01 mol) was dissolved in dry benzene (300 cm^3) in a 1 ℓ 3-necked flask. This solution was surrounded by an ice-bath and dry HBr gas bubbled in for 2 h. The suspension was stirred at room temperature for 12 h and at 60-75° for 3 h, followed by a further 6 h at room temperature. The benzene was removed on a rotary evaporator and the grey solid residue was recrystallised from a benzene/CH_2Cl_2 mixture. The white solid weighed 2.65 g; which corresponded to a quantitative yield, and melted at 193-195°; i.r. (nujol) 3600-2400 (bonded OH carboxylic acid), 1700 (aromatic carboxylic acid C=O), 840, 775 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.85-2.5 (m, 6, $C_{10}\underline{H}_6$), 4.89 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 265.981 (6, M_r ($^{12}C_{12}\,^{1}H_9\,^{16}O_2\,^{81}Br_1$) = 265.977), 264 (6), 185 (100), 141 (25), 140 (36), 115 (43).

Anal. Calcd. for $C_{12}H_9O_2Br$: C, 54.36; H, 3.42. Found: C, 54.11; H, 3.59.

1-Bromomethyl-4-methoxycarbonylnaphthalene (54) (4-Bromomethyl-1-methylnaphthoate)

1-Bromomethyl-4-carboxynaphthalene (0.53 g; 0.002 mol) was suspended in ether (100 cm^3) in an Erlenmeyer flask and cooled in an ice-bath for 30 min. Ice-cold CH_2N_2/ether solution (50 cm^3 of 0.4 M solution, i.e. 0.02 mol of CH_2N_2) was added with stirring. Copious volumes of N_2 were evolved and the clear yellow solution which resulted was left to stand overnight. By the next morning the colour had discharged but to ensure that no CH_2N_2 remained three drops of glacial CH_3COOH were added; no N_2 was evolved confirming the absence of CH_2N_2. The ethereal solution was worked-up by washing with water (2 x 50 cm^3), with 10% Na_2CO_3 solution (2 x 50 cm^3) and again with water (2 x 50 cm^3). The basic washings were acidified but there was no precipitate, indicating that all acid had been esterified. The ethereal solution was dried with anhydrous $MgSO_4$, filtered and evaporated to a yellow residue, weight 0.5 g (90%) which after two recrystallisations from 60-75° petroleum ether the methyl ester (54) melted at 83-85°; i.r. (nujol) 3050, 3020 (aromatic C-H), 1715 (aromatic ester C=O), 850, 780 (1,4-disubstituted naphthalene), 550 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.0-2.5 (m, 6, $C_{10}\underline{H}_6$), 4.95 (s, 2, $C\underline{H}_2Br$), 6.1 p.p.m. (s, 3, $COOC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 280 (8, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_2$ $^{81}Br_1$) = 280), 277.997 (8, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_2$ $^{79}Br_1$) = 277.994), 249 (2), 247 (2), 200 (16), 199 (100), 171 (43) 141 (8), 140 (40), 139 (45), 115 (5).

Anal. Calcd. for $C_{13}H_{11}O_2Br$: C, 55.95; H, 3.97. Found: C, 56.06; H, 3.85.

The CH_2N_2 solution used for this and for subsequent esterifications was prepared according to the method of Moore and Reed.[97] Further references consulted concerning the hazards and different precursors to CH_2N_2 were Fieser and Fieser[98] and de Boer and Backer.[99] The original account of the synthesis of CH_2N_2 and its use in the esterification of carboxylic acid was reported by von Pechmann[100] in 1894.

Diethyl ether (500 cm^3), diethylene glycol monoethyl ether ("carbitol") (90 cm^3) and 30% NaOH solution (120 cm^3) were chilled in a salt-ice bath to at least 0° in an apparatus specially designed for the preparation of CH_2N_2. This comprised a single continuous distillation apparatus fitted with rubber corks, and without ground glass joins or sharp edges. Bis-(N-methyl-N-nitroso)-terephthalamide (70% in mineral oil) (36 g; 0.1 mol) was added in one batch and the flask immediately transferred to heating mantle. The yellow ether-CH_2N_2 solution distilled over and was collected in an ice-cooled receiver which contained 100 cm^3 of ether such that the receiver was under the surface of the ether at all times. Approximately 400 cm^3 of the ethereal solution distilled over, leaving a white residue in the distillation flask. The molarity of the CH_2N_2 was determined by titration with 17.5 N AR CH_3COOH. When all the CH_2N_2 had been neutralised the solution was no longer yellow; the solution was approximately 0.4 M.

1-Fluoromethyl-4-methoxycarbonylnaphthalene (55) (4-Fluoromethyl-1-methylnaphthoate)

The fluoromethylnaphthalene (55) was prepared from the bromide (54) in 55% yield. The % conversion of bromide to fluoride was 60%; i.r.

(melt) 3075, 3010 (aromatic C-H), 2995, 2945, 2900 (aliphatic C-H), 1710 (aromatic ester C=O), 1060 (aliphatic C-F), 835, 780 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 0.8-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.2 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 6.0 p.p.m. (s, 3, $COOC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 218.072 (62, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_2$ $^{19}F_1$) = 218.074), 200 (11), 187 (100), 186 (21), 159 (46), 141 (16), 115 (7).

4-Ethoxycarbonyl-1-methoxymethylnaphthalene (56) (4-Methoxymethyl-1-ethylnaphthoate)

4-Methoxymethyl-1-naphthoic acid (1.08 g; 0.005 mol) was suspended in 40 cm^3 100% ethanol in a 3-necked, 100 cm^3 flask fitted with nitrogen inlet, reflux condenser, magnetic stirrer and heating mantle. Freshly distilled boron trifluoride-etherate was added and the solution stirred under reflux for 20 h. The reaction mixture was allowed to cool and 200 cm^3 of water was added. The solution became cloudy and was extracted with CH_2Cl_2 (2 x 100 cm^3). This extract was washed with water (2 x 100 cm^3), with 10% NaOH solution (2 x 75 cm^3) and again with water (2 x 50 cm^3). The basic washings were acidified and the white solid residue which precipitated was filtered to give 0.25 g of unreacted acid. The organic extract was dried and evaporated to give the ester (56) which was an oil (0.75 g; 62% yield); i.r. (film) 3010 (aromatic C-H), 2980, 2975 (aliphatic C-H), 1710 (aromatic ester C=O), 1125 ($-CH_2-O-CH_2-$, C-O), 835, 750 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 0.85-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.3 (s, 2, $C\underline{H}_2OCH_3$), 5.65 (q, 2, $COOC\underline{H}_2CH_3$; J = 7 Hz), 6.7 (s, 3, $CH_2OC\underline{H}_3$), 8.63 p.p.m. (t, 3, $COOCH_2C\underline{H}_3$, J = 7 Hz); mass spectrum (70 eV) m/e (relative intensity) 244.093 (90,

M_r ($^{12}C_{15}$ $^{1}H_{16}$ $^{16}O_3$) = 244.101), 213 (23), 199 (100), 183 (16), 171 (34), 159 (15), 141 (6), 139 (10), 115 (21). This method for the preparation of carboxylic esters was reported by Marshall et al.[101]

1-Bromomethyl-4-ethoxycarbonylnaphthalene (57) (4-Bromomethyl-1-ethylnaphthoate)

The bromomethylnaphthalene (57) was prepared from the methyl ether (56) by means of the reaction with dry hydrogen bromide gas in benzene. The product was recrystallised three times from 60-75° petroleum ether and was obtained in 75% yield. The white crystalline solid melted at 75.5-76.5°; i.r. (film) 3070 (aromatic C-H), 1725 (aromatic carboxylic ester C=O), 825, 770 (1,4-disubstituted naphthalene), 560 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 0.85-2.65 (m, 6, $C_{10}\underline{H}_6$), 5.18 (s, 2, $C\underline{H}_2Br$), 5.62 (q, 2, $C\underline{H}_2CH_3$, J = 7 Hz), 8.55 p.p.m. (t, 3, $COOCH_2C\underline{H}_3$, J = 7 Hz); mass spectrum (70 eV) m/e (relative intensity), 294 (13, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{81}Br_1$) = 294), 292.003 (13, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{79}Br_1$) = 292.010), 249 (4), 247 (4), 214 (22), 213 (100), 185 (25), 157 (13), 141 (10), 140 (22), 139 (20), 115 (3).

Anal. Calcd. for $C_{14}H_{13}O_2Br$: C, 57.38; H, 4.47. Found: C, 57.18; H, 4.40.

4-Ethoxycarbonyl-1-fluoromethylnaphthalene (58) (4-Fluoromethyl-1-ethylnaphthoate)

Fluoride-bromide exchange was carried out on 1-bromomethyl-4-ethoxycarbonylnaphthalene by heating with anhydrous KF in N-methyl-pyrrolidone at 140-150° for 4 h. The yield of fluoromethylnaphthalene

(58) obtained was 45% following chromatography of the crude product on silica gel with petroleum ether (30-35°) as eluent. The fluoromethylnaphthalene (58) was a clear liquid; i.r. (film) 3090, 3055, 3025 (aromatic C-H), 3000, 2945, 2840 (aliphatic C-H), 1705 (aromatic carboxylic ester C=O), 1058 (aliphatic C-F), 835, 775 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 0.8-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.25 (d, 2, $\underline{CH}_2F$; J = 48 Hz), 5.62 (q, 2, $COO\underline{CH}_2CH_3$, J = 7 Hz), 8.58 p.p.m. (t, 3, $COOCH_2\underline{CH}_3$, J = 7 Hz); mass spectrum (70 eV) m/e (relative intensity) 232.086 (92, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{19}F_1$) = 232.090), 214 (15), 204 (23), 188 (26), 187 (100), 169 (16), 159 (75), 141 (8), 139 (12), 133 (25), 115 (4).

1-Acetyl-4-methoxynaphthalene (60)

The methyl ketone (60) was prepared by Friedel-Crafts acetylation of 1-methoxynaphthalene (Eastman) in the manner previously described. The ketone (60) is a solid and was recrystallised twice from 60-75° petroleum ether to a pale-yellow crystalline solid which melted at 72-74° (lit.[96] m.p. 72-73°). The yield obtained was 85% of the theoretical; i.r. (nujol) 3090, 3025 (aromatic C-H), 1660 (aromatic ketone C=O), 1240 (aralkyl ether C-O), 818, 762 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 0.95-3.61 (m, 6, $C_{10}\underline{H}_6$), 6.13 (s, 3, $O\underline{CH}_3$), 6.2 p.p.m. (s, 3, $CO\underline{CH}_3$); mass spectrum (70 eV) m/e (relative intensity) 200 (7, M_r ($^{12}C_{13}$ $^{1}H_{12}$ $^{16}O_2$) = 200), 185 (59), 157 (26), 142 (26), 128 (40), 127 (35), 115 (18), 114 (100), 113 (20).

1-Bromo-4-methoxynaphthalene (61)

1-Bromo-4-methoxynaphthalene was prepared by the reaction between 1-methoxynaphthalene and iodine monobromide. The procedure adopted for the preparation of the reagent was that reported by Militzer.[102] The IBr was prepared in a 3 ℓ 3-necked flask fitted with thermometer, mechanical stirrer and heating mantle using Br_2 (B.D.H.) (25 cm^3; 0.5 mol), I_2 (B.D.H.) (127.5 g; 0.5 mol) and $CHCl_3$ (500 cm^3). The $CHCl_3$ had been washed with concentrated H_2SO_4 (5%) to remove ethanol, then with water, and then dried over anhydrous $MgSO_4$ and distilled at 61° just prior to the reaction.

The Br_2 was added to the $CHCl_3$ and then the I_2 was added with stirring. The red-brown solution turned darker as the I_2 dissolved. This solution was stirred at 20° for 30 min and at 40° for 10 min. It was then cooled to 20°. This suspension was added to a stirred solution of 1-methoxynaphthalene (Eastman) (80 g; 0.5 mol) in $CHCl_3$ (250 cm^3) in a 3 ℓ 3-necked flask fitted with mechanical stirrer, double-surface reflux condenser, dropping funnel, and an air inlet which was adjusted so that the constant stream removed the HBr as it was formed. The reaction vessel was maintained at 15-20° in a water bath; the addition of the iodine monobromide was made over a period of 30 min. The reaction mixture was stirred at this temperature for 45 min and was then washed with water (2 x 500 cm^3) after the precipitated I_2 had been filtered off. The dark purple $CHCl_3$ solution was washed with 10% aqueous NaOH solution (2 x 500 cm^3) in order to remove any remaining I_2. It was then washed with water (2 x 500 cm^3), dried with anhydrous $MgSO_4$, filtered and evaporated. The residue was analysed by n.m.r. and also by vapour phase chromatography on an SE 30 column. The n.m.r.

spectrum indicated that the mixture contained mainly one component with traces of another two; this was confirmed by v.p.c.

The dark brown reaction residue was distilled under vacuum at 1.7 mm. Three fractions were collected and analysed by v.p.c. The third fraction boiling between 160-163° (lit.[103] b.p. 159/4 mm;[104] 147-153/3 mm) was pure 1-bromo-4-methoxynaphthalene (87.75 g; 74%); i.r. (film) 3085, 3025 (aromatic C-H), 2975, 2952, 2925, 2825 (aliphatic C-H), 1245 (aralkyl ether C-O), 1090 (aromatic C-Br), 805, 770 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.8-3.68 (m, 6, $C_{10}\underline{H}_6$), 6.23 p.p.m. (s, 3, $OC\underline{H}_3$); mass spectrum (70 eV), m/e (relative intensity) 238 (99, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{16}O_1\ ^{81}Br_1$) = 238), 236 (100, M_r ($^{12}C_{11}\ ^{1}H_9\ ^{16}O_1\ ^{79}Br_1$) = 236), 223 (60), 221 (60), 195 (55), 193 (55), 126 (18), 114 (35).

4-Methoxy-1-naphthoic Acid (62)

Several attempts were made to prepare this compound from the methyl ketone (60) by refluxing with NaOCl solution. All of these failed. The only reaction detected was oxidation of the naphthalene system itself and so this route to the naphthoic acid (62) was abandoned.

4-Methoxy-1-naphthoic acid was eventually prepared by the Grignard synthesis described by Gray and Jones.[103] 4-Methoxy-1-naphthyl magnesium bromide was prepared by reacting magnesium (6.12 g; 0.25 g atom) with 1-bromo-4-methoxynaphthalene (5.3 g) in 25 cm^3 of anhydrous ether. The mixture was stirred under reflux in a 1 ℓ 3-necked flask fitted with double-surface reflux condenser, 500 cm^3 equilibrating dropping funnel, heating mantle and magnetic stirrer. After 30 min the ether had begun to appear cloudy and so the reaction was assumed to have

started. The remainder of the 1-bromo-4-methoxynaphthalene (59.25 g; 0.25 mol in all) dissolved in 350 cm^3 of anhydrous ether was added dropwise over a period of 1 h. The reaction mixture which was now light brown in colour was refluxed with stirring for a further 9 h. The reaction mixture now comprised two phases and was cooled and poured onto solid CO_2 (400 g) in 800 cm^3 of ether, with vigorous manual stirring. A milky white suspension was formed. This was left to stand overnight to allow the excess CO_2 to sublime. Hydrochloric acid (17%) (300 cm^3) was added and the two layers stirred. The upper ethereal layer was separated and the white solid was filtered from the aqueous layer, washed with water and dissolved in 800 cm^3 of boiling 10% aqueous NaOH solution. This solution was filtered hot, the filtrate cooled and acidified with concentrated HCl and the solid which separated, filtered off. The carboxylic acid was recrystallised twice from hot glacial CH_3COOH and dried under high vacuum. The yield of 4-methoxy-1-naphthoic acid was 24 g (48%) and it melted at 247-247.5° (lit.[103] m.p. 248°); i.r. (nujol) 3200 (aromatic C-H), 3100-2200 (hydrogen bonded OH carboxylic acid), 1270 (aralkyl ether C-O), 825, 785 cm^{-1} (1,4-disubstituted naphthalene); n.m.r.[$(CD_3)_2CO$] τ 0.7-3.2 (m, 6, $C_{10}H_6$), 5.93 p.p.m. (s, 3, OCH_3); mass spectrum (70 eV) m/e (relative intensity) 202 (100 M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_3$) = 202), 186 (15), 184 (38), 158 (20), 156 (12), 141 (5), 130 (25), 113 (36).

4-Methoxy-1-naphthylcarbinol (63)

4-Methoxy-1-naphthylcarbinol was prepared from the corresponding carboxylic acid (62) in 50% yield employing $LiAlH_4$ in anhydrous ether

as the reducing agent. The product was a viscous liquid which solidified on standing. Recrystallisation from 60-75° petroleum ether gave a white crystalline solid which melted at 34-35° (lit.[81] m.p. 35°); i.r. (film) 3400 (bonded OH) 3100, 3005 (aromatic C-H), 2900, 2850 (aliphatic C-H), 1280, 1250 (aralkyl C-O), 820, 765 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.65-3.6 (m, 6, $C_{10}\underline{H}_6$), 5.18 (s, 2, $C\underline{H}_2OH$), 5.23 (s, 1, $CH_2O\underline{H}$), 6.1 p.p.m. (s, 3, $OC\underline{H}_3$). The peak at τ 5.23 p.p.m. disappeared when D_2O was shaken with the solution; mass spectrum (70 eV) m/e (relative intensity), 188 (97, M_r ($^{12}C_{12}$ $^{1}H_{12}$ $^{16}O_2$) = 188), 171 (100), 159 (36), 149 (15), 144 (24), 141 (4), 128 (36), 115 (25).

1-Bromomethyl-4-methoxynaphthalene (64)

The reports in the literature[81] of this compound describe the tendency of this compound to undergo hydrolysis even in slightly damp air. For this reason it was necessary to store the product under nitrogen in a desiccator and to prepare the bromide by a method different from the one usually adopted for this transformation. The method was first described for this compound by Shoesmith and Rubli.[81] Hydrogen bromide gas was bubbled into 750 cm^3 dry benzene in an ice-bath for 1 h. 4-Methoxy-1-naphthylcarbinol was added (5.0 g; 0.027 mol) and the solution stirred at room temperature for 12 h. The light green solution was refluxed for 1 1/2 h and then the benzene was removed on a rotary evaporator. The residue was taken up in 100-110° petroleum ether and 5 g of "Norit" decolourising charcoal was added. The solution was filtered and the clear, colourless solution was cooled in a CH_2Cl_2

solid CO_2 ice bath. A white solid separated out and was filtered off and dried. This solid, which decomposed at 119.5-120.5° (lit.[81] m.p. 119-120°, dec.) weighed 6.21 g (93%); i.r. (nujol) 3050 (aromatic -H), 1255, 1235 (aralkyl ether C-O), 820, 810, 760 (1,4-disubstituted naphthalene), 550 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.5-3.45 (m, 6, $C_{10}\underline{H}_6$), 5.11 (s, 2, $C\underline{H}_2Br$), 6.0 p.p.m. (s, 3, $OC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity), 252 (6, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{16}O_1$ $^{81}Br_1$) = 252), 250 (6, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{16}O_1$ $^{79}Br_1$) = 250), 172 (82), 171 (100), 157 (29), 149 (7), 141 (4), 129 (27), 128 (37), 115 (5).

Attempted Preparation of 1-Fluoromethyl-4-methoxynaphthalene

Three separate attempts were made to prepare this compound from 1-bromomethyl-4-methoxynaphthalene. The reaction conditions for the first attempt were 130-140° for 3 1/2 h, for the second 140-150° for 3 1/2 h and finally 160° for 13 h. Trace amounts of 1-fluoromethyl-4-methoxynaphthalene were detected by n.m.r. spectroscopy of the residue of the first and third attempts. The n.m.r. doublet with a coupling constant J_{CH_2-F} = 48 Hz is characteristic of the $-CH_2F$ function and is readily distinguishable from all other methylene absorptions. The second fraction contained considerably more fluoromethyl compound, but the percentage (15%) was still low. The fractions were chromatographed on silica gel at -35° using 30-35° petroleum ether as eluent. The chromatographic column was maintained at this temperature by means of a jacket through which flowed methanol previously cooled to this temperature. No fluoromethylnaphthalene was detected in any fraction collected. However, appreciable quantities of a white solid melting at 149-150.5° were obtained. Spectroscopic investigation of this solid

indicated that it was a bis-(4-methoxynaphthyl) -methane. The i.r. spectrum of the solid showed absorptions at 825 cm^{-1} characteristic of 2 adjacent protons in the naphthalene system, absorptions at 762 and 752 cm^{-1} indicated 4 adjacent protons, peaks at 805 and 822 cm^{-1} were characteristic of 2 adjacent protons. These absorption patterns for the C-H out-of-plane deformation modes indicate 1,4-linkage in the ring systems through the methylene bridge; 1,3-linkage is excluded as there is no signal in the 860-835 cm^{-1} region.

The n.m.r. spectrum also indicated 1,4-substituted in both ring systems; i.r. (nujol) 3090, 3070, 3025 (aromatic C-H), 1270, 1255 (aralkyl ether C-O), 825, 805, 822, 762, 752 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.6-3.6 (m, 12, $C_{20}\underline{H}_{12}$), 5.42 (s, 2, $C\underline{H}_2$), 6.13 p.p.m. (s, 6, $OC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 328.145 (100, M_r ($^{12}C_{23}$ $^{1}H_{20}$ $^{16}O_2$) = 328.140), 313 (12), 297 (39), 281 (13), 265 (16), 171 (15), 149 (11), 141 (8), 115 (4).

4-Methyl-1-sulphonaphthalene (65) (4-Methyl-1-naphthalenesulphonic acid)

This compound (65) was prepared according to the method of Fieser and Bradsher.[105] Concentrated H_2SO_4 (125 cm^3) was added to 1-methyl-naphthalene (35.5 g; 0.25 mol) with stirring. The reaction vessel was a 250 cm^3 3-necked flask fitted with dropping funnel, thermometer and magnetic stirrer and was contained in an ice-bath. The concentrated H_2SO_4 was added from the dropping funnel over 5 h; the temperature of the reaction mixture was maintained at 4° throughout. The stirring of the reaction mixture was continued for 3 h, after this time the mixture became too viscous and then separated into two layers, one of which was dark brown. The reaction mixture was allowed to stand at

room temperature for 6 days during which time a white solid began to separate out. The green-grey mixture was cooled and poured onto 200 g ice. Copious amounts of a grey-white solid separated out and the suspension was filtered. The solid was washed and dried to a white crystalline solid (41.5 g; 75% yield). Unreacted 1-methylnaphthalene was recovered by extracting the aqueous residue with CH_2Cl_2.

Compound (65) ; i.r. (nujol) 3450 (bonded OH), 1140, 1035 (hydrated sulphonic acid S=O), 830, 760 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. (D_2O) τ 1.17 (s, 1, $SO_3\underline{H}$), 1.52-3.22 (m, 6, $C_{10}\underline{H}_6$), 7.84 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 222 (100, M_r ($^{12}C_{11}$ $^{1}H_{10}$ $^{16}O_3$ $^{32}S_1$) = 222), 157 (17), 141 (51), 140 (20), 139 (37), 129 (45), 128 (23), 115 (60).

4-Chlorosulpho-1-methylnaphthalene (66) (4-Methyl-1-naphthalenesulphonyl chloride)

The potassium salt of the sulphonic acid was first prepared according to Fieser and Bradsher's method[105] by adding 1-methyl-4-sulphonaphthalene (24 g; 0.108 mol) to a warmed solution of KCl (37.5 g) in 150 cm^3 water. The resulting white slurry was heated to almost boiling, allowed to cool and then cooled further in ice. The fine white precipitate was filtered off under suction and dried in an oven to give a quantitative yield of the potassium salt. The identity of the product was confirmed by i.r. spectroscopy. Strong bands at 1225, 1203, 1175, 1162, 1155, 1055, 1042 and 1031 cm^{-1} indicated an ionic sulphonate; bands at 832 and 752 cm^{-1} indicated a 1,4-disubstituted naphthalene compound.

The salt was dried in an oven at 100° overnight (13 g; 0.05 mol) and then treated with $POCl_3$ (6 g; 0.39 mol) in a 100 cm^3 flask fitted with reflux condenser in an oil-bath at 170-180° for 24 h. The flask and contents were shaken vigorously every 4 h. The reaction vessel was removed from the oil-bath and allowed to cool.

At the end of the reaction period a mud-coloured slurry was present in the flask. This was poured onto 150 g ice and 150 cm^3 CH_2Cl_2 was added. The two layers were stirred vigorously for 15 min and were then left to stand overnight. The two layers were separated and the aqueous layer extracted with CH_2Cl_2 (2 x 50 cm^3). The organic extracts were combined and washed with water (3 x 200 cm^3), with 10% aqueous NaOH solution (2 x 150 cm^3) and again with water (2 x 150 cm^3). The CH_2Cl_2 extract was dried with anhydrous $MgSO_4$, filtered and evaporated to a light-brown solid residue, weight 11.47 g (95.4% yield). The brown solid was recrystallised from 100-110° petroleum ether to clear crystalline platelets of the sulphonyl chloride (66) which melted at 80-81° (lit.[107] 81°); i.r. (nujol) 3095 (aromatic C-H), 1380, 1375, 1370, 1350, 1170 cm^{-1} (S=O sulphonyl chloride); n.m.r. (CCl_4) τ 1.15-2.85 (m, 6, $C_{10}\underline{H}_6$), 7.29 p.p.m. (s, 3, $C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 242 (6, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_2$ $^{32}S_1$ $^{37}Cl_1$) = 242), 240.006 (17, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_2$ $^{32}S_1$ $^{35}Cl_1$) = 240.001), 205 (14), 178 (3), 176 (8), 174 (3), 141 (100), 139 (30), 115 (61). This method for the preparation of sulphonyl chlorides is described by Adams and Marvel.[106]

Attempted Preparation of 1-Bromomethyl-4-chlorosulphonaphthalene (4-Bromomethyl-1-naphthalenesulphonyl chloride)

1-Methyl-4-chlorosulphonaphthalene (8.0 g; 0.03 mol) was stirred under reflux in a 250 cm^3 3-necked flask with N-bromosuccinimide (8.9 g; 0.045 mol) in 150 cm^3 CCl_4. Samples were withdrawn every 2 h and examined by n.m.r. over the next 48 h. At the end of the reaction period the proportion of bromomethylnaphthalene to methylnaphthalene was approximately 5 to 1. Large quantities of succinimide were present at the surface of the CCl_4; the solution was a deep orange colour by this time. The reaction mixture was washed with water (4 x 200 cm^3), dried with anhydrous $MgSO_4$ and evaporated to an amber coloured liquid residue which quickly solidified. The i.r. spectrum of this residue indicated the presence of sulphonyl chloride and bromomethyl functions but the absorptions were relatively weak and only two absorptions characteristic of sulphonyl chloride were present (cf. five for (66)). The n.m.r. spectrum showed a poor (too large) integration ratio of aromatic protons to methylene protons (9:1). The presence of a singlet at τ 2.95 p.p.m. overlapping the resonances due to aromatic protons was suspected as being due to the methine proton of the $CHBr_2$ function. No molecular ion peaks corresponding to the bromomethylnaphthalene were ever obtained on any mass spectrum run.

Separation of the different components was attempted by solid-liquid column chromatography on silica gel, by repeated fractional recrystallisation and by vacuum sublimation, but all attempts were in vain. 1-Bromomethyl-4-chlorosulphonaphthalene, although detected spectroscopically, was never isolated in a pure state.

1-Methoxymethylnaphthalene (67)

It was necessary to find the optimum method of preparation of the methoxymethyl function from the carbinol preferably, or if not, then from the bromide as it was found essential to protect this last functionality before several of the synthetic transformations were attempted. Three Organic Syntheses references were consulted;[108-110] and based on these descriptions a preparation using dimethylsulphate was attempted. Dimethylsulphate is both corrosive and poisonous and the reaction was therefore carried out in a fume-hood. Any liquid that splashed was treated immediately with dilute NH_4OH solution. The hands were also washed periodically with dilute ammonia.

1-Naphthylcarbinol (3.16 g; 0.02 mol) was dissolved in MeOH (40 cm^3) with stirring in a 3-necked 100 cm^3 flask. The flask was equipped with two dropping funnels and a reflux condenser. From the two dropping funnels were alternately added over 40 min solutions of NaOH (2.0 g; 0.05 mol) in water (15 cm^3) and $(CH_3)_2SO_4$ (5.04 g; 3.73 cm^3; 0.04 mol). As this addition proceeded the contents of the flask became slightly warm. A further 0.5 g (0.0125 mol) NaOH in water (5 cm^3) was added and the solution was refluxed for 3 h with continuous stirring. The reaction mixture was allowed to cool and the aqueous methanolic solution was diluted with water. The solution turned milky and was extracted with ether. The ethereal extract was washed with water (2 x 50 cm^3) with 10% HCl (2 x 25 cm^3) and again with water (2 x 50 cm^3). The n.m.r. spectrum of the reaction residue obtained after drying and evaporation indicated a ratio of approximately 5:1, carbinol to ether.

The reaction was repeated twice with reflux periods of 15 h and

32 h but the proportion of ether in the mixture could not be raised above 20%.

The methoxymethylnaphthalene (67) was successfully prepared in quantitative yield from 1-bromomethylnaphthalene by reaction of the bromide with a sodium methoxide solution. B.p. 1-methoxymethylnaphthalene 120°/3.5 mm (lit.[111] b.p. 101-3/1.5 mm); i.r. (film) 3100, 3050 (aromatic C-H), 2950, 2925, 2875 (aliphatic C-H), 1080 ($-CH_2-O-CH_2-$), 800, 790, 770 cm^{-1} (1-substituted naphthalene); n.m.r. (CCl_4) τ 2.0-3.0 (m, 7, $C_{10}\underline{H}_7$), 5.25 (s, 2, $C\underline{H}_2$), 6.74 p.p.m. (s, 3, $CH_2OC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 172 (8), 171 (2), 159 (7), 158 (43), 157 (10), 141 (20), 130 (14), 129 (100), 128 (20), 127 (20), 115 (3).

3-Bromo-1,8-naphthalic Anhydride (69)

Rule and Thompson[112] in their article entitled Bromo- and Nitro-derivatives of Naphthalic Acid describe three different methods for the bromination of naphthalic anhydride and they concluded "...Better results are obtained by carrying out the bromination in nitric acid solution: although the yield (20%) is still somewhat low, the preparation is rapidly effected and under the correct conditions, the product crystallizes from the reaction mixture in the pure state...".

1,8-Naphthalic anhydride (Koch-Light) (25 g; 0.13 mol) was stirred in concentrated nitric acid (500 cm^3 d. 1.418) and heated to 60-70° very rapidly. Bromine (15 g; 5.2 cm^3, 0.095 mol) was added to the reaction mixture from an equilibrating dropping funnel while the temperature was maintained at 60-70°. The reaction mixture changed from an off-white suspension to a yellow suspension and finally after

30 minutes at 60-70° to a dark brown solution. The reaction mixture was cooled and then left to crystallise overnight. The colourless needles were filtered and recrystallised from 95% EtOH. The yield of 3-bromo-1,8-naphthalic anhydride was 8.0 g (23%), 241-243° (lit.[113] m.p. 244°); i.r. (nujol) 3080 (aromatic C-H), 1775, 1740 (conjugated cyclic anhydride C=O), 1300, 1235 (cyclic anhydride C-O), 1049 (aromatic C-Br), 835, 785 cm^{-1} (1,3,8-trisubstituted naphthalene); n.m.r. ($CDCl_3$) τ 1.2-2.3 p.p.m. (m, $C_{10}\underline{H}_5$); mass spectrum (70 eV) m/e (relative intensity) 278 (14, M_r ($^{12}C_{12}\ ^{1}H_5\ ^{16}O_3\ ^{81}Br_1$) = 278), 277 (95), 276 (15, M_r ($^{12}C_{12}\ ^{1}H_5\ ^{16}O_3\ ^{79}Br_1$) = 276), 275 (100), 234 (93), 232 (95), 206 (52), 204 (53).

Anhydro-3-bromo-8-hydroxymercuri-1-naphthoic Acid (70)

The mercuration and subsequent hydrolysis of 3-bromo-1,8-naphthalic anhydride is described by Rule and Thompson[112] who referred to Whitmore and Fox[113,114] for essential practical details. The method used in this synthesis was therefore a similar combination of the two references.

3-Bromo-1,8-naphthalic anhydride (27.7 g; 0.1 mol) was heated until boiling in a solution of NaOH (13.6 g; 0.34 mol) in water (520 cm^3) in a 1 ℓ 3-necked flask equipped with heating mantle, magnetic stirrer, double-surface reflux condenser and dropping funnel. To this stirred suspension was added from the dropping funnel over 1 h, a solution of yellow mercuric oxide (Fisher) (23.8 g; 0.11 mol) in water (65 cm^3) and glacial CH_3COOH (25 cm^3). This suspension was stirred under reflux for 98 h during which time considerable volumes of CO_2 were evolved. The white suspension was filtered and

and dried to give the hydroxymercuri derivative (70) (45 g; 100%). The identity of the product was investigated by i.r. only as it was too involatile for a mass spectrum to be taken and too insoluble for an n.m.r.; i.r. (nujol) 3025, 3005 (aromatic C-H), 1650 (aromatic C=O), 1080 (aromatic C-Br), 835, 785, 770 cm^{-1} (1,3,8-trisubstituted naphthalene).

3-Bromo-1-naphthoic Acid (71)

Anhydro-3-bromo-8-hydroxymercuri-1-naphthoic acid (45 g; 0.1 mol) was boiled under reflux for 4 1/2 h with 400 cm^3 water and 150 cm^3 concentrated HCl. The reaction mixture was left to cool overnight and the white solid which had settled was filtered and washed with water. The crude solid was recrystallised from glacial CH_3COOH and four separate crystal fractions collected. 3-Bromo-1-naphthoic acid was less soluble than the 6-bromo-1-naphthoic acid also present in the crude solid, and so the first fractions collected contained the 1,3-isomer. The solid obtained from these fractions was vigorously dried and then melted at 230.5-232° (lit.[112] m.p. 231-2°). The yield of (71) was 50%; i.r. (nujol) 3200-2500 (bonded OH carboxylic acid), 1690 (aromatic carboxylic acid C=O), 1080 (aromatic C-Br), 855, 835, 745 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 0.5-2.5 p.p.m. (m, $C_{10}H_6$); mass spectrum (70 eV) m/e (relative intensity) 252 (98, M_r ($^{12}C_{11}\ ^{1}H_7\ ^{16}O_2\ ^{81}Br_1$) = 252), 251 (13), 250 (100, M_r ($^{12}C_{11}\ ^{1}H_7\ ^{16}O_2\ ^{79}Br_1$) = 250), 246 (34), 244 (35), 207 (21), 205 (21), 126 (67), 115 (18).

3-Bromo-1-methylnaphthoate (72)

3-Bromo-1-naphthoic acid was esterified in 95% yield by the addition of an ethereal solution of CH_2N_2 to an ethereal solution/suspension of the acid (72). The solid ester was recrystallised from 60-75° petroleum ether to give a white crystalline solid which melted at 58-59° (lit.[112] 59°); i.r. (nujol) 3050, 3010 (aromatic C-H), 1745 (aromatic carboxylic ester C=O), 1040 (aromatic C-Br), 855, 832, 750, 742 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.1-2.8 (m, 6, $C_{10}\underline{H}_6$), 6.18 p.p.m. (s, 3, $COOC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 266 (92, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_2$ $^{81}Br_1$) = 266), 264 (93, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_2$ $^{79}Br_1$)= 264), 235 (99), 233 (100), 207 (39), 205 (40), 126 (75).

3-Bromo-1-naphthylcarbinol (73)

3-Bromo-1-methylnaphthoate was reduced to 3-bromo-1-naphthylcarbinol in quantitative yield with $LiAlH_4$ in anhydrous ether. The buff coloured solid residue was recrystallised three times from 100-110° petroleum ether to fine white needles , m.p. 106-107°; i.r. (nujol) 3350 (bonded OH), 1065 (aromatic C-Br), 865, 850, 745 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.95-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.03 (s, 2, $C\underline{H}_2OH$), 8.51 p.p.m. (s, 1, $O\underline{H}$). The singlet at τ 8.51 p.p.m. disappeared on D_2O exchange; mass spectrum (70 eV) m/e (relative intensity) 238 (39, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{81}Br_1$) = 238), 236 (40, M_r($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{79}Br_1$) = 236), 221 (3), 219 (5); 209 (6), 207 (8), 157 (18), 139 (21), 129 (91), 128 (100), 127 (42).

Anal. Calcd. for $C_{11}H_9OBr$: C, 55.71; H, 3.83. Found: C, 55.74; H, 3.83.

3-Bromo-1-bromomethylnaphthalene (74)

Bromination of the carbinol (73) with PBr_3 in benzene gave an 85% yield of the bromide (74). This was recrystallised three times from a 10% benzene/100-110° petroleum ether mixture to white needles which melted at 94-96°; i.r. (nujol) 3010 (aromatic C-H), 1050 (aromatic C-Br), 865, 850, 765, 738 (1,3-disubstituted naphthalene), 540, 518 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.9-2.75 (m, 6, $C_{10}\underline{H}_6$), 5.25 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 301.897 (11, M_r ($^{12}C_{11}\ ^{1}H_8\ ^{81}Br_2$) = 301.896), 300 (24), 298 (12), 222 (25), 221 (100), 220 (26), 219 (100), 141 (21), 140 (44), 139 (45).

Anal. Calcd. for $C_{11}H_8Br_2$: C, 44.03; H, 3.09. Found: C, 44.20; H, 2.81.

3-Bromo-1-fluoromethylnaphthalene (75)

3-Bromo-1-fluoromethylnaphthalene was prepared from the bromide in the usual way. The yield of fluoromethylnaphthalene was 61% following column chromatography of the reaction residue on silica gel; i.r. (film) 3070 (aromatic C-H), 2975, 2925, 2860 (aliphatic C-H), 1060 (aliphatic C-F), 1020 (aromatic C-Br), 830, 760 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.9-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.55 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 240 (56, M_r ($^{12}C_{11}\ ^{1}H_8\ ^{81}Br_1\ ^{19}F_1$) = 240), 239 (15), 237.973 (58, M_r ($^{12}C_{11}\ ^{1}H_8\ ^{79}Br_1\ ^{19}F_1$) = 237.973), 160 (17), 159 (100), 158 (13), 157 (17), 133 (17).

Attempted Preparation of 3-Fluoro-1-methylnaphthoate

Sheppard and Sharts[115] state that "...Halogen atoms on aromatic rings may be readily replaced using potassium fluoride if there is an electron-withdrawing group in a position ortho- or para-...". Finger and Kruse[116] described the fluorine-chlorine exchange of p-chloronitrobenzene in dimethylsulphoxide with potassium fluoride at 185-190° for 14 hours.

Somewhat optimistically it was hoped that it might be possible to carry out a similar exchange on 3-bromo-1-methylnaphthoate to give the 3-fluoro compound, even though the electron-withdrawing group was not disposed either ortho- or para- to the exchanging group.

The 3-bromo compound (72) was heated with anhydrous potassium fluoride in N-methylpyrrolidone at 190° for 18 h. Following chromatography on 52% yield of 1-methylnaphthoate was obtained. Spectra of this compound were identical to those of the product of the reaction between CH_2N_2 and 1-naphthoic acid (28). The remainder of the material eluted from the column was unchanged starting material.

To determine whether this somewhat surprising result was some function of the solvent, the reaction was repeated using sulpholane as the solvent. The sulpholane was examined for oxidisable impurities by making a 1:1 solution with concentrated H_2SO_4. After 5 minutes a colour had appeared indicating that impurities were present and so the sulpholane was purified according to the procedure of Arnett and Douty[117] by distillation from powdered NaOH between 125-135° at 5.0 mm. The sulpholane was stored over molecular sieves under nitrogen.

Two attempts to prepare 3-fluoro-1-methylnaphthoate were made using sulpholane as the solvent. The first was carried out at 190° for 24 h.

Only a trace of 1-methylnaphthoate was detected in the product; mainly starting material was obtained following chromatography of the reaction residue. The second attempt was carried out at 185° for ten days, but only starting material was obtained from this attempt.

No trace of fluorinated compound was ever detected and so this synthesis was abandoned.

3-Cyano-1-naphthylcarbinol (76) (4-Hydroxymethyl-2-naphthonitrile)

3-Cyano-1-naphthylcarbinol was prepared in 51% yield from 3-bromo-1-naphthylcarbinol by cyanide-bromide exchange using cuprous cyanide in N-methylpyrrolidone. The reaction mixture was heated at 180-190° for 6 h. The pale-yellow solid residue was recrystallised from a 10% benzene/100-110° petroleum ether mixture to a white solid which melted at 87-89°; i.r. (nujol) 3425 (bonded OH), 3010 (aromatic C-H), 2220 (aryl nitrile C≡N), 875, 760, 740 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. ($CDCl_3$) τ 1.95-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.95 (d, 2, $C\underline{H}_2OH$, J = 0.6 Hz), 5.52 p.p.m. (t, 1, $CH_2O\underline{H}$, J = 0.6 Hz). On D_2O exchange the triplet at τ 5.52 p.p.m. disappeared and the doublet at τ 4.95 p.p.m. collapsed to a singlet. Mass spectrum (70 eV) m/e (relative intensity) 183.072 (48, M_r ($^{12}C_{12}$ $^{1}H_9$ $^{16}O_1$ $^{14}N_1$) = 183.068), 182 (18), 165 (11), 154 (30), 153 (100), 140 (13), 127 (54), 115 (6).

Anal. Calcd. for $C_{12}H_9ON$: C, 78.47; H, 4.95; N, 7.65. Found: C, 78.79; H, 5.26; N, 7.58.

1-Bromomethyl-3-cyanonaphthalene (77) (4-Bromomethyl-2-naphthonitrile)

1-Bromomethyl-3-cyanonaphthalene was prepared from the corresponding carbinol (76) with PBr_3 in benzene. The white solid residue was recrystallised three times from a 10% benzene/100-110° petroleum ether mixture to give a 90% yield of a white crystalline solid which melted at 151.5-153°; i.r. (nujol) 3010 (aromatic C-H), 2210 (aryl nitrile C≡N), 855, 770, 750 (1,3-disubsituted naphthalene), 565 cm^{-1} (aliphatic C-Br); n.m.r. [$(CD_3)_2CO$] τ 1.5-2.5 (m, 6, $C_{10}\underline{H}_6$), 4.82 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 247 (8, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{81}Br_1$) = 247), 244.978 (8, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{79}Br_1$) = 244.984), 167 (37), 166 (100), 144 (17), 141 (5), 140 (22), 139 (16), 115 (4).

Anal. Calcd. for $C_{12}H_8NBr$: C, 58.56; H, 3.28; N, 5.69. Found: C, 58.54; H, 3.32; N, 5.59.

3-Cyano-1-fluoromethylnaphthalene (78) (4-Fluoromethyl-2-naphthonitrile)

The fluoromethylnaphthalene (78) was prepared in 42% yield from its bromomethyl precursor (77). The reaction mixture was heated at 130-140°C for 4 h and then worked up with saturated NH_4Cl solution and chromatographed on silica gel to give a white solid; i.r. (nujol) 3030 (aromatic C-H), 2225 (aromatic C≡N), 1075 (aliphatic C-F), 835, 750 cm^{-1} (1,4-disubstituted naphthalene); n.m.r. ($CDCl_3$) τ 0.7-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.1 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 185.074 (100, M_r ($^{12}C_{12}$ $^{1}H_8$ $^{14}N_1$ $^{19}F_1$) = 185.058), 184 (86), 180 (10), 166 (9), 165 (29), 164 (10), 159 (7), 158 (37), 157 (20), 153 (12), 141 (2), 140 (6), 133 (5), 115 (1).

3-Cyano-1-methoxymethylnaphthalene (79) (4-Methoxymethyl-2-naphthonitrile)

The methyl ether (79) was prepared by reacting 1-bromomethyl-1-cyanonaphthalene with sodium in methanol. After the normal work-up the ether (79) was obtained as a colourless solid in 90% yield, m.p. 67.5-68.5°; i.r. (nujol) 3020 (aromatic C-H), 2220 (aryl nitrile C≡N), 1125 ($-CH_2-O-CH_2-$, C-O), 850, 770, 745 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.95-2.6 (m, 6, $C_{10}\underline{H}_6$), 5.22 (s, 2, $\underline{CH}_2OCH_3$), 6.71 p.p.m. (s, 3, $CH_2O\underline{CH}_3$); mass spectrum (70 eV) m/e (relative intensity) 197.070 (15, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{14}N_1$ $^{16}O_1$) = 197.084), 196 (88), 195 (48), 181 (15), 166 (80), 165 (100), 163 (15), 153 (28), 139 (35), 138 (20), 128 (22), 115 (1).

Anal: Calcd. for $C_{13}H_{11}ON$: C, 79.14; H, 5.62; N, 7.10. Found: C, 79.45; H, 6.00; N, 7.06.

3-Acetyl-1-methoxymethylnaphthalene (80)

Magnesium turnings (1.22 g; 0.05 g atom) were placed in a 50 cm^3 3-necked flask with 5 cm^3 anhydrous ether. The flask was fitted with a reflux condenser, 25 cm^3 equilibrating dropping funnel, magnetic stirrer and nitrogen inlet. The magnesium was stirred under the nitrogen atmosphere for 5 min and then 1 cm^3 of a solution of CH_3I (1.42 g; 0.05 mol) in ether (10 cm^3) was added from the dropping funnel. The ethereal solution became cloudy after about 3 min. The remainder of the CH_3I solution was added and the reaction mixture stirred for a further 3 h.

Anhydrous benzene (19 cm^3) was added and the condenser arranged for distillation. The ether was distilled off and the condenser

returned to the reflux position.

3-Cyano-1-methoxymethylnaphthalene (1.97 g; 0.01 mol) was added in one batch in 10 cm^3 benzene. This solution was stirred under reflux for 7 h. After 15 min the solution had turned green. At the end of the 7 h reaction period the mixture was cooled in an ice-bath. The reaction mixture was transferred to a 250 cm^3 flask and 6 N HCl (100 cm^3) was added very cautiously. There was considerable effervescence and the mixture turned yellow-brown in colour. This solution was stirred under reflux for 36 h. The two layers were separated and the benzene layer washed with water (2 x 200 cm^3), with 10% $NaHCO_3$ solution (4 x 100 cm^3) and again with water (3 x 100 cm^3). The pink benzene solution was dried with anhydrous $MgSO_4$ and was evaporated to a dark brown, thick viscous, liquid residue. N.m.r. analysis of this residue indicated several spurious peaks in both the methylene and methyl regions. The residue was chromatographed on silica gel using a 10% benzene/35-45° petroleum ether mixture as the eluent.

3-Acetyl-1-methoxymethylnaphthalene was obtained in 77% yield; i.r. (film) 3150, 3075 (aromatic C-H), 3000, 2940, 2900, 2825 (aliphatic C-H), 1680 (aromatic ketone C=O), 1115, 1095 ($-CH_2-O-CH_2-$), 845, 766, 760, 735 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.8-2.85 (m, 6, $C_{10}\underline{H}_6$), 5.42 (s, 2, $C\underline{H}_2OCH_3$), 6.79 (s, 3, $CH_2OC\underline{H}_3$), 7.56 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 214.108 (75, M_r ($^{12}C_{14}\ ^{1}H_{14}\ ^{16}O_2$) = 214.099), 199 (67), 186 (15), 183 (35), 181 (22), 171 (27), 149 (29), 141 (15), 139 (46), 115 (9), 84 (100). The procedure followed here is based on that of Callen et al.[120]

3-Acetyl-1-bromomethylnaphthalene (81)

The bromide (81) was prepared from the methyl ether (80) in quantitative yield with dry HBr gas in benzene. The solution was stirred at room temperature for 12 h and at 60° for 2 h. The solid residue was recrystallised three times from a 10% benzene/100-110° petroleum ether mixture to give colourless crystals of (81), m.p. 109-110.5°; i.r. (nujol) 3030 (aromatic C-H), 1680 (aromatic ketone), 845, 775, 730 (1,3-disubstituted naphthalene), 570 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.4-2.75 (m, 6, $C_{10}\underline{H}_6$), 5.17 (s, 2, $C\underline{H}_2Br$), 7.42 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity), 264 (1, M_r ($^{12}C_{13}\ ^{1}H_{11}\ ^{16}O_1\ ^{81}Br_1$) = 264), 262.009 (1, M_r ($^{12}C_{13}\ ^{1}H_{11}\ ^{16}O_1\ ^{79}Br_1$) = 261.999), 220 (1), 218 (1), 183 (93), 141 (13), 140 (84), 139 (100), 115 (14).

Anal. Calcd. for $C_{13}H_{11}OBr$: C, 59.35; H, 4.21. Found: C, 59.09; H, 4.01.

3-Carbamoyl-1-naphthylcarbinol (83) (4-Hydroxymethyl-2-naphthamide)

3-Carbamoyl-1-naphthylcarbinol was prepared from its 3-cyano precursor (76) by means of the reaction between the nitrile, caustic soda solution, and hydrogen peroxide, in ethanol. The yield of amide was low, only 50%. The product was recrystallised from 95% ethanol three times to give colourless crystals of carbinol (83), m.p. 155-156°; i.r. (nujol) 3400 (hydrogen bonded OH), 3150 (bonded NH), 3075, 3050, 3030 (aromatic C-H), 1695 (primary amide C=O), 1595 (primary amide), 850, 835, 735 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 1.4-2.5 (m, 6, $C_{10}\underline{H}_6$), 4.92 (s, 2, $C\underline{H}_2OH$), 7.0 p.p.m. (s, 3, $CONH\underline{_2}$ and $CH_2O\underline{H}$). The broad singlet at τ 7.0 p.p.m. disappeared when the solution

was shaken with D_2O; mass spectrum (70 eV) m/e (relative intensity) 201.088 (54, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{16}O_2$ $^{14}N_1$) = 201.079), 185 (15), 172 (38), 155 (20), 141 (3), 139 (25), 129 (100), 128 (48), 127 (44), 115 (11).

Anal. Calcd. for $C_{12}H_{11}O_2N$: C, 71.63; H, 5.50; N, 6.96. Found: C, 71.50; H, 5.43, N, 6.71.

3-Acetyl-1-fluoromethylnaphthalene (82)

3-Acetyl -1-fluoromethylnaphthalene was prepared from 3-acetyl-bromomethylnaphthalene by bromide-fluoride exchange at 130-140° for 4 h. The yield following chromatography on silica gel was 36%; i.r. (film) 3040 (aromatic C-H), 2985, 2980 (aliphatic C-H), 1680 (aromatic ketone C=O), 1060 (aliphatic C-F), 850, 765, 735 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.67-2.62 (m, 6, $C_{10}\underline{H}_6$), 4.45 (d, 2, $C\underline{H}_2F$, J = 48 Hz), 7.43 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 202.084 (90, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_1$ $^{19}F_1$) = 202.079), 188 (34), 187 (100), 160 (17), 159 (91), 157 (24), 141 (3), 139 (26), 133 (55), 115 (7).

1-Bromomethyl-3-carbamoylnaphthalene (84) (4-Bromomethyl-2-naphthamide)

The carbinol (83) was brominated with PBr_3 in benzene to give a 33% yield of the bromide (84). Re-extraction of the aqueous residue with CH_2Cl_2 plus soxhlet extraction of the residue following evaporation to dryness of the aqueous residue could not improve the yield obtained. The solid was recrystallised from a 10% benzene/100-110° petroleum ether mixture to give colourless crystals, m.p. 204-5°. Bromide-fluoride exchange was not attempted because of the small amount of the bromide

(84) available and because of the lack of success encountered during the attempted preparation of the 1,4-isomer of this compound; i.r. (nujol) 3350, 3180 (amide N-H), 3110 (aromatic C-H), 1665 (aromatic amide C=O), 860, 780, 750 (1,3-disubstituted naphthalene), 550 cm^{-1} (aliphatic C-Br); n.m.r. [$(CD_3)_2CO$] τ 1.4-2.6 (m, 6, $C_{10}\underline{H}_6$), 4.95 (s, 2, $C\underline{H}_2Br$), 6.8 p.p.m. (s, 2, $CONH_2$); mass spectrum (70 eV) m/e (relative intensity) 265 (10, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_1$ $^{14}N_1$ $^{81}Br_1$) = 265), 262.991 (10, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_1$ $^{14}N_1$ $^{79}Br_1$) = 262.995), 185 (17), 184 (100), 141 (6), 140 (20), 139 (22), 115 (2).

Anal: Calcd. for $C_{12}H_{10}ONBr$: C, 52.56; H, 3.26; N, 5.11. Found: C, 52.69; H, 3.48; N, 5.05.

3-Carboxy-1-naphthylcarbinol (85) (4-Hydroxymethyl-2-naphthoic Acid)

3-Carboxy-1-naphthylcarbinol was prepared from 3-cyano-1-naphthylcarbinol. This synthetic transformation was attempted by acidic hydrolysis of the nitrile, but all attempts were unsuccessful. The nitrile (76) was hydrolysed to the carboxylic acid in quantitative yield by refluxing the nitrile with 6 N solution of NaOH in water until only one phase was present in the reaction mixture (15 h). The white solid obtained after work-up was recrystallised from 95% ethanol to give colourless crystals of the acid (85), m.p. 293-295°; i.r. (nujol) 3050 (bonded OH), 1680 (aromatic carboxylic acid C=O), 860, 775, 740 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 1.47-2.65 (m, 6, $C_{10}\underline{H}_6$), 4.9 (s, 2, $C\underline{H}_2OH$), 5.95 p.p.m. (s, 1, $CH_2\underline{OH}$). The broad singlet at τ 5.95 p.p.m. disappeared on the addition of D_2O to the solution; mass spectrum (70 eV) m/e (relative intensity) 202.057 (86, M_r ($^{12}C_{12}$ $^{1}H_{10}$

$^{16}O_3$) = 202.063), 173 (52), 157 (25), 155 (42), 141 (13), 124 (100), 123 (52), 115 (21).

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.30; H, 4.47. Found: C, 71.60; H, 4.69.

3-Methoxycarbonyl-1-naphthylcarbinol (86) (4-Hydroxymethyl-2-methyl-naphthoate)

The methyl ester of 3-carboxy-1-naphthylcarbinol was prepared in 90% yield from the reaction between an ethereal suspension of the carboxylic acid and an ethereal solution of CH_2N_2. The white solid ester was recrystallised from a 10% benzene/petroleum ether mixture and was then vacuum sublimed to give colourless crystals, m.p. 79-80°; i.r. (nujol) 3200 (bonded OH), 1710 (aryl ester C=O), 850, 765, 735 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 1.3-2.7 (m, 6, $C_{10}\underline{H}_6$), 5.0 (s, 2, $C\underline{H}_2OH$), 6.15 (s, 3, $COOC\underline{H}_3$), 6.65 p.p.m. (s, 1, $CH_2\underline{O}H$). The singlet at τ 6.65 p.p.m. disappeared on addition of D_2O to the solution; mass spectrum (70 eV) m/e (relative intensity) 216.076 (100, M_r ($^{12}C_{13}\ ^1H_{12}\ ^{16}O_3$) = 216.079), 187 (61), 185 (31), 183 (20), 157 (29), 155 (42), 143 (19), 141 (9), 139 (21), 129 (32), 128 (46), 127 (32), 115 (5).

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.25; H, 5.59. Found: C, 71.97; H, 5.50.

1-Bromomethyl-3-methoxycarbonylnaphthalene (87) (4-Bromomethyl-2-methylnaphthoate)

1-Bromomethyl-3-methoxycarbonylnaphthalene was prepared from the corresponding carbinol (86) in 80% yield using PBr_3 in benzene as the reagent. The bromide (87) was recrystallised from 60-75° petroleum ether to long white needles, m.p. 125-126.5°; i.r. (nujol) 3070 (aromatic C-H), 1710 (aromatic ester C=O), 800, 775, 725, 715 (1,3-disubstituted naphthalene), 590 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.3-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.15 (s, 2, $C\underline{H}_2Br$), 6.12 p.p.m. (s, 3, $COOC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 280 (6, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_2$ $^{81}Br_1$) = 280), 277.997 (6, M_r ($^{12}C_{13}$ $^{1}H_{11}$ $^{16}O_2$ $^{79}Br_1$) = 277.994), 249 (2), 247 (2), 199 (100), 141 (13), 140 (22), 139 (23), 115 (3).

Anal. Calcd. for $C_{13}H_{11}O_2Br$: C, 55.95; H, 3.97. Found: C, 56.60; H, 4.05.

1-Fluoromethyl-3-methoxycarbonylnaphthalene (88) (4-Fluoromethyl-2-methylnaphthoate)

1- Fluoromethyl-3-methoxycarbonylnaphthalene was prepared from the bromide (87) in 40% yield by bromide-fluoride exchange with anhydrous KF. The fluoromethylnaphthalene was a clear liquid; i.r. (film) 3075, 3050 (aromatic C-H), 2960, 2925, 2865 (aliphatic C-H), 1725 (aryl ester C=O), 1055 (aliphatic C-F), 865, 850, 765, 753 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.5-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.3 (d, 2, $C\underline{H}_2F$, J = 48.0 Hz), 6.15 p.p.m. (s, 3, $COOC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 218.074 (94, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{16}O_2$ $^{19}F_1$) = 218.074), 200 (9), 187 (100), 159 (71), 157 (14), 141 (7), 139 (14), 133 (26), 115 (4).

3-Ethoxycarbonyl-1-ethoxymethylnaphthalene (89) and 3- Ethoxycarbonyl-1-naphthylcarbinol (90) (4-Ethoxymethyl-2-ethylnaphthoate and 4-Hydroxymethyl-2-ethylnaphthoate)

The carboxylic acid (85) (1.0 g; 0.005 mol) was dissolved in 100% ethanol (50 cm^3) in a 100 cm^3 3-necked flask equipped with double-surface reflux condenser, nitrogen inlet, magnetic stirrer and heating mantle. Freshly distilled boron trifluoride-etherate (4 cm^3) was added and the solution stirred under reflux for 20 h.

The reaction mixture was allowed to cool and was poured into distilled water (200 cm^3). This was extracted with CH_2Cl_2, washed and dried. N.m.r. spectroscopy of the residual oil, following evaporation of the solvent, showed that both carbinol-ester and ether-ester were present. Their identities were confirmed by accurate mass measurement of the molecular ion peaks of both species. Separation was not attempted as it was immaterial whether the bromide was prepared from the ether or the alcohol. Either function would be transformed to the bromide on treatment with anhydrous HBr in dry benzene; n.m.r. (CCl_4) τ 1.3-2.7 (m, $C_{10}\underline{H}_6$), 4.8 (s, $C\underline{H}_2OH$), 5.05 (s, $C\underline{H}_2OC_2H_5$), 5.2 (s, $O\underline{H}$), 5.72 (q, $COOC\underline{H}_2CH_3$ and $CH_2OC\underline{H}_2CH_3$, J = 0.6 Hz), 8.6 p.p.m. (t, $CH_2OCH_2C\underline{H}_3$ and $COOCH_2C\underline{H}_3$, J = 0.6 Hz); mass spectrum (70 eV) m/e (relative intensity) 258.142 ($^{12}C_{16}\ ^{1}H_{18}\ ^{16}O_3$) = 258.126), 230.001 ($^{12}C_{14}\ ^{1}H_{14}\ ^{16}O_3$) = 229.996.

1-Bromomethyl-3-ethoxycarbonylnaphthalene (91) (4-Bromomethyl-2-ethylnaphthoate)

Treatment of the mixture of ester-ether (89) and ester-alcohol (90) with HBr in benzene afforded 3-ethoxycarbonyl-1-bromomethyl-naphthalene in 98% overall yield, calculated from the carboxylic acid (85). The white solid bromide (91) was recrystallised twice from 60-75° petroleum ether to long white needles, m.p. 114-115°; i.r. (nujol) 3040 (aromatic C-H), 1710 (aryl ester C=O), 855, 770, 740 (1,3-disubstituted naphthalene), 555 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.2-2.8 (m, 6, $C_{10}\underline{H}_6$), 5.1 (s, 2, $\underline{CH}_2Br$), 5.6 (q, 2, $\underline{CH}_2CH_3$, J = 0.6 Hz), 8.55 p.p.m. (t, 3, $COOCH_2\underline{CH}_3$, J = 0.6 Hz); mass spectrum (70 eV) m/e (relative intensity) 294 (10, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{81}Br_1$) = 294), 292.010 (10, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{79}Br_1$) = 292.010), 250 (4), 248 (4), 214 (41), 213 (100), 183 (19), 169 (54), 141 (31), 140 (20), 139 (21), 115 (6

Anal. Calcd. for $C_{14}H_{13}O_2Br$: C, 57.35; H, 4.47. Found: C, 57.28; H, 4.43.

3-Ethoxycarbonyl-1-fluoromethylnaphthalene (92) (4-Fluoromethyl-2-ethylnaphthoate)

The fluoride (92) was prepared from the bromide (91) in 35% yield. The white solid fluoride melted at 72-73°; i.r. (melt) 3030 (aromatic C-H), 2980, 2920, 2850 (aliphatic C-H), 1720 (aromatic ester C=O), 1060 (aliphatic C-F), 800, 760, 740 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.6-2.9 (m, 6, $C_{10}\underline{H}_6$), 4.35 (d, 2, $\underline{CH}_2F$, J = 48.0 Hz), 5.7 (q, 2, $COO\underline{CH}_2CH_3$, J = 0.8 Hz), 8.65 p.p.m. (t, 3, $COOCH_2\underline{CH}_3$, J = 0.8 Hz); mass spectrum (70 eV) m/e (relative intensity)

232.088 (95, M_r ($^{12}C_{14}$ $^{1}H_{13}$ $^{16}O_2$ $^{19}F_1$) = 232.090), 214 (67), 204 (36), 188 (25), 187 (100), 186 (27), 169 (71), 159 (75), 141 (40), 139 (18), 133 (20), 115 (15).

1,3-Bisbromomethylnaphthalene (94), 3-Bromomethyl-1-methylnaphthalene (95) and 1-Bromomethyl-3-methylnaphthalene (96)

1,3-Dimethylnaphthalene (Aldrich) (6.04 g; 0.0396 mol) was dissolved in CCl_4 (500 cm^3) in a 1 ℓ flask equipped with double-surface reflux condenser, heating mantle and magnetic stirrer. N-Bromosuccinimide (6.89 g; 0.0396 mol) was added and the solution stirred under reflux for 10 h. A sample was withdrawn for n.m.r. analysis after 4 h and 10 h. The mixture was allowed to cool and the succinimide on the surface of the liquid was filtered off. The CCl_4 solution was washed with water (6 x 200 cm^3) and dried with anhydrous $MgSO_4$. The solution was evaporated to a pale yellow liquid residue (9.16 g).

N.m.r. analysis of this residue indicated that 1,3-dimethylnaphthalene, 1,3-bisbromomethylnaphthalene, 3-bromomethyl-1-methylnaphthalene and 1-bromomethyl-1-methylnaphthalene were all present in the mixture. The residue was subjected to solid-liquid chromatography using 400 g silica gel and eluting with 35-45° petroleum ether. Two 600 cm^3 fractions were collected and thereafter 200 cm^3 fractions. The fractions were analysed by n.m.r. spectroscopy. The first two contained unreacted 1,3-dimethylnaphthalene (0.94 g), the next nine the two 1,3-methyl bromomethyl isomers in approximately constant proportions. The last two fractions collected comprised 1,3-bisbromomethylnaphthalene (1.2 g).

Crystallisation of the mixture of the two isomers was attempted and this revealed that the 3-bromomethyl-1-methyl isomer was significantly less soluble in 60-75° petroleum ether than the 1,3 isomer. Fractional crystallisation of the combined chromatographic fractions was carried out. In all, nine crystallisation fractions were collected and these comprised 1.88 g 1-bromomethyl-3-methylnaphthalene, 1.05 g 3-bromomethyl-1-methylnaphthalene and the residue which was a mixture of the two.

All three compounds (94), (95) and (96) were recrystallised from 70-85° petroleum ether to long white needles.

1,3-Bisbromomethylnaphthalene (94) had a m.p. 111-112°; i.r. (nujol) 3020 (aromatic C-H), 850, 780, 755 (1,3-disubstituted naphthalene), 580 cm^{-1} (aliphatic C-Br); n.m.r. [$(CD_3)_2CO$] τ 1.7-2.7 (m, 6, $C_{10}\underline{H}_6$), 5.0 (s, 2, α-$C\underline{H}_2Br$), 5.28 p.p.m. (s, 2, β-$C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 315.914 (12, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{81}Br_2$) = 315.911), 314 (25), 312 (13), 235 (100), 233 (100), 154 (94), 153 (45), 152 (12), 141 (3), 128 (9), 115 (6).

Anal. Calcd. for $C_{12}H_{10}Br_2$: C, 45.9; H, 3.21. Found: C, 45.92; H, 3.19.

3-Bromomethyl-1-methylnaphthalene (95) had a m.p. 86.5-87°; i.r. (nujol) 3075 (aromatic C-H), 870, 850, 775, 752 (1,3-disubstituted naphthalene), 548 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 2.0-2.85 (m, 6, $C_{10}\underline{H}_6$), 5.55 (s, 2, β-$C\underline{H}_2Br$), 7.35 p.p.m. (s, 3, α-$C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 236 (8, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{81}Br_1$) = 236), 233.994 (8, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{79}Br_1$) = 234.004), 156 (29), 155 (100), 153 (13), 152 (11), 149 (7), 141 (15), 115 (9).

Anal. Calcd. for $C_{12}H_{11}Br$: C, 61.53; H, 4.73. Found: C, 61.82; H, 4.76.

1-Bromomethyl-3-methylnaphthalene (96) had a m.p. 63-63.5°; i.r. (nujol) 3060 (aromatic C-H), 872, 860, 849, 775, 745 (1,3-disubstituted naphthalene), 570 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.9-2.85 (m, 6, $C_{10}\underline{H}_6$), 5.28 (s, 2, α-$C\underline{H}_2Br$), 7.59 p.p.m. (s, 3, β-$C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 236 (11, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{81}Br_1$) = 236), 234.002 (11, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{79}Br_1$) = 234.004), 186 (9), 156 (25), 155 (100), 153 (17), 149 (20), 141 (14), 115 (10).

1,3-Bisfluoromethylnaphthalene (97)

Halogen exchange was carried out on 1,3-bis bromomethylnaphthalene by heating with anhydrous KF for 4 1/2 h. Chromatography of the reaction residue on silica gel and subsequent n.m.r. analysis of the products indicated that methylnaphthalene as well as fluoromethylnaphthalene had been formed during the course of this reaction. Altogether three chromatographic separations were necessary to obtain the 1,3-bisfluoromethylnaphthalene in a pure state. The overall yield of bisfluoromethyl compound (97) which was a clear liquid was very low, only 5%; i.r. (film) 3075, 3020 (aromatic C-H), 2975, 2950, 2900, 2850 (aliphatic C-H), 1060 (aliphatic C-F), 865, 850, 840, 765, 730 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 2.0-2.9 (m, 6, $C_{10}\underline{H}_6$), 4.45 (d, 2, α-$C\underline{H}_2F$, J = 48.0 Hz), 4.75 p.p.m. (d, 2, β-$C\underline{H}_2F$, J = 48.0 Hz). mass spectrum (70 eV) m/e (relative intensity) 192.073 (97, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{19}F_2$) = 192.075), 191 (20), 170 (13), 159 (100), 141 (6), 139 (5), 133 (8), 115 (2).

1-Fluoromethyl-3-methylnaphthalene (98)

1-Fluoromethyl-3-methylnaphthalene was prepared from 1-bromomethyl-3-methylnaphthalene in 38% yield. The fluoromethylnaphthalene was a clear liquid, and its identity was confirmed spectroscopically; i.r. (film) 3050, 3025 (aromatic C-H), 2975, 2920, 2860 (aliphatic C-H), 1065 (aliphatic C-F), 860, 850, 830, 769, 730cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 2.0-2.95 (m, 6, $C_{10}\underline{H}_6$), 4.45 (d, 2, α-CH_2F, J = 48.0 Hz), 7.65 p.p.m. (s, 3, β-$C\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 174.081 (100, M_r ($^{12}C_{12}$ $^{1}H_{11}$ $^{19}F_1$) = 174.084); 173 (27), 159 (90), 141 (31), 133 (9), 115 (9).

3-Nitro-1-naphthylcarbinol (100)

It was reported by Brown and Subba Rao[118] that by means of the reagent sodium borohydride and anhydrous aluminum chloride in diglyme, it was possible to selectively reduce a nitro function in the presence of a carboxylic acid or its derivative. Diglyme (diethylene glycol dimethyl ether) was dried with $LiAlH_4$, filtered, and distilled under vacuum, at 49-50°/3.3 mm. Sodium borohydride was dissolved in this and 3-nitro-1-methylnaphthoate (Alfred Bader) was added. Anhydrous $AlCl_3$ (BDH) dissolved in diglyme was added to the stirred mixture. This suspension was stirred at 10° for 1 h, 20° for 1 h, 40° for 2 h, and at 70° for 1 h. The reaction mixture was worked up by extraction with ether. N.m.r. and i.r. spectra of the residue indicated that no reduction had taken place.

The reaction was repeated at a higher temperature, 80° for 5 h and with larger and smaller amounts of solvent, but all attempts were unsuccessful. The purity of the reagents was checked by carrying out this reduction on p-nitrobenzoic acid (see page 124) which was readily reduced to p-nitrobenzyl alcohol.

This method was abandoned and a different reaction attempted. The procedure is that of Nystrom[119] in which the reducing agent is lithium aluminium hydride and anhydrous aluminium chloride in anhydrous ether. Nystrom described the selective reduction of p-nitrobenzaldehyde and the lack of reduction of p-nitrotoluene and nitrobenzene.

$LiAlH_4$ (0.38 g; 0.01 mol) was suspended in 10 cm^3 anhydrous ether in a 100 cm^3 3-necked flask fitted with reflux condenser and drying tube, 25 cm^3 equilibrating dropping funnel and magnetic stirrer. The suspension was stirred vigorously for 10 min; anhydrous $AlCl_3$ (1.33 g; 0.01 mol) in 15 cm^3 ether was added quickly and the mixture stirred for a further 5 min. A suspension of 3-nitro-1-methylnaphthoate (2.0 g; 0.0087 mol) in 50 cm^3 ether was added dropwise over 30 min. During this addition the reaction mixture effervesced and a yellow-green solid appeared on the surface of the liquid. This mixture was poured into a beaker and the beaker placed in an ice-bath. Ice-cold water (100 cm^3) was added cautiously and the two layers which resulted were separated and the aqueous layer extracted twice with ether. The combined organic extract was washed with water (2 x 50 cm^3) with 10% $NaHCO_3$ (2 x 100 cm^3) and again with water (2 x 50 cm^3). The ethereal solution was dried and evaporated to a yellow-brown solid residue (1.26 g; 84% yield) which was recrystallised from a 10% benzene/100-110° petroleum

ether mixture to light brown needles, m.p. 131.5-133.5°; i.r. (nujol) 3200 (bonded OH), 3010 (aromatic C-H), 1530, 1349 (aromatic nitro N-O), 860, 848, 765, 755 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. [$(GD_3)_2CO$] τ 1.2-2.4 (m, 6, $C_{10}\underline{H}_6$), 4.77 (d, 2, $C\underline{H}_2OH$, J = 6 Hz), 5.4 p.p.m. (t, 1, $CH_2O\underline{H}$, J = 6 Hz). On addition of D_2O the triplet centred at τ 5.4 p.p.m. disappeared and the doublet centred at τ 4.77 p.p.m. collapsed to a singlet; mass spectrum (70 eV) m/e (relative intensity) 203.065 (100, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_3$ $^{14}N_1$) = 203:058), 186 (20), 158 (25), 156 (23), 139 (36), 128 (98), 127 (80), 115 (10).

Anal. Calcd. for $C_{11}H_9O_3N$: C, 65.01; H, 4.47; N, 6.85. Found: C, 64.87; H, 4.48; N, 6.99.

1-Bromomethyl-3-nitronaphthalene (101)

The alcohol (100) was brominated in 87% yield using the standard reagents previously described. The yellow solid residue was recrystallised three times from a 10% benzene/100-110° petroleum ether mixture to pale yellow crystalline needles, m.p. 149-151°; i.r. (nujol) 3010 (aromatic C-H), 1515 (aromatic NO_2), 1345 (aromatic NO_2), 870, 855, 785, 770, 760 (1,3-disubstituted naphthalene), 545 cm^{-1} (aliphatic C-Br); n.m.r. [$(CD_3)_2CO$] τ 0.8-2.8 (m, 6, $C_{10}\underline{H}_6$), 4.8 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 267 (10, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{16}O_2$ $^{14}N_1$ $^{81}Br_1$) = 267), 264.981 (10, M_r ($^{12}C_{11}$ $^{1}H_8$ $^{16}O_2$ $^{14}N_1$ $^{79}Br_1$) = 264.968), 202 (8), 200 (8), 187 (13), 186 (100), 141 (4), 140 (28), 139 (19), 127 (6), 115 (2).

Anal. Calcd. for $C_{11}H_8O_2NBr$: C, 49.63; H, 3.03; N, 5.26. Found: C, 49.56; H, 3.13; N, 5.20.

1-Fluoromethyl-3-nitronaphthalene (102)

1-Fluoromethyl-3-nitronaphthalene was obtained from its bromomethyl precursor in 13% yield. The fluoromethylnaphthalene was a bright yellow solid which melted at 98.5-99°; i.r. (nujol) 3020 (aromatic C-H), 1510, 1345 (aromatic NO_2), 1060 (aliphatic C-F), 875, 855, 790, 775 cm^{-1} (1,3-disubstituted naphthalene); n.m.r. (CCl_4) τ 1.2-2.7 (m, 6, $C_{10}\underline{H}_6$), 4.25 p.p.m. (s, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 205.072 (100, M_r ($^{12}C_{11}\ ^{1}H_8\ ^{14}N_1\ ^{16}O_2\ ^{19}F_1$) = 205.054), 159 (90), 157 (30), 147 (35), 141 (8), 139 (35), 133 (90), 115 (10).

p-Nitrobenzyl alcohol (104)

This prepration was undertaken for two reasons: to ascertain if the reported selective reduction of a carboxylic acid function in the presence of a nitro function could be carried out. The previously attempted reductions of 3-nitro-1-methylnaphthoate (p. 121) were unsuccessful under the conditions reported by Brown and Subba Rao.[118] The reduction of p-nitrobenzoic acid to p-nitrobenzyl alcohol was one of the examples recorded by these authors and so verification of their procedure and, at the same time, the purity of the reagents used in this attempt was appropriate at this point. Secondly, the alcohol (104) could subsequently be brominated and fluorinated to yield p-nitrobenzyl fluoride. This compound could be used to verify the reported n.m.r. parameters by Béguin[45] and to compare benzyl fluoride and fluoromethylnaphthalene data directly.

Sodium borohydride (6.65 g; 0.175 mol) was suspended in diethylene-glycol dimethyl ether ("diglyme") (175 cm^3) in a 3-necked, 250 cm^3

flask fitted with thermometer, reflux condenser, dropping funnel and magnetic stirrer. p-Nitrobenzoic acid (Aldrich) (8.35 g; 0.05 mol) was added to the stirred suspension with considerable effervescence, which quickly subsided. A solution of aluminium chloride (7.74 g; 0.58 mol) in diglyme (29 cm^3) was added to the stirred mixture from the dropping funnel over 1/2 h; the reaction flask was maintained at 20° in a water bath. At the end of the addition the reaction mixture was pale yellow in colour. This mixture was heated and stirred at 75° for 1 h and was then poured onto crushed ice (250 g) and concentrated HCl (25 cm^3). The clear solution which resulted as left to stand overnight, much of the water and diglyme was then removed on a rotary evaporator, leaving a pale yellow slurry. This slurry was extracted three times with ether (3 x 100 cm^3), the solution was dried, filtered and evaporated to a clear solution which still contained diglyme. Petroleum ether (60-75°) (100 cm^3) was added to the solution and immediately a white solid precipitated out. The solid was filtered, dried and recrystallised from hot water to yield 4.7 g (76%) of p-nitrobenzyl alcohol which melted at 92.5-93° (lit.[118] m.p. 92-93°; i.r. (nujol) 3525 (hydrogen bonded O-H), 1500 (aromatic $-NO_2$), 1340 (aromatic $-NO_2$), 825 cm^{-1} (p-disubstituted benzene); n.m.r. ($CDCl_3$) τ 1.78-2.6 (m, 4, C_6H_4), 5.24 (s, 2, CH_2OH), 7.22 p.p.m. (s, 1, OH). The singlet at τ 7.22 p.p.m. disappeared when the solution was shaken with D_2O; mass spectrum (70 eV) m/e (relative intensity) 153 (73, M_r ($^{12}C_7$ $^{1}H_7$ $^{16}O_3$ $^{14}N_1$) = 153), 136 (17), 114 (11), 108 (22), 107 (42), 106 (37), 105 (18), 89 (70), 79 (30), 78 (50), 77 (100).

p-Nitrobenzyl bromide (105)

p-Nitrobenzyl alcohol (3.06 g; 0.02 mol) was dissolved in benzene (50 cm^3) and brominated with PBr_3 in the usual way to give 3.65 g (85%) of the bromide (105) as long white needles which melted at 98.5-99.5° (lit.[41] 97.5-99) after two recrystallisations from petroleum ether (60-75°); i.r. (nujol) 3125, 3100, 3075 (aromatic C-H), 1540 (aromatic $-NO_2$), 1350 (aromatic $-NO_2$), 805 (p-disubstituted benzene), 590 cm^{-1} (aliphatic C-Br); n.m.r. (CCl_4) τ 1.7-2.6 (m, 4, $C_6\underline{H}_4$), 5.5 p.p.m. (s, 2, $C\underline{H}_2Br$); mass spectrum (70 eV) m/e (relative intensity) 217 (9, M_r ($^{12}C_7$ $^{1}H_6$ $^{16}O_2$ $^{14}N_1$ $^{81}Br_1$) = 217), 215 (9, M_r ($^{12}C_7$ $^{1}H_6$ $^{16}O_2$ $^{14}N_1$ $^{79}Br_1$) = 215), 171 (1), 169 (1), 137 (15), 136 (100), 106 (15), 90 (35), 89 (27), 78 (30).

p-Nitrobenzyl fluoride (106)

p-Nitrobenzyl bromide (105) was fluorinated with anhydrous KF in N-methylpyrrolidone. The first compound eluted from the chromatographic column in 20% yield was p-nitrotoluene. Spectra and the m.p. were identical to those of an authentic sample. The fluoride was isolated as a solid in 35% yield, m.p. 37-38° (lit.[40,41,44] m.p. 38-38.5°); i.r. (melt) 3040 (aromatic C-H), 2950, 2925 (aliphatic C-H), 1530 (aromatic $-NO_2$), 1330 (aromatic $-NO_2$), 1065 (aliphatic C-F), 805 cm^{-1} (p-disubstituted benzene); n.m.r. (CCl_4) τ 1.65-2.7 (m, 4, $C_6\underline{H}_4$), 4.62 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 155 (82, M_r ($^{12}C_7$ $^{1}H_6$ $^{16}O_2$ $^{14}N_1$ $^{19}F_1$) = 155), 154 (26), 136 (100), 125 (10), 109 (5), 91 (3), 65 (2).

Benzyl Fluoride (108)

Benzyl fluoride was prepared from benzyl bromide (Aldrich) in 50% yield by fluorination with anhydrous KF; i.r. (film) 3120, 3100, 3050 (aromatic C-H), 2975, 2980, 2920 (aliphatic C-H), 1065 (aliphatic C-F), 745, 695 cm^{-1} (monosubstituted benzene); n.m.r. (CCl_4) τ 2.5-3.2 (m, 5, $C_6\underline{H}_5$), 4.76 p.p.m. (d, 2, $C\underline{H}_2F$, J = 48.0 Hz); mass spectrum (70 eV) m/e (relative intensity) 110 (100, M_r ($^{12}C_7\ ^1H_7\ ^{19}F_1$) = 110), 109 (63), 91 (10), 63 (8).

Other Syntheses

Several syntheses involving 1-naphthonitrile were carried out prior to the attempted reaction with the disubstituted naphthalenes in order to establish the appropriate reaction conditions. Not all of these were used subsequently but are included here.

1-Acetylnaphthalene (110)

Magnesium turnings (0.3 g; 0.013 g atom) were placed in a dry 50 cm^3 3-necked flask fitted with magnetic stirrer, reflux condenser with drying tube, 25 cm^3 equilibrating dropping funnel and a nitrogen inlet. The magnesium turnings were covered with anhydrous ether (5 cm^3) and stirred under nitrogen. A solution of CH_3I (0.85 g; 0.006 mol) in ether (5 cm^3) was added from the dropping funnel over 1 1/2 h. Dry benzene (15 cm^3) was added and the ether was distilled off. 1-Naphthonitrile (0.5 g, 0.003 mol) was added and the solution refluxed for 5 h. This solution was cooled and 6 N HCl (6 cm^3) added. Refluxing was continued for a further 8 h. The two layers were separated and the aqueous layer extracted with benzene. The combined benzene extracts were washed with water, with 10% Na_2CO_3, and again with water. The benzene solution was dried and evaporated to a brown viscous residue. This residue was

distilled under vacuum between 100-103° at 4 mm (lit.[121] b.p. 143-5°/6 mm) to give an 80% yield of the methyl ketone (110); i.r. (film) 3040 (aromatic C-H), 2975, 2950 (aliphatic C-H), 1680 (aromatic ketone C=O), 800, 768 cm^{-1} (1-substituted naphthalene); n.m.r. (CCl_4) τ 1.8-2.85 (m, 7, $C_{10}\underline{H}_7$), 7.4 p.p.m. (s, 3, $COC\underline{H}_3$); mass spectrum (70 eV) m/e (relative intensity) 170 (30, M_r ($^{12}C_{12}$ $^{1}H_{10}$ $^{16}O_1$) = 170), 169 (2), 155 (100), 129 (10). This method[120] was described on page 109 for the preparation of 3-acetyl-1-methoxymethylnaphthalene.

1-Naphthamide (111)

1-Naphthonitrile (1.53 g; 0.01 mol) was dissolved in 95% EtOH (5.5 cm^3) and 6 N NaOH (0.5 cm^3) in a 50 cm^3 3-necked flask fitted with magnetic stirrer, reflux condenser and thermometer. This solution was cooled in an ice bath to about 10°. Hydrogen peroxide solution (30%) (4 cm^3; 0.035 mol) was added and the mixture stirred at 10-20° for 1 h. Gradually a suspension formed which subsequently cleared. The mixture was warmed and stirred at 50-55° for 3 h, it was then cooled, the EtOH removed on a rotary evaporator and the aqueous solution made neutral to litmus with 5% H_2SO_4. A white precipitate formed which was filtered off and recrystallised from boiling water to a white crystalline solid which melted at 202-3° (lit.[122] 204°); i.r. (nujol) 3350, 3175 (primary amide N-H), 3060 (aromatic C-H), 1660, 1655 (aromatic primary amide C=O), 810, 775 cm^{-1} (1-substituted naphthalene); n.m.r. [$(CD_3)_2CO$] τ 1.45-2.95 (m, 7, $C_{10}\underline{H}_7$), 7.25 p.p.m. (s, 2, $CONH_2$). The singlet at τ 7.25 p.p.m. disappeared on addition of D_2O; mass spectrum (70 eV) m/e (relative intensity) 171 (62, M_r ($^{12}C_{11}$ $^{1}H_9$ $^{16}O_1$ $^{14}N_1$) = 171), 169 (18), 155 (56), 127 (100), 126 (25).

1-Naphthoic Acid (28)

This compound was prepared in two ways:-

(a) 1-Naphthamide (111) was diazotised and hydrolysed to 1-naphthoic acid by the method of Whitmore and Langlois.[123] Treatment of 1-naphthamide (0.34 g; 0.002 mol) with a solution of $NaNO_2$ (0.2 g; 0.003 mol) in water (5 cm^3) and 15% H_2SO_4 (5 cm^3) at 70-80° for 36 h gave a 50% yield of 1- naphthoic acid.

(b) 1-Naphthonitrile (109) was hydrolysed in 25% yield to 1-naphthoic acid by the method of Clarke and Taylor.[124] 1-Naphthonitrile (1.5 g; 0.01 mol) was added to a stirred solution of 75% H_2SO_4 (3.5 g) at 100°. The solution was stirred at 100° for 4 h and at 150° for 1 h. The reaction mixture was poured onto ice and the white, solid carboxylic acid filtered off. After recrystallisation from 95% EtOH both samples gave spectra identical to an authentic sample of 1-naphthoic acid and melted at 161°.

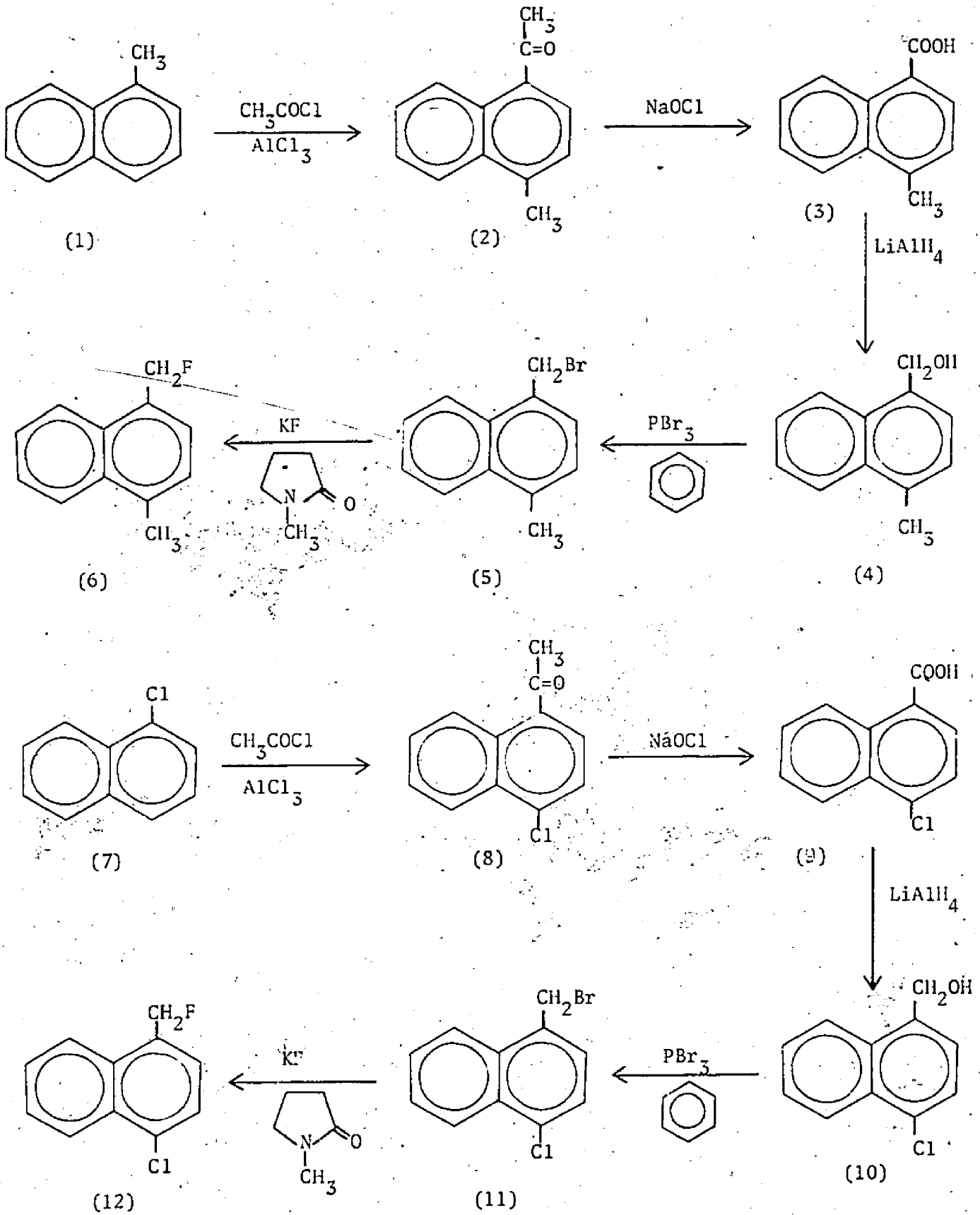
1-Aminomethylnaphthalene (112)

The reagents and the method in this reduction of the nitrile to the amine were the same as those used in the selective reduction of 3-nitro-1-methylnaphthoate (p. 122). A mixture of $LiAlH_4$, $AlCl_3$ and 1-naphthonitrile were reacted together in equimolar proportions. The reaction mixture was taken up in CH_2Cl_2 and the acidic solution extracted. The aqueous solution was made basic with 10% NaOH solution and extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried with anhydrous $MgSO_4$, filtered and evaporated to an oily liquid. The yield was 40%; the liquid was distilled under vacuum, b.p. 150°/10 mm (lit.[125] b.p. 155°/12 mm);

i.r. (film) 3090 (bonded N-H), 3030 (aromatic C-H), 2975, 2880 (aliphatic C-H), 800, 785 cm^{-1} (1-substituted naphthalene); n.m.r. (CCl_4) τ 1.8-2.9 (m, 7, $C_{10}\underline{H}_7$), 4.82 (s, 2, $C\underline{H}_2$), 8.76 p.p.m. (s, 2, $N\underline{H}_2$); mass spectrum (70 eV) m/e (relative intensity) 157 (85, M_r ($^{12}C_{11}$ $^{1}H_{11}$ $^{14}N_1$) = 157), 156 (100), 141 (28), 129 (90), 128 (65), 127 (40), 115 (22).

The schemes depicted on pages 132-145 represent the synthetic routes followed and the essential reagents required to effect the transformations.

A key for the purpose of nomenclature of all compounds is to be found on pages 146-149.



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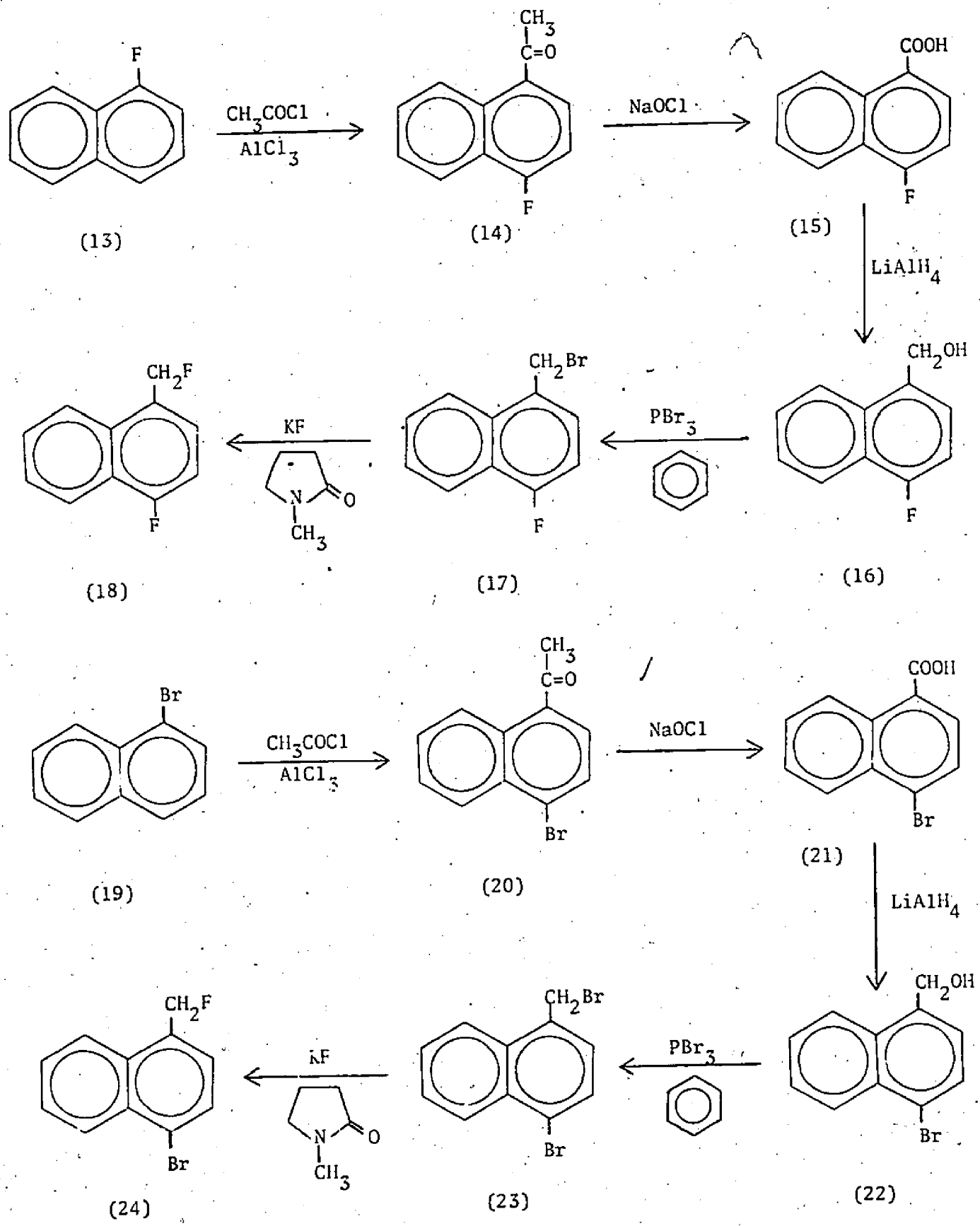

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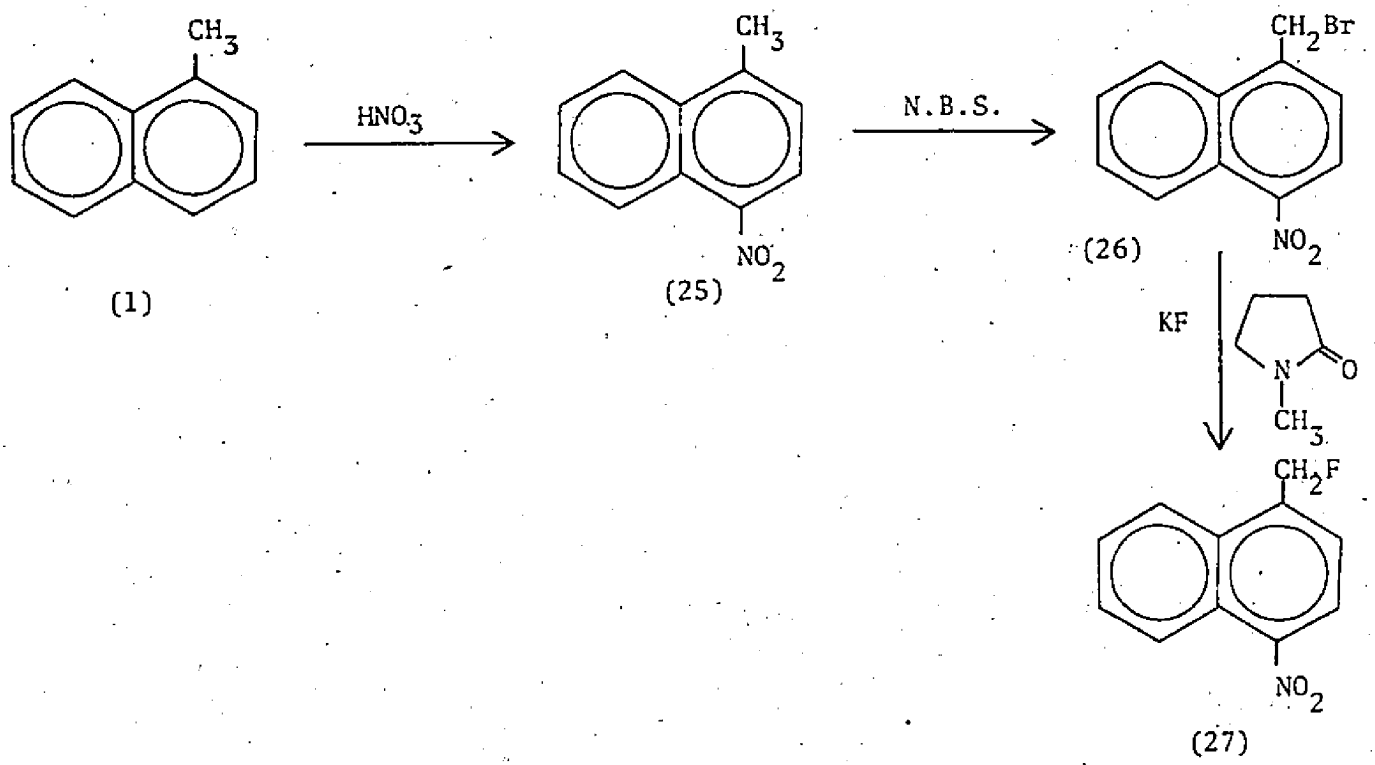

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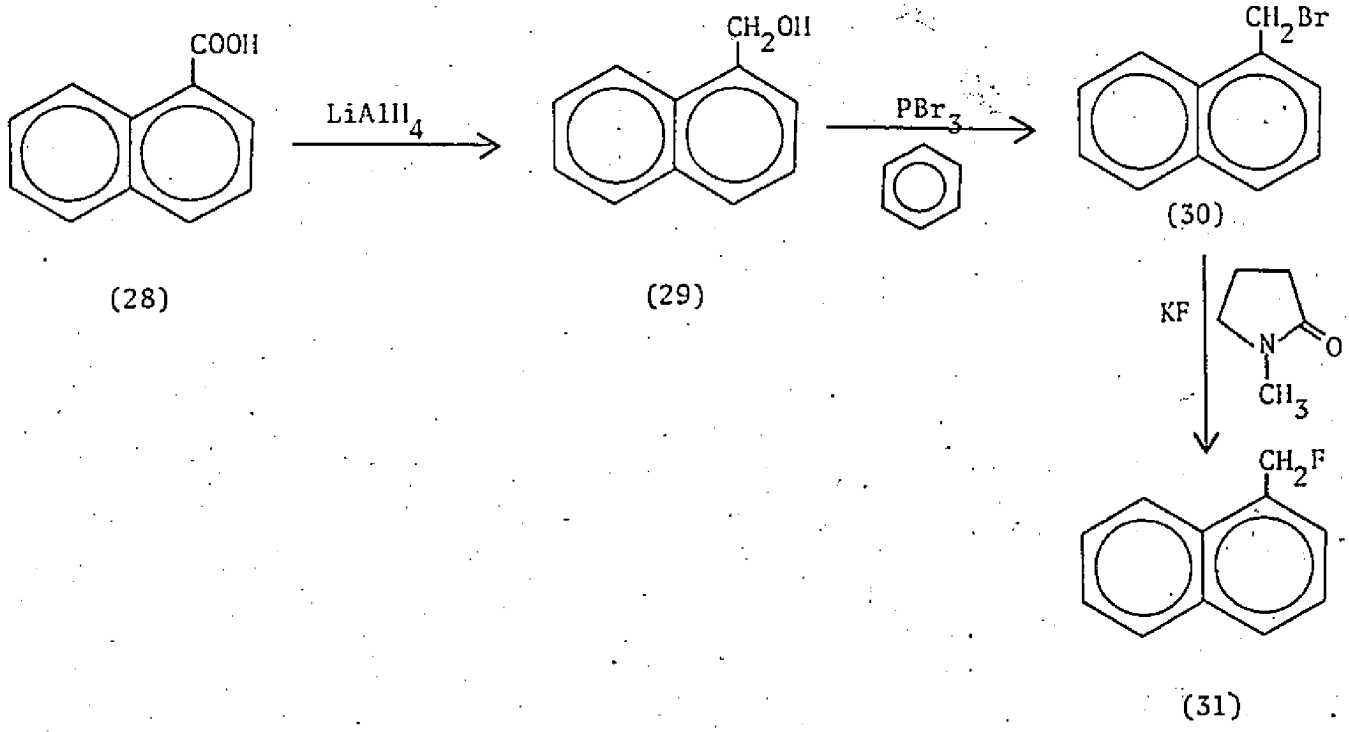

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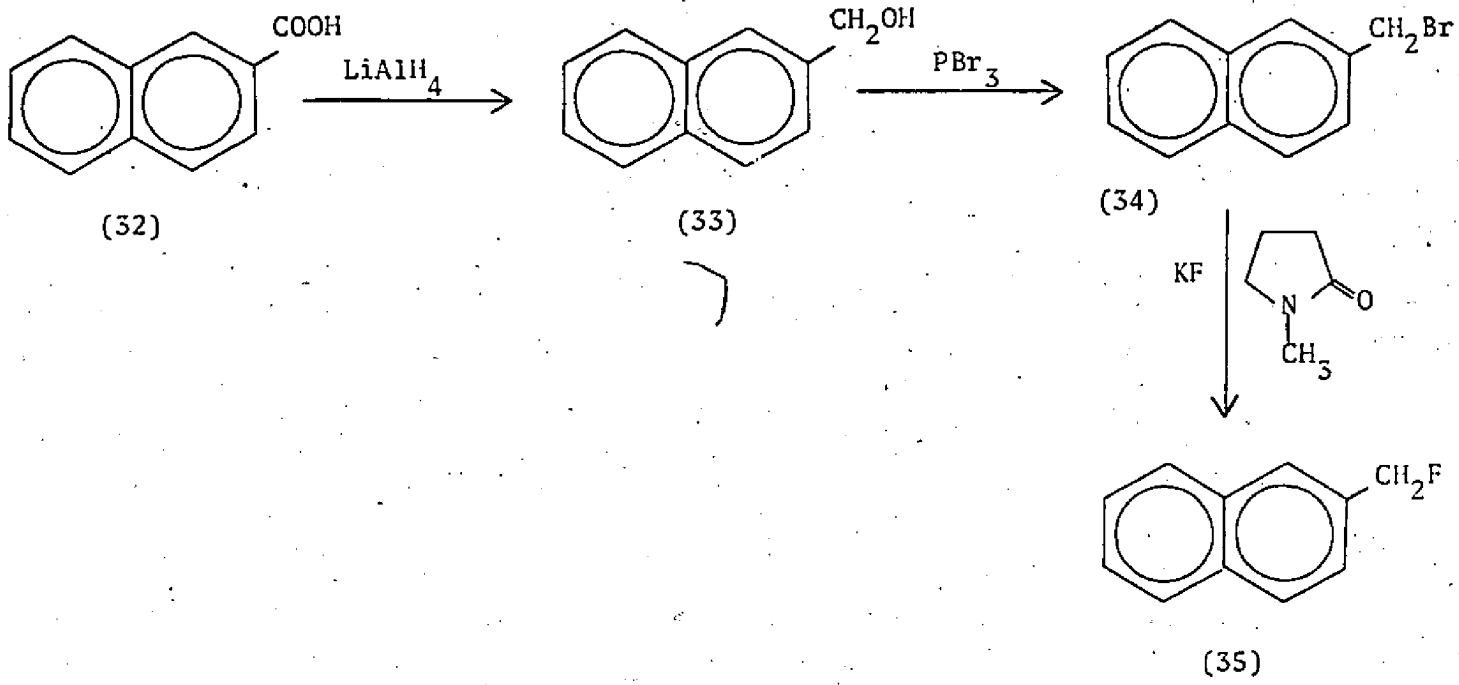
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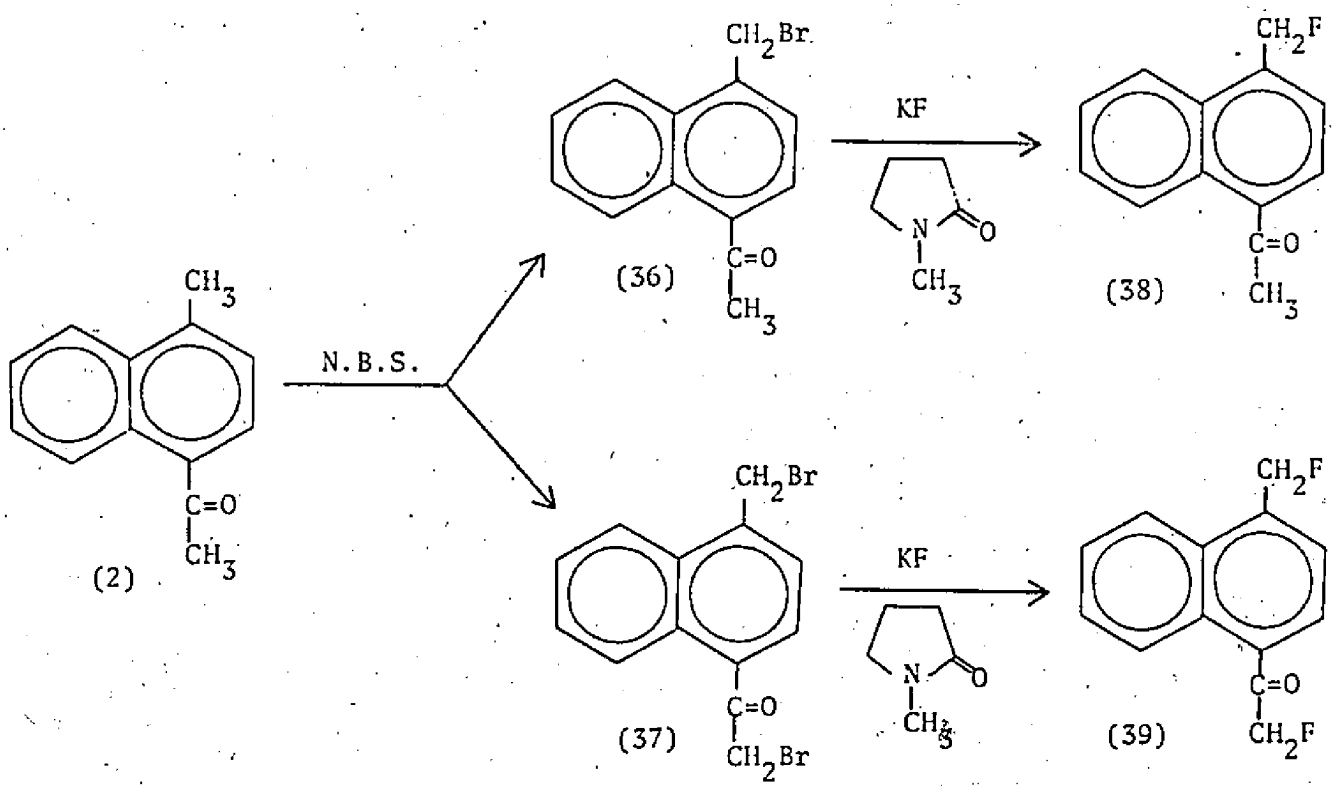
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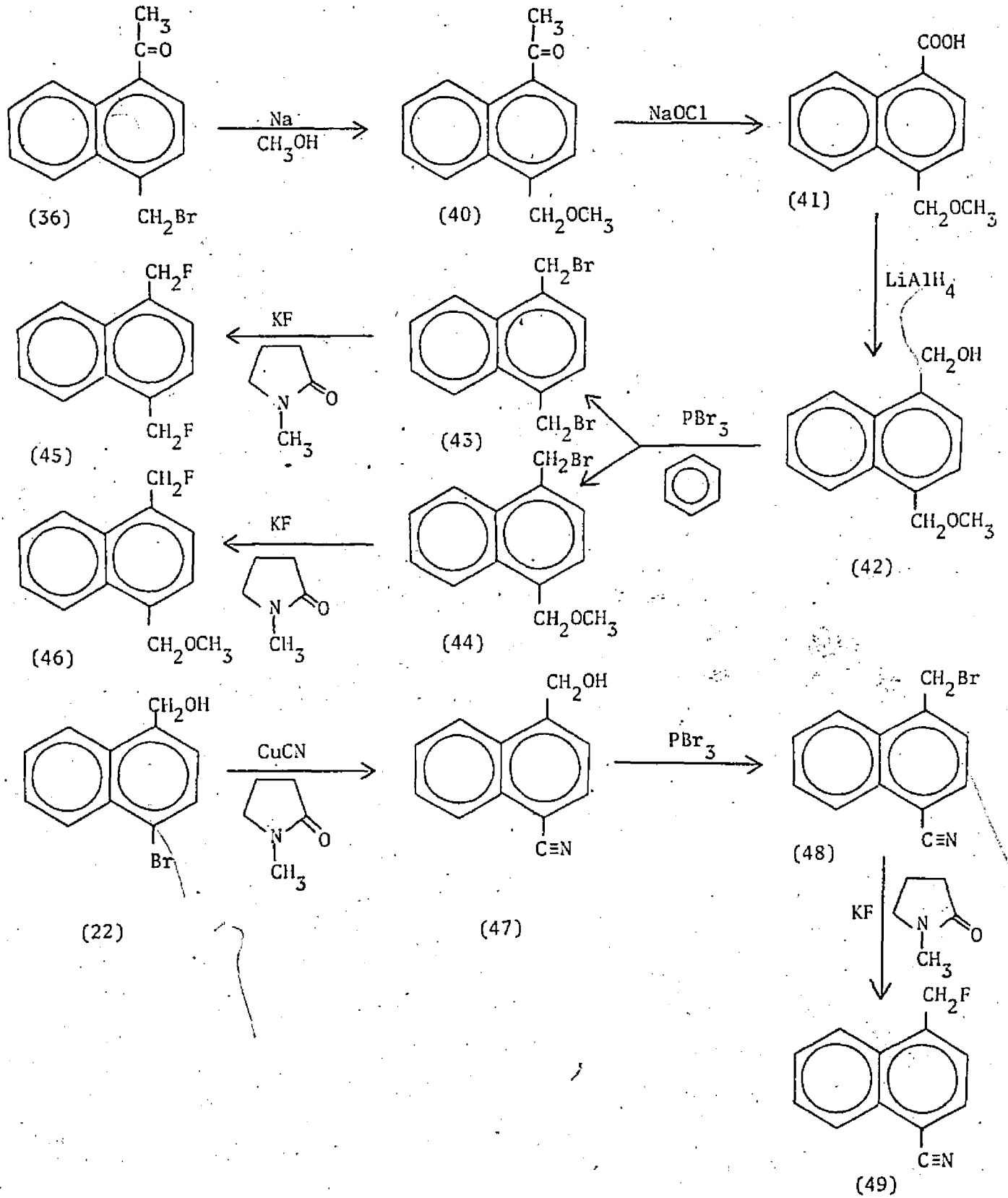
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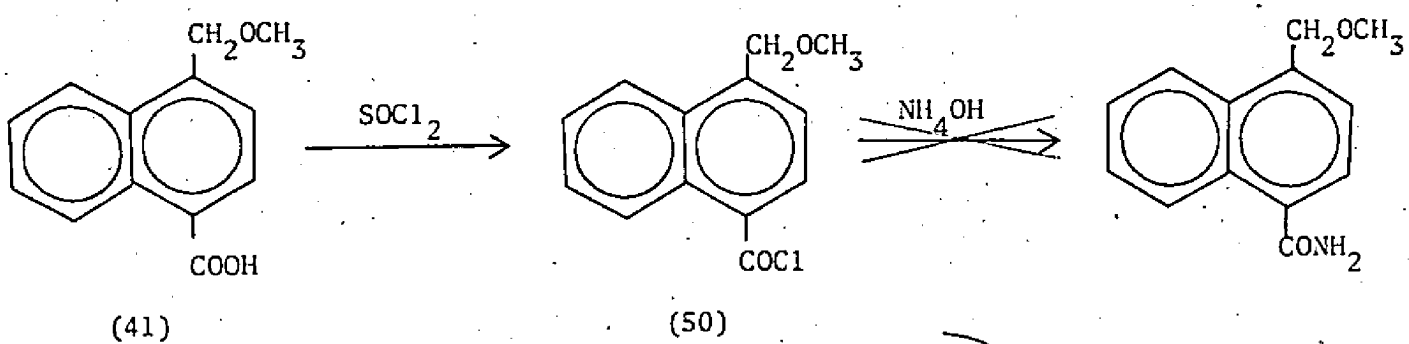

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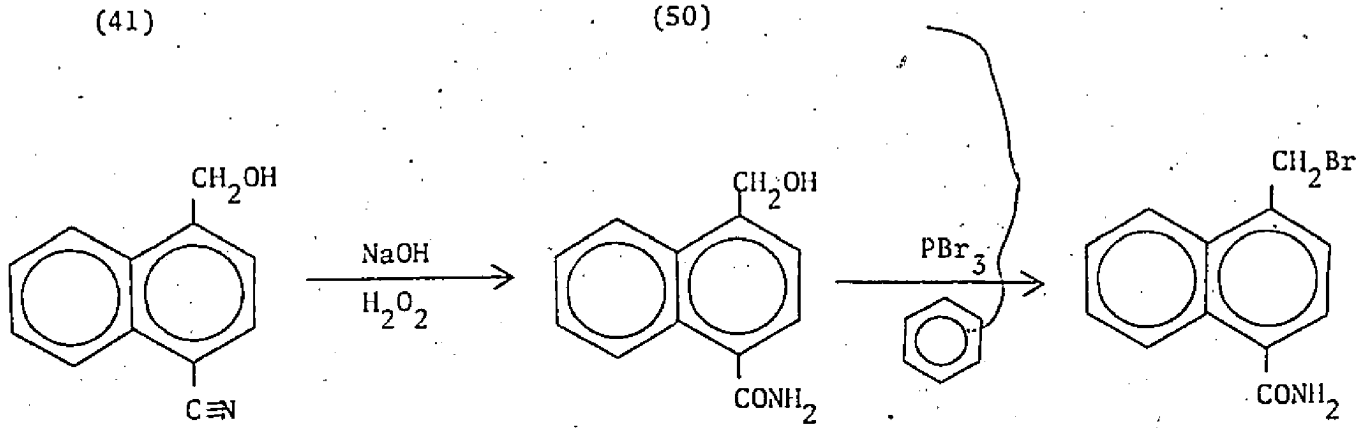

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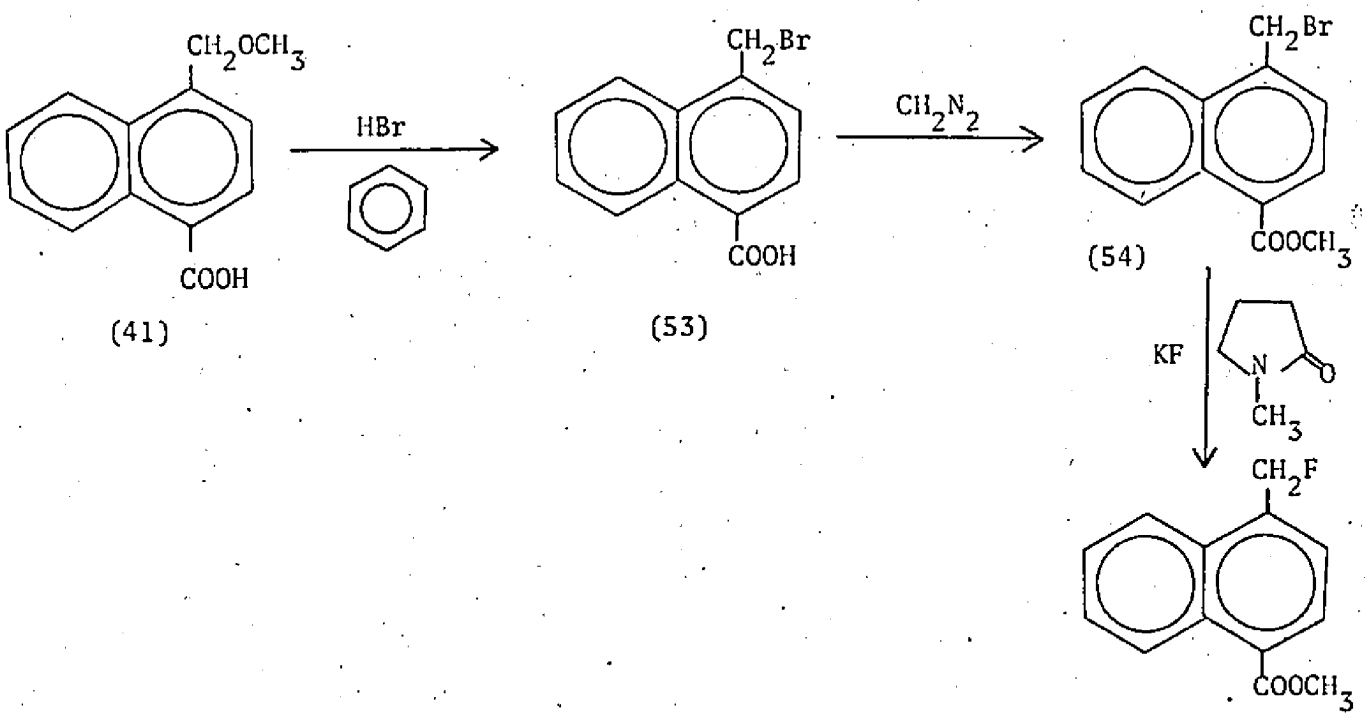

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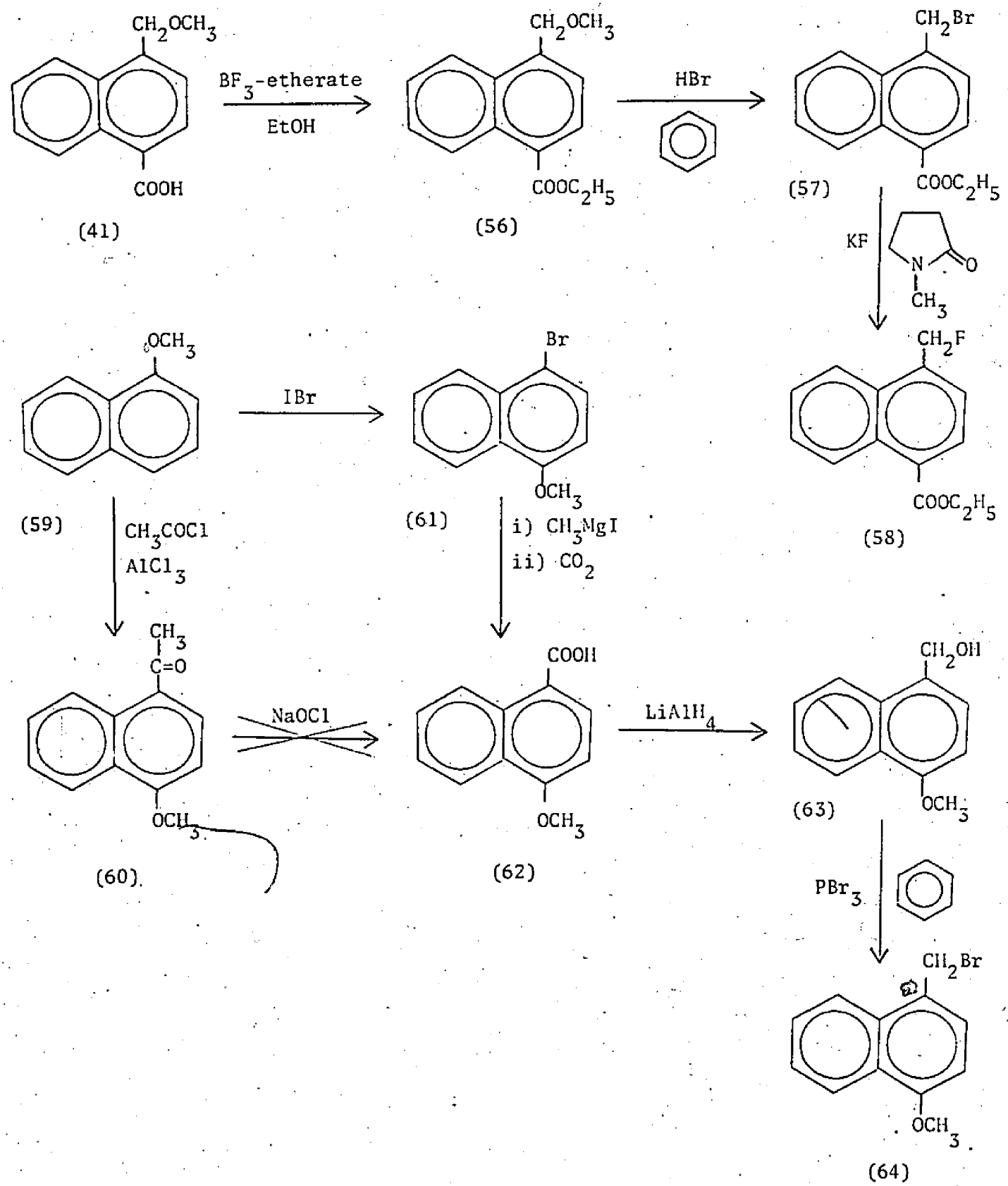
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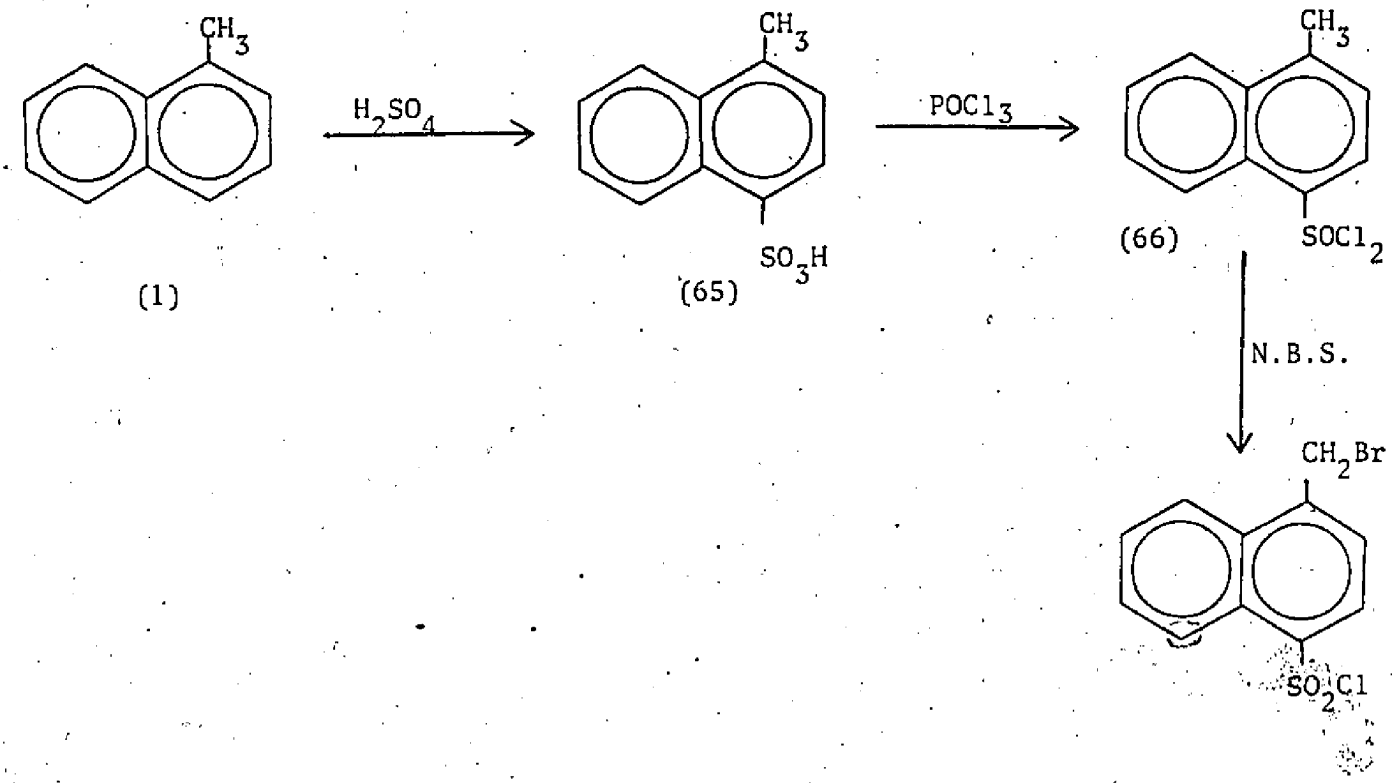
COOC2H5
(56)
HBr
CH2Br
COOC2H5
(57)
KF
N
O
CH3
CH2F
COOC2H5
(58)
OCH3
(59)
IBr
Br
OCH3
(61)
CH3COCl
AlCl3
i) CH3MgI
ii) CO2
CH3
C=O
OCH3
(60)
NaOCl
COOH
OCH3
(62)
LiAlH4
CH2OH
OCH3
(63)
PBr3
CH2Br
OCH3
(64)



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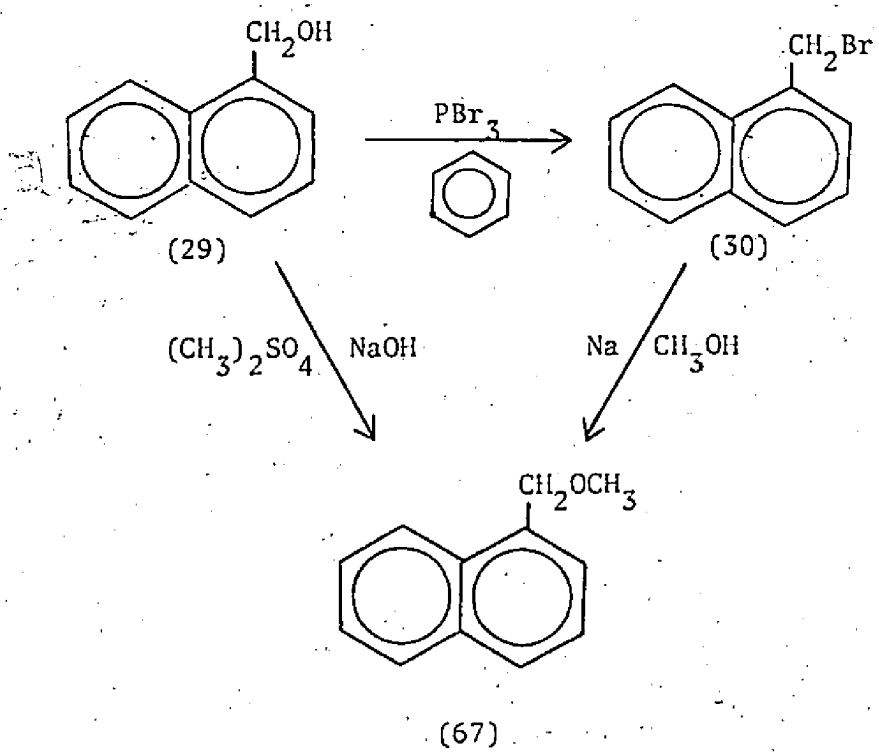

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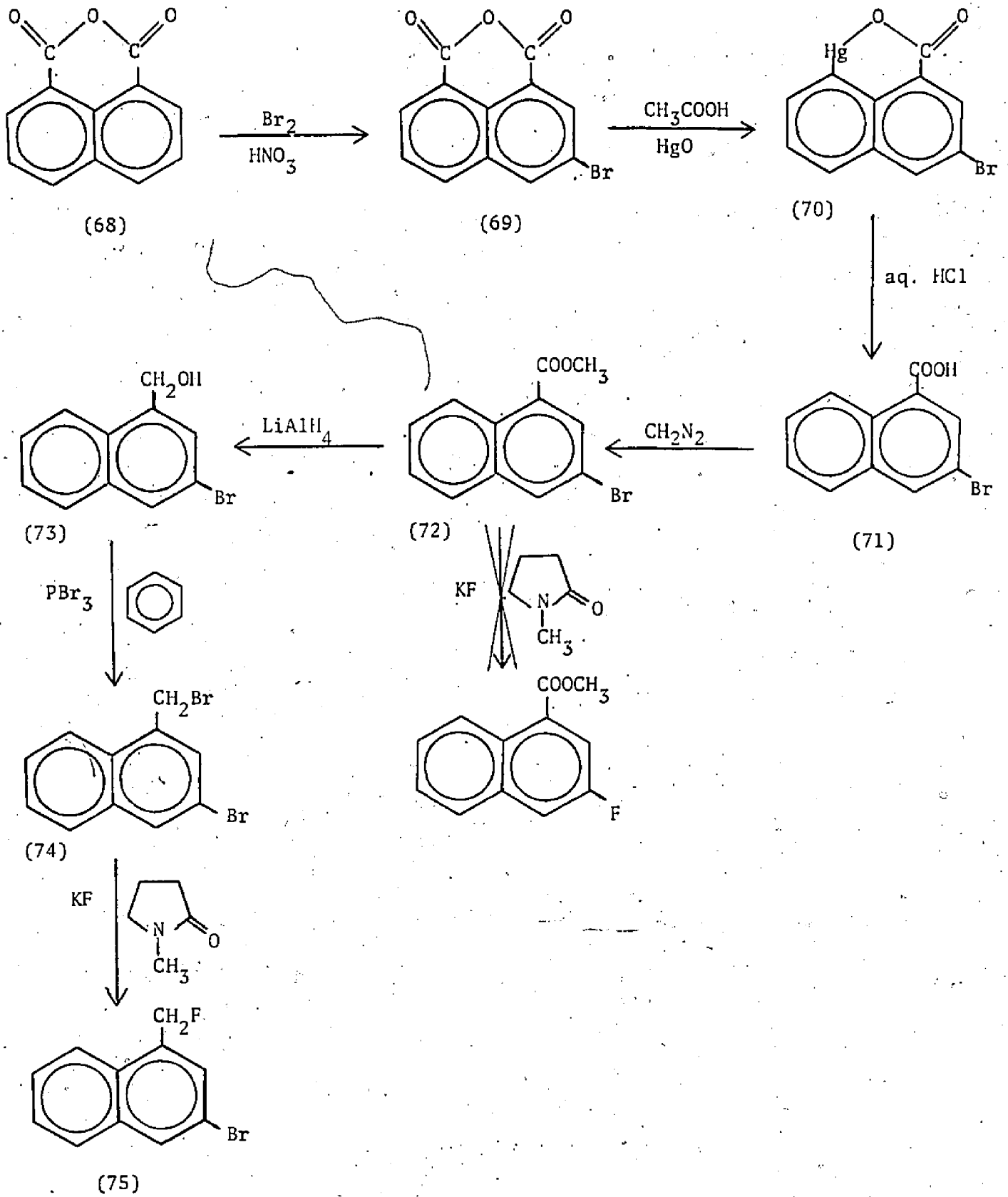
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HgO
aq. HCl
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PBr3
KF
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(69)
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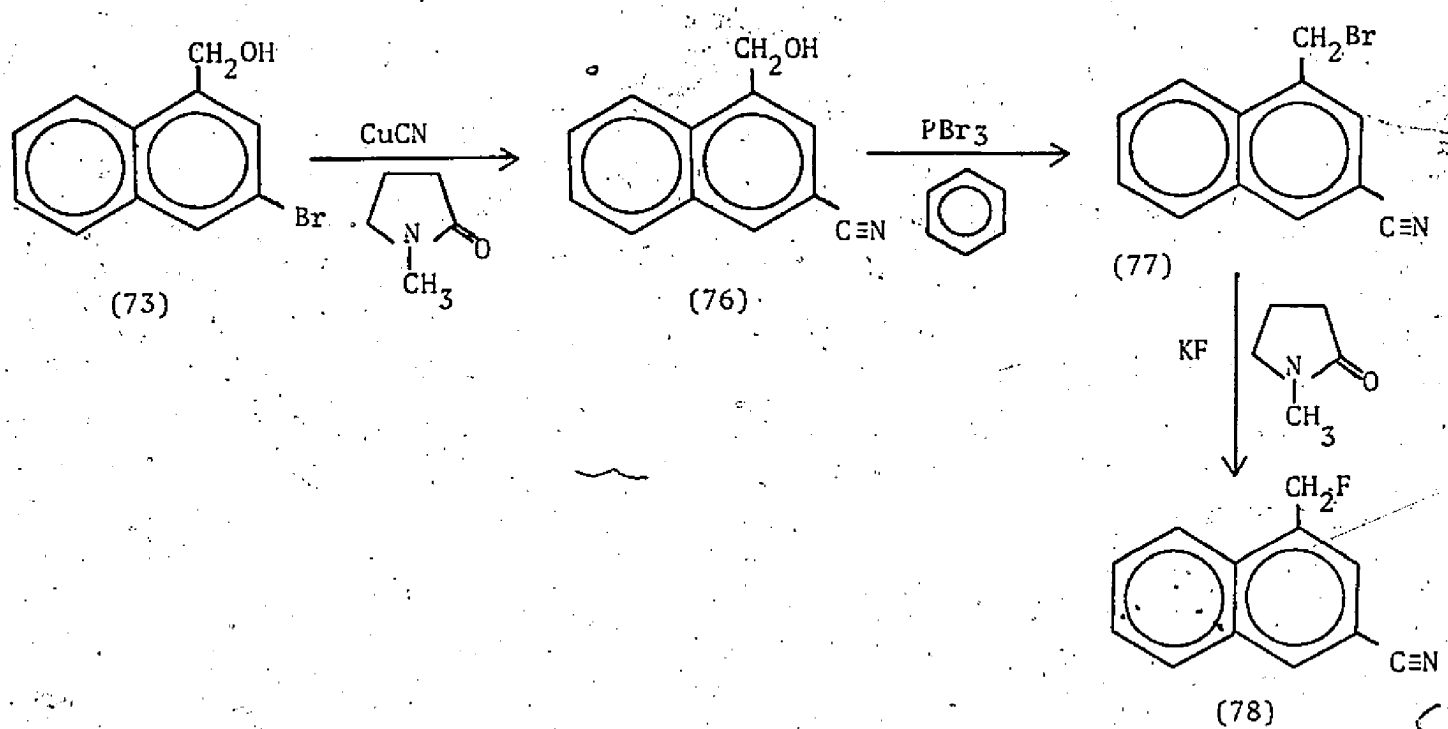
(72)
(73)
(74)
(75)



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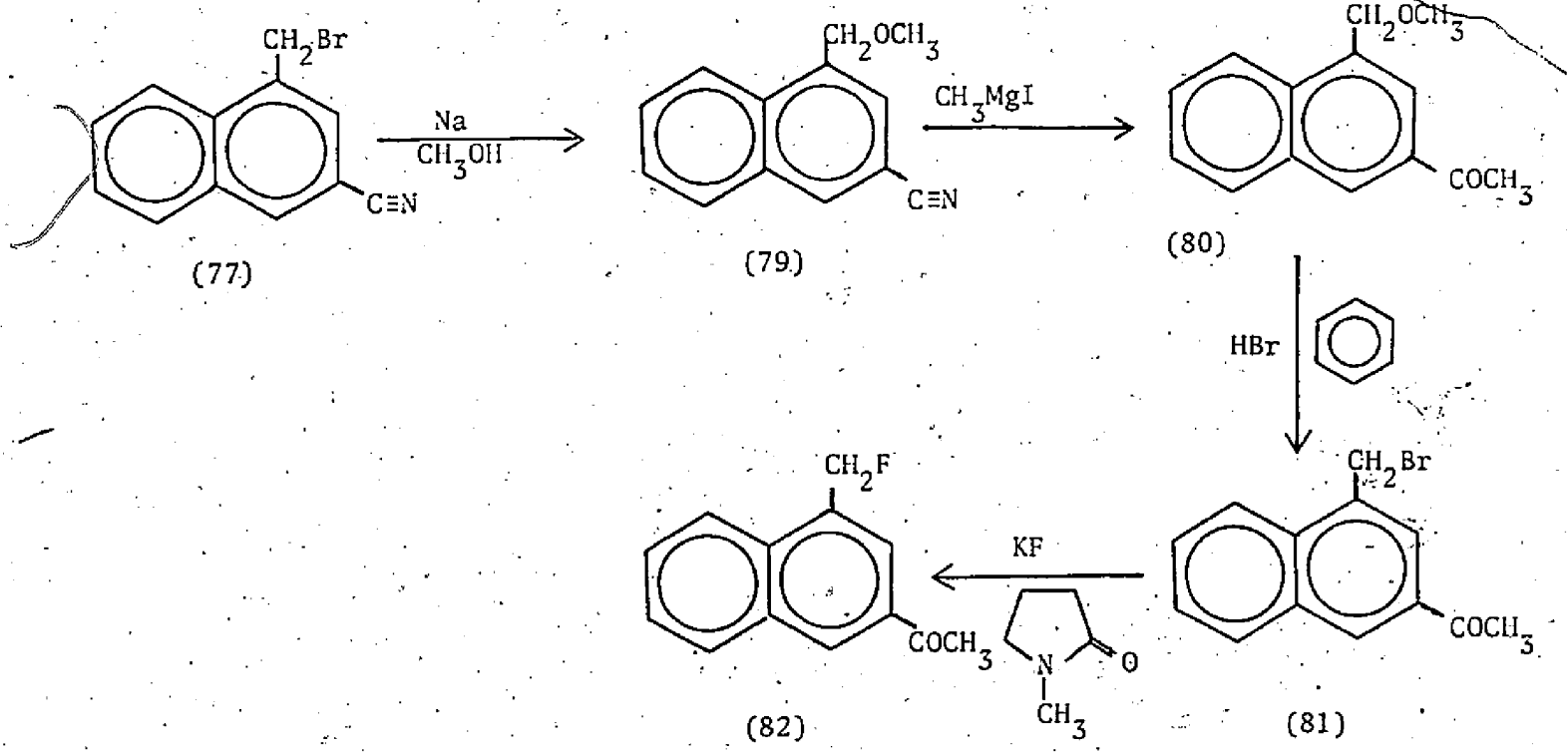

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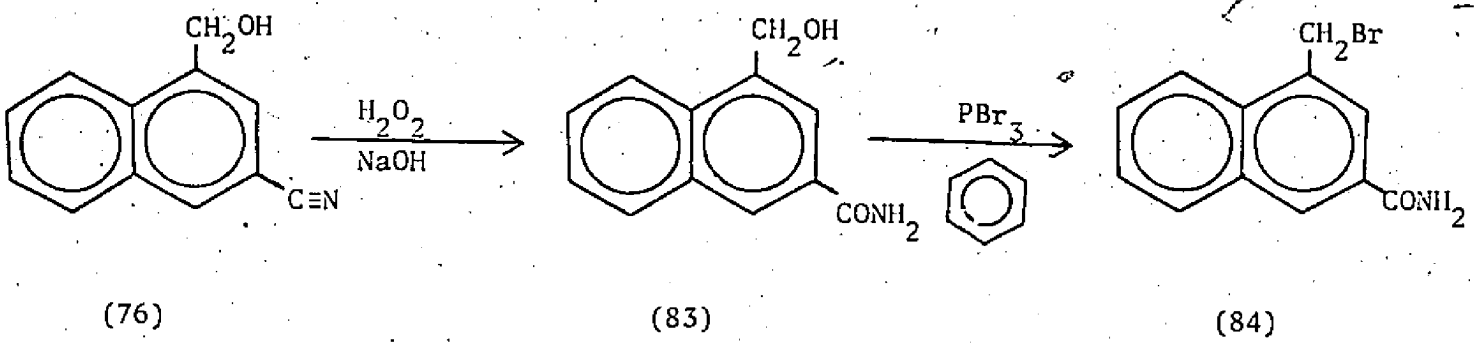

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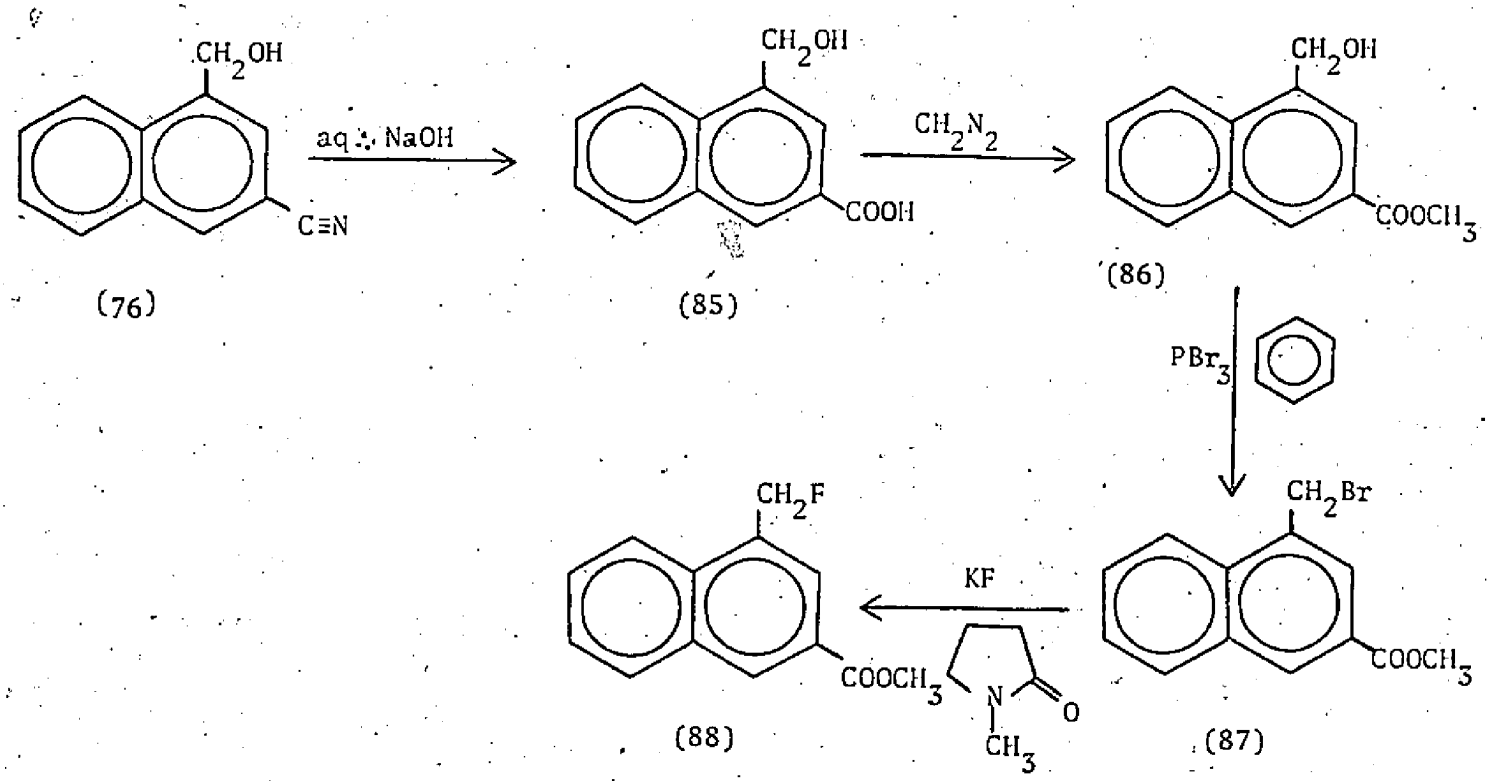

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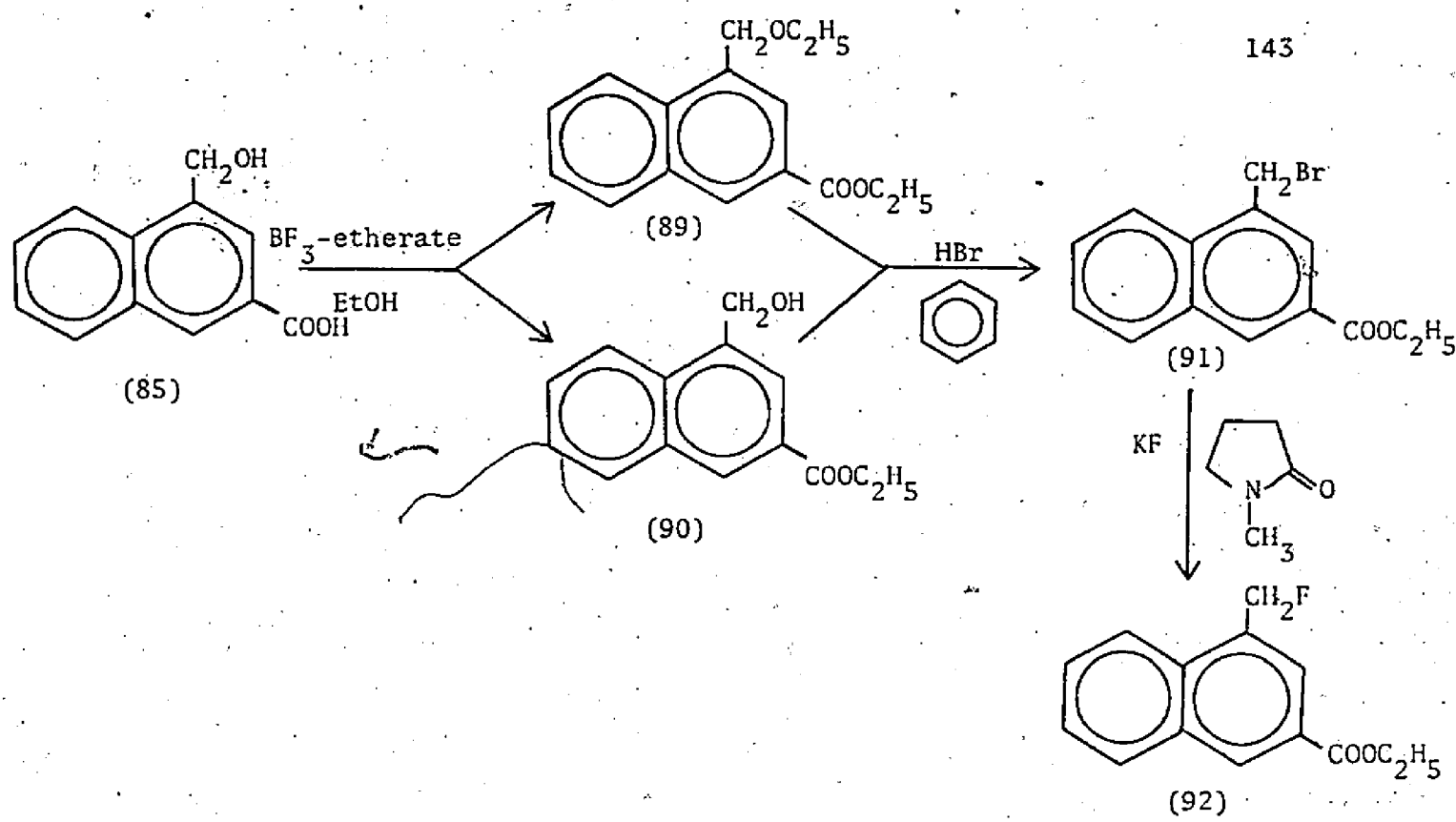
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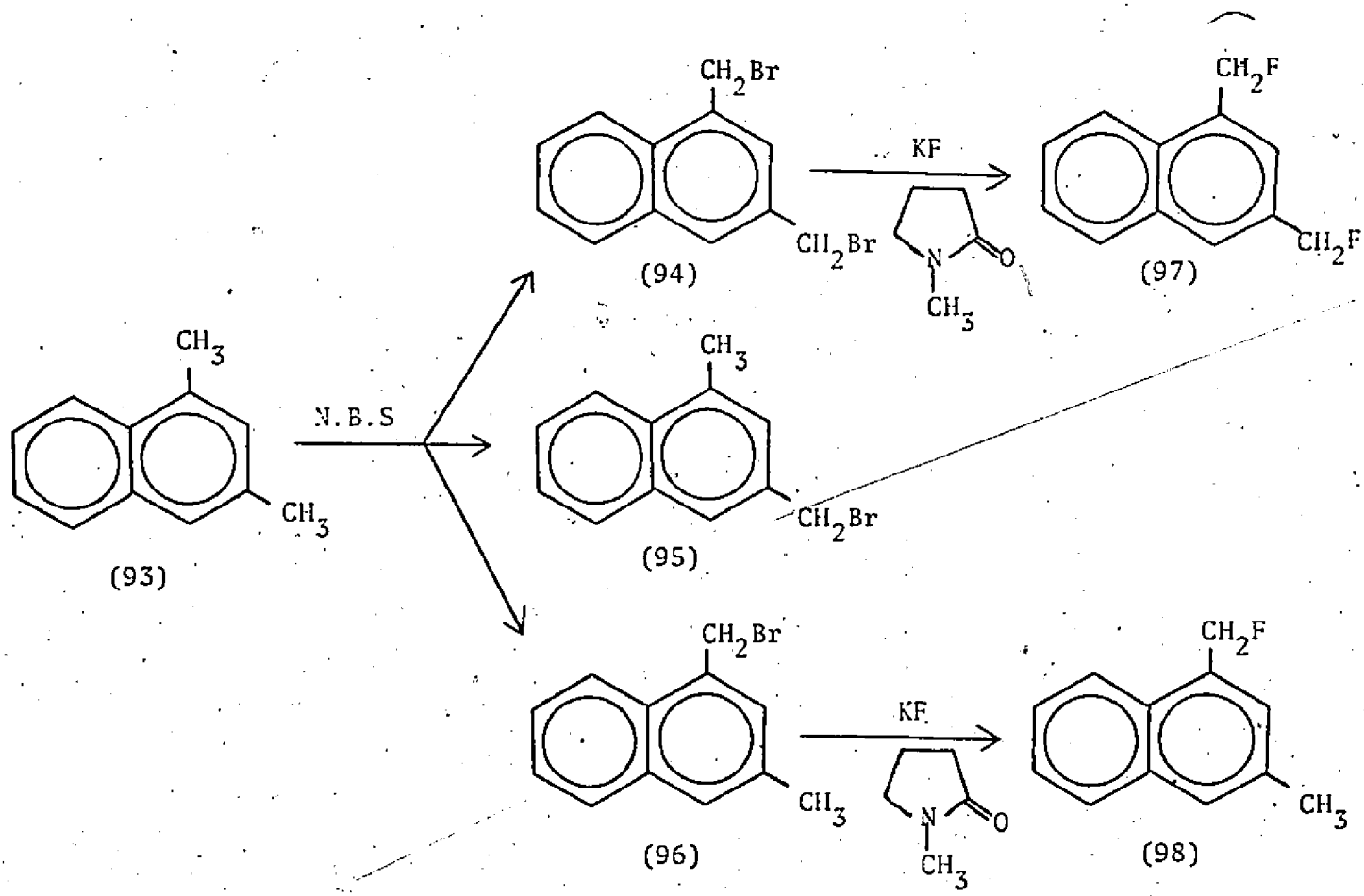
BF3-etherate
EtOH
(85)
CH2OC2H5
COOC2H5
(89)
CH2OH
COOC2H5
(90)
HBr
CH2Br
COOC2H5
(91)
KF
N
O
CH3
CH2F
COOC2H5
(92)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(93)
N.B.S
CH2Br
CH2Br
(94)
KF
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CH3
CH2F
CH2F
(97)
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(95)
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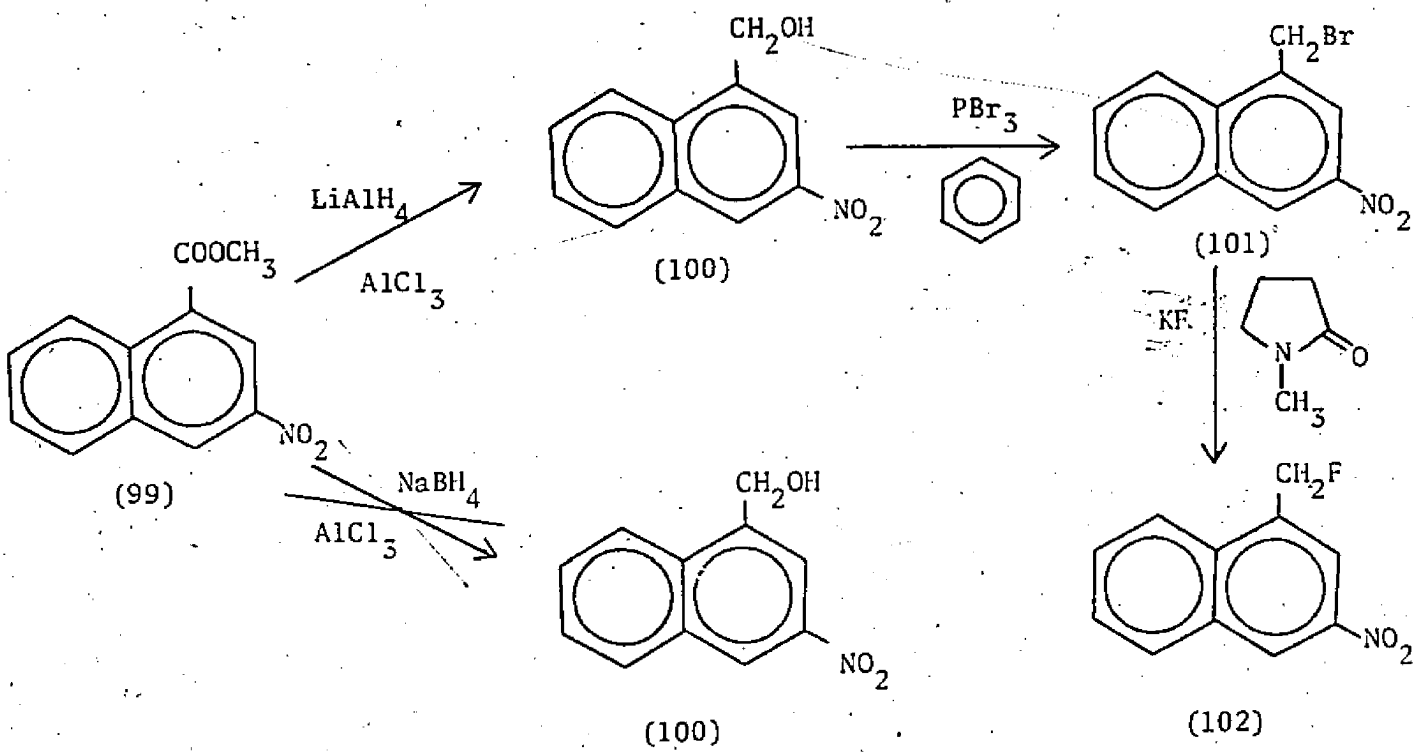
CH3
(96)
KF
N
O
CH3
CH2F
CH3
(98)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AlCl3
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(100)
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PBr3
CH2Br
NO2
(101)
KF
N
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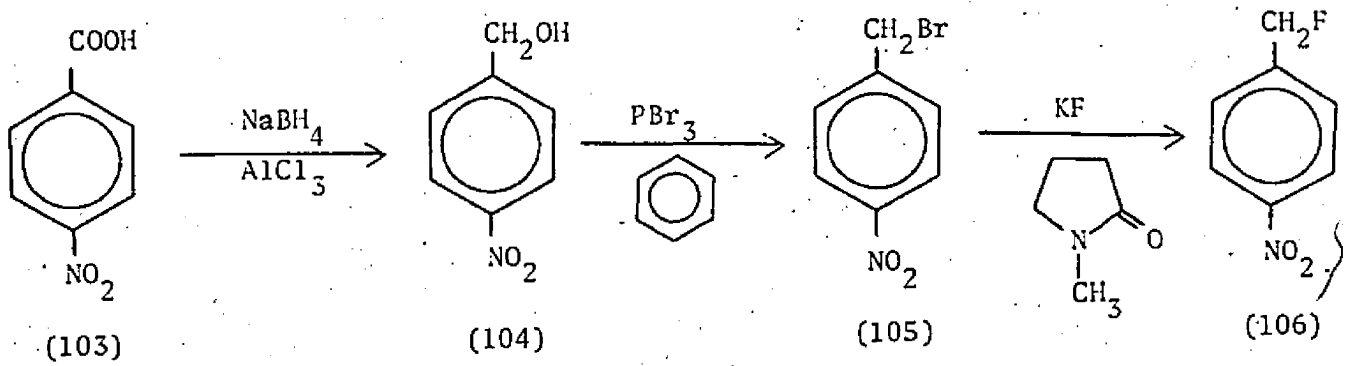
CH3
CH2F
NO2
(102)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(105)
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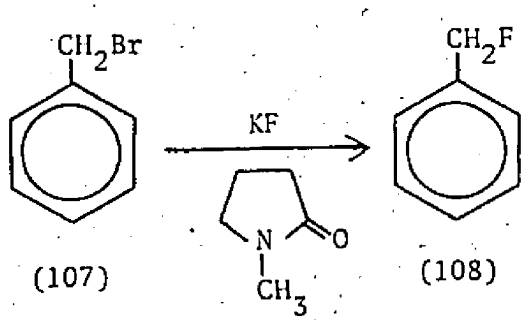
CH2F
NO2
(106)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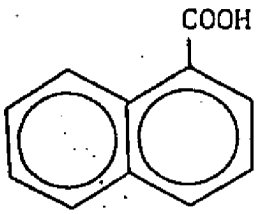
(107)
KF
N
O
CH3
CH2F
(108)



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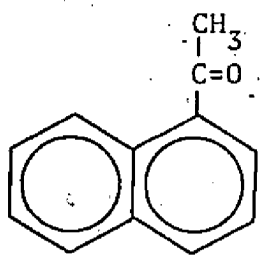
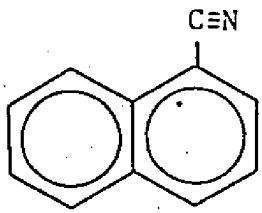


(110)

H_2SO_4

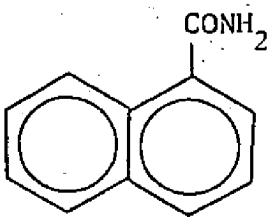
CH_3MgI



(109)

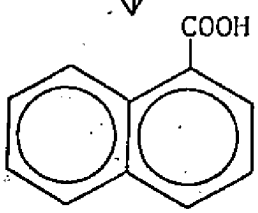
NaOH
H_2O_2

$LiAlH_4$
$AlCl_3$



(111)

$NaNO_2$
H_2SO_4



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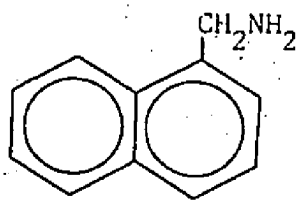

(112)

NOMENCLATURE

1. 1-Methylnaphthalene
2. 1-Acetyl-4-methylnaphthalene
3. 4-Methyl-1-naphthoic acid
4. 4-Methyl-1-naphthylcarbinol
5. 1-Bromomethyl-4-methylnaphthalene
*6. 1-Fluoromethyl-4-methylnaphthalene
7. 1-Chloronaphthalene
8. 1-Acetyl-4-chloronaphthalene
9. 4-Chloro-1-naphthoic acid
*10. 4-Chloro-1-naphthylcarbinol
*11. 1-Bromomethyl-4-chloronaphthalene
*12. 4-Chloro-1-fluoromethylnaphthalene
13. 1-Fluoronaphthalene
14. 1-Acetyl-4-fluoronaphthalene
15. 4-Fluoro-1-naphthoic acid
*16. 4-Fluoro-1-naphthylcarbinol
*17. 1-Bromomethyl-4-fluoronaphthalene
*18. 4-Fluoro-1-fluoromethylnaphthalene
19. 1-Bromonaphthalene
20. 1-Acetyl-4-bromonaphthalene
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23. 4-Bromo-1-bromomethylnaphthalene
*24. 4-Bromo-1-fluoromethylnaphthalene
25. 1-Methyl-4-nitronaphthalene
*26. 1-Bromomethyl-4-nitronaphthalene
*27. 1-Fluoromethyl-4-nitronaphthalene
28. 1-Naphthoic acid
29. 1-Naphthylcarbinol
30. 1-Bromomethylnaphthalene
*31. 1-Fluoromethylnaphthalene
32. 2-Naphthoic acid
33. 2-Naphthylcarbinol
34. 2-Bromomethylnaphthalene

*35. 2-Fluoromethylnaphthalene
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*39. 4-Fluoroacetyl-1-fluoromethylnaphthalene
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*41. 4-Methoxymethyl-1-naphthoic acid
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*44. 1-Bromomethyl-4-methoxymethylnaphthalene
*45. 1,4-Bisfluoromethylnaphthalene
*46. 1-Fluoromethyl-4-methoxymethylnaphthalene
*47. 4-Cyano-1-naphthylcarbinol (4-Hydroxymethyl-1-naphthonitrile)
*48. 1-Bromomethyl-4-cyanonaphthalene (4-Bromomethyl-1-naphthonitrile)
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*55. 1-Fluoromethyl-4-methoxycarbonylnaphthalene (4-Fluoromethyl-1-methylnaphthoate).
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*58. 4-Ethoxycarbonyl-1-fluoromethylnaphthalene (4-Fluoromethyl-1-ethylnaphthoate).
59. 1-Methoxynaphthalene
60. 1-Acetyl-4-methoxynaphthalene
61. 1-Bromo-4-methoxynaphthalene

62. 4-Methoxy-1-naphthoic acid
63. 4-Methoxy-1-naphthylcarbinol
64. 1-Bromomethyl-4-methoxynaphthalene
65. 1-Methyl-4-sulphonaphthalene (4-Methyl-1-naphthalenesulphonic acid)
66. 4-Chlorosulpho-1-methylnaphthalene (4-Methyl-1-naphthalenesulphonyl chloride)
67. 1-Methoxymethylnaphthalene
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69. 3-Bromo-1,8-naphthalic anhydride
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71. 3-Bromo-1-naphthoic acid
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*74. 3-Bromo-1-bromomethylnaphthalene
*75. 3-Bromo-1-fluoromethylnaphthalene
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*82. 3-Acetyl-1-fluoromethylnaphthalene
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*90. 3-Ethoxycarbonyl-1-naphthylcarbinol (4-Hydroxymethyl-2-ethylnaphthoate)

*91. 1-Bromomethyl-3-ethoxycarbonylnaphthalene (4-Bromomethyl-2-ethylnaphthoate)

*92. 3-Ethoxycarbonyl-1-fluoromethylnaphthalene (4-Fluoromethyl-2-ethylnaphthoate)

93. 1,3-Dimethylnaphthalene

*94. 1,3-Bisbromomethylnaphthalene

*95. 3-Bromomethyl-1-methylnaphthalene

*96. 1-Bromomethyl-3-methylnaphthalene

*97. 1,3-Bisfluoromethylnaphthalene

*98. 1-Fluoromethyl-3-methylnaphthalene

99. 3-Nitro-1-methylnaphthoate

*100. 3-Nitro-1-naphthylcarbinol (4-Hydroxymethyl-2-nitronaphthalene)

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*102. 1-Fluoromethyl-3-nitronaphthalene

103. p-Nitrobenzoic acid

104. p-Nitrobenzyl alcohol

105. p-Nitrobenzyl bromide

106. p-Nitrobenzyl fluoride

107. Benzyl fluoride

108. Benzyl bromide

109. 1-Naphthonitrile

110. 1-Acetylnaphthalene

111. 1-Naphthamide

112. 1-Aminomethylnaphthalene

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* New Compounds

CHAPTER 3

RESULTS

Recording of Nuclear Magnetic Resonance Spectra

^{19}F spectra were recorded on a Varian HA-100 spectrometer operating at 94.08 MHz in frequency sweep mode and on a Varian HA-60-IL spectrometer operating at a frequency of 56.45 MHz in frequency sweep mode at a probe temperature of 27.5 ± 1°. External hexafluorobenzene and trichlorofluoromethane respectively were used as lock and reference peaks. To avoid solvent effects on the chemical shifts as far as possible, measurements of ^{19}F substituent chemical shifts were carried out on carbon tetrachloride solutions containing 8% by weight substituted 1-fluoromethylnaphthalene and 4% by weight 1-fluoromethylnaphthalene. The carbon tetrachloride used was Fisher "Spectranalyzed" and was not purified further before use. The substituent chemical shifts were measured directly from the spectra of these solutions as the distance between the positions of the central peaks of the two triplets. The substituent chemical shift, $\Delta\phi$, was considered to be a positive value if the signal due to the substituted derivative appeared at higher field than that due to 1-fluoromethylnaphthalene itself.

Proton spectra were recorded on the same spectrometers operating at 100 MHz in frequency sweep mode and 60 MHz in field sweep mode. The

internal reference and lock was the signal due to tetramethylsilane. ^{1}H measurements were carried out on the same solutions as the ^{19}F measurements. Proton substituent chemical shifts, $\Delta\tau$, were measured directly as the distance between the centres of the doublets of the methylenic protons. The substituent chemical shift, $\Delta\tau$, was considered to be a positive value if the signal due to the substituted derivative appeared at higher field than that due to 1-fluoromethylnaphthalene itself.

The conditions of measurement of proton and fluorine substituent chemical shifts and the sign conventions correspond to those described by Béguin[45] for the benzyl fluorides.

Resonance signals were integrated in order to assign signals to either the substituted or unsubstituted derivative. Proton-fluorine coupling constants were measured for all compounds from both the fluorine and the proton spectra.

Measurements were repeated on solutions containing 4% substituted fluoromethylnaphthalene and 6% 1-fluoromethylnaphthalene by weight in carbon tetrachloride using the Varian HA-60-IL spectrometer. This was done for two reasons: to determine if there were significant solvent shifts, and to confirm the signal assignments made on the criterion of spectral integration.

The chemical shifts of 1-fluoromethylnaphthalene, 2-fluoromethylnaphthalene and benzyl fluoride were recorded under the standardisation conditions of Filipovich and Tiers[126] who report a simplified, internally referenced procedure for determining and tabulating reliable fluorine n.m.r. shielding values. They found trichlorofluoromethane to be an

excellent solvent for fluorine compounds; at the same time the solvent peak was used as internal reference and lock. Chemical shifts were recorded on a 5% solution by weight of fluoromethylnaphthalene or benzyl fluoride in trichlorofluoromethane.

To facilitate the measurement of substituent chemical shifts the proton signals were decoupled from the fluorine by means of the application of an auxilliary field oscillating at the frequency of the fluorine resonances. By this means of heteronuclear decoupling the methylene doublets collapsed to two singlets. Reciprocal experiments were carried out by observing fluorine absorptions and irradiating with a radiofrequency field corresponding to the frequency of proton absorptions. The two characteristic triplets collapsed to two singlets. Substituent chemical shifts could then be measured as the distance between the two singlets. Heteronuclear decoupling experiments were carried out while observing both proton and fluorine resonances using the 100 MHz spectrometer. Difficulty was encountered while attempting to decouple fluorine from proton signals using the 60 MHz spectrometer. Only partial decoupling could be obtained with the result that either the doublet did not coalesce to a singlet, the distance between the two lines of the doublet signals decreased, or the lines only partially coalesced to form a broad singlet which prevented shift differences from being measured accurately. The heteronuclear decoupling of proton splitting of fluorine spectra was successfully accomplished on the Varian HA-60-IL spectrometer.

Tables of Results

The results of these experiments are to be found in Tables I-XI on the following pages. The results for benzyl fluorides[45] are included as Table XII. The contents of the tables are as follows:-

Table I, 100 MHz ^{19}F N.m.r. substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Table II, 60 MHz ^{19}F Chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Table III, 60 MHz ^{19}F Chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 6% by weight 1-fluoromethylnaphthalene and 4% by weight substituted-1-fluoromethylnaphthalene.

Table IV, Substituent chemical shift values of substituted fluoromethylnaphthalenes taken from Tables I, II and III.

Table V, $[F]_H$ Heteronuclear decoupling frequencies and coupling constants of substituted fluoromethylnaphthalenes.

Table VI, 100 MHz ^{1}H N.m.r. substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Table VII, 60 MHz ^{1}H N.m.r. chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Table VIII, 60 MHz ^{1}H N.m.r. chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 6% by weight 1-fluoromethylnaphthalene and 4% by weight substituted-1-fluoromethylnaphthalene.

Table IX, Substituent chemical shift values of substituted fluoromethylnaphthalenes taken from Tables VI, VII, and VIII.

Table X, $[H]_F$ Heteronuclear decoupling frequencies and coupling constants of substituted fluoromethylnaphthalenes.

Table XI, Chemical shift values measured under standard conditions.

Table XII, 60 MHz ^{19}F and ^{1}H Substituent chemical shifts and coupling constants for substituted benzyl fluorides.

^{19}F Substituent chemical shifts were measured to $\pm$ 0.5 Hz. H_{ref} - distance between signal due to 1-fluoromethylnaphthalene and that due to trichlorofluoromethane measured in Hz. H_{sample} - distance between signal due to substituted-1-fluoromethylnaphthalene and that due to trichlorofluoromethane measured in Hz, i.e. sample resonant frequency relative to CCl_3F as standard. 94.08 MHz and 56.45 MHz are the spectrometer operating frequencies for observing ^{19}F absorptions at 1.4092 Tesla. $\Delta\phi$ values are labelled:-

$\Delta\phi$ (a) Measured at 100 MHz on a solution containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

$\Delta\phi$ (b) Measured at 60 MHz - concentrations as in (a).

$\Delta\phi$ (c) Measured at 60 MHz on a solution containing 6% by weight 1-fluoromethylnaphthalene and 4% by weight substituted-1-fluoromethylnaphthalene.

$\Delta\tau$ and J_{HF} values are labelled similarly.

Table I. 100 MHz ^{19}F N.m.r. substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Substituent	Δφ(a) Hz	Δφ/94.08 Hz	J_{HF}(a) Hz
4 CH_3	-236.0	-2.51	48.2
4 F	-264.0	-2.81	48.4
4 CH_2OCH_3	- 18.0	-0.19	47.8
3 $COOC_2H_5$	- 12.0	-0.13	48.0
3 $COOCH_3$	- 6.5	-0.07	48.1
3 CH_3	-	-	-
3 CH_2F	+118.0	+1.25	47.7
d	+118.0	+1.25	47.75
4 Cl	+ 24.0	+0.25	48.0
2 CH_2F	+ 28.0	+0.30	48.0
3 $COCH_3$	+ 28.0	+0.30	48.1
4 Br	+ 71.5	+0.76	48.0
4 CH_2F	+122.5	+1.30	47.75
3 Br	+271.5	+2.89	47.5
3 NO_2	-	-	-
3 CN	+372.0	+3.95	47.1
4 $COOC_2H_5$	+523.0	+5.56	47.0
4 $COCH_3$	+533.0	+5.67	47.0
4 $COOCH_3$	+554.0	+5.89	47.1
4 $COCH_2F$	+630.0	+6.70	47.2
4 CN	+668.0	+7.10	47.0
4 NO_2	-	-	-

d. Shift for the β-CH_2F group.

Table II. 60 MHz ^{19}F Chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Substituent	$H_{ref.}$ Hz	H_{sample} Hz	Δφ(b) Hz	Δφ/56.45 Hz	J_{HF}(b) Hz
4 CH_3	11696.0	11551.0	-145.0	-2.57	48.5
4 F	11704.0	11542.5	-161.5	-2.86	48.2
4 CH_2OCH_3	11702.0	11686.0	- 16.0	-0.28	47.7
3 $COOC_2H_5$	11697.5	11693.5	- 4.0	-0.07	48.0
3 $COOCH_3$	11709.0	11700.5	- 8.5	-0.15	48.0
3 CH_3	11691.5	11699.0	+ 7.5	+0.13	47.9
3 CH_2F	11683.0	11753.5	+ 70.5	+1.25	47.7
d		11755.5	+ 72.5	+1.28	47.75
4 Cl	11688.0	11702.0	+ 14.0	+0.25	48.0
2 CH_2F	11668.5	11683.0	+ 14.5	+0.26	48.0
3 $COCH_3$	11689.0	11706.0	+ 17.0	+0.31	47.9
4 Br	11689.5	11736.0	+ 46.5	+0.82	47.6
4 CH_2F	11700.5	11774.5	+ 74.0	+1.31	47.8
3 Br	11693.0	11860.0	+167.0	+2.59	47.7
3 NO_2	11702.5	11895.5	+193.0	+3.42	47.0
3 CN	11702.0	11926.5	+224.5	+3.98	47.1
4 $COOC_2H_5$	11697.5	12016.5	+319.0	+5.65	47.5
4 $COCH_3$	11682.0	12007.0	+325.0	+5.76	47.0
4 $COOCH_3$	11681.0	12022.5	+341.5	+6.05	47.1
4 $COCH_2F$	11683.0	12071.0	+388.0	+6.87	47.6
e		12580.0	+897.0	+15.85	48.0
4 CN	11690.0	12090.0	+400.0	+7.09	47.1
4 NO_2	11678.0	12099.0	+421.0	+7.46	47.0

d Shift for β-CH_2F group.
e Shift for $COCH_2F$ group.

Table III. 60 MHz ^{19}F Chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 6% by weight 1-fluoromethylnaphthalene and 4% by weight substituted-1-fluoromethylnaphthalene.

Substituent	$H_{ref.}$ Hz	H_{sample} Hz	$\Delta\phi$(c) Hz	$\Delta\phi/56.45$ Hz	J_{HF}(c) Hz
4 CH_3	11708.0	11562.5	-145.5	-2.58	48.2
4 F	11713.0	11552.0	-161.0	-2.85	48.2
4 CH_2OCH_3	11707.0	11690.5	- 16.5	-0.29	47.75
3 $COOC_2H_5$	11695.0	11707.5	- 12.5	-0.22	48.0
3 $COOCH_3$	11710.0	11707.5	- 2.5	-0.04	48.0
3 CH_3	11702.0	11711.5	+ 9.5	+0.17	48.0
3 CH_2F	11700.5	11767.5	+ 67.0	+1.19	47.52
d		11769.0	+ 68.5	+1.22	47.62
4 Cl	11701.5	11711.5	+ 10.0	+0.18	48.0
2 CH_2F	11695.5	11711.5	+ 16.0	+0.28	48.0
3 $COCH_3$	11700.5	11718.0	+ 17.5	+0.31	48.4
4 Br	11704.0	11744.5	+ 40.5	+0.72	47.75
4 CH_2F	11707.0	11781.0	+ 74.0	+1.31	49.0
3 Br	11710.5	11875.5	+165.0	+2.92	47.5
3 NO_2	11706.5	11892.5	+186.0	+3.30	47.0
3 CN	11712.0	11933.0	+232.0	+4.11	47.2
4 $COOC_2H_5$	11701.0	12018.0	+317.0	+5.62	47.2
4 $COCH_3$	11704.0	12027.5	+323.5	+5.73	47.0
4 $COOCH_3$	11700.0	12034.0	+334.0	+5.92	47.1
4 $COCH_2F$	11710.0	12096.0	+386.0	+6.84	47.1
e		12562.0	+852.0	+15.09	48.0
4 CN	11706.5	12100.0	+393.5	+6.97	47.2
4 NO_2	11709.0	12111.0	+402.0	+7.12	46.8

d Shift for β-CH_2F group.
e Shift for $COCH_2F$ group.

Table IV. Substituent chemical shift values of substituted fluoromethylnaphthalenes taken from Tables I, II and III.

Substituent	Δφ(a)	Δφ(b)	Δφ(c)
4 CH_3	-2.51	-2.57	-2.58
4 F	-2.81	-2.86	-2.85
4 CH_2OCH_3	-0.19	-0.28	-0.29
3 $COOC_2H_5$	-0.13	-0.07	-0.22
3 $COOCH_3$	-0.07	-0.15	-0.04
3 CH_3	-	+0.13	+0.17
3 CH_2F	+1.25	+1.25	+1.19
d	+1.25	+1.28	+1.22
4 Cl	+0.25	+0.25	+0.18
2 CH_2F	+0.30	+0.26	+0.28
3 $COCH_3$	+0.30	+0.31	+0.31
4 Br	+0.76	+0.82	+0.72
4 CH_2F	+1.30	+1.31	+1.31
3 Br	+2.89	+2.59	+2.92
3 NO_2	-	+3.42	+3.30
3 CN	+3.95	+3.98	+4.11
4 $COOC_2H_5$	+5.56	+5.65	+5.62
4 $COCH_3$	+5.67	+5.76	+5.73
4 $COOCH_3$	+5.89	+6.05	+5.92
4 $COCH_2F$	+6.70	+6.87	+6.84
e	-	+15.85	+15.09
4 CN	+7.10	+7.09	+6.97
4 NO_2	-	+7.46	+7.12

d Shift for β-CH_2F group.
e Shift for $COCH_2F$ group.

Table V. $[F]_H$ Heteronuclear decoupling frequencies and coupling constants of substituted fluoromethylnaphthalenes.

Substituent	Decoupling frequencies MHz		J_{HF}(a) Hz	J_{HF}(b) Hz	J_{HF}(c) Hz
4 CH_3	-	99.999309	48.2	48.5	48.2
4 F	-	99.999	48.4	48.2	48.2
4 CH_2OCH_3	59.9968310	99.999	47.8	47.7	47.75
3 $COOC_2H_5$	59.996974	99.999	48.0	48.0	48.0
3 $COOCH_3$	59.996974	99.999	48.1	48.0	48.0
3 CH_3	59.996867	-	-	47.9	48.0
3 CH_2F	59.996964	99.999	47.70	47.70	47.52
d			47.75	47.75	47.62
4 Cl	59.9968310	99.999	48.0	48.0	48.0
2 CH_2F	59.996952	99.999	48.0	48.0	48.0
3 $COCH_3$	59.996967	99.999	48.1	47.9	48.4
4 Br	59.996978	99.999	48.0	47.6	47.75
4 CH_2F	59.996976	99.999	47.75	47.8	49.0
3 Br	59.99680	99.999	47.5	47.7	47.5
3 NO_2	59.99697	-	-	47.0	47.0
3 CN	59.9969810	99.999	47.1	47.1	47.2
4 $COOC_2H_5$	59.9964974	99.999	47.0	47.5	47.2
4 $COOCH_3$	59.996972	99.999	47.1	47.1	47.1
4 $COCH_3$	59.996994	99.999865	47.0	47.0	47.0
4 $COCH_2F$	59.997014	99.999	47.2	47.6	47.1
e	59.996984		-	48.0	48.0
4 CN	59.996770	99.999	47.0	47.1	47.2
4 NO_2	-	-	-	47.0	46.8

d Coupling constant for β-CH_2F group.
e Coupling constant for $COCH_2F$ group.

Table VI. 100 MHz ^{1}H N.m.r. chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene

Substituent	$H_{ref.}$ Hz	H_{sample} Hz	Δτ(a) Hz	Δτ/100 Hz	J_{HF}(a) Hz
4 CH_3	595.0	592.5	+2.5	+0.025	48.0
4 F	613.0	604.0	+9.0	+0.090	48.1
4 CH_2OCH_3	607.5	607.5	0.0	0.0	47.8
3 $COOC_2H_5$	628.5	628.5	0.0	0.0	47.75
3 $COOCH_3$	610.5	607.0	+3.5	+0.035	48.7
3 CH_3	-	-	-	-	-
3 CH_2F	606.5	603.0	+3.5	+0.035	47.75
d	..	572.0	+34.5	+0.345	47.5
4 Cl	600.0	591.0	+9.0	+0.090	48.0
2 CH_2F	626.5	596.5	+30.0	+0.30	47.75
3 $COCH_3$	631.5	628.5	+3.0	+0.030	47.75
4 Br	616.5	610.0	+6.5	+0.065	47.75
4 CH_2F	580.5	578.5	+2.0	+0.020	49.6
3 Br	612.0	604.0	+8.0	+0.080	47.0
3 NO_2	616.0	615.0	+1.0	+0.010	47.5
3 CN	615.5	610.5	+5.0	+0.050	47.3
4 $COOC_2H_5$	630.5	630.0	+0.5	+0.005	47.5
4 $COCH_3$	606.0	605.0	+1.0	+0.010	46.95
4 $COOCH_3$	631.0	630.5	+0.5	+0.005	47.3
4 $COCH_2F$	-	-	-	-	-
4 CN	613.0	613.0	0.0	0.0	47.25
4 NO_2	-	-	-	-	-

d Shift for β-CH_2F group.

Table VII. 60 MHz ^1H N.m.r. chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 4% by weight 1-fluoromethylnaphthalene and 8% by weight substituted-1-fluoromethylnaphthalene.

Substituent	$H_{ref.}$ Hz	H_{sample} Hz	$\Delta\tau$ (b) Hz	$\Delta\tau$/60.0 MHz	J_{HF} (b) Hz
4 CH_3	337.0	335.5	+1.5	+0.025	49.0
4 F	344.0	339.0	+5.0	+0.083	48.7
4 CH_2OCH_3	340.0	340.0	0.0	0.0	47.8
3 $COOCH_3$	340.5	339.0	+1.5	+0.025	48.7
3 $COOC_2H_5$	340.5	340.0	+0.5	+0.008	48.0
3 CH_3	336.0	334.5	+1.5	+0.025	49.0
3 CH_2F	338.0	335.5	+2.5	+0.042	47.6
d		317.0	+21.0	+0.350	48.2
4 Cl	339.5	334.0	+5.5	+0.092	48.8
2 CH_2F	339.5	321.5	+18.0	+0.30	48.2
3 $COCH_3$	340.5	338.0	+2.5	+0.042	48.6
4 Br	344.0	340.5	+3.5	+0.058	48.05
4 CH_2F	340.5	339.5	+1.0	+0.017	50.3
3 Br	339.5	333.0	+6.5	+0.108	48.15
3 NO_2	342.5	342.5	0.0	0.0	48.4
3 CN	343.5	340.5	+3.0	+0.050	48.05
4 $COOC_2H_5$	343.0	342.75	+0.25	+0.004	48.7
4 $COCH_3$	338.0	336.0	+2.0	+0.033	48.2
4 $COOCH_3$	337.5	336.0	+1.5	+0.025	48.3
4 $COCH_2F$	341.5	340.0	+1.5	+0.025	46.8
e		313.0	+28.5	+0.475	48.6
4 CN	343.5	343.5	0.0	0.0	48.05
4 NO_2	343.5	343.5	0.0	0.0	47.25

d Shift for β-CH_2F group.
e Shift for $COCH_2F$ group.

Table VIII. 60 MHz ^{1}H N.m.r. chemical shifts, substituent chemical shifts and coupling constants for carbon tetrachloride solutions containing 6% by weight 1-fluoromethylnaphthalene and 4% by weight substituted-1-fluoromethylnaphthalene.

Substituent	$H_{ref.}$ Hz	H_{sample} Hz	Δτ(c) Hz	Δτ/60.0 MHz	J_{HF}(c) Hz
4 CH_3	340.0	338.5	+1.5	+0.025	49.0
4 F	343.5	338.5	+5.0	+0.083	49.0
4 CH_2OCH_3	341.0	341.0	0.0	0.0	47.75
3 $COOCH_3$	341.0	340.5	+0.5	+0.008	48.9
3 $COOC_2H_5$	340.5	340.0	+0.5	+0.008	48.2
3 CH_3	340.0	338.0	+2.0	+0.033	49.0
3 CH_2F	340.0	338.0	+2.0	+0.033	47.4
d		319.5	+20.5	+0.342	48.1
4 Cl	341.0	336.0	+5.0	+0.083	48.8
2 CH_2F	340.0	322.5	+17.5	+0.292	48.4
3 $COCH_3$	341.0	339.0	+2.0	+0.033	48.5
4 Br	343.5	339.0	+4.5	+0.075	48.5
4 CH_2F	342.5	341.0	+1.5	+0.025	50.3
3 Br	341.0	334.5	+6.5	+0.108	48.15
3 NO_2	342.0	338.5	+3.5	+0.058	48.3
3 CN	342.5	336.5	+6.0	+0.10	48.2
4 $COOC_2H_5$	340.5	340.5	0.0	0.0	48.7
4 $COCH_3$	339.5	338.0	+1.5	+0.025	48.2
4 $COOCH_3$	339.5	338.0	+1.5	+0.025	48.3
4 $COCH_2F$	340.0	338.5	+1.5	+0.025	47.2
e		310.5	+30.0	+0.50	48.4
4 CN	342.5	342.0	+0.5	+0.008	47.7
4 NO_2	343.0	343.0	0.0	0.0	48.7

d Shift for β-CH_2F group.
e Shift for $COCH_2F$ group.

Table IX. Substituent chemical shift values of substituted fluoromethylnaphthalenes taken from Tables VI, VII and VIII.

Substituent	Δτ(a)	Δτ(b)	Δτ(c)
4 CH_3	+0.025	+0.025	+0.025
4 F	+0.090	+0.083	+0.083
4 CH_2OCH_3	0.0	0.0	0.0
3 $COOCH_3$	+0.035	+0.025	+0.008
3 $COOC_2H_5$	0.0	+0.008	+0.008
3 CH_3	-	+0.025	+0.033
3 CH_2F	+0.035	+0.042	+0.033
d	+0.345	+0.350	+0.342
4 Cl	+0.090	+0.092	+0.083
2 CH_2F	+0.30	+0.30	+0.292
3 $COCH_3$	+0.030	+0.042	+0.033
4 Br	+0.065	+0.058	+0.075
4 CH_2F	+0.020	+0.017	+0.025
3 Br	+0.080	+0.108	+0.108
3 NO_2	+0.010	0.0	+0.058
3 CN	+0.050	+0.050	+0.10
4 $COOC_2H_5$	+0.005	+0.004	0.0
4 $COCH_3$	+0.010	+0.033	+0.025
4 $COOCH_3$	+0.005	+0.025	+0.025
4 $COCH_2F$	-	+0.025	+0.025
e	-	+0.475	+0.50
4 CN	0.0	0.0	+0.008
4 NO_2	-	0.0	0.0

d Values for β-CH_2F group.
e Values for $COCH_2F$ group.

Table X. $[H]_F$ Heteronuclear decoupling frequencies and coupling constants of substituted fluoromethylnaphthalenes.

Substituent	Decoupling frequency MHz	J_{HF}(a) Hz	J_{HF}(b) Hz	J_{HF}(c) Hz
4 CH_3	94.0770050	48.0	49.0	49.0
4 F	94.0764020	48.1	48.7	49.0
4 CH_2OCH_3	94.050330	47.8	47.8	47.75
3 $COOCH_3$	94.0764700	48.7	48.7	48.9
3 $COOC_2H_5$	94.0763850	47.75	48.0	48.2
3 CH_3	-	-	49.0	49.0
3 CH_2F	94.0763500	47.75	47.6	47.4
d		47.5	48.2	48.1
4 Cl	94.0767200	48.0	48.8	48.8
2 CH_2F	94.0763350	47.75	48.2	48.4
3 $COCH_3$	94.076400	47.75	48.6	48.5
4 Br	94.0763600	47.75	48.05	48.5
4 CH_2F	94.0765000	49.6	50.3	50.3
3 Br	94.0764955	47.0	48.15	48.15
3 NO_2	94.0762150	47.5	48.4	48.3
3 CN	94.0759998	47.3	48.05	48.20
4 $COOC_2H_5$	94.0760000	47.5	48.7	48.7
4 $COCH_3$	94.0699000	46.95	48.2	48.2
4 $COOCH_3$	94.0760950	47.3	48.3	48.3
4 $COCH_2F$	-	-	46.8	47.2
e		-	48.6	48.4
4 CN	94.0759995	47.25	48.05	47.7
4 NO_2	-	-	47.25	48.7

d Values for β-CH_2F group.
e Values for $COCH_2F$ group.

Table XI. Chemical shift values measured under standard conditions - 5% in CCl_3F or CCl_4.

Compound	ϕ_o [d]	τ_o [d]	J_{HF} [e]
1-Fluoromethylnaphthalene	208.7	4.35	48.0
2-Fluoromethylnaphthalene	209.2	4.68	48.0
Benzyl fluoride	211.0 211.3[f]	4.76 4.76[f]	48.0 48.0[f]

[d] Measured in p.p.m.

[e] Measured in Hz.

[f] Values from C. Beguin, Bull. Soc. chim. France, (3), 4214 (1967).

Table XII. 60 MHz ^{19}F and ^{1}H Substituent chemical shifts and coupling constants for substituted benzyl fluorides[d]

Substituent	$\Delta\phi_e$	$\Delta\tau_e$	HF Hz
p-OCH_3	-7.79	+0.095	48.7
p-CH_3	-2.95	+0.048	48.3
p-F	-2.82	+0.044	48.2
p-Cl	+0.49	+0.042	48.1
p-Br	+0.98	+0.050	47.9
p-CN	+7.68	-0.085	47.2
p-NO_2	+8.10	-0.140	46.9
m-OCH_3	+0.94	+0.030	48.2
m-CH_3	-0.44	+0.038	48.0
m-F	+2.82	0.00	48.0
m-Cl	+2.99	+0.023	47.2
m-CN	+5.03	-0.047	47.4
m-NO_2	+5.10	-0.125	47.2

d Values from C. Béguin, Bull. Soc. chim. France, (3), 4214 (1967)

e Measured in p.p.m.

Analysis of the Data

(i) Dual Substituent Parameter Correlations

Fluorine substituent chemical shifts, proton substituent chemical shift and coupling constant values were correlated with the sets of resonance and polar effect parameters described by Taft et al.[16] and with the resonance and inductive parameters of Swain and Lupton.[127]

The dual substituent parameter treatment describes substituent effects in terms of an additive blend of polar and pi delocalisation effects each of which is the product of a reaction parameter and a substituent parameter : specifically for ^{19}F substituent chemical shift data:-

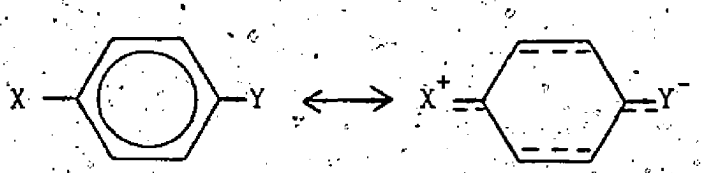
$$\Delta\phi = \rho_I\sigma_I + \rho_R\sigma_R$$

The σ_I scale of polar effects has been shown to be widely applicable in cases where the substituent is bonded to an sp^2 or sp^3 carbon atom. In contrast, Taft et al.[16] demonstrated that a single σ_R parameter scale applied only to systems which were similar in reaction type and in particular in their π-electronic frameworks and that four such scales were both practicable and discernible. These authors also claimed that these different scales were of particular advantage in that they were capable of discriminating between different reaction types and transition states.

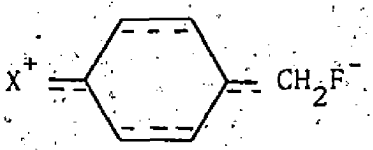
The four different resonance parameter sets are: $\sigma_{R(BA)}$, σ_R^o, σ_R^+, and $\sigma_{R(A)}^-$ and are applicable to the following pi delocalisation classes:-

$\sigma_{R(BA)}$ Scale

These parameters are generally applicable to benzoic acid (BA) type reactions in which the side chain (Y) is a weak to moderate pi electron acceptor group.

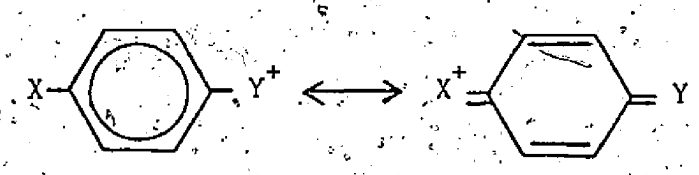


Y-groups of this type included $-COC_6H_4F(p)$, $-SF_5$, $-C_6H_4F(p)$, $-SC_6H_4F(p)$, and $-CH_2F$. The fluoromethyl group was presumed to act as a weak pi electron acceptor through contributions from a hyperconjugative form:



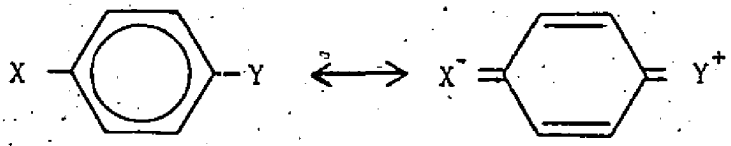
σ_R^+ Scale

This group includes strong pi electron accepting groups such as N_2^+ and several electrophilic aromatic substitution transition states.



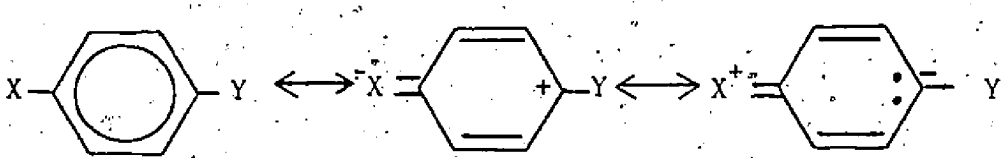
$\sigma_{R(A)}^-$ Scale

These values apply to reactions involving strong pi electron donating side chains.



σ_R^o Scale

These values apply in cases where there is no resonance interaction across the Ar Y bond, between the side chain and the aromatic system,



The different sets of values for the substituents involved in this study are listed in Table XIII.

Swain and Lupton[127] have recently proposed a dual substituent parameter treatment of substituent effects. They claimed that all previous scales of substituent effect "constants" could be reduced to just two scales, F and R, where e.g.

$$\sigma = fF + rR$$

F and R are field (or "inductive") and resonance constants which differ for each substituent, and f and r are empirical weighing factors which are independent of the substituent but different for each set of substituent constants (σ, σ^*, σ_I, σ_R, etc.) which are to be expressed in terms of F and R. A single universal resonance parameter scale is

Table XIII. Values of substituent parameters.

Substituent	σ_I	$\sigma_{R(BA)}$	σ_R^o	σ_R^+	$\sigma_{R(A)}^-$	F	R
$-OCH_3$	+0.27	-0.61	-0.45	-1.02	-0.45	+0.413	-0.500
$-CH_3$	-0.04	-0.11	-0.11	-0.25	-0.11	-0.052	-0.141
-F	+0.50	-0.45	-0.34	-0.57	-0.45	+0.708	-0.336
-Cl	+0.46	-0.23	-0.23	-0.36	-0.23	+0.690	-0.161
-Br	+0.44	-0.19	-0.19	-0.30	-0.19	+0.727	-0.176
-COOR	+0.30	+0.14	+0.14	+0.14	+0.34	+0.552	+0.140
-CN	+0.56	+0.13	+0.13	+0.13	+0.33	+0.847	+0.184
$-NO_2$	+0.65	+0.15	+0.15	+0.15	+0.46	+1.109	+0.155
$-COCH_3$	+0.28	+0.16	+0.16	+0.16	+0.47	+0.534	+0.202
$-CH_2F$	+0.12	-0.02					
$-CH_2OCH_3$	-0.01	-0.06					

	σ_m^+	σ_p^+
$-OCH_3$	+0.047	-0.778
$-CH_3$	-0.066	-0.311
-F	+0.352	-0.073
-Cl	+0.399	+0.114
-Br	+0.405	+0.150
-COOMe	+0.368	+0.489
-COOEt	+0.366	+0.482
-CN	+0.562	+0.659
$-NO_2$	+0.674	+0.790

applied in this treatment, a significant difference from Taft's treatment. In order to determine the applicability of these values to the fluoromethylnaphthalene system $\Delta\phi$'s were also correlated with the F and R values of Swain and Lupton.

Substituent constants for the $-CH_2F$ and $-CH_2OCH_3$ groups are not listed in ref. 16. However, Sheppard[52] has reported σ_I and σ_R values for these substituents derived from ^{19}F measurements of meta- and para-fluorotoluenes and these values were used in the correlations.

The dual substituent parameter correlations were carried out on an IBM System/370 Model 145 computer using the University of Victoria program 'MULREG', a program which performs a multiple linear regression for a set of independent variables (in this case σ_I and σ_R) and a dependent variable ($\Delta\phi$, $\Delta\tau$ or J). Ouput from the program as listed in Tables XIV-XXI includes the following:-

R - multiple correlation coefficient for the multiple linear regression.

FPROB - a confidence measure of the total regression derived from computed t-values.

ρ_I - the regression coefficient associated with σ_I.

FPROB ρ_I - a measure of confidence in the regression coefficient ρ_I. This parameter is the significance level associated with the regression coefficient ρ_I. Based on a null hypothesis, i.e. that ρ_I is zero, this parameter is the statistical measure of the probability that the null hypothesis is true - the chances that these data or any similar subsequent data would confirm the null hypothesis. A small value of FPROBρ_I rejects the null hypothesis and at the same time confirms the magnitude of ρ_I. A suitable

acceptance criterion is chosen and values outside this limit are rejected and indicate that ρ_I is not significantly different from zero. For physical data of this type an acceptable value is 0.001, i.e. that only 1 in 1000 cases would confirm the null hypothesis and that the value of ρ_I is significantly different from zero by the magnitude indicated.

FPROBρ_R - a measure of confidence in the regression coefficient ρ_R.

INTERCEPT.

S.E. of INTERCEPT - Standard error of intercept.

S.D. - Standard deviation of total regression correlation.

Two other quantities are listed in the results tables.

n - the number of data points included in the correlation.

λ - the ratio ρ_R/ρ_I.

In the dual substituent parameter analysis reported by Taft et al.[16] the fitting of the data was constrained to zero intercept behaviour. While recognising that the data for the unsubstituted member of any set may be as subject to experimental error as any other member, they remarked that such error is generally relatively small for a set of reliable data. In a data set the point P=0 for the H substituent is critical and valuable in locating the scale origins. This point cannot influence the rho values (all sigmas are constrained to zero) and so this point does not affect the statistics.

We chose to adopt a slightly different approach to the fitting of the data to this equation. We believe that by allowing a free fit and by not restraining the equation to zero intercept behaviour this

provides yet another measure of the "goodness of fit". The multiple correlation coefficient, R, and the statistical confidence measures of the form of the overall equation and for the separate coefficients of the independent variables allows one to analyse the different aspects of the fitting of the data to the dual substituent parameter equation. The value of the intercept and the comparison of this value to the standard error for the intercept affords another means of monitoring "a good fit" or probably more importantly in what respects a fit was not "a good fit". The hydrogen data point was included as a normal data point in order to permit this free fitting to the equation.

The blending factor, λ, defined as ρ_R/ρ_I is an indication of the relative transmission of resonance and polar effects. For para-substituents λ is normally 1 or greater whereas for meta-substituents it is typically less than 0.4. This reflects the poorer transmission of pi-delocalisation effects from the meta- than from the para-position. Large λ values are associated with physical property measurements which involved predominantly the π electrons; ionisation equilibria are characterised by a value of λ much closer to unity indicating a higher blend of polar effects. An interesting study in this respect is the ionisation of α-substituted p-toluic acids in 50% aqueous ethanol.[128] For this series $\lambda \rightarrow 0$ indicating no substituent resonance effects are possible; the interposition of the methylene moiety between the substituent and the aromatic nucleus does eliminate conjugation of the substituent-X with the ring.

If ρ_I and ρ_R are of opposite sign λ will be a negative quantity. This stresses the fact that the transmission of I and R effects from any substituent need not necessarily be closely related.

Fluoromethylnaphthalene parameters correlated by this equation include ^{19}F 100 MHz and 60 MHz substituent chemical shifts ($\Delta\phi$), ^{1}H 100 MHz and 60 MHz substituent chemical shifts ($\Delta\tau$), average coupling constant values (J_{HF}) measured from ^{19}F spectra and ^{19}F 100 MHz substituent chemical shifts for substituents not subject to steric twisting by peri-hydrogens. ^{19}F 60 MHz $\Delta\phi$ and J values for substituted benzyl fluorides were also correlated by the multiple linear regression treatment. Results of these correlations are shown in Tables XIV-XXV. The contents of the tables are as follows:

Table XIV. Multiple linear regression of 100 MHz ^{19}F substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes.

Table XV. Multiple linear regression of 100 MHz ^{19}F substituent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes.

Table XVI. Multiple linear regression of 60 MHz ^{19}F substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes.

Table XVII. Multiple linear regression of 60 MHz ^{19}F substitutent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes.

Table XVIII. Multiple linear regression of 60 MHz ^{19}F substituent chemical shifts of p and m-substituted benzyl fluorides.

Table XIX. Multiple linear regression of 100 MHz and 60 MHz ^{1}H substituent chemical shifts of 3- and 4-substituted-1-fluoromethyl-naphthalenes.

Table XX. Multiple linear regression of 100 MHz and 60 MHz J_{HF} coupling constants of 3- and 4-substituted fluoromethylnaphthalenes and p- and m-

substituted benzyl fluoride.

Table XXI. Multiple linear regression of 100 MHz substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes. Substituents not subject to steric twisting by peri-hydrogens - Br, Cl, F, CN, CH_3.

Table XXII. Multiple linear regression of 100 MHz and 60 MHz ^{19}F substituent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes.

Table XXIII. Linear least squares correlation of substituent chemical shifts and Brown σ^+ values for substituted-1-fluoromethylnaphthalenes and substituted benzyl fluorides, and calculated σ^+ values.

Table XXIV. Observed and calculated substituent chemical shift values for 4-substituted-1-fluoromethylnaphthalenes.

Table XXV. Observed and calculated substituent chemical shifts values for 3-substituted-1-fluoromethylnaphthalenes.

Table XIV. Multiple linear regression of 100 MHz ^{19}F substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)}^{+} + \sigma_I$	10	0.993	0.0000	8.48	0.00003	16.91	0.00000	2.00	0.25	0.32	0.53
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2F$ data[a]	11	0.993	0.0000	8.32	0.00001	16.91	0.00000	2.03	0.34	0.28	0.51
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2OCH_3$ data[a]	11	0.992	0.0000	8.11	0.00001	16.85	0.00000	2.08	0.43	0.27	0.54
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2OCH_3$ and CH_2F data[a]	12	0.992	0.0000	8.03	0.00000	16.85	0.00000	2.10	0.47	0.24	0.51
Taft $\sigma_R^{+} + \sigma_I$	10	0.992	0.0000	8.02	0.00007	13.21	0.00000	1.65	0.97	0.35	0.58
Taft $\sigma_R^{+} + \sigma_I$ with $-CH_2OCH_3$ data[a]	11	0.992	0.0000	8.19	0.00001	13.21	0.00000	1.61	0.90	0.28	0.55
Taft $\sigma_R^{+} + \sigma_I$ with $-CH_2F$ data[a]	11	0.991	0.0000	8.17	0.00001	13.19	0.00000	1.61	0.89	0.31	0.56
Taft $\sigma_R^{+} + \sigma_I$ with $-CH_2F$ and CH_2OCH_3 data[a]	12	0.992	0.0000	8.27	0.00000	13.19	0.00000	1.59	0.84	0.25	0.53
Taft $\sigma_R^{o} + \sigma_I$	10	0.991	0.0000	7.87	0.00008	18.91	0.00000	2.40	0.31	0.36	0.60
Taft $\sigma_{R(A)}^{-} + \sigma_I$	10	0.986	0.0000	5.87	0.00145	10.76	0.00001	1.83	-0.32	0.46	0.77
Swain and Lupton F and R[b]	10	0.995	0.0000	4.32[b]	0.00005	17.73[b]	0.00000	-	0.28	0.29	0.46

a i.e. using σ_I and σ_R values from ref. 52 for $-CH_2F$ and $-CH_2OCH_3$ substituents.

b These parameters do not have the same significance as in Taft's analysis.

Table XV. Multiple linear regression of 100 MHz ^{19}F substituent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$	8	0.899	0.0173	7.08	0.00656	-5.34	0.10928	-0.75	-0.61	0.55	0.92
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2F$ data[a]	9	0.881	0.0118	6.78	0.00414	-5.55	0.08422	-0.82	-0.42	0.50	0.90
Taft $\sigma_R^o + \sigma_I$	8	0.899	0.0173	7.08	0.00656	-5.34	0.10928	-0.75	-0.61	0.55	0.92
Taft $\sigma_R^o + \sigma_I$ with $-CH_2F$ data[a]	9	0.881	0.0118	6.78	0.00414	-5.55	0.08422	-0.82	-0.42	0.50	0.90
Taft $\sigma_R + \sigma_I$	8	0.902	0.0159	7.00	0.00601	-3.60	0.11731	-0.51	-0.76	0.55	0.89
Taft $\sigma_R^+ + \sigma_I$ with $-CH_2F$ data[a]	9	0.868	0.0158	6.60	0.00556	-3.68	0.12096	-0.56	-0.55	0.54	0.95
Taft $\sigma_{R(A)}^- + \sigma_I$	8	0.908	0.0141	7.67	0.00540	-3.14	0.08506	-0.41	-0.43	0.53	0.88
Taft $\sigma_{R(A)}^- + \sigma_I$ with $-CH_2F$ data[a]	9	0.898	0.0080	7.52	0.00283	-3.33	0.05261	-0.44	-0.28	0.46	0.90
Swain and Lupton F and R[b]	8	0.829	0.0555	4.24[b]	0.02167	-4.75[b]	0.21885	-	-0.65	0.74	1.17

a i.e. using σ_I and σ_R values from ref. 52 for $-CH_2F$ and $-CH_2OCH_3$ substituents.

b These parameters do not have the same significance as in Taft's analysis.

Table XVI. Multiple linear regression of 60 MHz ^{19}F substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$	10	0.992	0.0000	8.49	0.00005	17.09	0.00000	2.01	0.28	0.35	0.59
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2F$ data[a]	11	0.991	0.0000	8.35	0.00001	17.09	0.00000	2.05	0.36	0.31	0.56
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2OCH_3$ data[a]	11	0.991	0.0000	8.18	0.00001	17.04	0.00000	2.08	0.43	0.29	0.57
Taft $\sigma_{R(BA)} + \sigma_I$ with $-CH_2F$ and $-CH_2OCH_3$ data[a]	12	0.991	0.0000	8.11	0.00000	17.05	0.00000	2.10	0.45	0.26	0.55
Taft $\sigma_R^+ + \sigma_I$	10	0.991	0.0000	8.03	0.00001	13.36	0.00000	1.66	1.01	0.38	0.63
Taft $\sigma_R^+ + \sigma_I$ with $-CH_2OCH_3$ data[a]	11	0.991	0.0000	8.26	0.00001	13.36	0.00000	1.62	0.90	0.31	0.60
Taft $\sigma_R^+ + \sigma_I$ with $-CH_2F$ data[a]	11	0.990	0.0000	8.19	0.00002	13.33	0.00000	1.63	0.92	0.33	0.60
Taft $\sigma_R^+ + \sigma_I$ with $-CH_2OCH_3$ and CH_2F data[a]	12	0.990	0.0000	8.35	0.00000	13.34	0.00000	1.60	0.85	0.28	0.58
Taft $\sigma_R^o + \sigma_I$	10	0.981	0.0000	7.88	0.00013	19.11	0.00001	2.43	0.33	0.39	0.65
Taft $\sigma_{R(A)} + \sigma_I$	10	0.984	0.0000	5.86	0.00192	10.87	0.00001	1.86	-0.30	0.48	0.80
Swain and Lupton F and R[b]	10	0.994	0.0000	4.33[b]	0.00008	17.94[b]	0.00000	-	0.30	0.32	0.51

a i.e. using σ_I and σ_R values from Ref. 52 for $-CH_2F$ and $-CH_2OCH_3$ substituents.

b These parameters do not have the same significance as in Taft's analysis.

Table XVII. Multiple linear regression of 60 MHz ^{19}F substituent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$	8	0.882	0.0241	6.86	0.00914	-4.64	0.17124	-0.68	-0.62	0.58	0.97
Taft $\sigma_{R(BA)} + \sigma_I$ with CH_2F data[a]	9	0.861	0.0179	6.54	0.00633	-4.87	0.13858	-0.75	-0.40	0.53	0.96
Taft $\sigma_R^o + \sigma_I$	8	0.882	0.0241	6.86	0.00914	-4.64	0.17124	-0.68	-0.62	0.58	0.97
Taft $\sigma_R^o + \sigma_I$ with CH_2F data[a]	9	0.861	0.0179	6.54	0.00633	-4.87	0.13858	-0.75	-0.40	0.53	0.96
Taft $\sigma_R^+ + \sigma_I$	8	0.880	0.0253	6.84	0.00958	-3.27	0.18179	-0.48	-0.78	0.61	0.98
Taft $\sigma_R^+ + \sigma_I$ with CH_2F data[a]	9	0.886	0.0106	6.82	0.00371	-3.26	0.13995	-0.48	-0.77	0.51	0.90
Taft $\sigma^-_{R(A)} + \sigma_I$ with CH_2F data[a]	9	0.878	0.0127	7.22	0.00461	-2.98	0.09039	-0.41	-0.28	0.49	0.90
Taft $\sigma^-_{R(A)} + \sigma_I$	8	0.891	0.0202	7.39	0.00787	-2.77	0.13633	-0.37	-0.46	0.56	0.94
Swain and Lupton F and R[b]	8	0.819	0.0683	4.07[b]	0.02735	-4.08[b]	0.29437	-	-0.64	0.76	1.21

a i.e. using σ_I and σ_R values from Ref. 52 for $-CH_2F$ and $-CH_2OCH_3$ substituents.

b These parameters do not have the same significance as in Taft's analysis.

Table XVIII. Multiple linear regression of 60 MHz ^{19}F substituent chemical shifts of p and m-substituted benzyl fluorides.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
p-X											
Taft $\sigma_{R(BA)} + \sigma_I$	8	0.998	0.0000	9.87	0.00007	16.51	0.00002	1.67	-0.34	0.25	0.35
Taft $\sigma_R^o + \sigma_I$	8	0.990	0.0002	9.25	0.00127	20.41	0.00010	2.21	-0.17	0.62	0.87
Taft $\sigma_R^+ + \sigma_I$	8	0.992	0.0002	9.35	0.00089	11.23	0.00007	1.20	0.26	0.58	0.80
Taft $\sigma_{R(A)}^- + \sigma_I$	8	0.962	0.0022	6.94	0.04899	13.04	0.00172	1.88	0.96	1.19	1.74
Swain and Lupton F and R[a]	8	0.998	0.0000	4.98[a]	0.00016	18.92[a]	0.00002	-	0.00	0.28	0.39
m-X											
Taft $\sigma_{R(BA)} + \sigma_I$	7	0.996	0.0005	7.60	0.00031	2.18	0.00340	0.29	0.09	0.18	0.26
Taft $\sigma_R^o + \sigma_I$	7	0.996	0.0005	7.48	0.00030	2.75	0.00319	0.37	0.12	0.18	0.25
Taft $\sigma_R^+ + \sigma_I$	7	0.993	0.0007	7.54	0.00047	1.45	0.00625	0.19	0.16	0.23	0.32
Taft $\sigma_{R(A)}^- + \sigma_I$	7	0.994	0.0007	7.14	0.00052	1.80	0.00910	0.25	0.02	0.21	0.31
Swain and Lupton F and R[a]	7	0.990	0.0012	4.64[a]	0.00083	2.16[a]	0.02475	-	0.13	0.29	0.39

a These parameters do not have the same significance as in Taft's analysis.

Table XIX. Multiple linear regression correlation of 60 MHz and 100 MHz ^{1}H substituent chemical shifts of 3- and 4-substituted-1-fluoromethylnaphthalenes.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTERCEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$ 100 MHz 4-X	8	0.976	0.0009	0.08	0.01189	-0.15	0.00125	-1.97	0.01	0.01	0.01
Taft $\sigma_{R(BA)} + \sigma_I$ 60 MHz 4-X	8	0.922	0.0099	0.08	0.04475	-0.11	0.02550	-1.29	0.01	0.01	0.02
Taft $\sigma_{R(BA)} + \sigma_I$ 100 MHz 3-X	7	0.740	0.1380	0.06	0.10751	-0.14	0.07969	-2.12	0.02	0.01	0.02
Taft $\sigma_{R(BA)} + \sigma_I$ 60 MHz 3-X	7	0.907	0.0330	0.13	0.02464	-0.18	0.02956	-1.45	0.01	0.01	0.02

Table XX. Multiple linear regression of 100 MHz and 60 MHz J_{HF} coupling constants of 3- and 4-substituted fluoromethylnaphthalenes and m- and p-substituted benzyl fluorides.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$ 4-X-fluoromethylnaphthalene	12	0.954	0.0000	-0.99	0.00184	-2.38	0.00002	+2.33	47.81	0.08	0.18
Taft $\sigma_{R(BA)} + \sigma_I$ 3-X-fluoromethylnaphthalene	9	0.803	0.0448	-1.54	0.01647	0.90	0.33217	-0.58	48.13	0.16	0.28
Taft $\sigma_{R(BA)} + \sigma_I$ p-X-benzyl fluoride	8	0.994	0.0001	-1.08	0.00050	-2.20	0.00007	+2.03	48.01	0.06	0.08
Taft $\sigma_{R(BA)} + \sigma_I$ m-X-benzyl fluoride	7	0.827	0.1010	-0.95	0.10341	-0.89	0.12852	+0.94	47.93	0.71	0.30

Table XXI. Multiple linear regression of 100 MHz ^{19}F substituent chemical shifts of 4-substituted-1-fluoromethylnaphthalenes.
Substituents not subject to steric twisting by peri-hydrogens, Br, Cl, F, CN, CH_3.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Taft $\sigma_{R(BA)} + \sigma_I$	6	0.999	0.0010	9.24	0.00100	16.28	0.00072	1.76	-0.18	0.11	0.16
Taft $\sigma_R^o + \sigma_I$	6	0.990	0.0057	8.67	0.00693	18.89	0.00264	2.18	0.02	0.45	0.64
Taft $\sigma_R^+ + \sigma_I$	6	0.993	0.0041	8.67	0.00491	12.64	0.00184	1.46	0.54	0.39	0.53
Taft $\sigma_{R(A)}^- + \sigma_I$	6	0.993	0.0045	6.84	0.00827	11.98	0.00273	1.75	-0.42	0.39	0.56

Table XXII. Multiple linear regression of 100 MHz and 60 MHz ^{19}F substituent chemical shifts of 3-substituted-1-fluoromethylnaphthalenes omitting -COOMe and -COOEt points.

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
$\sigma_{R(BA)} + \sigma_I$ 100 MHz	6	0.946	0.0383	6.51	0.01913	-3.03	0.32342	-0.47	-0.20	0.50	0.77
$\sigma_{R(BA)} + \sigma_I$ 100 MHz with CH_2F[a]	7	0.937	0.0168	6.28	0.00762	-3.03	0.27550	-0.48	-0.05	0.43	0.72
$\sigma_R^o + \sigma_I$ 100 MHz	6	0.946	0.0383	6.51	0.01913	-3.03	0.32342	-0.47	-0.20	0.50	0.77
$\sigma_R^o + \sigma_I$ 100 MHz with CH_2F[a]	7	0.937	0.0168	6.28	0.00762	-3.03	0.27550	-0.48	-0.05	0.43	0.72
$\sigma_R^+ + \sigma_I$ 100 MHz	6	0.944	0.0394	6.48	0.01972	-2.11	0.33670	-0.33	-0.30	0.54	0.78
$\sigma_R^+ + \sigma_I$ 100 MHz with CH_2F[a]	7	0.932	0.0193	6.15	0.00867	-1.92	0.33800	-0.31	-0.10	0.46	0.75
$\sigma^-_{R(A)} + \sigma_I$ 100 MHz	6	0.960	0.0269	6.98	0.01431	-2.03	0.19347	-0.29	-0.09	0.43	0.67
$\sigma^-_{R(A)} + \sigma_I$ 100 MHz with CH_2F[a]	7	0.954	0.0099	6.85	0.00490	-2.11	0.12892	-0.31	0.02	0.35	0.62
$\sigma_{R(BA)} + \sigma_I$ 60 MHz	6	0.935	0.0479	6.26	0.02455	-2.22	0.48064	-0.36	-0.18	0.54	0.82
$\sigma_{R(BA)} + \sigma_I$ 60 MHz with CH_2F[a]	7	0.924	0.0232	6.01	0.01091	-2.22	0.44084	-0.37	-0.01	0.46	0.77
$\sigma^-_{R(A)} + \sigma_I$ 60 MHz	6	0.947	0.0372	6.68	0.02038	-1.62	0.32073	-0.24	-0.11	0.48	0.75
$\sigma^-_{R(A)} + \sigma_I$ 60 MHz with CH_2F[a]	7	0.939	0.0158	6.53	0.00814	-1.72	0.24163	-0.26	0.03	0.40	0.69

Table XXII. (Continued)

Correlation	n	R	FPROB	ρ_I	FPROBρ_I	ρ_R	FPROBρ_R	$\lambda = \frac{\rho_R}{\rho_I}$	INTER-CEPT	S.E. of INTERCEPT	S.D.
Swain and Lupton F and R[b] 100 MHz	6	0.903	0.0816	3.91[b]	0.04208	-2.67[b]	0.45746	-	0.18	0.68	1.01
Swain and Lupton F and R[b] 60 MHz	6	0.893	0.0934	3.74[b]	0.05039	-1.95[b]	0.58915	-	-0.16	0.70	1.05

a i.e. using σ_I and σ_R values from Ref. 52 for $-CH_2F$ and $-CH_2OCH_3$ substituents.

b These parameters do not have the same significance as in Taft's analysis.

Table XXIII. Linear least squares correlation of substituent chemical shifts and Brown[129] σ^+ values for substituted-1-fluoromethylnaphthalenes and substituted benzyl fluorides and calculated σ^+ values.

Correlation	n	ρ	INTERCEPT	r	S.D.
Δφ Substituted-1-fluoromethylnaphthalene[a] vs. σ^+	13	9.34	-0.25	0.916	1.48
Δφ Substituted benzyl fluoride vs. σ^+	14	9.92	-0.30	0.982	0.86

[a] Data for 3-COOMe and 3-COOEt omitted.

Calculated σ^+ values

	σ^+
3-$COCH_3$	+0.059
4-$COCH_3$	+0.634
3-CH_2F	+0.161
4-CH_2F	+0.166
4-CH_2OCH_3	+0.006
4-$COCH_2F$	+0.744

Table XXIV. Observed and calculated substituent chemical shift values for 4-substituted-1-fluoromethylnaphthalenes measured at 100 MHz.

ρ_I = 8.477, ρ_R = 16.912, INTERCEPT = 0.252

Substituent	σ_I	$\sigma_{R(BA)}$	Δφ calculated	Δφ observed	Difference
CH_3	-0.04	-0.11	-1.95	-2.51	.56
F	+0.05	-0.45	-3.12	-2.81	.31
Cl	+0.46	-0.23	+0.26	+0.25	.01
Br	+0.44	-0.19	+0.77	+0.76	.01
CN	+0.56	+0.13	+7.20	+7.10	.1
$COOCH_3$	+0.30	+0.14	+5.16	+5.89	.73
$COOC_2H_5$	+0.30	+0.14	+5.16	+5.56	.40
NO_2	+0.65	+0.15	+8.30	+7.46	.84
$COCH_3$	+0.28	+0.16	+5.33	+5.67	.34

Table XXV. Observed and calculated substituent chemical shift values for 3-substituted-1-fluoromethylnaphthalenes measured at 100 MHz.

(a) ρ_I = 7.080, ρ_R = -5.341, INTERCEPT = -0.613

Substituent	σ_I	$\sigma_{R(BA)}$	Δφ calculated	Δφ observed	Difference
CH_3	-0.04	-0.11	-0.31	+0.13	.44
Br	+0.44	-0.19	+3.52	+2.89	.63
CN	+0.56	+0.13	+2.66	+3.95	1.29
$COOCH_3$	+0.30	+0.14	+0.76	-0.07	.83
$COOC_2H_5$	+0.30	+0.14	+0.76	-0.13	.89
NO_2	+0.65	+0.15	+3.19	+3.42	.23
$COCH_3$	+0.28	+0.16	+0.51	+0.30	.21

(b) ρ_I = 7.672, ρ_R = -3.141, INTERCEPT = -0.434

Substituent	σ_I	$\sigma^-_{R(A)}$	Δφ calculated	Δφ observed	Difference
CH_3	-0.04	-0.11	-0.40	+0.13	.53
Br	+0.44	-0.19	+3.54	+2.89	.65
CN	+0.56	+0.33	+2.83	+3.95	1.12
$COOCH_3$	+0.30	+0.34	+0.80	-0.07	.87
$COOC_2H_5$	+0.30	+0.34	+0.80	-0.13	.93
NO_2	+0.65	+0.46	+3.11	+3.42	.31
$COCH_3$	+0.28	+0.47	+0.24	+0.30	.06

(c) ρ_I = 6.978, ρ_R = -2.026, INTERCEPT = -0.094

Substituent	σ_I	$\sigma^-_{R(A)}$	Δφ calculated	Δφ observed	Difference
CH_3	-0.04	-0.11	-0.15	+0.13	.28
Br	+0.44	-0.19	+3.36	+2.89	.47
CN	+0.56	+0.33	+3.14	+3.95	.81
NO_2	+0.65	+0.46	+3.51	+3.42	.09
$COCH_3$	+0.28	+0.47	+0.91	+0.30	.61

(ii) Single Substituent Parameter Correlations.

In his analysis of ^{19}F substituent chemical shifts Béguin[45] reported a good correlation with the σ^+ constants of Brown and Okamoto[129]:-

$$\Delta\phi = +9.76\ \sigma^+ - 0.27 \quad (r = 0.976)$$

A similar correlation was undertaken with the fluoromethylnaphthalene data using a program to calculate the slope and intercept for linear free energy single substituent parameter correlations by a linear least squares method.

Analysis of benzyl fluoride data was also repeated using this computer program. Results for both data sets are shown in Table XXIII. From the values of slope and intercept obtained for the fluoromethylnaphthalenes, σ^+ values were calculated for m-CH_2F, p-CH_2F, p-$COCH_2F$, p-CH_2OCH_3, m-$COCH_3$ and p-$COCH_3$ substituents. A graph of this relationship was drawn (Fig. 3) and these substituents are indicated on this graph.

(iii) Comparison of Fluoromethylnaphthalene and Benzyl Fluoride Data

A graph (Fig. 4) of substituent chemical shifts was plotted for substituents where both benzyl fluoride and fluoromethylnaphthalene data were available. This was in order to determine if there were any specific deviations between the two data sets. In fact, it appears that the fluoromethylnaphthalene data correlates quite well with the benzyl fluoride data and hence the differences between the dual substituent parameter correlations for the two series must arise from the behaviour of those substituents which are not common to the two series.

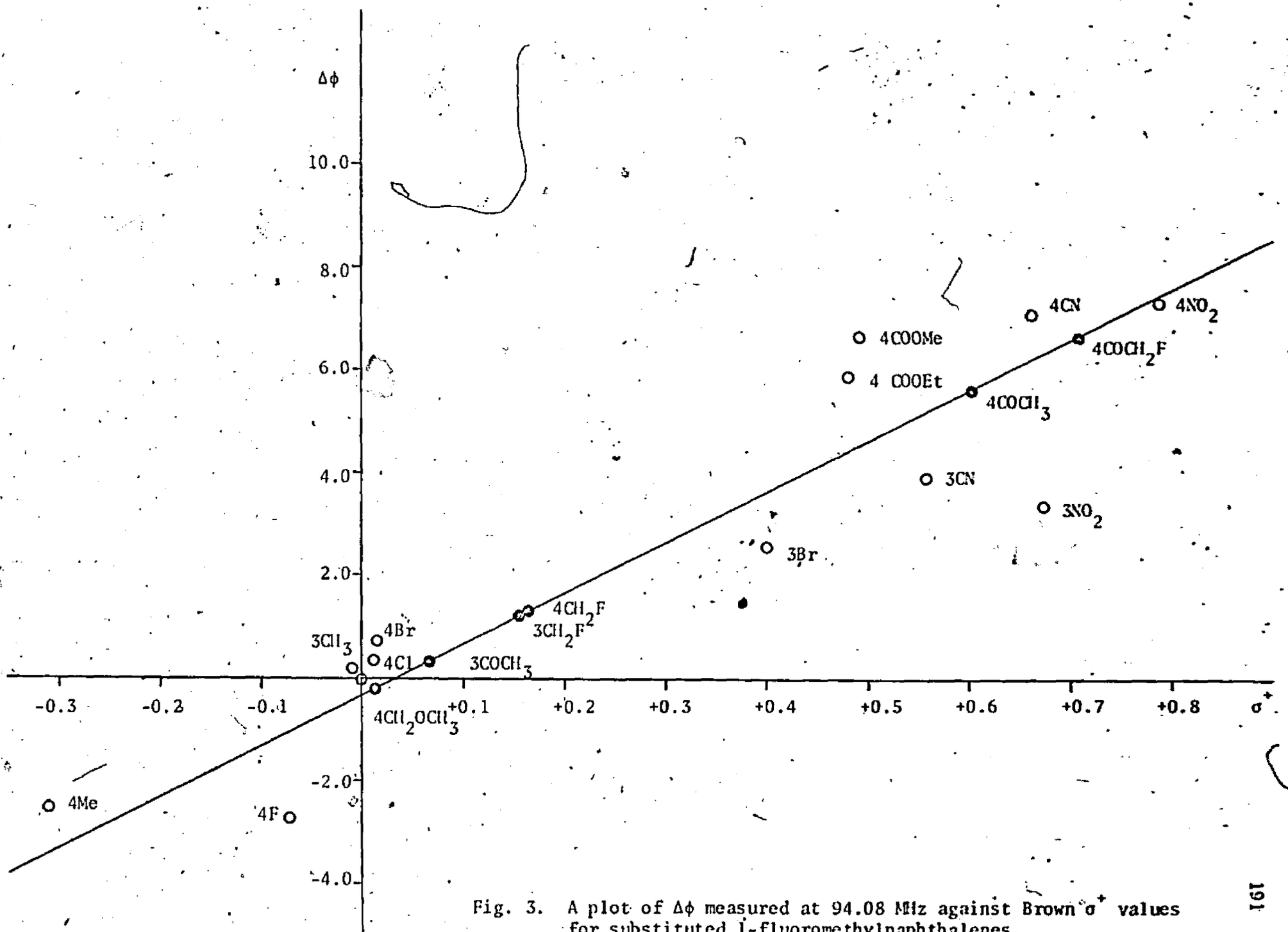


Fig. 3. A plot of Δφ measured at 94.08 Mhz against Brown σ^+ values for substituted 1-fluoromethylnaphthalenes.

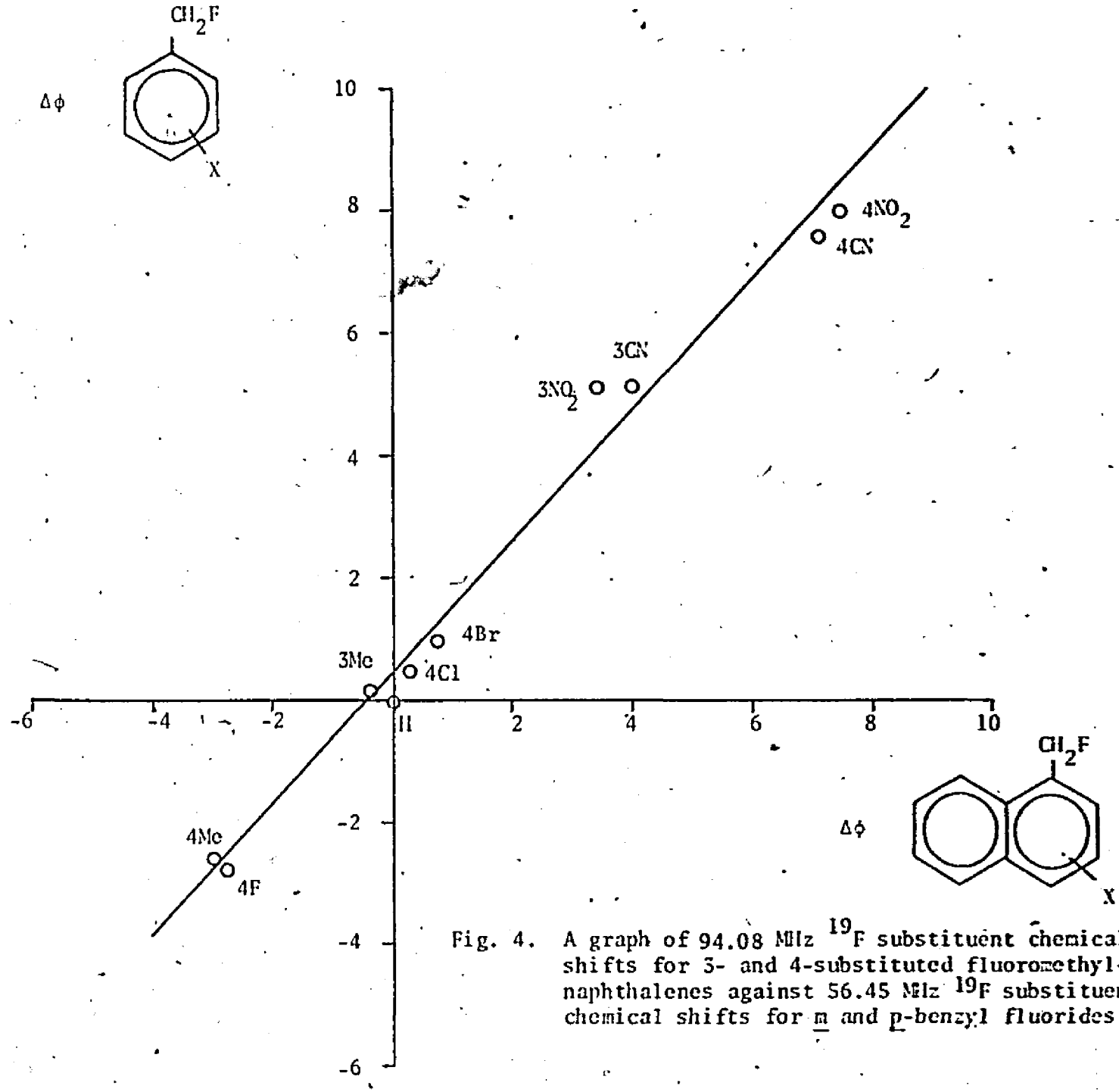


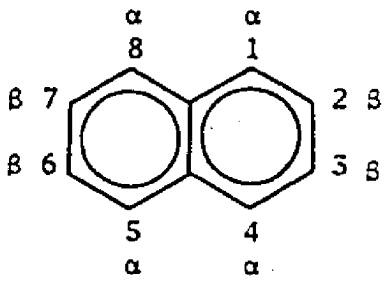
Fig. 4. A graph of 94.08 MHz ^{19}F substituent chemical shifts for 3- and 4-substituted fluoromethylnaphthalenes against 56.45 MHz ^{19}F substituent chemical shifts for m and p-benzyl fluorides.

CHAPTER 4

DISCUSSION

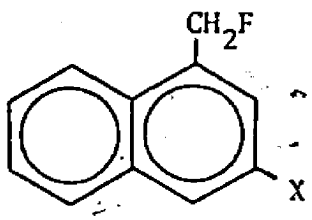
Spectral Characteristics of Substituted Naphthalenes

It is appropriate at this point to mention several of the terms used to describe the various positions and positional relationships in the naphthalene system. Naphthalene positions are numbered as shown and may also be referred to generally as α and β positions.

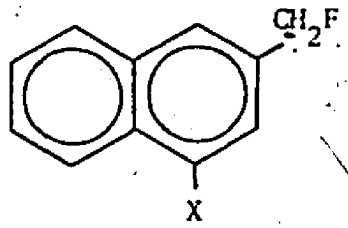


The 1,8-α,α interaction and the 4,5-α,α interaction are the 'peri' interactions in the naphthalene system.

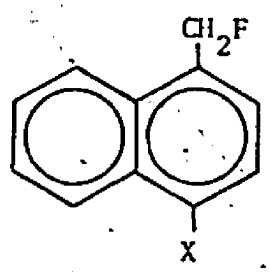
Relative dispositions of substituent and reaction site referred to in this study are:-



3α



4β



4α

In this system of nomenclature for the disubstituted naphthalenes the position of the side-chain functional group (CH_2F) is designated as α or β as appropriate and the position of the substituent is then indicated by the position number, the ring being numbered from the functional group position as 1 (for α) or 2 (for β).

i) Infrared Spectra

Infrared spectra were recorded of all substituted naphthalenes synthesised and details of these spectra are included in the experimental section. In most cases these spectra were used to confirm the identity of the compounds. Absorptions were assigned based on group absorption frequencies recorded in 'An Introduction to Practical Infra-Red Spectroscopy' by Cross and Jones.[130] However, one or two of the infrared spectroscopic characteristics are worthy of particular note.

Absorptions in the 860-730 cm^{-1} region of the spectrum are due to C-H out-of-plane vibrations. The hydrogen substitution pattern for each ring can be considered separately. 1-Substituted naphthalenes show absorptions in the regions 810-785 and 780-760 cm^{-1}, characteristic of three and four adjacent hydrogens respectively. 2-Substituted naphthalenes absorb at 860-835, 835-805 and 760-735 cm^{-1}, characteristic of an isolated hydrogen atom, two adjacent hydrogen atoms and four adjacent hydrogen atoms respectively.[*] 1,4-Disubstituted naphthalenes therefore show absorptions in the regions 835-805 and 780-735 cm^{-1}, and 1,3-disubstituted naphthalenes in the regions 860-835 and 780-735 cm^{-1}.

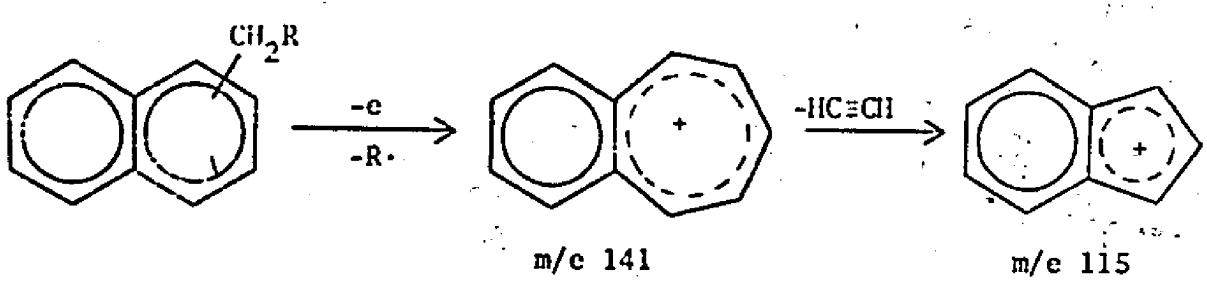
Two substituent group frequencies that were of considerable value in spectral assignments were those due to the aliphatic C-Br stretching

vibration between 600-615 cm^{-1} and the aliphatic C-F stretching vibration at 1070-1060 cm^{-1}. This latter band was very strong and varied very little in its position. The force constants for the CH_2-X bonds calculated from the measured CH_2-Br and CH_2-F stretching frequencies and from that listed for CH_2-Cl[130] (690 cm^{-1}) are C-F, 1.29×10^6; C-Br, 1.23×10^6 and C-Cl, 8.01×10^5 dynes/cm. These values follow trends for other bond characteristics of C-halogen bonds, such as bond energy and bond length.

The spectrum of 1-fluoromethylnaphthalene is shown in Figs. 5 and 6 as characteristic of the spectra of this class of compounds.

ii) Mass Spectra

As is characteristic of aromatic compounds, and in particular alkyl substituted aromatic hydrocarbons, the fluoromethylnaphthalenes gave mass spectra which exhibited strong molecular ion peaks. The most characteristic cleavage of the alkyl benzenes occurs at the bonds beta to the aromatic ring, the fragment ion rearranges to the tropylium ion, which itself loses acetylene in a metastable transition. An analogous fragmentation pattern is observed in methylene substituted naphthalenes and has been described by Budzikiewicz, Djerassi and Williams.[131]



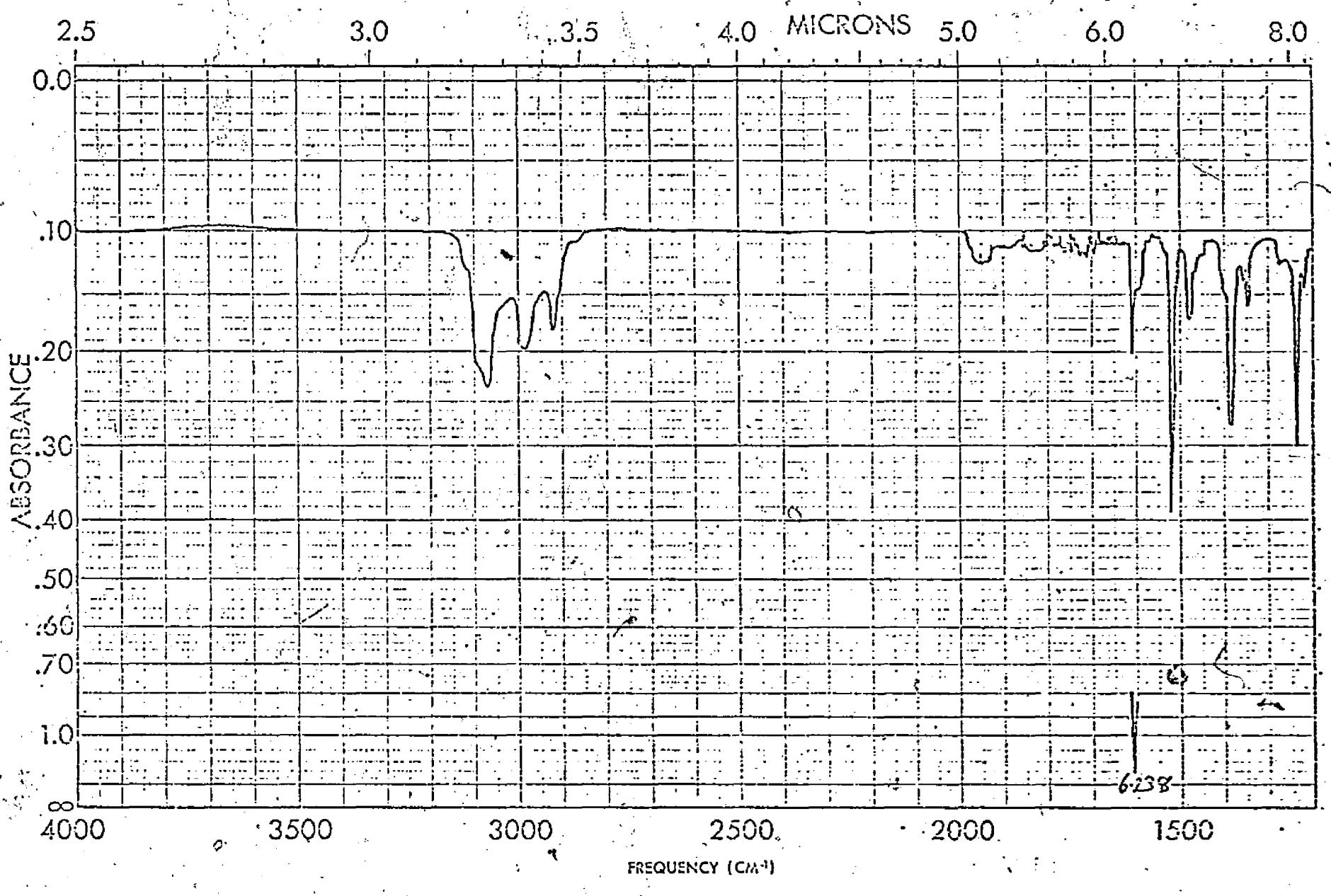


Fig. 5. Infrared spectrum of 1-fluoromethylnaphthalene between 4000-1200 cm^{-1}.

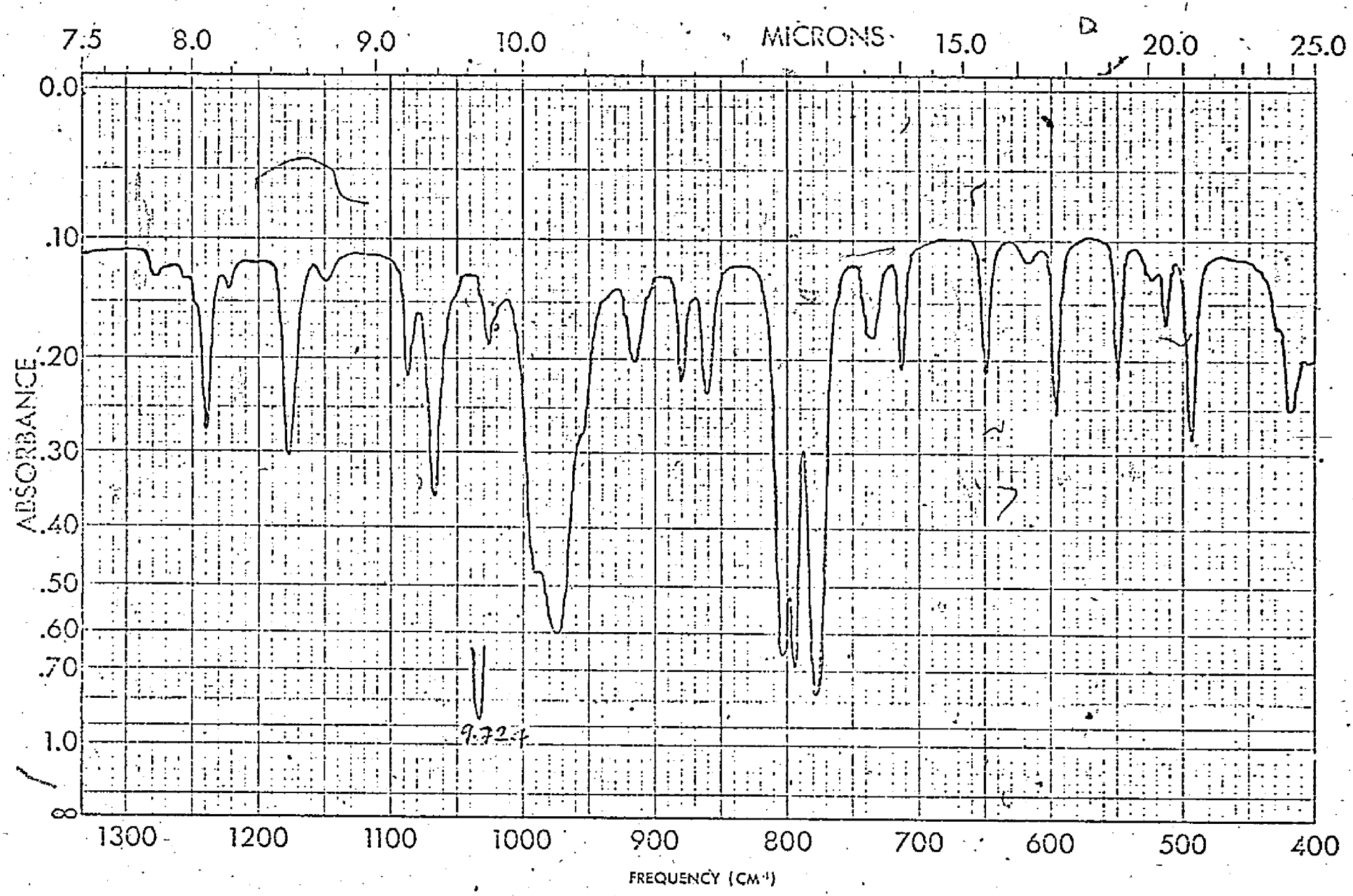


Fig. 6. Infrared spectrum of 1-fluoromethylnaphthalene between 1330-400 cm^{-1}.

The metastable peak corresponding to this fragmentation has an m/e value of $(115)^2/141 = 93.8$. This peak was not observed and so must have been of very low intensity. Numerous relatively intense doubly charged peaks are very prominent in the spectra of most of the naphthalene derivatives prepared. Another mass spectral feature worthy of mention is the increased relative abundance of the molecular ion peak of the fluoromethylnaphthalenes compared to naphthalenes bearing other substituents; in many instances the molecular ion peak is also the base peak. Presumably this is due to the strength of the C-F bond. The mass spectrum of 1-fluoromethylnaphthalene is shown in Fig. 7 and exhibits many of these spectral features discussed. Details of the most prominent peaks to be found in the spectra of the substituted naphthalenes prepared, together with values for their relative abundances, are given in the experimental section.

iii) Nuclear Magnetic Resonance Spectra

Naphthalene itself is an eight spin system with the chemical shifts of the two multiplets due to the α and β protons being found at τ 2.315 p.p.m. and τ 2.66 p.p.m. respectively. It is only recently[132] that naphthalene has been analysed as an eight spin system and the sign and magnitudes of the various coupling constants assigned. Previous to this study, this system had always been considered as an AA'BB' case.

In the absence of strongly deshielding substituents two groups of multiplets corresponding to four β and two α protons could be discerned in the spectra of 1,4-disubstituted naphthalenes, and two multiplets each integrating for three protons in 1,3-disubstituted naphthalenes.

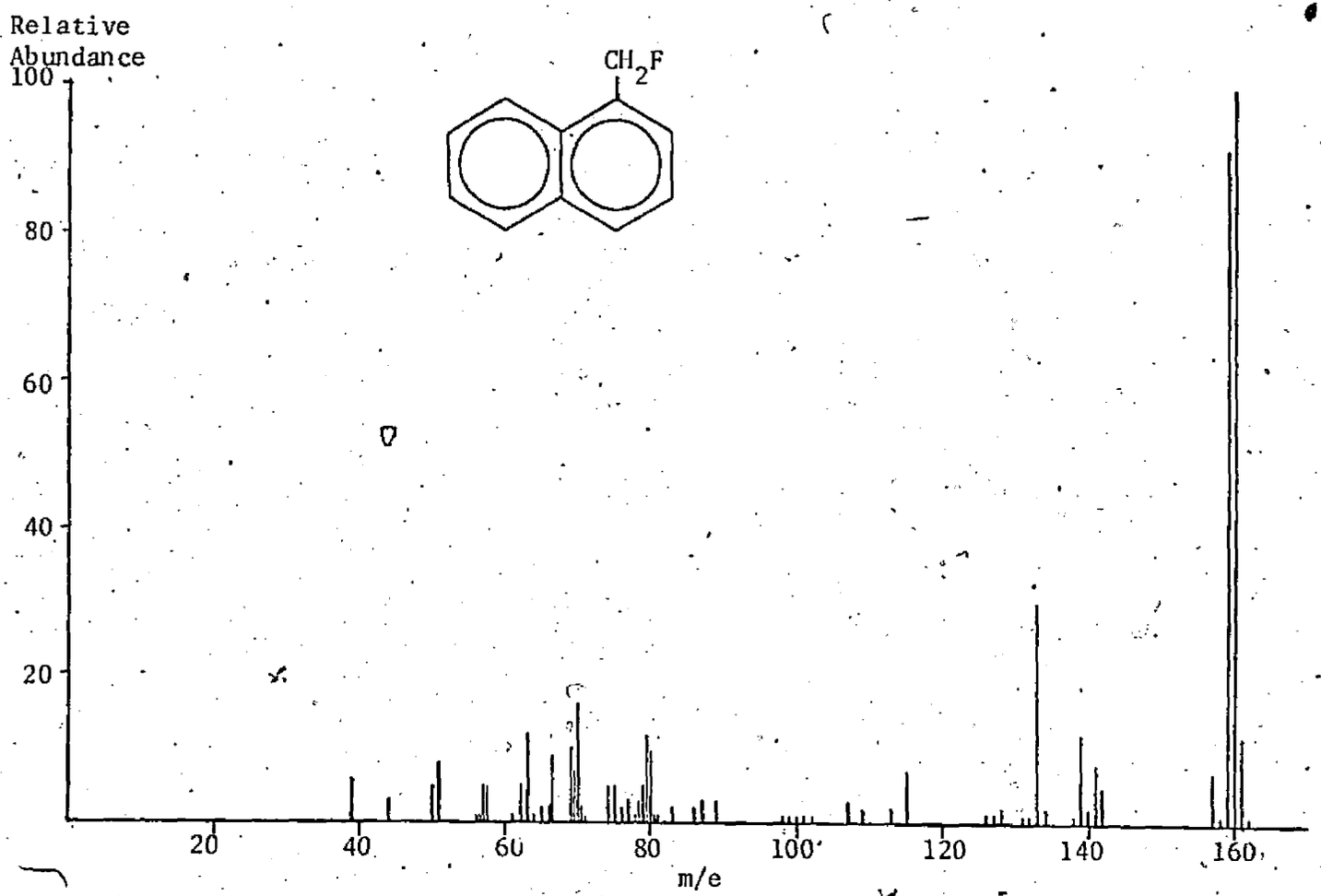


Fig. 7. Mass spectrum of 1-fluoromethylnaphthalene.

m/e	%		m/e	%
162	1	P+2	81	1
161	12	P+1	80.5	1
160	100		80	10
159	92		79.5	12
158	1		79	5
157	7		78.5	3
142	5		78	1
141	8		77	3
140	2		76	2
139	12		75	5
138	1		74	5
134	2		71	1
133	30		70.5	2
132	1		70	16
131	1		69.5	7
128	2		69	10
127	1		66.5	9
126	1		65	2
115	7		64	1
113	2		63	12
109	2		62	5
107	3		61	1
102	1		57.5	5
101	1		57	5
100	1		56.5	1
99	1		56	1
98	1		51	8
89	3		50	5
87	3		44	3
86	2		39	6
83	2			

In most cases deshielding substituents were present and so these patterns were obscured. The n.m.r. signals due to the substituents of the substituted naphthalenes were simple in nature.

The spectra of methyl substituted naphthalenes showed an unusual characteristic, which at first was thought due to an impurity in the samples. Subsequently a paper appeared in the literature[133] which reported this signal as real and not an artefact. In the n.m.r. spectrum of methyl substituted naphthalenes the α-methyl absorption is unusually complex as a result of benzylic coupling. The signal is an asymmetric doublet. By use of an iterative computer technique coupling constants of

$$J_{CH_3,2\text{-}H} = -0.75 \text{ Hz}, \quad J_{CH_3,3\text{-}H} = +0.40 \text{ Hz}, \quad J_{CH_3,4\text{-}H} = 0.65 \text{ Hz}$$

were obtained for 1,8-dimethylnaphthalene. To illustrate this benzylic coupling the region τ 7-8 p.p.m. of the spectrum of 4-methyl-1-naphthylcarbinol is shown in Fig. 8. The splitting, as shown, is about 0.75 Hz.

Multiple regression analysis of the 3-substituted-1-fluoromethylnaphthalene series gave rise to results that indicated serious deviations from the predicted model for this system. The source of five of the compounds in this series was via a common route which involved the separation of isomers, and so it was considered necessary to establish the authenticity of these derivatives. The 3-acetyl, 3-bromo, 3-cyano, 3-methyl ester and 3-ethyl ester derivatives were all prepared indirectly from 3-bromo-1-methylnaphthoate. This ester was prepared from naphthalic anhydride by bromination to yield 3-bromo-1,8-naphthalic anhydride. One

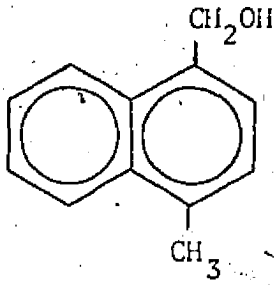


Fig. 8. ^{1}H N.m.r. spectrum of 4-methyl-1-naphthylcarbinol in the region τ 7-8 p.p.m.

J = 0.75 Hz

of the carboxylate functions was removed by mercuration and subsequent hydrolysis to yield the 3-bromo- and 6-bromo-1-naphthoic acids; the isomers were separated by recrystallisation from glacial acetic acid and the 3-bromo-1-naphthoic acid obtained was esterified with diazomethane to yield 3-bromo-1-methylnaphthoate. It was therefore necessary to confirm the identity of the 3-bromo-1-methylnaphthoate obtained in this manner. Two n.m.r. spectral methods were used in this confirmation of the orientation of the substituents in the naphthalene nucleus.

A lanthanide shift reagent, europium tris[1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate] [$Eu(fod)_3$] was added to a solution of 3-bromo-1-methylnaphthoate in carbon tetrachloride in one study and to an authentic sample of 3-nitro-1-methylnaphthoate in a parallel experiment. The shift reagent is known to coordinate preferentially via the carbonyl oxygen of the ester function[134]; it has also been shown by n.m.r. studies[39] that in 1-naphthaldehyde the carbonyl function spends more time in the plane of the naphthalene nucleus and pointing towards the 8-(peri) hydrogen. If one assumes a similar preferred conformation in the case of the ester function the proton closest to the coordinated shift reagent is the 8-hydrogen.

It has been shown that the main contribution to the observed lanthanide chemical shift is the pseudo-contact term which shows strong dependence on the geometrical position of the observed nucleus with respect to the central ion. There is a r^{-3} dependence of this shift and therefore the magnitude decreases rapidly with distance. For this reason it is possible to assign the various protons within a molecule; the proton closest to the lanthanide ion will show the largest downfield shift.

In the case of the two compounds investigated the spectra recorded in the absence of shift reagent do not resemble each other, nor do they appear to consist of similar components. However, on addition of shift reagent the signals moving to lower field at a more rapid rate are virtually identical. The order of the magnitude of the induced chemical shift was assigned 8H > 2H > 4H > 5H∿7H > 6H. The signals were then assigned to the various protons in the spectrum (Fig. 11) with no shift reagent added. The spectra with shift reagent added are shown in Figs. 9, 10.

The second study involved the recording of the n.m.r. spectrum of 3-bromo-1-methylnaphthoate in carbon tetrachloride solution at 220 MHz. At this field strength the spectrum is approaching first order and is thus far more readily interpreted. The spectrum with its assignments appears as Fig. 11. The signals were assigned on the basis of the magnitude of coupling constants reported by Crecely[132] and Goldstein and chemical shift considerations. The largest coupling is between adjacent α- and β-protons; for naphthalene itself this value is 8.28 Hz. Couplings of 8.5 and 8.2 Hz were measured in the spectrum of 3-bromo-1-methylnaphthoate. The doublet of doublets at 1896.2 Hz was assigned to the 8-H on the basis of its chemical shift. This α-proton is positioned adjacent to the carbonyl group of the ester function and therefore experiences a large downfield shift. The coupling of the 7-H and 8-H (8.5 Hz) identifies the group of signals due to the 7-H centred at 1599.75 Hz. The 8-H is also split by the 6-H with a coupling constant of 1.1 Hz (1.24 Hz in the case of naphthalene); this splitting identifies the 6-H centred at 1579.5 Hz. The 6-H shows three different splittings: $J_{6,7}$ (6.7 Hz), $J_{5,6}$ (8.2 Hz) and $J_{6,8}$ (1.1 Hz). The corresponding

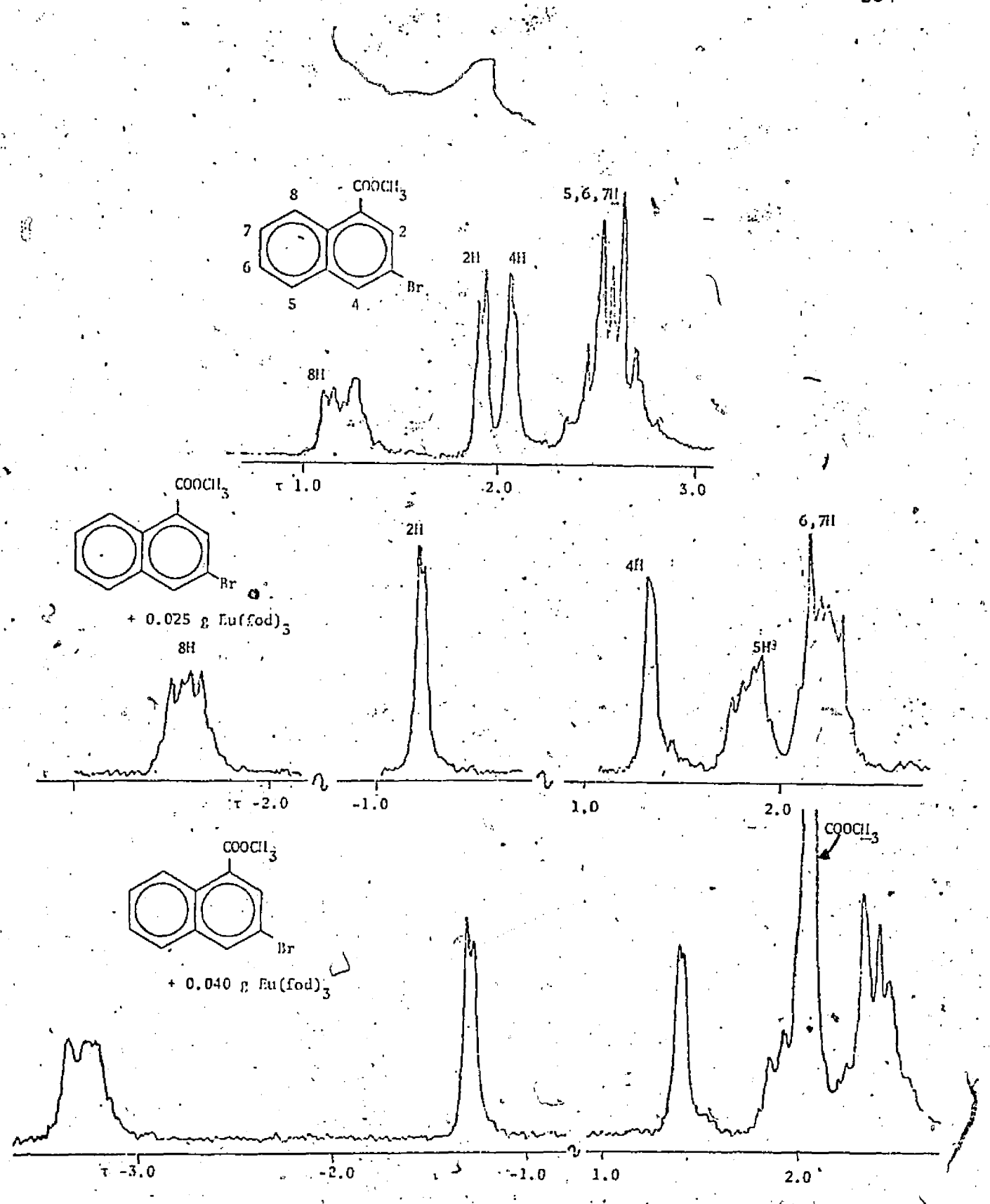


Fig. 9. 60 MHz ^{1}H N.m.r. spectra of 3-bromo-1-methylnaphthoate with different concentrations of Eu(fod)$_3$ added.

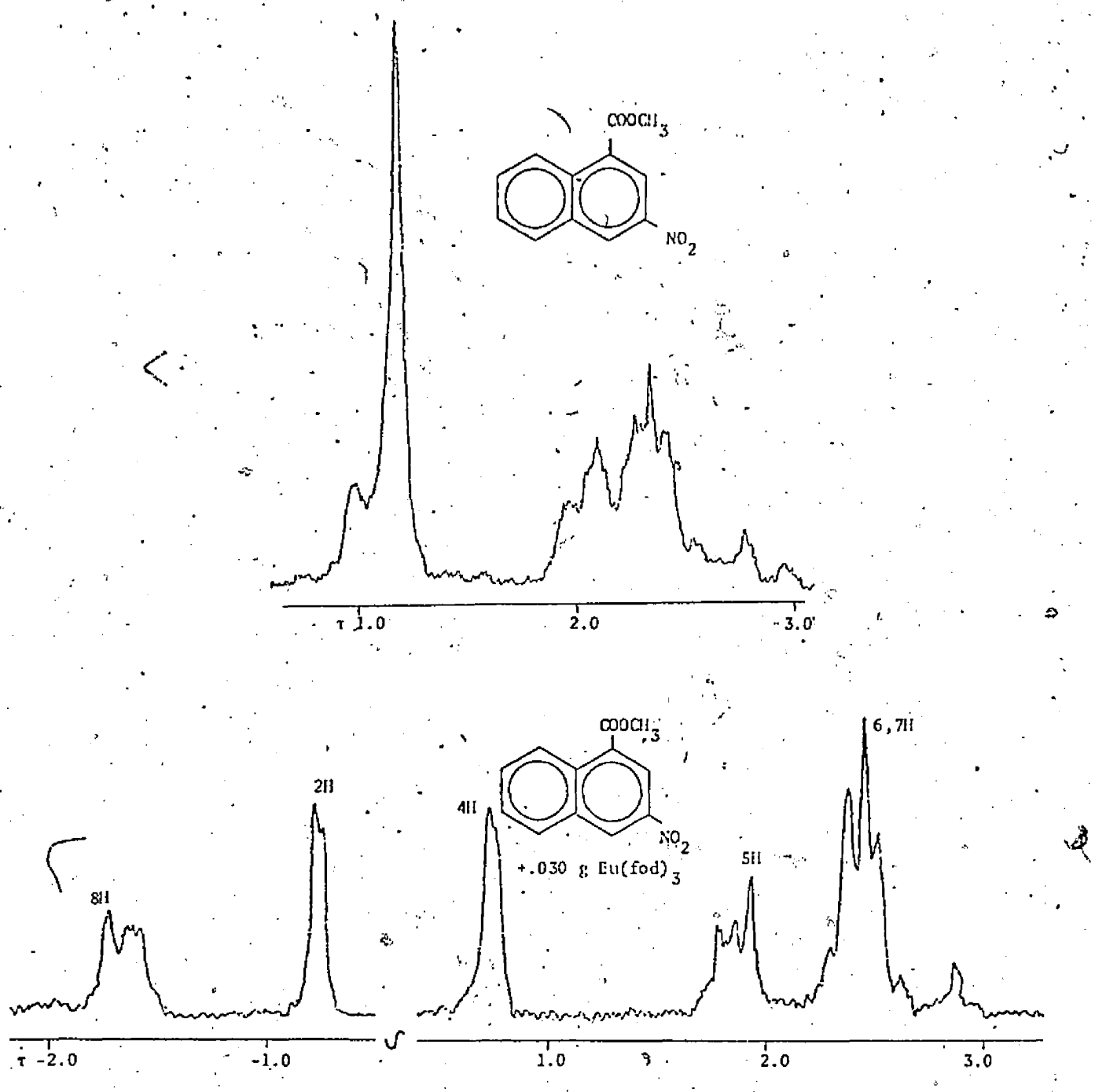


Fig. 10. 60 MHz ^{1}H n.m.r. spectra of (i) 3-nitro-1-methylnaphthoate, (ii) 3-nitro-1-methylnaphthoate with 0.030 g $Eu(fod)_3$ added to the $CDCl_3$ solution.

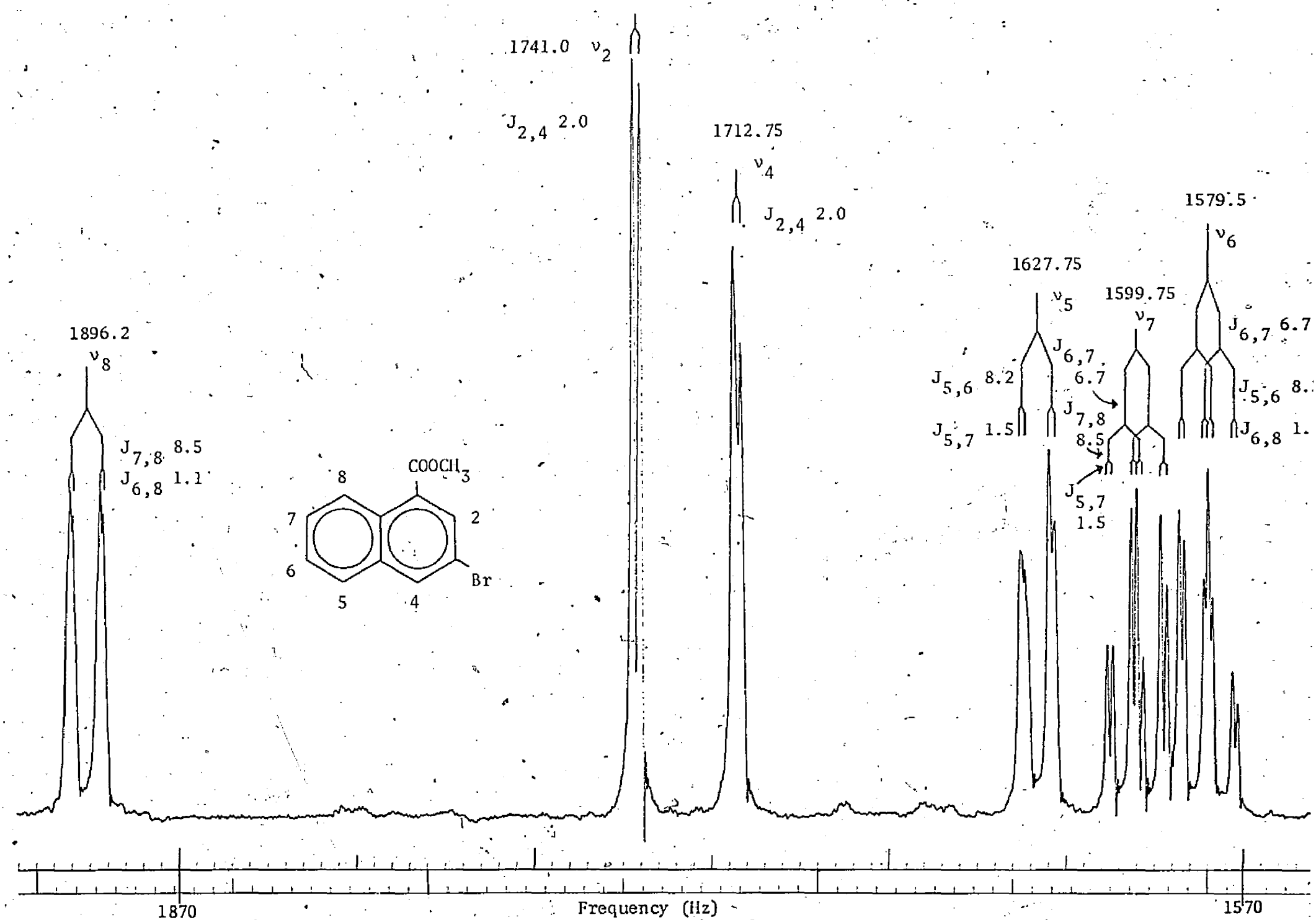


Fig. 11. 220 MHz ^{1}H n.m.r. spectrum of 3-bromo-1-methylnaphthoate.

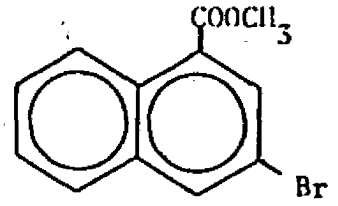
splittings are seen in the 5-H, 6-H and 7-H signals. The coupling constant $J_{5,6}$ (8.2 Hz) assigns the signal at 1627.75 to the 5-H. This signal is further split by the 7-H, $J_{5,7}$ = 1.5 Hz. The only peaks left unassigned are those at 1741.0 Hz and 1712.75 Hz, these being due to the 2- and 4-protons, coupled to each other with a coupling constant of 2.0 Hz. The doublet at lower field was assigned to the 2-H on chemical shift criteria (this proton is adjacent to the deshielding ester function) and on the criterion of the two peaks of the doublet being sharper than in the case of the 4-H. The 2-H will only be coupled to the 4-H, whereas the latter will show coupling with the 5-H (in naphthalene $J_{4,5}$ = -0.45 Hz) and thus show broadening of the doublet.

These values of coupling constants and chemical shifts measured from the 220 MHz spectrum of 3-bromo-1-methylnaphthoate were used as input data for the iterative computer program for the calculation of n.m.r. spectra developed by Harris and Woodman[135] at the University of East Anglia. The computed spectrum of 3-bromo-1-methylnaphthoate is shown in Fig. 12 and the refined chemical shifts and coupling constants together with the values measured from the experimental spectrum appear in Fig. 13.

As was mentioned previously, the n.m.r. pattern of the aromatic protons of 1,3- and 1,4-disubstituted naphthalenes was in most instances complex. However there were one or two exceptions of symmetrically substituted naphthalenes that showed both distinctive and relatively more simple patterns in the aromatic region of their spectra. Two examples of these 1,4-bisbromomethylnaphthalene and 1,4-dinaphthoic acid are shown in Fig. 14. Also included is the Varian catalogue[95] spectrum

Fig. 12. 220 ^{1}H N.m.r. spectrum of 3-bromo-1-methylnaphthoate generated by iterative n.m.r. computer program UEAVIC

Sweep width = 500 Hz



208

1910 Frequency (Hz) 1410

Figure 13. ^{1}H n.m.r. chemical shifts and coupling constants for 3-bromo-1-methylnaphthoate (a) measured at 220 MHz and, (b) generated by iterative n.m.r. computer program UEAVIC.

(a) Values measured at 220 MHz

ν_2	1741.0 Hz	J_{24}	2.0 Hz
ν_4	1712.75 Hz	J_{56}	8.2 Hz
ν_5	1627.75 Hz	J_{57}	1.5 Hz
ν_6	1579.5 Hz	J_{67}	6.7 Hz
ν_7	1599.75 Hz	J_{68}	1.1 Hz
ν_8	1896.2 Hz	J_{78}	8.5 Hz

(b) Values generated by UEAVIC

REFINED PARAMETERS AFTER 4 ITERATIONS

ν_2	1740.843 Hz	J_{24}	2.048 Hz
ν_4	1712.905 Hz	J_{25}	0.119 Hz
ν_5	1627.596 Hz	J_{26}	-0.004 Hz
ν_6	1580.638 Hz	J_{27}	-0.004 Hz
ν_7	1599.353 Hz	J_{28}	-0.092 Hz
ν_8	1896.165 Hz	J_{45}	-0.123 Hz
		J_{46}	-0.005 Hz
		J_{47}	-0.001 Hz
		J_{48}	0.337 Hz
		J_{56}	8.613 Hz
		J_{57}	1.088 Hz
		J_{58}	0.207 Hz
		J_{67}	6.789 Hz
		J_{68}	0.557 Hz
		J_{78}	8.894 Hz

of 1,4-dinitronaphthalene. These three spectra show two separate multiplets due to the α and β protons on the unsubstituted ring (the α protons at lower field) and a sharp singlet arising from the β protons on the substituted ring. The chemical shift of this signal is dependent upon the nature of the 1,4-substituents.

In Fig. 15 is the spectrum of naphthalene itself and below this the computed spectrum of naphthalene with the relevant parameters as reported by Crecely and Goldstein.[132]

Fig. 16 shows a typical ^{19}F spectrum from which $\Delta\phi$ and J values were recorded during this study. The lower spectrum shows the triplets due to 1-fluoromethyl-4-methoxymethylnaphthalene and 1-fluoromethyl-naphthalene. The central peaks of the two triplets are separated by 16.0 Hz, but this value is far more readily measured from the decoupled spectrum. This comprises a pair of sharp singlets which integrate in a ratio of approximately 2:1. The coupling constant in the lower spectrum is 47.7 Hz for the 4-substituted derivative. Not all the spectra were as well resolved as this example but the decoupled spectra were in most cases sharp singlets.

The proton spectra were far more troublesome in that chemical shift differences were very small and most of the spectra could not be decoupled so that measurements were often made on poorly resolved spectra.

Fig. 14. ^{1}H N.m.r. spectrum of (a) 1,4-bisbromomethylnaphthalene, (b) 1,4-dinaphthoic acid, (c) 1,4-dinitronaphthalene.[95]

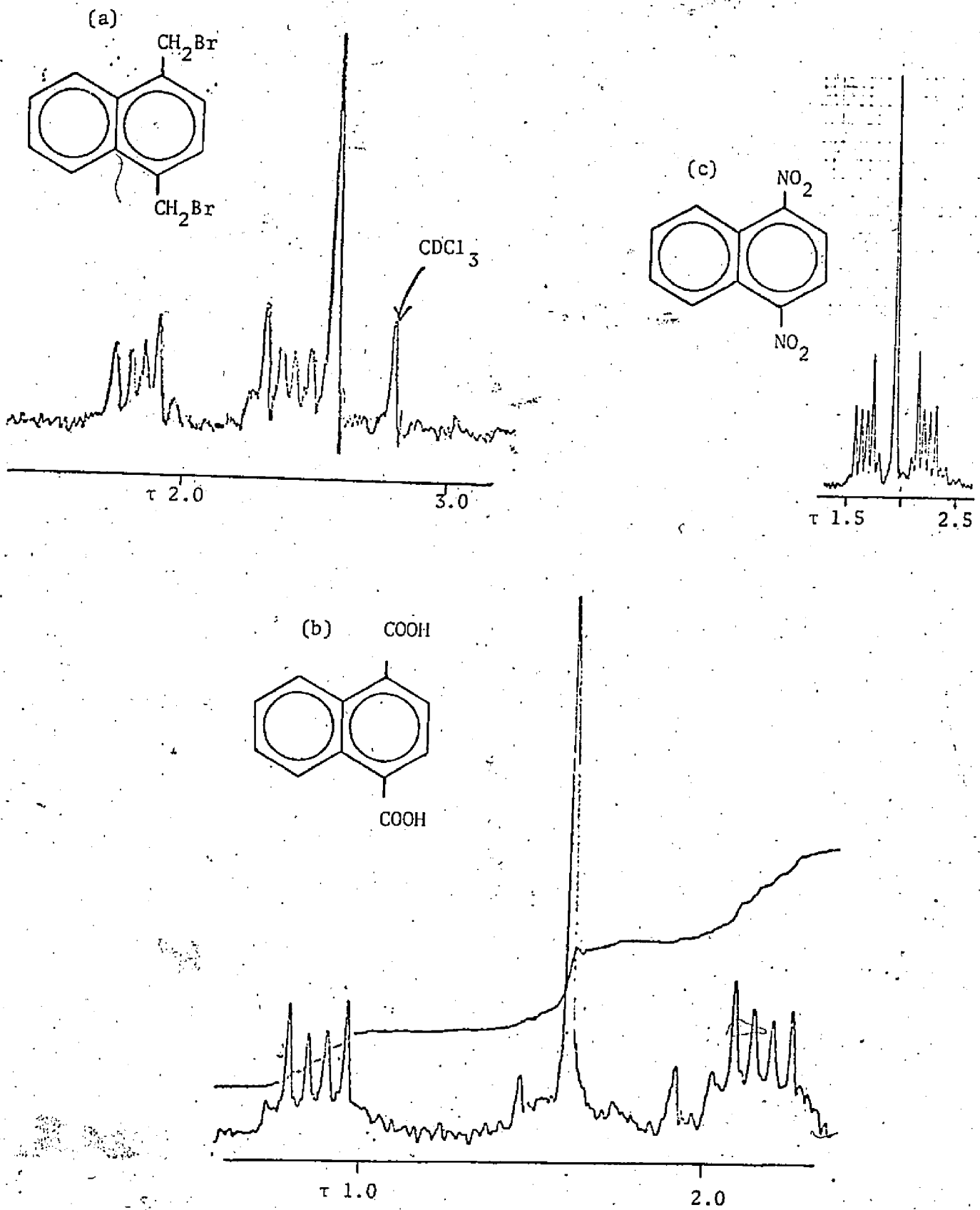
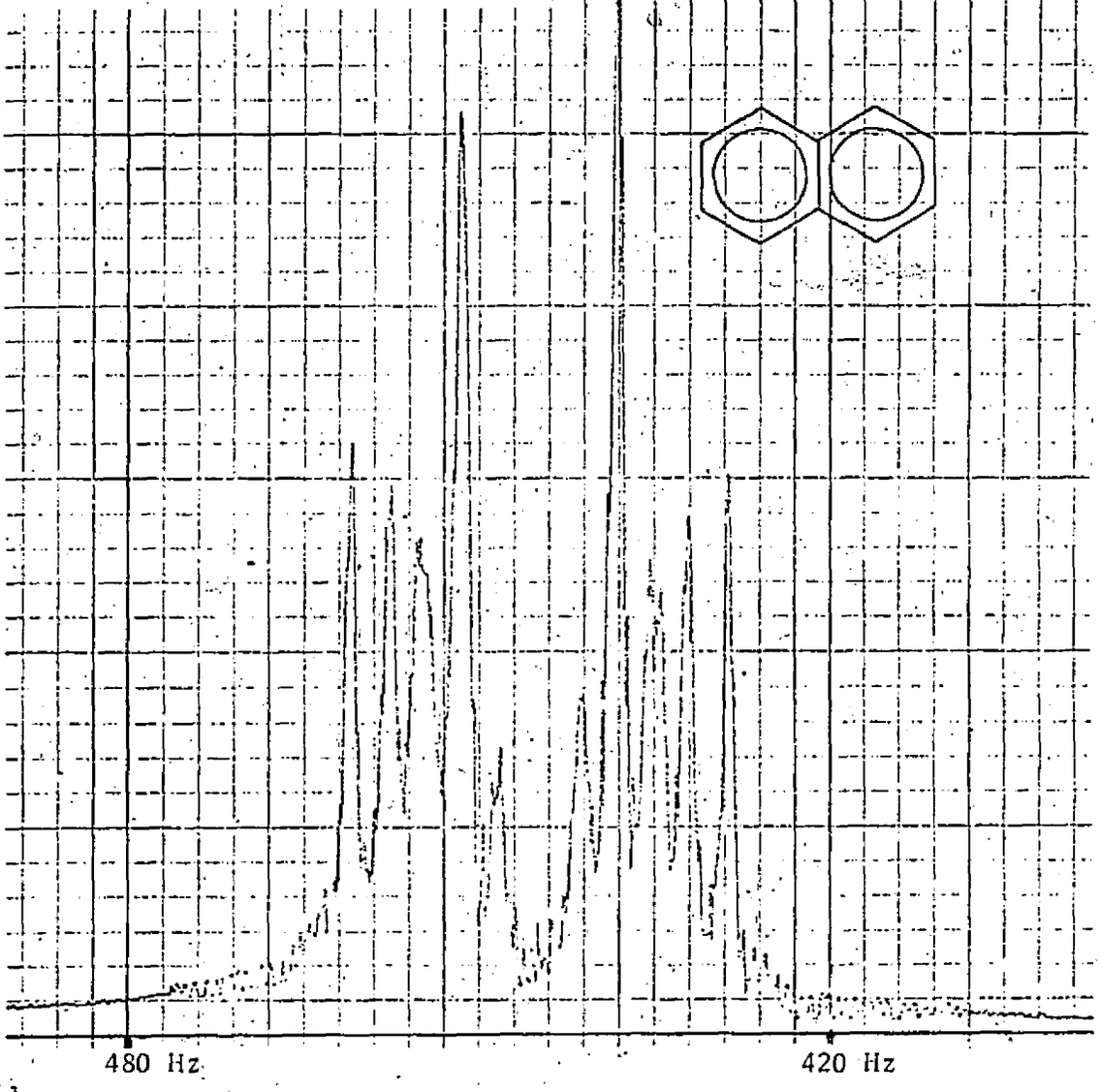
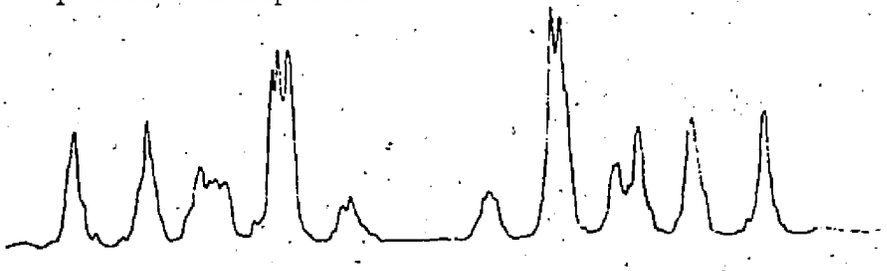


Fig. 15. (a) ^{1}H N.m.r. spectrum of naphthalene, (b) Calculated spectrum of naphthalene with values for chemical shifts and coupling constants.



(a) ^{1}H N.m.r. spectrum of naphthalene

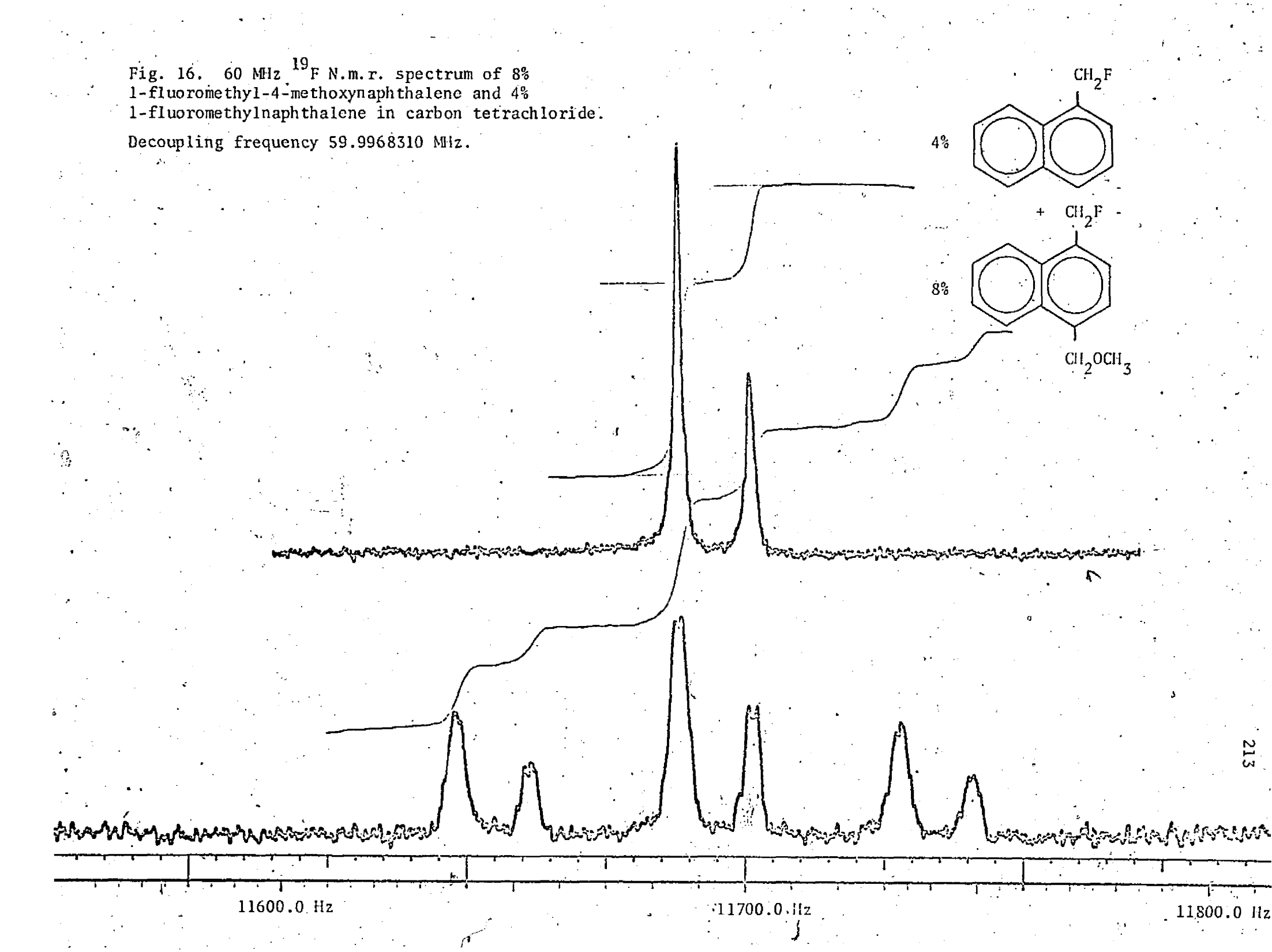


(b) Calculated spectrum and parameters[132] measured in Hz.

ν_1,ν_4,ν_5,ν_8	461.1	J_{18},J_{45}	-0.45	J_{14},J_{58}	0.74
ν_2,ν_3,ν_6,ν_7	440.3	J_{23},J_{67}	6.85	J_{15},J_{48}	0.85
$J_{12},J_{34},J_{56},J_{78}$	8.28	J_{26},J_{37}	0.25	$J_{16},J_{25},J_{38},J_{47}$	-0.10
$J_{13},J_{24},J_{57},J_{68}$	1.24	J_{27},J_{36}	0.10	$J_{17},J_{28},J_{35},J_{46}$	0.23

Fig. 16. 60 MHz ^{19}F N.m.r. spectrum of 8% 1-fluoromethyl-4-methoxynaphthalene and 4% 1-fluoromethylnaphthalene in carbon tetrachloride.

Decoupling frequency 59.9968310 MHz.



Fluoromethylnaphthalene N.M.R. Parameters

The ^{19}F substituent chemical shift values, $\Delta\phi$, are listed together in Table IV. With only a few exceptions discussed further below the degree of correspondence between shifts measured at 100 MHz and 60 MHz is extremely good (in most cases $\pm$ 0.06 p.p.m.; in the case of 3-Br $\pm$ 0.30 p.p.m.). The substituent chemical shifts are discussed below in groups according to their electronic effects in this system:-

(a) Substituents with a net electron-donating effect (4-CH_3, 4-F, 4-CH_2OCH_3)

These substituents all give rise to a fluoromethylnaphthalene signal at lower field than in the reference compound. Both -CH_3 and -F exhibit strong electron-donating influences through resonance interactions with the aromatic nucleus; the -CH_3 group does this by means of proton hyperconjugation and the -F group by means of resonance overlap between electrons in the 2p orbitals on the fluorine and 2p orbitals on the carbon atom. The 4-CH_2OCH_3 group, according to Sheppard,[52] has a σ_I value of -0.01 and a σ_R value of -0.06. This substituent is therefore thought to exert an electron-donating influence through inductive and resonance interactions. The small values for the sigma constants indicate that this influence is small and this is observed in the substituent chemical shift which is only -0.29 p.p.m. at 56.45 MHz. Presumably the electron-donating resonance effect is through hyperconjugation as in the methyl group itself; the electron-withdrawing effect of the electronegative ether oxygen must be more than offset by the electron-donating effect of the methylene moiety. The 3-CH_3 substituent surprisingly does not fall into this group. This is a departure from expected behaviour which is difficult to explain.

(b) 4-Halogen Substituents (4-Cl, 4-Br)

The fluorine signal is shifted to higher field by these substituents and this is consistent with the effect of the electron-donating substituents discussed under (a). These substituents have net electron-withdrawing effects, since the electron-withdrawing inductive effect is only partially offset by the electron-donating resonance effect. Orbital overlap with the orbitals of the carbon atom is considerably less good for chlorine or bromine than for fluorine, for which the resonance effect can offset the inductive effect. The p-orbitals are much larger with chlorine and bromine and do not correspond in size to those on carbon as well as do those of fluorine.

(c) Electron-withdrawing 3-substituents (3-Br, 3-NO_2, 3-CN, 3-$COCH_3$)

All substituents give a shift displacement towards high field as would be expected from the behaviour of the substituents discussed above. The order of decreasing magnitude of substituent chemical shift is 3-CN > 3-NO_2 > 3-$COCH_3$ > 3-Br. This is the order that would be expected based on electron-withdrawing effects, except that the positions of the CN and NO_2 groups appear to be reversed. The NO_2 group is usually accepted as having a greater electron-withdrawing effect than CN.

(d) Strongly electron-withdrawing 4-substituents (4-$COOCH_3$, 4-$COOC_2H_5$, 4-$COCH_3$, 4-$COCH_2F$, 4-CN, 4-NO_2)

All substituents in this group show the large, positive substituent chemical shift as would be expected. Inductive and particularly resonance withdrawal is an important characteristic of these functionalities. From their $\Delta\phi$ values the order of increasing electron withdrawal is 4-COOEt < 4-$COCH_3$ < 4-$COOCH_3$ < 4-$COCH_2F$. Their magnitudes differ by very little; in the same substituent order the values are 5.65, 5.76,

6.05, 6.87. The first three all have a similar electron-withdrawing effect, only 4-$COCH_2F$ exerts a slightly larger influence than the other three substituent groups.

(e) Fluoromethyl substituents

In a bisfluoromethyl substituted naphthalene it is possible to view either fluoromethyl group as substituent or side-chain probe. Thus the 3α-derivative is also a 4β-bisfluoromethylnaphthalene. The resonance position of the β-CH_2F group was measured in β(2)-fluoromethylnaphthalene itself for comparison. The β-CH_2F group ^{19}F resonance appears at higher field than that for the α-CH_2F. In the ^1H n.m.r. spectrum of naphthalene itself the β protons resonate at higher field than the α-protons.

The σ_I value for -CH_2F is +0.12 and σ_R value is -0.02,[52] thus this substituent is electron-withdrawing overall. The 3-CH_2F substituent displaces the probe resonance signal (of the α-CH_2F group) towards high field as a result of its strong inductive influence. If the CH_2F group interacts with the aromatic system via hyperconjugation then the sign of the σ_R constant should in fact be positive, as is not the case. The substituent chemical shift of the CH_2F of the 1,4-bis CH_2F derivative reflects this large inductive withdrawal. However, the magnitude of the shift is a little surprising considering the resonance electron-withdrawing effect of this substituent.

As has been noted, the β-CH_2F probe resonates at higher field than the α-CH_2F. The difference is +14.5 Hz, at 56 MHz, or +0.257 p.p.m., a considerable shift. One would therefore expect to see two quite distinct separate groups of triplets for the 1,3-bis CH_2F compound. This is, in fact, not the case. The observed shifts for each -CH_2F group

are very similar at 56 MHz, one triplet appears 72.5 Hz towards higher field than the standard, the other triplet at 70.5 Hz, and at 94 MHz the two triplets are superimposed and cannot be resolved. The 56 MHz values correspond to $\Delta\phi$ values of +1.28 and +1.25 respectively. Clearly, in 1,3-bisfluoromethylnaphthalene the substituent chemical shift of the 3-CH_2F substituent acting on the α-CH_2F probe is greater than the substituent chemical shift of the 4-CH_2F substituent acting on the β-CH_2F probe, the difference between the substituent chemical shifts being 0.257.

For the β-CH_2F group regarded as a functional group in 1,3-bisfluoromethylnaphthalene the measured substituent chemical shift (from 1-fluoromethylnaphthalene) is +1.28. Of this, +0.257 is attributed to the fluoromethyl probe being located in the β- rather than the α-position, and the remainder (1.28-0.26 = 1.02) is therefore attributed to the substituent effect of the 4-CH_2F group acting on the β-CH_2F probe. We may compare this 4β effect(1.02 p.p.m.) with that of 4α (1.31 p.p.m.) and 3α (1.25 p.p.m.). The response of the ^{19}F n.m.r. signal to the substituent effect of the -CH_2F function is greater when the functional centre or probe is situated in the α-position in the naphthalene. A similar observation was noted by Wells, Ehrenson and Taft[17] regarding the data of Adcock and Dewar[25] concerning the ^{19}F shifts of substituted fluoronaphthalenes and also for data concerning naphthalene reactivities (see below).*

It is impossible to assign the two signals due to 1,3-bisfluoromethylnaphthalene on chemical shift criteria and so a comparison

* It is of interest to attempt to assign the two CH_2F signals of 1,3-bisfluoromethylnaphthalene measured at 56 MHz, even though the signals are nearly coincident and have been assumed so in the above discussion.

of various coupling constants was made. The J_{HF} coupling constants of 1-fluoromethylnaphthalene and 2-fluoromethylnaphthalene are both 48.0 Hz and so J_{HF} appears to be independent of position. For the two signals due to $-CH_2F$ in 1,3-bisfluoromethylnaphthalene to appear so close to one another the 3α (i.e. considering the 3-CH_2F function as the substituent) orientation must be more sensitive to the influence of the substituent than the 4β orientation (the (1)4-CH_2F function being the substituent in this case). The value of J appeared to correlate with the substituent chemical shift, being larger for negative shifts and smaller as the shifts became more positive. Hence the $-CH_2F$ group with the larger J value was the one which had suffered a smaller substituent chemical shift effect, i.e. the β-CH_2F group.

This assignment is supported by the J_{HF} values measured from ^1H n.m.r. spectra. The chemical shifts for these two functions are readily distinguishable in the proton n.m.r. spectrum. The J_{HF} value assigned to the α-CH_2F in the ^1H n.m.r. spectrum was smaller, in agreement with the assignment arrived at above.

(f) The $COCH_2F$ substituent

Although substituent constants for the $COCH_2F$ group are not known the group would be expected to be electron-withdrawing, as is $-COCH_3$. In accordance with this expectation the substituent chemical shift of this group is large and positive (+6.87 p.p.m.). The influence of the 4-$COCH_2F$ substituent appears to be the sum of the substituent effects of what might be considered its 'components', i.e. $-COCH_3$ and $-CH_2F$. The substituent effect of introducing a fluorine atom into the 4-methyl group of 4-methyl-1-fluoromethylnaphthalene is given by the shift difference

between 4-methyl-1-fluoromethylnaphthalene and 1,4-difluoromethyl-naphthalene, i.e. 3.81 p.p.m. Substituent effects are attenuated by a factor of approximately 1/3 per carbon-carbon bond, thus the effect of introducing a fluorine into 4-acetyl-1-fluoromethylnaphthalene at the acetomethyl group should be 3.81/3 = 1.27 p.p.m. Thus the total substituent effect of the FCH_2CO substituent is calculated to be +5.67 (the substituent chemical shift for 4-$COCH_3$ itself) + 1.27 = 6.94. The measured value is 6.70 and the good agreement suggests that the substituent effects for this form of multiple substitution are additive.

(g) Substituents showing deviations from expected behaviour

(4-CH_2OCH_3, 3-$COOCH_3$, 3-$COOC_2H_5$)

The two ester substituents show serious deviations from predicted behaviour. They appear to have an overall electron-donating effect in this system, the substituent chemical shift having the same sign as those for the 4-F and 4-CH_3 substituents. Both functions are normally electron-withdrawing through inductive (-I) and resonance (-M) mechanisms, and yet here they appear to display electron-donating behaviour. The shifts for these substituents exhibit the most serious deviations from from predicted behaviour, and the reason for this is not readily apparent. They exhibit opposite behaviour in dilution shift (Table IV) which is most surprising considering the structural and electronic similarities of these two systems. An explanation is offered (p. 235) for these observations. It is not obvious why the 60 and 100 MHz values for the 4-CH_2OCH_3 substituent should be so different (Table IV); the spectra were recorded on the same sample.

Effect of Dilution

Comparison of the values of n.m.r parameters measured from ^{19}F n.m.r. spectra obtained from the two different concentrations of solute would suggest that solvent effects are not appreciable in this system. The general trend of the effect of dilution appears to decrease the magnitude of $\Delta\phi$ values. As mentioned above the substituents which appear to have anomalous effects (-COOMe and -COOEt) also show the most drastic dilution effects.

Proton N.M.R. Parameters

Proton n.m.r. parameters show considerably greater deviations from consistent behaviour. J_{HF} values measured from the ^{1}H spectra differ at different spectrometer operating frequencies and when different dilutions are observed at a single operating frequency; it is not surprising that these J values do not exhibit respectable correlations. Furthermore $\Delta\tau$ values show chemical shifts due to dilution effects comparable in size to the shift values themselves. Values of zero for the 3-NO_2, 4-NO_2 and 4-CN substituents are impossible to rationalise except perhaps in terms of magnetic anisotropy, and yet -$COCH_3$ and -COOR do not appear so aberrant and the arbitrary exclusion of these data from the correlations severely limits the value of any conclusions (Table XIX). The values for the halogens are particularly interesting. These are very large and it is well established that halogens show deviations in plots of substituent chemical shifts which cannot be attributed to magnetic anisotropy effects[136,137]; these effects are, however, magnetic in origin.[138]

Correlations of N.M.R. Parameters of Substituted Fluoromethylnaphthalenes

Correlations carried out are shown in Tables XIV-XXIII. Sigma values for $-CH_2F$ and $-CH_2OCH_3$ substituents were those of Sheppard[52] and so these data points were not included in the initial correlation for two reasons. Since these were not values derived by Taft et al. and so did not correspond to any of the four distinct pi-delocalisation behaviour scales, inclusion of these values might tend to obscure different trends apparent from the data when analysed in conjunction with substituent constants derived from Taft's analysis. A preliminary analysis of the data excluding these points allowed a comparison to be made with results of other workers for similar analyses of other data sets.

Correlation of 4-substituted-1-fluoromethylnaphthalene 100 MHz data (Table XIV) clearly shows a better correlation with Taft's $\sigma_{R(BA)}$ values; σ_R^+ values are the next best data set in describing fluoromethylnaphthalene behaviour. Inclusion of the 4-CH_2F and 4-CH_2OCH_3 data points does not improve the correlation but changes the ρ values and statistical parameters very slightly. In the correlation of these data with $\sigma_{R(BA)}$ and σ_I substituent constants all the statistical confidence measures tend to an optimum. These statistical confidence measures, and specifically the correlation coefficient (R) of 0.993 indicate a very good fit. Moreover, the value of the intercept (ideally zero) is within the standard error. The sign and magnitudes of the regression coefficients, ρ_I and ρ_R, are +8.477 and +16.912 respectively, and the significance of these will be discussed later.

The corresponding 60 MHz data correlate slightly less well with the Taft parameters (Table XVI), R = 0.992, but again the best correlation

is observed with $\sigma_{R(BA)}$ values. For this data set the ρ values are slightly larger than those derived in the 100 MHz analysis; ρ_I is +8.489 and ρ_R +17.094. The next best fit is again achieved with the σ_{R^+} set for which R = 0.990.

Correlation of the 3-substituted fluoromethylnaphthalenes is far less good (Tables XV and XVII). The $\sigma_{R(A)}^-$ scale fit for the 100 MHz data (Table XV) is associated with a correlation coefficient of 0.908 and the confidence measures locate most of the departures from the model in the ρ_R parameter. It is interesting to note that by omitting the two aberrant data values for 3-$COOCH_3$ and 3-$COOC_2H_5$ the correlation coefficient is improved to a value of 0.959, a barely respectable correlation but a far better fit than is obtained when the two points are included.

Analysis of Béguin's benzyl fluoride data (Table XVIII) indicates a good correlation with $\sigma_{R(BA)}$, R = 0.998. The regression coefficients are ρ_I +9.868, ρ_R +16.512 for <u>para</u>-substituted derivatives. For the <u>meta</u>-substituted benzyl fluorides the best fit is achieved with σ_R^o substituent parameters but the resulting correlation is only marginally better than that using the $\sigma_{R(BA)}$ scale. The correlation coefficient in the former case is 0.996 with ρ_I = +7.599 and ρ_R = +2.176.

The influence of a peri, steric-twisting, resonance-inhibiting effect is observed in the 4-substituted-1-fluoromethylnaphthalene data. A correlation of data (Table XXI) for substituents not subject to this effect: Br, Cl, F, CN and CH_3, gives a correlation coefficient of 0.999. The associated regression coefficients are ρ_I +9.243 and ρ_R +16.284. Exclusion of strongly resonance interacting groups such as 4-NO_2, 4-$COCH_3$,

and 4-COOR results in a proportionately larger part of the total effect being located in the inductive parameter at the expense of the resonance parameter.

Proton substituent chemical shift and J_{HF} coupling constant correlations were carried out (Table XIX) although little hope of obtaining successful correlations was anticipated since there are very few reports of good correlations with these parameters. However, correlation of 100 MHz $\Delta\tau$ values for 4-substituted fluoromethylnaphthalenes gives a correlation coefficient of 0.976 with ρ_I = +0.08 and ρ_R = -0.15. 60 MHz 3-substituted derivative correlations with $\sigma_{R(BA)}$ show only a poor correlation, R = 0.907 and ρ_I = +0.13 and ρ_R = -0.18.

Coupling constant correlations are also surprisingly good (Table XX); the 4-substituted series show a correlation coefficient of 0.965, with ρ_I = -0.99 and ρ_R = -2.38. For benzyl fluorides the <u>para</u>-substituent correlation coefficient is 0.994 with ρ_I = -1.08 and ρ_R = -0.22 and for the <u>meta</u> series, R = 0.827 with ρ_I = -0.95 and ρ_R = -0.89. The 3-substituted-1-fluoromethylnaphthalene data also show a poor fit with substituent constants: R = 0.80, ρ_I = -1.54 and ρ_R = 0.90.

It should be noted that correlations with the F and R parameters of Swain and Lupton in most cases are appreciably poorer than with Taft's values for substituent constants. The ^{19}F $\Delta\phi$ data for the 4-substituted-1-fluoromethylnaphthalenes measured at both 60 MHz and 100 MHz give slightly better fits with the F and R parameters than with Taft's values.

Béguin reported a good correlation between $\Delta\phi$ values for substituted benzyl fluorides and Brown σ^+ values. The results of the linear least

squares correlation of these data and the fluoromethylnaphthalene data (Table XXIII) indicate a substantially poorer fit for the fluoromethylnaphthalenes than for the benzyl fluorides. The correlation coefficients are 0.916 and 0.982 respectively. With the values of $\Delta\phi$, and the slope (ρ) and intercept generated in this correlation, Brown σ^+ values were calculated for 4-CH_2OCH_3, 3-$COCH_3$, 3-CH_2F, 4-CH_2F, 4-$COCH_3$, and 4-$COCH_2F$ substituents (Table XXIII).

Interpretation of the Results

(i) Proton Substituent Chemical Shifts

It has been shown[139,140] that the substituent dependence of proton chemical shifts for many aliphatic compounds may be described in terms of the dipolar electric field effect and the anisotropic magnetic susceptibility of the substituent. The nature of this dependence for aromatic compounds is less certain. A study of the transmission of electronic effects in benzyl halides involving proton magnetic resonance substituent chemical shifts has been carried out by Yokoyama et al.[46] These workers established that at finite concentration molecules of the same or different compounds interact specifically with solvents so that the substituent chemical shifts are solvent dependent and not merely the shifts themselves. Even when comparing substituent effects with substituent chemical shifts measured at infinite dilution benzyl halides were shown to interact with the solvent in a manner peculiar to the particular compound. The attempted correlations of infinite dilution substituent chemical shifts according to Hammett and Yukawa-Tsuno* relations

* A dual substituent parameter treatment.

were poor. Yokoyama et al. carried out a literature survey of approximately one hundred Hammett correlations of proton n.m.r. data and found that the majority of these had unsatisfactory correlation coefficients < 0.90-0.95. The ρ values appeared to have no pattern and in general could not be used in the same fashion as reactivity ρ's are used as an index of efficiency of transmission of substituent effects in aryl systems. Plots of ρ-values against chain length between the proton and the aromatic nucleus showed no relationship between ρ and chain length. One would expect such a relationship if the substituted electronic effects on the proton n.m.r. are regular and systematic. Examples where ρ is radically influenced by geometry, and through-space and solvents effects were also cited.

In the light of these observations we report a correlation coefficient of 0.976 for the dual substituent parameter treatment for the substituent chemical shifts of the methylenic protons of the 4-substituted-1-fluoromethylnaphthalene series. The ρ_I value is +0.076 and the ρ_R is -0.15. The small magnitudes of the regression coefficients reflect the low sensitivity of proton magnetic resonance chemical shifts to substituent effects and the blending factor, λ = -1.975, indicates the dominant role of resonance effects. The sign of ρ_R for ^1H n.m.r. substituent chemical shifts is negative whereas that for the ^{19}F $\Delta\phi$ values is positive. The sign of the slopes of the graph of σ^+ against substituent chemical shift for the methylenic protons and the fluorine atom in benzyl fluoride are correspondingly opposite in sign. The reason for the positive value of ρ_I is not clear nor is the reason these two correlation coefficients are opposite in sign. Suffice it to say that

it appears that the introduction of +M (-R) resonance interacting groups into the naphthalene nucleus para to the $-CH_2F$ function results in a shift towards high field of the methylenic proton signal as one might predict. Increased π-electron density is transmitted along the C-C bond from the aromatic nucleus towards the methylenic protons, resulting in increased shielding. In view of the uncertainty surrounding the nature of the response of proton chemical shifts further analysis of the parameters would be inappropriate.

J_{HF} Coupling Constants

Proton-proton spin-spin coupling in high resolution nuclear magnetic resonance spectra[141] is due to interactions of molecular electrons. There are three possible mechanisms.

1. Nuclear magnetic moment interaction with orbital electronic currents.

2. The dipole interaction between nuclear magnetic moments and the electron spin magnetic moment.

3. An additional interaction between nuclear magnetic moments and the electron spins in s orbitals due to non-zero values of the electronic wave function at the nucleus. This last term is known as the contact term and for ^1H-^1H couplings dominates to such an extent that the other two terms are negligible. In fluorocarbons the complex mechanism for F-F and H-F coupling also involves the electron orbital and dipole-electron spin terms. At the present time the theoretical interpretation of observed coupling constants is inadequate. It has been shown that the value of the coupling constant decreases with increased

electronegativity of the substituent group in a manner analogous to vicinal ^{1}H-^{1}H coupling. Geminal H-F coupling constants have not been discussed in detail in the literature and so the observed substituent effects will be interpreted in terms of the ideas associated with ^{1}H-^{1}H geminal couplings.

Pople and Bothner-By[142] have developed a theory for the nuclear spin coupling between geminal hydrogen atoms. This theory suggests that the value of the geminal coupling constant provides a means of distinguishing between inductive and hyperconjugative electron transfer. They predict that withdrawal of electrons from orbitals symmetric between hydrogen atoms (generally inductive effects) should lead to a positive change in the coupling constant and that withdrawal of electrons from orbitals antisymmetric between hydrogen atoms (generally hyperconjugative effects) should lead to a negative change in the coupling constant.

If one assumes that the sign of the coupling constant J_{HF} in fluoromethylnaphthalenes is positive, as was found for the H-F geminal coupling in 2,6-dichlorobenzyl fluoride,[143] then these foregoing ideas would fully account for the direction of the trend in the value of the coupling constant (i.e. the value is reduced, becomes more negative, with the introduction of resonance electron-withdrawing substituents). The opposite effects on coupling constant for inductive and resonance withdrawal are not reflected in the ρ-values - both are negative. However, λ = +2.328 and reflects the dominant role of the resonance effect.

(iii) Fluorine Substituent Chemical Shifts

The 3-substituted-1-fluoromethylnaphthalene substituent chemical shift values were found to correlate with the $\sigma^{-}_{R(A)}$ pi delocalisation behaviour scale of Taft marginally better than the σ^{+}_{R} scale. The 4-substituted derivatives achieved the best fit to the dual substituent parameter equation when correlated with $\sigma_{R(BA)}$ substituent constant values. Values of ρ_I, ρ_R, λ, and the correlation coefficient for these systems plus the best fit values for the benzyl fluoride data are shown below. Data for fluoronaphthalenes and fluorobenzenes are included for comparison.

System	ρ_I	ρ_R	λ	R	Source
4-X-1-fluoromethyl-naphthalene	+8.48	+16.91	+1.20	0.993	this work
3-X-1-fluoromethyl-naphthalene	+6.98	- 2.03	-0.28	0.959	this work
p-X-benzyl fluorides	+9.87	+16.51	+1.67	0.998	this work*
m-X-benzyl fluorides	+7.48	+ 2.75	+0.37	0.996	this work*
4-α-fluoronaphthalenes	-12.77	-30.44	+2.65		ref. 17
3-α-fluoronaphthalenes	-6.85	- 2.68	+0.41		ref. 17
p-X-fluorobenzene (in MeOH)	-9.02	-31.17	+3.46		ref. 16
p-X-fluorobenzene (in cyclohexane)	-7.03	-30.58	+4.35		ref. 16

* The data used in these correlations were those of Béguin.[45]

From these data it can be seen that the nature of either the response to the substituent or the response to the fluorine chemical shift is totally different for the situations where the fluorine atom is bonded directly to the aromatic nucleus and the situation when a methylene moiety is interposed between the aromatic nucleus and the fluorine probe. Attention will first be directed towards the relative magnitudes of the ρ-values, and the striking difference in sign of the ρ-values between fluoroaryl and fluoromethylaryl series will be discussed separately

Comparison of Fluorobenzenes and Fluoronaphthalenes

From reactivity studies carried out on naphthalene derivatives it has been shown that resonance interactions are more important than in the corresponding benzene system. This is attributed to the considerably greater stability, and therefore greater contribution to the resonance hybrid, of the naphthoquinoid resonance structure over the quinoid resonance structure. On this basis ρ_R would be expected to be larger in the 4α naphthalene series than in the para benzene series. On the other hand, since the 4α and para distance relationships are closely similar, ρ_I values for 4α naphthalenes and para benzene series should be closely similar. However, the p-substituted fluorobenzenes show a larger ρ_R value than the 4α-fluoronaphthalenes. This is most surprising, but even more surprising is the comparison of the ρ_I values for the 3α- and 4α-fluoronaphthalene series and the p-X-fluorobenzenes. It is inconceivable that the inductive effect from the 4-position should be nearly twice that from the 3-position or twice that in fluorobenzenes as these ρ_I values imply.

In their analysis of substituent effects in the naphthalene series Taft et al.[17] make reference to the effect which gives rise to these discrepancies. "...A third effect on $\sigma_I\rho_I$ (of a somewhat indirect nature) may be expected in the substituted naphthalenes. In the cases where the substitution is in the 4,5 and 8 positions, the peri-hydrogen exerts a twisting effect on those systems having planarity demands with the ring system. This effect would tend to decrease the effective σ_R value for these substituents...Consequently, we would expect that in the usual cases where ρ_I and ρ_R are of the same sign, this steric inhibition of the resonance effect would be reflected in an increase in the magnitude of ρ_I, concomitant with a partial decrease in ρ_R. This would have the effect of making the 4α, 5α and 8β ρ_I proportionality factors appear somewhat greater than they would in the absence of such steric effect, as well as contributing to somewhat decreased values of ρ_R. Such an influence appears to exist for the ρ values for the 4α- and 8β- cases...". It seems clear that peri steric twisting is an important factor influencing transmission of electron effects in fluoronaphthalenes.

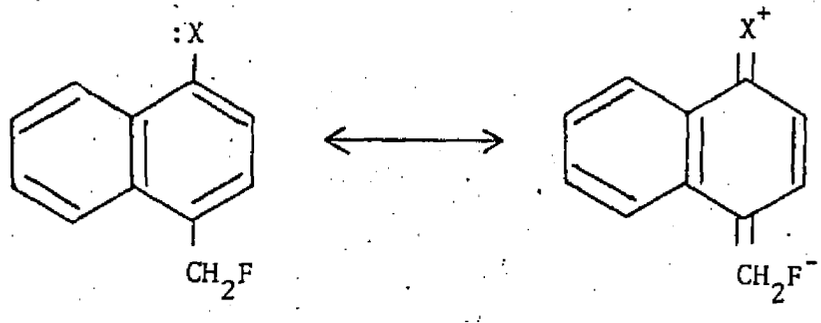
Fluoromethyl Derivatives

The fluoromethylnaphthalene and benzyl fluoride fluorine substituent chemical shifts correlate best with the $\sigma_{R(BA)}$ pi delocalisation parameter series. The most obvious interpretation of this is that the CH_2F function behaves as a weak π electron acceptor through the hyperconjugative form already discussed (p. 33). Correlation of the 3α-series with the $\sigma^-_{R(A)}$ set is marginally better than with the $\sigma_{R(BA)}$ set and in turn better than with the σ_R^+ set (Table XXII). However, since the differences between these three correlations are almost certainly not significant

(for $\sigma^-_{R(A)}$ R = 0.959, for σ_R^+ R = 0.944, for $\sigma_{R(BA)}$ R = 0.946, but the standard error of the estimate of the ρ_R values are 1.21, 1.84 and 2.57 respectively), no interpretation is offered. The effects of m-substituents have been considered generally to be of the σ^o_R type but various meta series were subjected to multiple linear regression statistical analysis by Taft who concluded that meta data do not discriminate between the different series, probably mainly because meta resonance effects are small. He concluded that while the assignment of meta-substituent effects to the σ^o_R type is not inconsistent, the available data did not provide a sound basis of support for the unique applicability of the σ^o_R scale to meta series. In fact, a $\sigma_{R(meta)}$ scale derived from the meta basis sets themselves did not fit the meta sets significantly better.

Comparison of the ρ values of the fluoromethylnaphthalene series with the fluoromethylbenzenes reveals some unexpected results. For the 4α-naphthalene series ρ_R is slightly larger than in the para benzene series. It is not surprising that ρ_R is larger in the naphthalene system and the reasons for this expectation have been dealt with earlier (p. 44). What is surprising is that ρ_I for the 4α-naphthalenes is smaller than that for para benzenes, and the same is true when the 3α-series is compared with the meta benzenes. The 4α- and para distance relationship should be the same as should the 3α- and meta and no difference in inductive effects would be anticipated. Moreover, somewhat unexpectedly the ρ_I values for 4α- are larger than the 3α- and similarly for para are larger than for meta. The ρ_R for the 3α- series is negative but this value is probably not significantly different from zero; ρ_R is equal to -2.0 and the standard error in this estimate is 1.2.

The steric influence of the peri-hydrogen was detected in the 4-substituted-1-fluoromethylnaphthalene data by the improvement of the correlation by the exclusion of +R groups such as $-NO_2$, -COOR and $-COCH_3$. It might be noted here that the $-CH_2F$ group itself may be subject to a slight peri-effect, since there are specific steric requirements at the functional centre associated with hyperconjugative forms of the type, -

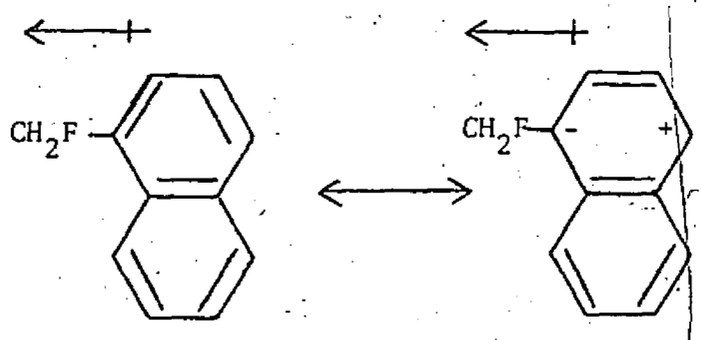


Fluoromethylnaphthalenes which contained suitable strong -R substituents which would provide a test for this effect were unfortunately not available.

The sign of the ρ values for the benzyl fluorides and fluoromethylnaphthalenes is not readily rationalised in the terms usually applied to shielding effects of the fluorine nucleus. The behaviour shown by the fluorobenzenes and fluoronaphthalenes where ρ's are negative is "normal" behaviour for the effect of a substituent on the fluorine chemical shift. In fluorobenzene the introduction of an electron-donating substituent into the system results in increased shielding of the fluorine nucleus and a corresponding upfield shift relative to the unsubstituted derivative. Introduction of an electron-donating substituent into the fluoromethylnaphthalenes induced a fluorine n.m.r. signal at lower field than the signal due to 1-fluoromethylnaphthalene itself.

These observations could be rationalised in terms of alternation of charge effect at adjacent carbon atoms along the chain of transmission. This explanation is precluded by the data for p-substituted-1-phenyl-2-fluoroethanes[45] (fluorides of ethyl benzene) where correlation with the Hammett σ parameter gave a positive ρ value (+0.73), the substituent chemical shifts being in the same direction as those for correspondingly substituted benzyl fluorides. Absence of an alternating effect is also supported by the charge density calculations of Brownlee and Taft[37] for m- and p-substituted fluorobenzenes and p-substituted fluorostilbenes, among others. These authors noted that neither the pi-electron density at the carbon bonded to the fluorine nor the fluorine σ-orbital charge density appeared related to the electron density at any of the intervening carbon atoms.

The π-inductive model (p. 38) would not appear to rationalise the observations to any better degree than the more generally accepted theories of transmission of electronic effects.



In this model the dipole due to the CH_2F function acts externally on the naphthalene ring polarising the π-system and in this manner induces the withdrawal of electrons from the 4-position through the right-hand dipolar resonance structure. This would result in the increased

shielding of the fluorine nucleus by electron-donating substituents as in the fluorobenzenes and contrary to observations.

Sheppard's theory of fluorine p-π interaction (p. 38) is a more attractive alternative in explaining the reversal in the response to substituent effects in going from fluoroaryl to fluoromethylaryl series. The chemical shifts of both basal and apical fluorines of $-SF_5$ exhibit positive ρ value behaviour, likewise the $-CF_3$ and $-SO_2F$ substituents as this theory would predict. The distances involved in the overlap and the size of the orbitals on the halogen appear to be important in the degree of electronegativity returned to the ring through the Sheppard mechanism.

This mechanism would explain the ^{19}F resonance signal of the fluoromethylarenes appearing at lower field with the introduction of electron-donating substituents. If this mechanism is operating, electron density increases at the carbon atom bearing the fluorine and at the fluorine atom itself. This charge is centred on the $2p_y(\sigma)$ orbitals rather than the $2p_z(\pi)$ orbitals since the charge density is transmitted from the aromatic ring through the sigma bonds of the system. The electron return via p-π interaction reduces the charge density in the $2p_z(\pi)$ orbitals on fluorine. Electron density-chemical shift correlations of Karplus and Das,[33] Paleta et al.,[36] Brownlee and Taft,[37] and Dewar and Kelemen[38] all report correlation with the π electron density on fluorine rather than the total charge density. Thus electron-donating substituents which increase the overall charge density at fluorine do so by increasing the σ charge density which is partially offset by a decrease in π charge density. It is the decrease in π charge density which is of major importance in determining the chemical shift and the

signal therefore appears at lower field.

The 3-substituted-1-fluoromethylnaphthalene data which exhibit a small negative ρ_R value may also be rationalised in terms of the p-π interaction model. If the electron return from the fluorine $2p_z(\pi)$ orbitals to the aromatic ring is by means of this mechanism, then the fluorine atom of the fluoromethyl group will be disposed very close to the 2-proton on the naphthalene nucleus and will distort this proton from its original sp^2 hybridised position. Substituents in the 3-position will begin to experience steric effects as a result of this proximity to both the hydrogen and the highly electronegative fluorine. This will tend to reduce their resonance interaction with the aromatic nucleus. Likewise, the proximity of the 3-substituent will reduce the tendency of the fluorine atom to return electron density to the aromatic ring. Both these effects will result in the fluorine exhibiting the 'normal' n.m.r. response, i.e. it will be shielded by electron-donating substituents. Of the 3-substituted derivatives the two ester substituents show the most serious deviations. This is not surprising, considering their steric bulk and electronic character. The values for 3-$COCH_3$ and 3-NO_2 are both smaller than anticipated; again this could be due to their relative bulk and subsequent steric interaction with the CH_2F function. The only substituents which appear to behave in the same manner as the 4-substituted derivatives are the 3-CN and 3-Br groups; both are linear and would show the smallest tendency to interact with the CH_2F function.

It is not surprising that this phenomenon is not observed with the benzyl fluorides since there are two ortho positions in these compounds through which electron return may take place. In one of these steric

interactions would not be involved and so return would take place through this position preferentially. Also, in the case of the benzyl fluorides all of the 3-substituents investigated, apart from 3-NO_2 and 3-CH_3, were linear.

In the fluoroarene systems the $2p_z(\pi)$ orbitals on fluorine are directly conjugated with the aromatic π system. Introduction of resonance electron-donating substituents increases the π electron density at fluorine, resulting in increased shielding and the signal appearing at higher field.

Sheppard offered his model as an alternative explanation for the observed apparent electron-withdrawing resonance effect of the -CF_3 substituent. The more accepted explanation for the resonance effect of this substituent is fluorine hyperconjugation (p. 35). Fluorine hyperconjugation cannot, at first sight, explain the reversal in substituent effect between the fluoromethylarenes and the fluoroarenes. Electron-donating 4-substituents should increase the electron density at fluorine in this model and should produce increased shielding at the fluorine nucleus. However, if, as is likely, the shielding experienced by the fluorine nucleus is not solely a function of the total electron density then it is possible to rationalise the downfield shift produced by electron-donating substituents in the fluoromethylarenes, within the framework of the hyperconjugation model. The hyperconjugative model predicts that the introduction of a resonance electron-donating substituent should decrease the $ArCH_2$-F bond order and increase the π charge on fluorine. HMO calculations of Bĕguin support this conclusion based on "pictorial" resonance theory.

If we now consider the equation of Prosser and Goodman[34]

$$\delta = \frac{488}{\Delta E} [11.9\Delta P_F + 0.1\ \Delta P_C + 3.9\Delta P_{CF}]$$

where ΔP_F and ΔP_{CF} are changes in the π electron density at F and the C-F π bond order respectively, these terms are important but strongly opposed. If the relative magnitudes of these two terms are sufficiently dependent upon the electronic structure of the chemical bonds in the vicinity of the fluorine and not solely on the value of the electron density on fluorine itself, then possibly either term might predominate over the other. For a negative ρ value ΔP_F would be the dominant term whereas a change in sign would indicate ΔP_{CF} was the leading term. In the original presentation of this equation, Prosser and Goodman[34] use such a rationale to explain the difference in sign of ρ values for p-substituted benzoyl fluorides and p-substituted benzenesulphonyl fluorides and obviously a similar rationale might well apply to the fluoromethylarenes and fluoroarenes.

The complexity of this problem is illustrated by the following table which gives the sign of the ρ values for various substituted fluoroaromatic series.

Substituent	F	CH_2F	CF_3	COF	SO_2F	SF_5(apex)	SCF_3	SO_2CF_3
ρ	-	+	+	-	+	+	-	-

It is not likely that this problem will be resolved until the nature of the factors affecting the chemical shift of a fluorine nucleus are better understood.

Conclusions

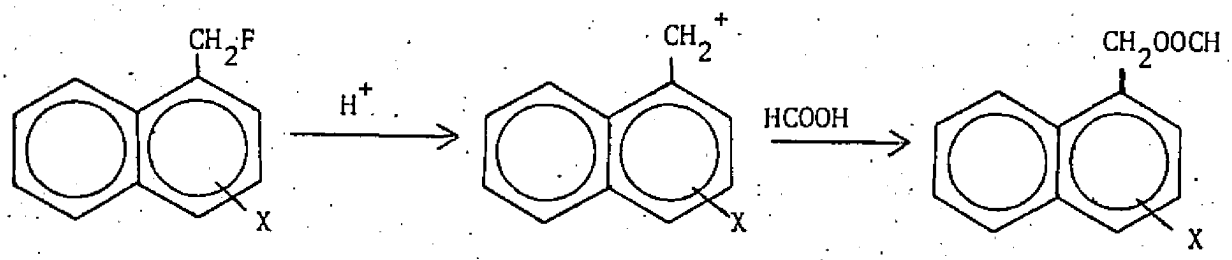
The study of the ^{19}F and ^{1}H n.m.r. spectra of a series of 22 substituted-1-fluoromethylnaphthalenes has yielded information of considerable interest in the context of ^{19}F nuclear magnetic resonance, of substituent effects in aromatic compounds, and of the effects peculiar to the naphthalene system itself.

This work substantiated and extended the observations of earlier workers which arose from investigations of the benzene analogue of the fluoromethylnaphthalene system. The data from this study were analysed using different substituent parameter scales, and subsequently interpreted in terms of the series which gave the best fit to the dual substituent parameter model. In several instances the fit obtained with one scale was only marginally better than that with another. If it had been possible to synthesise compounds with strong +M(-R) resonance electron-donating substituents these differences would have been much greater.

The nature of the response of the fluorine n.m.r. signal to the substituent effect is the same in both fluoromethylaryl series. We have offered an interpretation of the sign of the response of the substituent chemical shift to the substituent effect in terms of currently accepted models. The unexpected nature of the ^{19}F n.m.r. response (the positive ρ value) of this and other phenyl fluorine derivatives is difficult to interpret in terms of the current theories of substituent effects in aromatic systems and the factors contributing to the screening of the fluorine nucleus. Further work will be necessary in both fields before all experimental observations are adequately rationalised.

A further study in the fluoromethylnaphthalene system which would

give more insight into this problem would be the solvolysis of the series of compounds synthesised in this work. Very few side-chain reactions of naphthalenes have been studied previously which involve an electron deficient transition state. The solvolysis reaction would provide an example of this type of reaction. The reaction is carried out in formic acid:-



and thus allows one to observe the enhanced resonance effects of +M(-R) substituents presumed to operate in a naphthalene system of this type.

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