

A KINETIC STUDY OF THE SOLVOLYSIS OF SOME
DIPHENYLMETHYL CHLORIDES

by

Rita E. M. Burley

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ABSTRACT

A study has been made of the electronic effect of substituents upon the first-order rates of solvolysis of a number of formal derivatives of benzyl chloride. These solvolyses, which proceed through a unimolecular mechanism, were studied in a mixture of 90% ethanol and 10% acetone at various temperatures, allowing the energies of activation to be calculated. A good linear free-energy correlation was found using the Brown-Okamoto substituent constant, σ^+ .

A comparison of substituent effects in the α -(2-fluorenyl)- and α -(4-biphenyl)- systems ($\rho = -1.7$ and -1.2 respectively) shows that the transmission of electronic substituent effects across the aryl systems is enhanced by increased ^{co-}planarity of the aryl fragment. The relative effects of substituents upon the observed rate are proportional, but not identical, in the two systems. This proportionality factor may be linked with an interplanar angle of 45° in biphenyl.

The effect of inserting the p-C₆H₄- group between the substituent and the reaction centre is the same in the benzhydryl system ($\rho = -4.4$), cf. -1.2 for the (α -(4-biphenyl)benzyl chlorides) and in the t-cumyl system, where $\rho = -1.21$ for substituent effects in the solvolysis of α -(4-biphenyl)-isopropyl chloride.

Transmission of substituent effects in the 2,6-dimethylbenzhydryl chlorides is less ($\rho = -3.6$) than in the benzhydryl chlorides, allowing the estimation of a mean transmission coefficient. Using this, together with allowances for both the steric and the electronic effects of the two ortho-methyl groups, an attempt was made to calculate the various contributions of steric and electronic factors to the observed reaction rate.

The average discrepancy between calculated and experimental values of the free energy of activation is ± 0.13 kcal mole⁻¹. No saturation of electronic effect occurs in those derivatives of 2,6-dimethylbenzhydryl chloride studied here.

A general mechanism for the transmission of electronic effects of substituents across aryl systems is discussed.

Twenty-four new chlorides and their precursors have been synthesised; new routes have been investigated in the preparation of α -(6-substituted-2-fluorenyl)benzyl chlorides.

CHAPTER IINTRODUCTIONThe Generalised Displacement Reaction andDuality of Mechanism

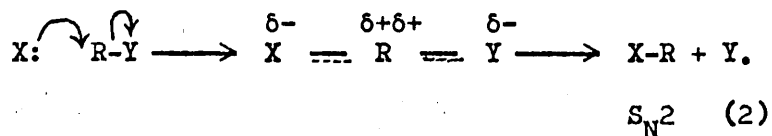
The generalised displacement reaction may be defined as a reaction in which a bond between two groups is replaced by a bond between one of these groups and a third:



In nucleophilic displacements the group X and the displaced group Y are nucleophiles or Lewis bases, that is, groups possessing an unshared electron pair. One pair of electrons is transferred from X to the reaction centre and another from the reaction centre to Y. The bond-breaking is thus heterolytic as opposed to homolytic (where bond rupture proceeds with both fragments retaining one electron from the original covalent pair).

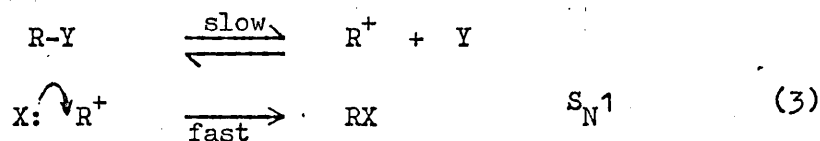
The mechanism of the solvolytic reaction has been studied for a wide range of substrates under a variety of experimental conditions. It was in the early 1930s and due mainly to the work of E.D. Hughes and C.K. Ingold¹ with alkyl halides that the two, now established, mechanisms, namely bimolecular and unimolecular displacements or substitutions, received precise formulation and experimental substantiation.

Bimolecular substitution involves only one stage, in which the two groups simultaneously undergo covalency change. It is labelled S_N2 .

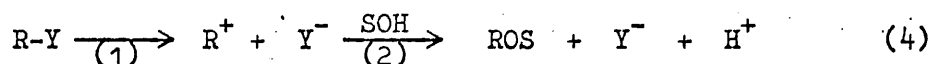


The bond formation between the incoming nucleophile X and R is synchronous with the heterolytic fission of the R-Y bond.

The second mechanism involves two stages: a slow reversible rate-determining heterolysis of the compound undergoing substitution followed by a rapid coordination between the formed carbonium ion and the substituting agent, X. Since in the rate-determining stage only one molecule is undergoing covalency change, the mechanism is unimolecular, and labelled S_N1 .



The generalised displacement reaction could have been represented as:



where SOH represents a solvent molecule or other nucleophilic species. The time lag between reaction 1 and 2 determines the lifetime of the carbonium ion. A long time-lag enables the carbonium ion to become completely free. Such is the pure S_N1 displacement of which the solvolysis of benzhydryl halides is an example. When the time-lag vanishes, reactions 1 and 2 are synchronous and the mechanism is pure S_N2 displacement.

Thus the S_N1 - S_N2 mechanisms are intended to be extremes of a continuous spectrum with no dividing line defining the extremes. Intermediate or borderline cases are known. Such are the solvolyses of secondary alkyl halides.

The Kinetic Form and Stereochemical Consequences of the Two Mechanisms

The transition state for an S_N2 displacement has the three groups, R_1, R_2, R_3 (in $R_1R_2R_3CY$ with X the incoming nucleophile) held in a plane, by bonds with sp^2 hybridisation. The groups X and Y are attached by the two electrons which are in a p-orbital at right angles to this plane.

As a direct result of the stereochemistry of the transition state S_N2 reactions must proceed with inversion of configuration. The latter is not due to electrostatic repulsion between the entering and leaving groups because reactions involving positively or negatively charged substrates have been shown to proceed with inversion rather than retention of configuration.

The stereochemistry of S_N1 reactions follows no unique rule. The limiting situation arises when the carbonium ion attains a planar configuration and can be attacked by the nucleophile equally readily from either direction leading to a racemic product. In any series of S_N1 displacements the amount of racemisation increases with increasing stability of the carbonium ion.

Net inversion of configuration in S_N1 reactions can be explained either as a shielding effect of the carbonium ion by the displaced group or alternatively in terms of an ion-pair between the carbonium ion and the displaced anion.

Partial inversion of configuration occurs when the carbonium ion at the time of capture has not attained its most stable configuration nor completely separated from the leaving group.

Retention of configuration is also possible, as when a neighbouring group interacts with the carbonium ion centre and forces the incoming nucleophile to attack from the side originally occupied by the displaced group.

Polar solvents solvate the formed or forming carbonium ion thus increasing its stability but the extent of racemisation depends on the stability of the solvated ion. Unstable intermediates will cause an increase in the amount of racemisation, as occurs with an ether solvent, whereas the stable solvated ions obtained using an hydroxy solvent increase the net amount of inversion.

The typical kinetic form of the S_N2 mechanism is expressed by the second order rate equation:

$$\text{Rate} = k_2[X][RY] \quad (5)$$

where k_2 is the rate constant for the reaction

[X] is the concentration of the attacking nucleophile

[RY] is the concentration of the molecule undergoing substitution.

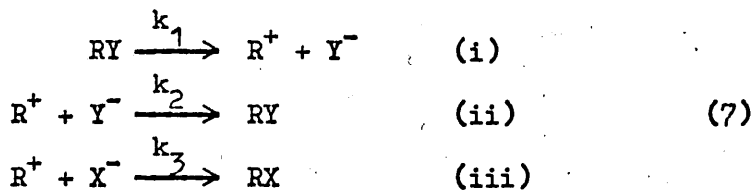
However, first order kinetics may also be followed if, for example, one of the reactants is in constant large excess: or if one reactant is a buffered component of a chemical equilibrium: or if the two reactants are not kinetically independent, as when they form ion pairs or other electrostatic clusters in a non-polar solvent.

The unimolecular process can also lead to first order kinetics with an overall rate equal to the heterolysis rate.

$$\text{Rate} = k_1[RY] \quad (6)$$

This is a limiting law obeyed to an approximation when the rate of reversal of heterolysis is much smaller than the rate of coordination of the carbonium ion with the substituting agent. Such is the general kinetic form when the substituting agent is in large excess as when it is an important constituent of the solvent.

A more general situation arises when the rate of reversal of heterolysis is comparable with that of combination of the carbonium ion with the substituting agent. Considering the following equations:



The kinetic expression for this situation is:

$$\frac{-d[\text{RY}]}{dt} = \frac{k_1 [\text{RY}]}{k_2/k_3 [\text{Y}^-] + 1}$$

If reaction 7(ii) is insignificant compared to reaction 7(iii) then $k_2[\text{Y}^-] \ll k_3$ and the equation reduces to equation (6). If, however, the ratio k_2/k_3 is appreciable its effect will become increasingly so as the reaction proceeds giving rise to a progressively smaller instantaneous rate of ionisation. Such is a "mass action" effect or an "external return".

The addition of a common anion, Y^- to the reaction, will also give rise to a retardation in the overall rate of substitution. The explanation is the same as that for "external return".

Any such ionic retardation effect will always be offset by an ionic-strength accelerating effect. In some instances the retardation can be completely swamped as in the hydrolysis of t-butyl halides. However, the use of a high concentration of an inert salt, e.g. lithium perchlorate can itself swamp out the ionic-strength accelerating effect. This is useful, since the presence of a retardation effect is good evidence of a carbonium ion intermediate and hence of an $\text{S}_{\text{N}}1$ mechanism. Further proof of $\text{S}_{\text{N}}1$ mechanism is afforded by adding a second nucleophile to the reaction so that there is competition for the carbonium ion. The ratio of the products, but not their overall rates of formation, are determined by the relative concentrations of the nucleophiles. In this respect, the addition of the azide ion has been widely used.

The $\text{S}_{\text{N}}1$ reaction is favoured relative to $\text{S}_{\text{N}}2$ by large electron release from alkyl groups, strong electron affinity in the leaving group, a low nucleophilic activity in the incoming nucleophile and conducting the reaction in a highly ionizing solvent.

The carbonium ion formed in the rate-determining step may form a product in one of two ways. If it possesses a β -hydrogen atom, it may, by an elimination process, form an olefin product, otherwise it will react with a nucleophile. The S_N1 mechanism necessitates that the proportion of products via either process must be independent of the leaving group and that the proportions of isomeric olefins formed by elimination should also be invariant with respect to the leaving group.

In this thesis, the compounds whose rates of solvolysis are to be compared belong to the benzhydryl chloride system. In ionizing solvents, this system undergoes solvolysis according to the unimolecular mechanism².

Carbonium Ions

(a) Substituent Effects

Carbonium ions are derivatives of the trivalent positively charged species CH_3^+ in which the hydrogen atoms may be replaced by other organic residues. The carbon atom on which the charge formally resides is sp^2 hybridised. The ease of formation of the ion is directly related to its stability.

The stability of a carbonium ion increases with increasing charge delocalisation. This can be achieved both within a molecule by electrical induction, conjugation and related phenomena and externally by solvation, ion association and charge transfer.

Substituent groups within a molecule which facilitate delocalisation of charge will thus stabilise the carbonium ion. Such can be achieved in two ways:

- (i) by inductive or field effects;
- (ii) by resonance or conjugation effects.

Inductive and field effects are electrostatic in origin arising either from ionic charges or from the dipole moments of electronegative atoms. They are short range effects and obey an inverse square law. Inductive effects act through the sigma electrons of a molecule whilst field effects are transmitted through space or through solvent molecules.

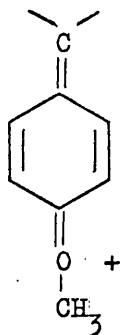
Resonance effects are transmitted through the π -orbitals of unsaturated molecules, are long range effects and are of particular importance in aromatic systems. The disturbance of π -electron density at one atom in a conjugated system may become distributed over the π -electron orbitals associated with the whole system giving rise to an alternation of polarised carbon atoms. When a group gives rise to a permanent displacement of electrons within a molecule by resonance conjugation, it is described as having a mesomeric effect. The methoxyl group, being electron releasing as a result of a resonance effect, is said to be a +M substituent and its +M effect opposes its inductive (-I) effect.

Symmetrical molecules, for example, biphenyl may be resonance stabilised but have no resultant polarity in the ground state. However, during the course of a reaction, e.g. electrophilic substitution, the molecule may be able to accommodate charge delocalisation in the transition state. For biphenyl, this is so if the addition of an electrophile occurs at the ortho or para position of one nucleus and biphenyl is said to be ortho-para directing and is activated relative to benzene. Since this property of the phenyl substituent is effective only when the reagent begins to bond to the ring, it is termed a polarisability or electromeric effect, to distinguish it from the permanent polarisation effect already discussed.

The nomenclature introduced by C.K. Ingold³ to describe these effects is as follows:

State of Molecule	Effect of Substituent	
	Inductive	Resonance
Ground State	Inductive ($^{\pm}I_s$)	Mesomeric ($^{\pm}M$)
Transition State	Inductomeric ($^{\pm}I_d$)	Electromeric ($^{\pm}E$)

Groups which exhibit a +E and/or a +I_d effect in the transition state will best stabilise a carbonium ion. Thus, in benzhydryl chloride, the *p*-methoxy group (+M, +E) causes a rate enhancement to solvolysis. This is because the oxygen atom can accept a considerable fraction of the possible charge via resonance structures such as:



i.e. an electron rich oxygen 2p-orbital becomes part of the overall π -bonding. Such resonance is also possible for an *o*-methoxy group, but the inductive effect (-I), strongest in this position of close proximity to the reacting centre, causes a large decrease in the rate of ionization relative to that of the *p*-methoxy group.

The electronic effects of halogen substituents are similar to those of methoxy but less intense which is reflected in a less marked change in relative rates. The electron attracting p-nitro group ($-I_d$, $-E$) causes a marked decrease in rate.

Resonance effects will be maximal from those substituents whose p-orbitals can overlap most effectively with the π -orbitals associated with the unsaturated carbon atom, i.e. from substituents involving the first row elements (i.e. $-F$, $-OH$, $-NH_2$; cf. $-Cl$, $-Br$, $-SH$).

The Baker-Nathan Order

The inductive effect of alkyl groups is in the order $Me < Et \sim iso-Pr < tert-Bu$ which is consistent with their dipole moments. However, the rates of unimolecular hydrolyses of the p-alkyl substituted benzhydryl chlorides are in the order $H < tert-Bu < iso-Pr < Et < Me$ ⁴. The same order is observed for the hydrolysis rates of p-alkyl benzoates in 85% ethanol⁵ and in detritiation reactions⁶. This inverted order first noted by J.W. Baker and W.S. Nathan in 1935⁴ is known as the Baker-Nathan order. The ortho-alkyl substituents have a similar but much diminished effect whilst the m-alkyl compounds follow the inductive order.

Conventional resonance interactions are impossible since the carbon atom of the alkyl group is saturated. However, the charge at the 4-position may be delocalised by an interaction with the carbon-hydrogen and carbon-carbon bonding orbitals of the alkyl groups. This delocalisation of the positive charge is known as hyperconjugation.

Belief in hyperconjugation is not unanimous and some workers hold the view that solvation and subtle steric effects are responsible for the reversal in reactivity between the meta and para positions^{4,7}.

The Linear Free Energy Principle and Substituent Constants

According to the relation:

$$\Delta F^{\circ} = -RT \ln K$$

where ΔF° is the standard free energy of reaction

R is the universal gas constant

T is the absolute temperature

K is the equilibrium constant,

the equilibrium constant for a reaction depends only on the difference in the standard free energies of the reactants and products. In a rate process the activated complex is in equilibrium with the reactants and thus the rate constant similarly depends on the free-energy difference between the reactants and the activated complex. Estimates of rate and equilibrium constants are equivalent to estimates of free-energy differences between various species.

Interactions between groups which are bonded together include their internal bond energies, steric interactions and energies of interaction with the solvent. Groups which are not bonded to each other may interact in three ways: polar (including inductive, polarisability and field or direct electrostatic effects); resonance (only that resonance involving both groups simultaneously); and steric (including interference with internal rotations etc., as well as steric compressions).

The Linear Free Energy Principle is concerned with the reactivity of molecules whose structure can be divided into a reacting group X and a non-reacting residue, R.

In the absence of strong specialised interactions between R and X:

1. The effects of the substituent X upon the standard free energy of a reaction and upon the free energy of activation of that reaction are linearly related.
2. The differences in the overall energy of reaction involving a reacting group X, produced by a series of changes in R are linearly related to the changes in the corresponding values for another reaction involving X, and also to those for a reaction involving a different group, X₂.

The Hammett Equation

Two series of rate or equilibrium constants which are both linearly related to a third series are linearly related to each other. The Hammett equation⁸

$$\log k/k_0 = \rho \sigma \quad (9)$$

takes as the single series of reference the ionization constants of substituted benzoic acids in water at 25°. The equation defines the substituent constant σ , as $\log k'/k_0'$ where k' is the ionization constant of the meta or para substituted benzoic acid and k_0' that of benzoic acid itself. σ is a measure of the electron-donating or electron-withdrawing power of the substituent. ρ , the reaction constant, is a measure of the sensitivity of the equilibrium constant to changes in the σ -value of the substituent.

In general, neither aliphatic nor ortho-substituted benzene derivatives adhere to the Hammett equation. To a large extent this is attributed to steric interactions, for if the reaction zone is widely removed from the region in which the change in structure occurs, the equation does become applicable. Thus, the specific rates of reaction

of various aliphatic and aromatic esters, including ortho-substituted compounds, with triethylamine do follow the Hammett equation⁹.

Hammett noted^{8b} that the ionization of anilines and phenols required enhanced values for the para-nitro and para-cyano groups. This requirement was extended to cover all groups which were capable of direct resonance interaction with the O⁻ and NH₂ groups in this series. Jaffe¹⁰ designated these σ^* but they were later changed to σ^- . Biggs¹¹ later reported several other σ^- -values for other substituents based on the same ionization reactions. The σ^- -values are presumed to be applicable to those reaction series in which direct conjugation between the substituent and the reaction site group, with a lone pair of electrons, can occur. The direct conjugation must be important in either the reactant or the product, but not in both. In such reactions, the meta-substituents still require the ordinary Hammett values.

In 1953, Brown¹² suggested that electrophilic aromatic substitution reactions might be correlated by a selectivity relationship:

$$\log p_f^{\text{Me}} = b \log \left(\frac{p_f^{\text{Me}}}{m_f^{\text{Me}}} \right) \quad (10)$$

p_f^{Me} = rate constant for substitution in the para position of toluene relative to that of benzene.

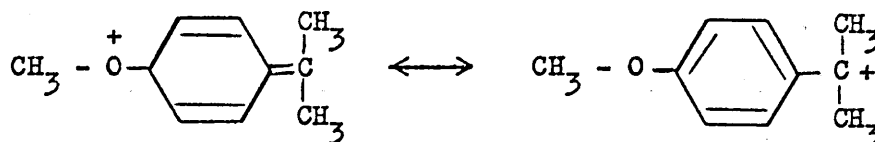
m_f^{Me} = rate constant for substitution in the meta position of toluene relative to that of benzene.

b = a constant for all electrophilic reagents.

A value for the constant, b , could be calculated from the Hammett equation

$$b = \frac{\sigma_{\text{p-Me}}}{\sigma_{\text{p-Me}} - \sigma_{\text{m-Me}}} \quad (11)$$

The calculated and experimental values did not agree¹³. In order to correlate these electrophilic reactivities Brown and Okamoto defined a new series of substituent constants for those substituents in the para-position which exerted a +T electronic effect. The reaction used was the first-order solvolysis of phenyldimethylcarbonyl chlorides in 90% aqueous acetone¹⁴. A plot of $\log_{10} k/k_0$ values for this reaction using meta-substituent constants was linear with a slope of -4.54. +T para-substituents deviated widely from the line. The transition state involving such groups should be resonance stabilised, e.g. for para-methoxy.



Substitution of the $\log k/k_0$ values for those +T substituents in the relation:

$$\sigma^+ = \frac{\log k/k_0}{-4.54} \quad (12)$$

leads to the σ^+ -constants.

A study of the same solvolysis reaction in various other ionizing solvents (anhydrous methanol, ethanol and propan-2-ol) led to similar substituent effects¹⁵.

In this system there are no complications due to steric effects and there is no possibility of rearranged products in the solvolysis reaction. These substituent constants give a measure of the effect of substituent groups on the stability of carbonium ion or carbonium ion-like transition states, and the original Hammett equation is modified to:

$$\log k/k_H = \sigma^+ \rho \quad (13)$$

Excellent $\log k/k_H$ versus σ^+ linear plots have been obtained for many aromatic substitution reactions yielding reliable reaction constants¹⁶, e.g. -12.1 for non-catalytic bromination,¹⁷ -2.4 for Friedel-Crafts ethylation,¹⁸ -10.0 for non-catalytic chlorination,^{19,20} -9.1 for Friedel-Crafts acetylation,²¹ -8.2 for detritiation¹⁶, -6.0 for nitration,¹⁶ -4.0 for mercuration,¹⁶ -4.6 for protodesilylation,¹⁶, -5.2 for protodeboronation¹⁶ and -6.2 for bromodesilylation¹⁶.

Deno showed that the σ -values derived from ionizations of triarylmethanols gave comparable σ^+ -values²².

Only the para-phenyl group appears to show consistent deviations from the relationship although other substituents e.g. para-fluoro in Friedel-Crafts ethylation, do show some real deviations.

The para-phenyl group shows deviant behaviour in the non-catalytic bromination¹⁷ and chlorination reactions¹⁹ and also in the Friedel-Crafts acetylation in ethylene dichloride²¹.

The σ^+ -values must be used to correlate reactions in which an electron-deficient reaction site can directly conjugate with substituents in either the reactant or the product, but not, presumably in both. In many cases, conclusions concerning the nature of the transition states, or products of an equilibrium, have been drawn based on the necessity of using σ^+ -values for correlation of the rate or equilibrium data. These conclusions are all based on the requirement of direct conjugation of substituents with an electron deficient site²³.

The Extended Selectivity Treatment²⁴ was introduced to assess the reliability and validity of the σ^+ parameters. In this approach the $\log (k_R/k_H)$ observations for a single substituent are plotted

against ρ for a variety of reactions. Such an approach probes the dependence of the response of each substituent to variations in the selectivity of the reagents and conditions.

When data for a series of selected side-chain reactions are plotted according to the Extended Selectivity Treatment small displacements from a correlation line based on the Hammett σ -constants are evident¹⁶. The scatter is random for all substituents and the extent of the displacement from the correlation line is independent of the value of the reaction constant. Such side-chain reactions include the ionization of anilinium ions in water at 25°, ionization of phenols in 48% ethanol at 100°, ethanolysis of benzoyl chlorides at 0° and alkaline hydrolysis of ethylbenzoates in 87.83% ethanol at 30°. For these reactions, conventional Hammett plots of $\log_{10}(k/k_H)$ versus σ yield good linear correlations. The Extended Selectivity Treatment examines the constancy of the contribution of a substituent over a series of reactions and is thus a more sensitive probe of the applicability of a free-energy relationship than the conventional Hammett treatment.

An attempted synthesis of the three distinct σ -scales, σ , σ^+ , σ^- , into a continuous range of σ -values, where σ^+ and σ^- represent limiting values, has been suggested by many authors. This subject is amply reviewed by Van Bekkum²⁵. Taft was led to a similar conclusion in his attempts to separate resonance and inductive effects in aromatic reactivities²⁶. Both Taft and Van Bekkum point out that direct conjugation is in fact of some importance in substituent effects on the ionizations of benzoic acids and that the substituent constants obtained in this way should not be considered normal.

Various attempts have been made to represent these varying conjugative effects by means of a single equation. Yukawa and Tsuno²⁷ have suggested the following:

$$\log_{10} k/k_0 = \rho[\sigma + r(\sigma^+ - \sigma)] \quad (14)$$

in which r can vary from one reaction to another. r is the ratio of conjugation in a particular series to that in the limiting cases requiring σ^+ . Several authors²⁸ have adopted this equation and tried to rationalise the values of ' r ' obtained in various types of reactions. It is agreed that r is not a function of the reaction constant, ρ .

Yoshioto et. al.²⁹ have proposed an analogous equation for reaction-series involving a negative reaction site:

$$\log_{10} k/k_0 = \rho[\sigma + r(\sigma^- - \sigma)] \quad (15)$$

Other equations have been suggested by Knowles et. al.³⁰ and Hine³¹. Both correlate a good deal of experimental data on electrophilic reactivities but have been shown to be limited.

The extension of the Hammett equation to poly-substituted benzene derivatives has been made for side-chain reactions¹⁰. The contributions of each substituent is assumed to be constant and the postulate is an example of the Additivity Principle. In the case of electrophilic substitution, assuming additivity, the equation may be written:

$$\log_{10} k_j = \rho \sum_i \sigma^+ i \quad (16)$$

where $\sum_i \sigma^+ i$ is the summation of substituent constants of the various substituents in the aromatic ring and k_j is the partial rate factor for a given position, ρ is assumed to be constant.

However, the non-catalytic bromination of polymethyl-substituted benzenes^{16,32} yields a ρ -value of -8.7 to be compared with -12.1 for the mono-substituted compounds. The dependence of ρ on the nature of the substrate is evidently complex. This suggests that the sensitivity of a reaction to substituent effects can be affected by the presence of other substituents, although it is not clear whether this effect arises from saturation of the electronic effect by the many contributing substituents or from either primary or secondary steric effects.

Resonance Effects in the Phenyl Substituent

Until the early 1950s the chemical reactivity of biphenyl had been explained by considering the two rings of biphenyl to act independently³³. The typical example was nitration³⁴.

Nitration of biphenyl yields 4-nitrobiphenyl. Nitration of 4-nitrobiphenyl produces 37% 2,4'- and 63% of 4,4'-dinitrobiphenyl. Similar results are obtained if the nitro-group is in the 3- or 4-position, or if two nitro-groups, or other meta-directing groups, are present in one of the rings, showing that one phenyl group is ortho-para-directing irrespective of its substituents. As if to underline this rule of independence, the 4-nitro group was shown not to activate a bromine atom in the 4'-position.

However, resonance interaction between the rings had been used to successfully explain the results obtained from physical measurements such as, dipole moments³⁵, thermochemical data,³⁶ X-ray measurements³⁷ and absorption spectroscopy³⁸.

In 1951, Berliner and Blommers³⁹ measured the dissociation constants of several 4-substituted-4'-biphenylcarboxylic acids and found that the data fitted a Hammett plot. This indicated that the effects of

substituents were transmitted through the biphenyl system. However, these effects were quantitatively less than in benzoic acid.

Such work showed that the independence of the two rings of biphenyl was probably due to the electronic requirements of the particular electrophilic substitution, since all $X-C_6H_4$ -substituents showed the same mildly activating effect. Berliner went on to study the rates of hydrolysis of 4'-substituted ethyl-4-biphenylcarboxylates⁴⁰ and showed that the transmission of substituent effects in the biphenyl system was present but was merely a quarter as large as in the analogous ethyl benzoates.

Work done by Kreiter et. al.⁴¹ on the dissociation constants of hydroxy and nitrohydroxy biphenyls and fluorenes was thought to show that through-resonance in biphenyl was minimal in the ground state.

In 1954, de la Mare⁴² first pointed out a major discrepancy in the observations for the para-chlorination of biphenyl which did not correlate with the Hammett equation.

Later, Eaborn and his school reviewed the behaviour of biphenyl in several reported substitution reactions by examining the ratio $\log f_p^{Me} / \log f_p^{Ph}$ ^{43,44}. He concluded that the reactivity of the para-position of biphenyl did not conform to a linear free energy relationship since no single substituent constant of the Hammett type could adequately represent the para-phenyl group in these reactions.

Using data from substitution reactions of biphenyl in the Extended Selectivity Treatment, H.C. Brown⁴⁵ showed that the reactivity of the para-position increases significantly with an increase in the electron demand of the substitution reaction (ρ). Such a variation had been noticed by Knowles³⁰ in 1960, who suggested that this was a reflection of the variability of resonance stabilisation merely as a function of electron demand.

Not only does the reactivity of the para-phenyl group depend on the reaction constant, ρ , but it is appreciably diminished compared with that of the α -phenyl substituent. While the ethanolysis of benzhydryl chloride is 270 times more rapid than that of α -phenylethyl chloride⁴⁶ and triphenylmethyl chloride solvolyses 39 times more rapidly than benzhydryl chloride,⁴⁷ the situation is very different for electrophilic substitution in the para-position of toluene and biphenyl. Here the para-methyl and para-phenyl substituents activate to about the same extent with the methyl slightly greater.

In 1964, Stock and Brown⁴⁵ suggested that both these anomalies were due to the energy barrier for achievement of coplanarity between the phenyl nuclei. Reduced reactivity is explained as the result of steric inhibition to resonance stabilisation in the transition state and the variations in the angle between the rings explains the variation in resonance interaction as a function of electron demand.

One of the formal rules for resonance is the requirement of coplanarity among contributory structures. Although non-coplanar structures make significant contributions to the hybrid, their importance is dependent upon the deviation from coplanarity. For biphenyl, the estimated energy barrier, 3.9 kcal mole,⁴⁸ and predicted deviation from coplanarity⁴⁹ (this value is the difference in energy between the barrier to rotation and the consequent resonance energy) are not large but sufficient to cause changes in reactivity. Extra stabilisation is probably present due to a shortening of the interannular bond⁵⁰.

In α -phenyl-substituted alkyl carbonium ions a high degree of resonance stabilisation from the aryl substituent is obtained because the ortho-hydrogens are easily accommodated in a planar conformation. In the carbonium ion obtained from biphenyl the full contribution from the phenyl substituent is impeded because of the steric repulsions among the four ortho-hydrogens. Such is reflected in reduced reactivity. As the

selectivity of the electrophilic reaction increases, the steric forces are, in part, overcome by the increased energy requirements of the transition state. Thus in the highly selective bromination reaction for which ρ is -12 ,¹⁷ the effects of the p-methyl and p-phenyl groups are reversed. The overall result in the reactions of biphenyl is the observed variation in the degree of stabilisation by the phenyl group.

In the acylation reaction⁵¹, as in mercuration⁵² and ethylation¹⁸, biphenyl is considerably less reactive than toluene. Acylation is a more selective reaction than either mercuration or ethylation; however, the same pattern of reactivity is maintained as evidenced by the respective partial rate factors. That is, the inductive influence of the substituent phenyl and methyl groups control relative rate in the meta-position. On the other hand, the para-position in both compounds is activated toward electrophilic substitution with the methyl group possessing the ability to stabilise the transition state to a slightly greater extent.

Stock and Brown¹⁶ tested these hypotheses by applying the Extended Selectivity Treatment to reactions at the 2-position in the planar, bridged biphenyl, fluorene. This position is structurally equivalent to the para-position in biphenyl, for the hydrocarbon contains the elements of the biphenyl system forced into coplanarity by the methylene bridge. In contrast to biphenyl, the 2-position of fluorene conforms to the Extended Selectivity Treatment and is considerably more reactive.

Fluorene as a Planar Biphenyl

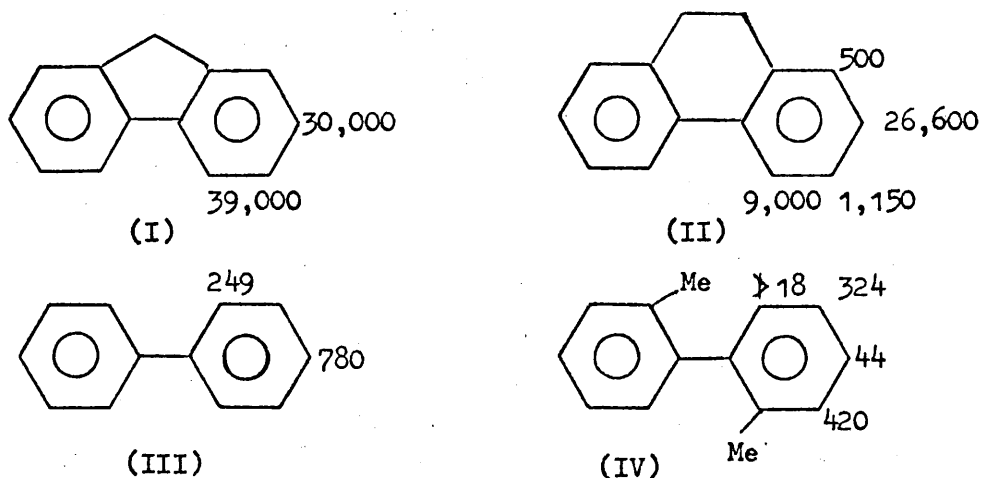
Fluorene is a planar hydrocarbon⁵³ containing the elements of the biphenyl system forced into coplanarity by the methylene bridge. The two aromatic rings are not exactly collinear but the π -electron system of one ring is able to release electrons conjugatively to the other. It is

therefore possible to regard fluorene as a substituted biphenyl in which the reactivity toward electrophiles is modified by:

- (a) the CH_2Ar group
- (b) the planarity of the system.

The arylalkyl group acts as an electron-releasing substituent activating the 2-position both inductively and hyperconjugatively.

In a series of papers P.B.D. de la Mare⁵⁴ measured the products and rates of molecular chlorination in acetic acid at 25° of a series of bridged biphenyls including biphenyl, fluorene, 2,2'-dimethylbiphenyl and 9,10-dihydrophenanthrene. The measured rates relative to benzene showed a wide range of reactivity; a factor of 170 separating the most reactive, fluorene, from the least reactive, 2,2'-dimethylbiphenyl, showing that the most important factor to the rate is the conjugative power of the aryl group which in turn is determined by the angle between the aryl rings during the transition state. Steric inhibition to resonance within the series is minimal in fluorene and maximal in 2,2'-dimethylbiphenyl.



The lack of resonance in 2,2'-dimethylbiphenyl causes a change in the orientation of chlorination whereby the alkyl group takes over the ortho-para directive role from the aryl group.

The chlorination data show that fluorene is more reactive than is expected for a planar alkyl-bridged biphenyl by an amount involving a free energy increment of about 1 kcal mole^{-1} and a rate enhancement factor of 5.

This cannot be totally explained by hyperconjugation since acting against hyperconjugation is the inductive effect of the aryl group acting through the methylene bridge as well as the diminished conjugation arising from the non-linearity of the fluorene molecule. De la Mare suggested that the extra rate enhancement factor was the distortion of the aromatic systems by the methylene bridge.

In a consideration of the Arrhenius parameters for the chlorination of these biphenyls⁵⁵ it is found that the difference in reactivity is determined by factors of enthalpy and that the entropies of activation vary very little. This is not an obvious conclusion since the angle between the planes of the aryl groups is important in determining their power of mutual conjugation and hence strongly affects the rate of chlorination. A similar observation is made by H.C. Brown⁵².

Berliner and Shieh⁵⁶ observed that the S_N1 solvolysis of α -(2-fluorenyl)ethyl chloride in 80% aqueous acetone was 60 times more rapid than the 4-biphenyl-yl-analogue. In a more extensive work on the solvolysis of the α -arylphenylmethyl chloride system, Berliner⁵⁷ found that the absolute rates were greater than in the α -arylethyl chloride system. Also, under identical conditions, the solvolysis of diphenylmethyl chloride proceeds about 400 times faster than the solvolysis of α -phenylethyl chloride. However, the rate differences in the arylphenylmethyl system are greatly compressed, e.g. the ratio of rates of the 2-fluorenyl to the phenyl compound is 700 in the α -arylethyl series and 138 in the arylphenylmethyl series. Such confirms that the greater reactivity of the diaryl carbonium system is accompanied by a lower selectivity⁵⁷.

When the relative rates of solvolysis of 4-biphenyl-yl, 2-fluorenyl and 2-(9,10-dihydrophenanthryl)-phenylmethyl chlorides are compared to that of the phenyl compound, the relative rates are 7.0, 138 and 38 respectively. That 9,10-dihydrophenanthrylphenylmethyl chloride occupies an intermediate position shows that forced coplanarity is the

main rate enhancer in the 2-fluorenyl analogue⁵⁷. A similar situation is obtained in the protodesilylation⁵⁸ and molecular chlorination of these three compounds⁵⁴ showing that the two carbon bridge allows some twisting of the phenyl groups. Earlier work on u.v. absorption spectra had shown conjugation to be present in such 2,2'-bridged biphenyls⁵⁹.

A plot of the relative rates of solvolysis of these α -arylphenylmethyl chlorides against (the Brown-Okamoto substituent constant) σ^+ is linear showing that the three solvolyses are similarly affected by changes in the hydrocarbon structure. The reaction constant, ρ , for the arylphenylmethyl system (-4.26) is expectedly lower than that for the arylethyl chloride system (-5.78).

The results of other electrophilic substitution reactions⁴⁵ confirm the greater reactivity of fluorene over biphenyl and this is ascribed to enforced coplanarity rather than to hyperconjugative or inductive effects. This is particularly evidenced in the highly selective bromination reaction where electron demand is at a maximum yet the partial rate factor for the 2-fluorenyl position relative to the 4-biphenyl position is 2×10^3 . Work on the molecular chlorination of 9,9-dimethyl fluorenes has shown hyperconjugation effects to be small⁶⁰. A similar order is observed in the relative rates of protodesilylation of the 2-SiMe₃ derivatives and 9-methyl and 9,9-dimethyl substituted fluorenes⁶¹. Furthermore, there is evidence that in some respects the methylene group in fluorene shows more analogy to a para than a meta-methyl group in toluene^{61,62}.

The planarity of fluorene makes the 2-fluorenyl system more effective than the 4-biphenyl-analogue in delocalising charge in the derived carbonium ion. Kinetic studies on the solvolysis of (biphenylenyl)benzyl chloride⁶³ which like the fluorenyl system can be considered a planar biphenyl show a rate enhancement of the same order.

The fluorenyl and biphenylenyl halides have lower energies of activation toward solvolysis than the biphenyl chloride. This implies that the former have ground states which are more polarised or that the derived carbonium ions have a lower resonance energies. Apart from the planarity of the system this could also be due to the strain inherent in the two systems. However, data on the solvolysis of the almost planar 4,5,9,10-tetrahydropyrenylbenzyl chloride⁶⁴ show it to be almost as effective as the fluorenyl system in stabilising the incipient carbonium ion. Both the rates of solvolysis and the derived Arrhenius parameters for the two chlorides are similar indicating that both hydrocarbon residues assist in the formation of the carbonium ion to a similar extent. Since the tetrahydropyrenyl system is not subjected to strain, there is no need to postulate any strain factor to explain the high reactivity of the fluorenyl derivative.

Substituent Effects in Biphenyl and Fluorene

The effects of 4-substituents on the 4'-position in biphenyl are related in a fairly simple way to the effects of the same substituents on the para position of benzene derivatives. A combination of inductive and tautomeric effects does not account for this⁶⁵.

Such a relationship is explicable if it is held that in the transition state the substituent influences the 1-position of biphenyl in the usual way, that the effect is then relayed to the 1'-position and thence, say, to the 4'-position of the other ring. The experimentally observed effect is much weaker than in the benzene system. For example, in the nitration of 4-nitrobiphenyl⁶⁶ in acetic anhydride, the 4'-position is deactivated by a factor of 30, whereas the nitro group in nitrobenzene deactivates the para position by a factor of 10^7 .

A similar pattern is observed for other reactions, e.g. protodesilylation, molecular chlorination and detritiation.

Protodesilylation in acetic acid-aqueous sulphur dioxide

at 50° 67

	k_{rel}
Trimethylsilylbenzene	1
4-Methyltrimethylsilylbenzene	18
4-Nitrotrimethylsilylbenzene	1.22×10^{-4}
4-Trimethylsilylbiphenyl	1
4'-Methyl-4-trimethylsilylbiphenyl	1.79
4'-Nitro-4-trimethylsilylbiphenyl	0.092

Molecular Chlorination 68

	k_{rel}
Benzene	1
Toluene	820
Biphenyl	1
4-Methylbiphenyl	7.5

Detritiation by Trifluoroacetic Acid 67

	k_{rel}
Tritiobenzene	1
4-Methyltritiobenzene	450
4-Tritiobiphenyl	1
4'-Methyl-4-tritiobiphenyl	4.0
4'-Chloro-4-tritiobiphenyl	0.29

2-Tritiofluorene	1
7-Methyl-2-tritiofluorene	3.8
7-Chloro-2-tritiofluorene	0.27

The diminished magnitude in the transmission of substituent effects in biphenyl relative to the phenyl system has been explained as due to the non-coplanarity of the biphenyl ring system.

The conjugative interactions across the 1,1'-bond in biphenyl are not greatly dependent on the nature of the substituent as the data for detritiation of similarly substituted fluorenes show. Further, a plot of $\log_{10} k_{rel}^T$ of biphenyl versus $\log_{10} k_{rel}^T$ of fluorene is an excellent straight line, showing that for this reaction the non-coplanarity of the rings in biphenyl does not have an important influence on the 4'-substituents.

If it is assumed that the two rings of biphenyl are near coplanarity in the transition state then it is expected that the relative effect of analogous substituents will be the same in the biphenyl and planar fluorene systems, for effects on the transition state are much more important than effects on the initial ground state^{67,69}. The data from the detritiation reaction shows that the effect of the substituent must be dampened in its transmission through the interannular bond and is not connected with the extent of coplanarity of the system.

The ionization constants of 2-aminofluorene (pK_a 4.31) is greater than that of 4-aminobiphenyl (pK_a 4.05). Similarly, fluorene-2-carboxylic acid (pK_a 5.8) is a weaker acid than biphenyl-4-carboxylic acid (5.62). However, the differences in the relative magnitudes of the ionization constants can be explained solely on the basis of the electronic effect of the meta-methylene group of fluorene and offer no evidence for greater conjugative interactions resulting from the planarity of the rings in fluorene⁷⁰.

4'-Substituents in biphenyl-4-carboxylic acid and 4-aminobiphenyl affect pK_a values in much the same way as 4-substituents in benzoic acid and aniline, although the range of values is much smaller. The same difference in relative magnitude is observed in the pK_a values of 4'-substituted-4-carboxylic acids and 7-substituted-2-fluorene carboxylic acids. This is in general accord with the results from the detritiation and desilylation reactions. Concerning the ionization reaction it is estimated that only 45% of the electronic effect is transmitted from the 4'-position to the 4-position in biphenyl. Similar work on 3'-substituted biphenyl-4-carboxylic acids show only 30% transmission.

The ionization reaction is not one in which there is a maximum electronic demand and thus is not very sensitive toward changes in substituents. Substituent effects are best studied in the context of an electrophilic substitution reaction. Whilst molecular chlorination, bromination, nitration etc., are the most sensitive reactions toward changes in substituents, more than one product can often be obtained and results are thus unduly complicated. Solvolysis of substituted benzyl halides in good ionizing solvents is a more efficient reaction and is one in which substituent effects are maximal.

The Scope of this Work

In the solvolysis of some α -arylbenzyl chlorides the 2-fluorenyl-derivative reacts more rapidly than the 4-biphenyl-derivative. As this is attributed to more complete conjugation across the aryl system in the former case, the transmission of substituent effects across the systems ought similarly to be improved by increased planarity of the aryl fragment.

A study was therefore begun on the effect of substituents upon the rates of solvolysis of α -(2-fluorenyl)- and α -(4-biphenyl)-benzyl chlorides.

The 2,6-dimethylbenzhydryl system resembles the α -(4-biphenyl)-benzyl system since non-planarity inhibits resonance stabilisation. The effect of para-substituents in both rings of the former system should show similar effects to those in the latter system. A second part of this work was a study of such effects.

Finally, in order to check that the results were not unique to one biphenyl system a second study was made of substituent effects in the 4-(α -chloro-iso-propyl)biphenyl system (ArCMe_2Cl). Similarly a number of para-substituted benzhydryl chlorides were studied so that the effect of the 2,6-dimethyl substituents could be assessed directly.

CHAPTER IIDISCUSSIONComparison of the 4-Biphenyl and 2-Fluorenyl Systems

The rate data from electrophilic displacement and solvolytic reactions^{15, 17} show that whilst the biphenyl and fluorenyl systems are both more reactive than phenyl, the fluorenyl system shows the greater rate enhancement. This has been ascribed¹⁷ to the coplanarity of the two phenyl nuclei in the fluorenyl structure, which in the carbonium ion transition state facilitates maximum delocalisation of charge.

Substituents in the biphenyl and fluorenyl systems show similar relative effects both in protodetrition⁶⁷ and in the ionization constants of the corresponding aroic acids.⁶⁹ These effects are much weaker than in the benzene analogues.

The solvolytic reaction of substituted benzyl chlorides in good ionizing solvents is a reaction in which substituent effects are maximal. A study was made of the effect of substituents on the rates of solvolysis of arylbenzyl chlorides (Ar.CHPhCl where Ar = (7-X-2-fluorenyl), (6-X-2-fluorenyl), (4-X-4'-biphenyl) and (3-X-4'-biphenyl)) in ethanol - acetone (9:1 v/v). Tables 1 and 2 list the substituents, the corresponding rates of solvolysis at 25^o, the derived thermodynamic parameters, and σ^+ for the substituent for the fluorene and biphenyl derivatives.

Table 1

Results of Kinetic Studies of Some α -(-X-2-Fluorenyl)Benzyl Chlorides

Substituent (X)	$k_1(25^\circ)(\text{sec}^{-1})$	$\Delta E(\text{kcal mole}^{-1})$	$-\Delta S(\text{e.u.})$	σ^+
H	9.9×10^{-3}	17.8 ± 0.2	8	0
7-Chloro	4.0×10^{-3}	18.0 ± 0.4	9	+0.114
7-Ethyl	3.4×10^{-2}	20.1 ± 0.2	2	-0.295
7-Fluoro	7.8×10^{-3}	17.7 ± 0.2	9	-0.07
7-Methoxy	160×10^{-3}	16.9 ± 0.4	6	+0.78
7-Nitro	3.3×10^{-4}	19.6 ± 0.3	9	-0.78
6-Chloro	9.7×10^{-4}	16.8 ± 0.3	15	+0.399

Table 2

Results of Kinetic Studies of some (-X-4'-Biphenyl)Benzyl Chlorides

Substituent (X)	$k_1(25^\circ)(\text{sec}^{-1})$	$\Delta E(\text{kcal mole}^{-1})$	$-\Delta S(\text{e.u.})$	σ^+
H	5.13×10^{-4}	19.8 ± 0.2	8	0
3-Bromo	1.45×10^{-4}	17.7 ± 0.7	17	+0.399
3-Fluoro	1.88×10^{-4}	18.2 ± 0.2	10	+0.352
3-Methyl	1.16×10^{-3}	15.8 ± 0.8	18	-0.065
3-Methoxy	4.5×10^{-4}	19.2 ± 0.4	10	+0.047
3-Nitro	5.6×10^{-5}	18.3 ± 0.9	16	+0.662
4-Bromo	2.8×10^{-4}	17.4 ± 0.5	16	+0.148
4-Chloro	2.5×10^{-4}	19.8 ± 0.3	9	+0.114
4-Fluoro	3.9×10^{-4}	18.7 ± 0.8	11	-0.079
4-Methyl	9.87×10^{-4}	19.9 ± 0.4	2	-0.316
4-Methoxy	3.51×10^{-3}	19.6 ± 0.3	5	-0.778
4-Nitro	5.0×10^{-5}	20.8 ± 1.0	8	+0.778
4-Phenyl	6.12×10^{-4}	20.1 ± 0.2	6	-0.135

Substituents influence the rate of solvolysis in the expected direction, i.e. methoxyl and alkyl enhance whereas nitro and halogeno depress the rate. 3'-Substituents in the α -(3'-X-4-biphenyl)benzyl system have a ~~much~~ smaller effect than the analogous 4'-substituents. This is expected since only inductive effects are predominant in the 3'-position. Due to synthetic difficulties (page 67) it was impossible to study the analogous α -(6-X-2-fluorenyl)benzyl system in depth. Only α -(6-chloro-2-fluorenyl)benzyl chloride was successfully prepared; its first order rate of solvolysis at 25° ($9.68 \times 10^{-4} \text{ sec}^{-1}$) is, as expected, reduced (24%) compared to α -(7-chloro-2-fluorenyl)benzyl chloride. Although a compound corresponding empirically to α -(6-methyl-2-fluorenyl)benzyl chloride was prepared, its first order rate of solvolysis was too slow to be measurable, indicating that the orientation of the chloride was suspect. A similar situation was encountered for α -(1-methyl-2-fluorenyl)benzyl chloride. Neither result could be explained.

In the biphenyl system, the only anomalous compound appears to be the 3-methyl biphenyl derivative, which, in one preparation, showed an unexpectedly high rate of reaction. However, this result must be treated with caution since the orientation of the chloride was not unambiguous (page 66).

A comparison of the rates of solvolysis in the α -(4'-X-4-biphenyl) and α -(7-X-2-fluorenyl) systems shows that relative substituent effects are greater in the fluorenyl than in the biphenyl system. A plot of $\log_{10} k_1$ (biphenyl) (k_1 is the first-order rate constant for solvolysis at 25°) vs. $\log_{10} k_1$ (fluorenyl) is linear with a slope of 1.45 ± 0.04 . This is compared (Graph 1) with a similar plot by Eaborn using rate data from the detritiation reaction of substituted biphenyls and fluorenes where a slope of unity was obtained⁶⁷. From this, Eaborn concluded that the relative substituent effects across the fluorene and biphenyl systems are identical. He explained this by assuming that the maximum effect

GRAPH 1Plot:

- (i) First-order rates of solvolysis of
 α -arylbenzyl chlorides.

$\log_{10} k_1(25^\circ)$ α -(4'-X-4-biphenyl)-
vs. $\log_{10} k_1(25^\circ)$ α -(7-X-2-fluorenyl)benzyl
chlorides.

- (ii) Relative rates of detritiation.

$\log_{10} k_{rel}(70^\circ)$ biphenyl
vs. $\log_{10} k_{rel}(70^\circ)$ fluorene

of substituents was shown in the transition state, which for biphenyl apparently involves a planar configuration of the two rings, thereby resembling the fluorenyl system.

The present results indicate that in the solvolytic reaction the relative effects of substituents in the two systems are proportional but not identical. The proportionality factor is most reasonably linked with the interplanar angle in the biphenyl system. The linearity also indicates that interaction between the two sets of compounds and the medium are proportional.

Plots of $\log_{10} k_1$ vs. σ^+ , the Brown-Okamoto substituent constant¹⁴ (Graph 2) for both the biphenyl and fluorenyl systems in the present work are linear. The numerical values of the slopes are evidence that the solvolysis of 3'- and 4'-substituted biphenylbenzyl chlorides ($\rho = -1.17 \pm 0.07$) is less sensitive to substituent effects than that of the fluorenyl compounds ($\rho = -1.73 \pm 0.09$). Transmission of electronic effect across the two phenyl nuclei in fluorene is greater than in biphenyl in agreement with the hypothesis that delocalisation of charge and the interplanar angles are linked. For the 3'-substituents alone, however, a Hammett treatment yields a value for the reaction constant, ρ , of -1.43 ± 0.06 , to be compared with -1.17 ± 0.07 for the 4'-substituents. This could indicate that either substituent effects are not relayed so easily from the 4'-position or that α -(3'-X-4-biphenyl)benzyl is a flatter system than the analogous α -(4'-X-4-biphenyl) system. However, the necessary extrapolations of the Arrhenius plots required in order to estimate the rates at 25°, the small range of σ^+ used in the Hammett plot (0.66, compared with 1.56 for the 4'-substituents) and the smaller number of points comprising the line all suggest a higher real margin of error than the probable error obtained statistically.

GRAPH 2Hammett Plot

(i) $\log_{10} k_1(25^\circ)$ (biphenyl)- vs. σ^+

$$\rho = 1.17 \pm 0.07$$

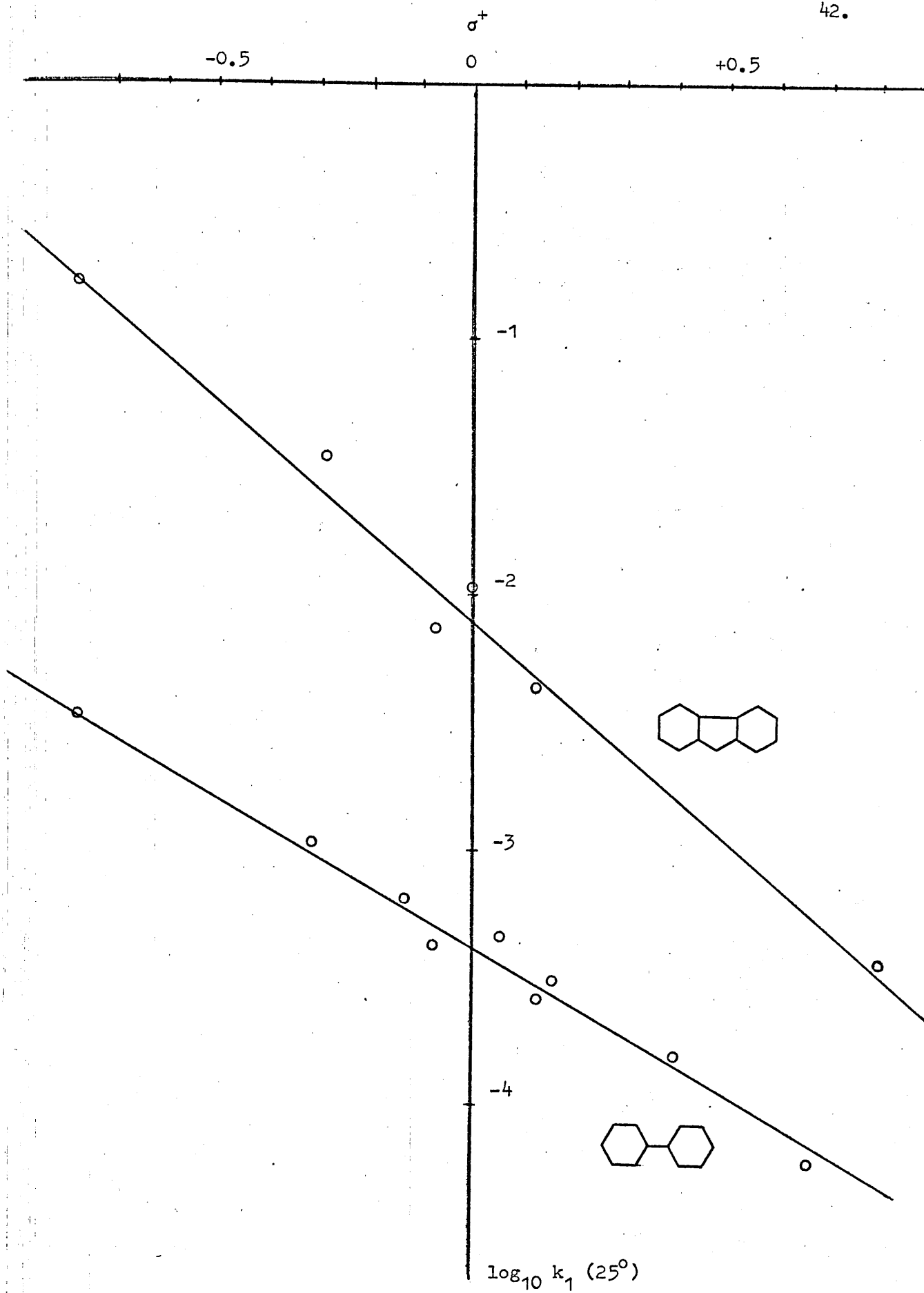
(ii) $\log_{10} k_1(25^\circ)$ (fluorenyl)- vs. σ^+

$$\rho = 1.73 \pm 0.09$$

k_1 = first-order rate constant at 25° for the solvolysis of substituted α -(4-biphenyl) and α -(2-fluorenyl)-benzyl chlorides.

σ^+ = Brown-Okamoto substituent constant.

ρ = Reaction constant.



GRAPH 2

Brown derived σ^+ from data obtained from the rates of solvolysis of substituted t-cumyl chlorides. For this system the reaction constant, ρ , is -4.54^{14} . The benzhydryl chloride system was investigated. Table 3 is a list of the monosubstituted compounds studied and their respective first-order rates of solvolysis at 25° in ethanol:acetone (9:1 v/v). A plot of $\log k_1$ vs. σ^+ for the benzhydryl system (Graph 3) gives a slope of -4.36 ± 0.41 . From this graph, values for the substituent constants of 4-biphenyl, 2-fluorenyl, 4,5,9,10-tetrahydro-2-pyrenyl, 2-(9,10-dihydrophenanthryl) and 2-biphenylenyl are obtained and compared with the literature values (Table 4).

Using the rates of chlorination of toluene and of fluorene as standard points to define the Hammett plot ($\sigma_{p\text{-Me}}^+ = -0.316$, $\sigma_{2\text{Fl}}^+ = -0.600$), calculated values of other aryl substituents were obtained which were in very good agreement with those obtained from solvolysis studies in ethanol:acetone, but in poor agreement with previously derived values. The cause of this discrepancy is obscure.

The rates of solvolysis of a number of α -(4'-X-4-biphenyl)isopropyl chlorides were also investigated. Table 5 is a list of the compounds together with their respective first-order rates of solvolysis at 25° . A Hammett plot (Graph 4) yields a reaction constant, ρ of -1.21 ± 0.05 .

The ρ -values for the four systems studied together with the t-cumyl chloride system are collected in Table 6.

In the benzhydryl system, a para- C_6H_4 group placed between the substituent, X, and the phenyl system, decreases the substituent effect ($\Delta\Delta G$) by a factor of 0.27 ($\rho/2\rho_1$). This factor, sometimes called the transmission coefficient, is the same as the value arising from a similar

Table 3

Results of Kinetic Studies of Some Substituted Benzhydryl Chlorides

Substituent	$k_1(25^\circ)$ (sec^{-1})	$\Delta E(\text{kcal mole}^{-1})$	$-\Delta S$
4-Chloro	$7.86 \times 10^{-6} \pm 0.12$	21.81 ± 0.20	9
4-Methoxy	$7.80 \times 10^{-2}^*$	14.00 ± 1.5	16
4-Fluoro	$5.62 \times 10^{-5}^*$		
4-Methyl	$8.93 \times 10^{-4}^{**}$		
4-Hydrogen	$0.38 \times 10^{-4}^{**}$		
4-t-Butyl	$7.01 \times 10^{-4}^{**}$		
3,3-Dimethyl	$1.61 \times 10^{-4}^{**}$		
3-Methyl	$0.77 \times 10^{-4}^{**}$		

* Value obtained by extrapolation of the Arrhenius plot.

** Williams, N.J., Ph.D. Thesis, London, 1974.

GRAPH 3A Hammett Plot for the Benzhydryl Chloride System

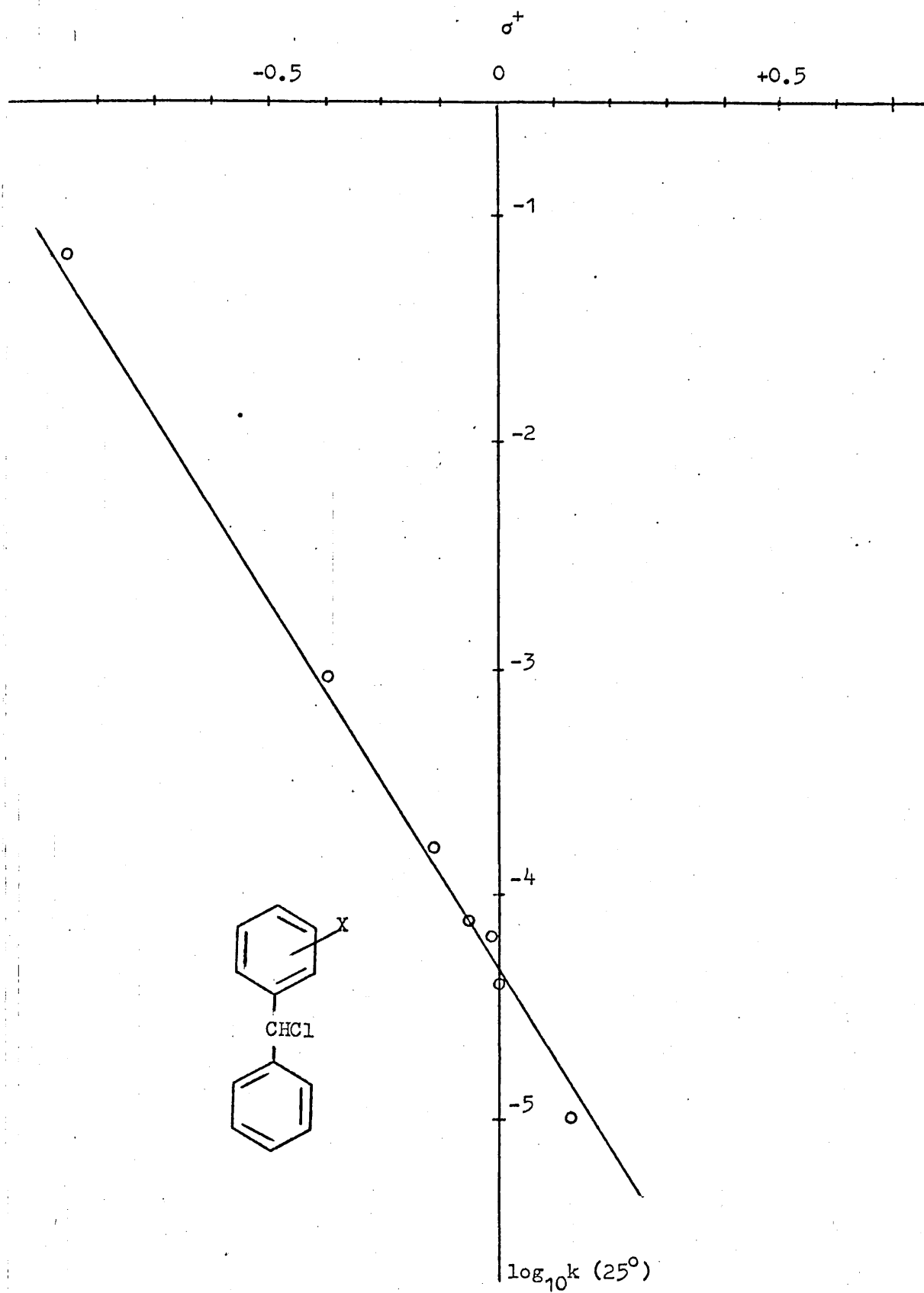
$$\log_{10} k_1(25^\circ) \text{ vs. } \sigma^+$$

$$\rho = -4.36 \pm 0.41$$

k_1 = first-order rate constant at 25° for the solvolysis of substituted benzhydryl chlorides.

σ^+ = Brown-Okamoto substituent constant.

ρ = reaction constant.



GRAPH 3

Table 4
Substituent Constants Derived from the Hammett Plot for the
Benzhydryl Chloride System Compared with some Literature Values

	$\log_{10} k_{25}^{\circ(1)}$	σ^+	$\sigma_{lit}^{+(2)}$	$\sigma_{lit}^{+(3)}$
4-Biphenyl	-3.33	-0.258	-0.179	-0.286
2-Fluorenyl	-2.022	-0.570	-0.60	-0.6
4,5,9,10-Tetrahydro-2-pyrenyl	-2.027	-0.571	-	-0.6
2-(9,10-Dihydrophenanthryl)	-2.466	-0.470	-0.352	-0.48
2-Biphenylenyl	-1.652	-0.680	-	-0.70

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1964, 5316.

Table 5

Results of Kinetic Studies of Some $\alpha(-X-4^{\circ}\text{-Biphenyl})\text{-}$
Isopropyl Chlorides

Substituent	$k_1(25^{\circ}) (\text{sec}^{-1})$	σ^+
4-Hydrogen	$1.44 \times 10^{-3} \pm 0.02$	0
4-Bromo	$8.53 \times 10^{-4} \pm 0.10$	+0.148
4-Chloro	$9.48 \times 10^{-4} \pm 0.03$	+0.114
4-Methoxy	$1.12 \times 10^{-2} \pm 0.01$	-0.778
4-Methyl	$2.77 \times 10^{-3} \pm 0.09$	-0.316

* k_1 = first-order rate constant.

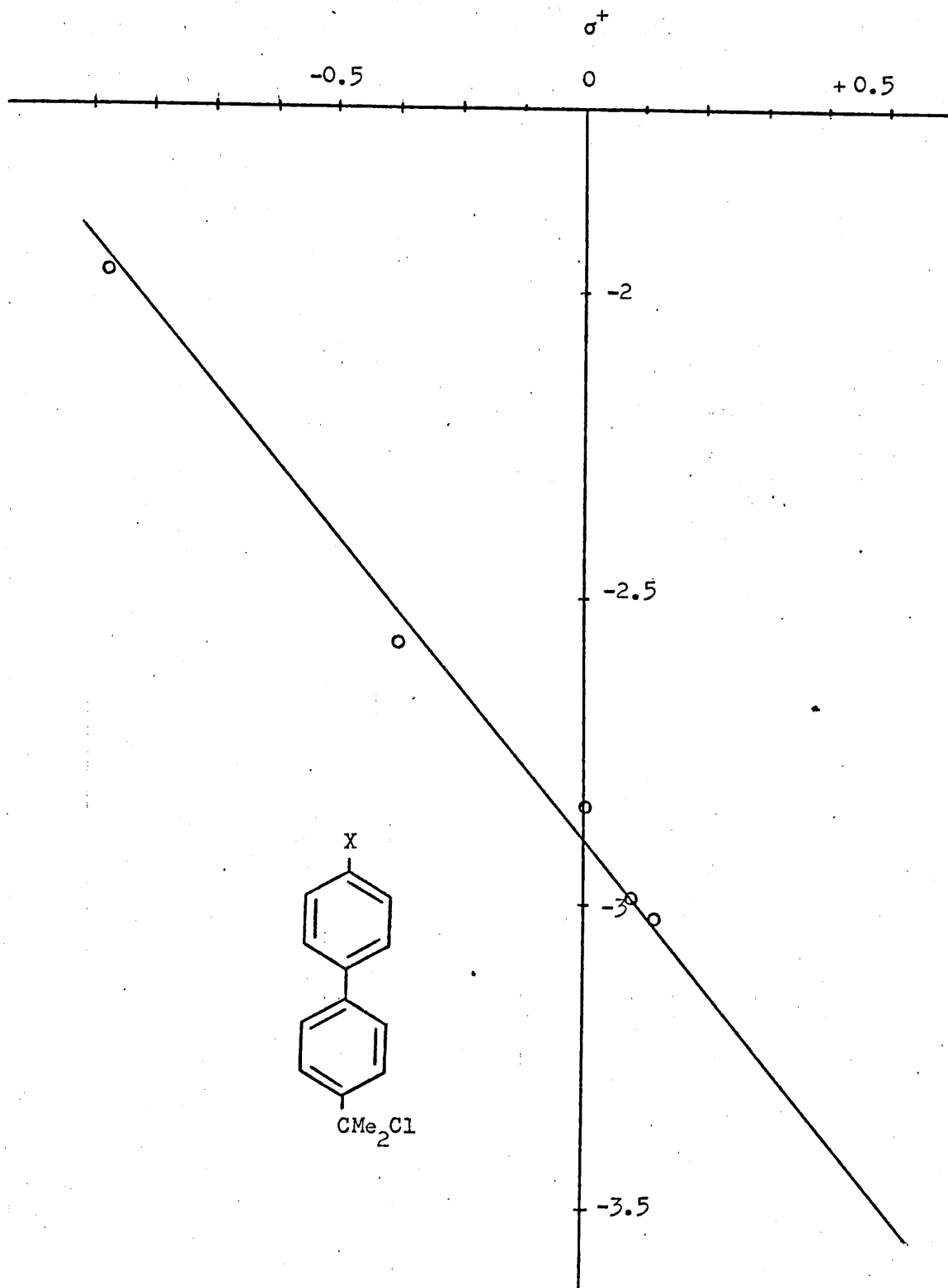
GRAPH 4A Hammett Plot for the α -(4-Biphenyl)-Isopropyl Chloride System $\log_{10} k_1(25^\circ)$ vs. σ^+

$$\rho = -1.21 \pm 0.05$$

k_1 = first-order rate constant at 25° for the solvolysis of substituted α -(4-biphenyl)-isopropyl chlorides.

σ^+ = Brown-Okamoto substituent constant.

ρ = reaction constant.

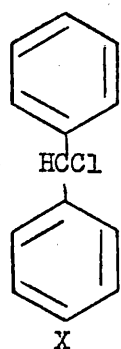


GRAPH 4

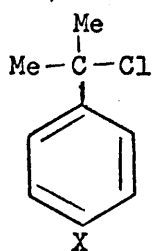
Table 6

Reaction Constants

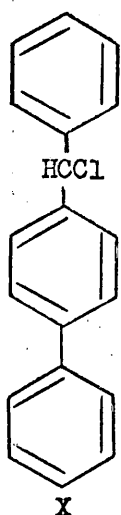
Transmission Coefficients



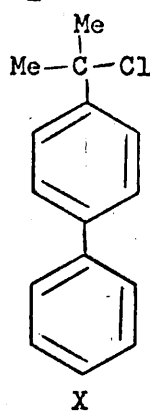
$$\rho_1 = -4.36$$



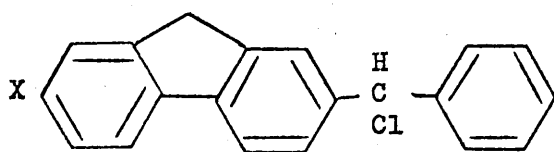
$$\frac{\rho_1}{\rho_3} = 0.96$$



$$\rho_2 = -1.17 \pm 0.07$$



$$\rho_4 = -1.21 \pm 0.05$$



$$\rho_5 = 1.73 \pm 0.09$$

$$\frac{\rho_2}{\rho_1} = 0.268$$

$$\frac{\rho_4}{\rho_3} = 0.267$$

$$\frac{\rho_5}{\rho_1} = 0.40$$

interposition in the t-cumyl system ($\frac{\rho_4}{\rho_3}$). It is also close to earlier values found in the ionization constants of 4-substituted benzoic acids. However, the transmission coefficient for the fluorenyl system ($\frac{\rho_5}{\rho_1}$) is 0.40. Further, since the ratios $\frac{\rho_1}{\rho_3}$ (0.96) and $\frac{\rho_2}{\rho_4}$ (0.94) approximate to each other, the effects of substituents over the two systems (4'-X-biphenyl)benzyl chloride and (4'-X-4-biphenyl)isopropyl chloride are parallel.

These results are all consistent with the hypothesis that the transmission of electronic effect in biphenyl and bridged hydrocarbons is linked with the value of the interplanar angle.

There are various equations reported⁴⁹ linking the interplanar angle of biphenyl with physical measurements. The equation which has received the greatest attention is:

$$E = E_0 \cos^2 \theta \quad (17)$$

where E = the energy of conjugation between the two rings.

E_0 = the energy of conjugation when $\theta = 0^\circ$

θ = the value of the interplanar angle in degrees.

Other equations involving higher powers of $\cos \theta$ have been proposed but fail to give more consistent results.

The data from the solvolysis of the α -(4'-X-4-biphenyl)benzyl halides and the α -(7-X-2-fluorenyl)benzyl halides may be used to deduce the interplanar angle θ' of biphenyl.

The magnitude of a substituent effect is reflected in the change in the free energy of activation between the substituted and unsubstituted system. Thus,

$$\Delta \Delta G = RT \log k_X/k_H \quad (18)$$

where k_X = the first order rate of solvolysis at 25° of the substituted system.

k_H = the first order rate of solvolysis at 25° of the unsubstituted system.

If in the fluorene system, the result of a substituent effect, ΔG , is dependent upon some function of Θ , then the corresponding result, $\Delta G'$ in the biphenyl system, depends similarly upon Θ' , the interplanar angle in biphenyl. As fluorene is planar, Θ is zero.

Because the solvolysis reaction is one in which electronic demands are maximal, the biphenyl residue will be as nearly coplanar as steric interactions will permit - that is, Θ' will be minimal and nearly constant for all 3'- and 4'-substituted-4-biphenylbenzyl carbonium ionic intermediates.

This suggests that the two free energy terms will be linearly linked for all substituents:

$$\Delta \Delta G = RT \log k_X/k_H = f(\Theta) \quad (19)$$

$$\Delta \Delta G' = RT \log k'_X/k'_H = f(\Theta') \quad (20)$$

i.e. $\frac{\Delta \Delta G}{\Delta \Delta G'} = \text{constant}$

A plot of $\log k_1$ (biphenyl) vs. $\log k_1$ (fluorenyl) is linear, with a slope of 1.45 ± 0.04 . The linearity implies that proportional changes in the various energetic contributions are occurring in the fluorene and biphenyl series.

Using the relationship that $f(\theta) = \cos^2 \theta$ and $\theta = 0^\circ$ for the fluorenyl system:

$$\text{Then, } \frac{\Delta \Delta G}{\Delta \Delta G'} = \frac{\cos^2 \theta}{\cos^2 \theta'} = \frac{1}{\cos^2 \theta'} \quad (21)$$

$$\begin{aligned} \frac{1}{\cos^2 \theta'} &= \text{slope of graph} \\ &= 1.45 \pm 0.04 \end{aligned}$$

This gives a value of θ' (45°) in complete agreement with that found in the molecular chlorination studies and close to various estimates from spectroscopic work⁷¹.

The increase in the percentage of transmission of substituent effects in fluorene over biphenyl is a consequence of the coplanarity of the two nuclei in fluorene, allowing greater resonance interaction.

Transmission of Effects in the 2,6-Dimethylbenzhydryl System.

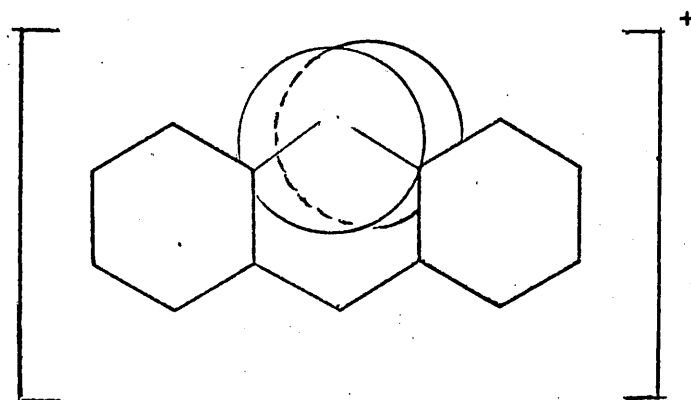
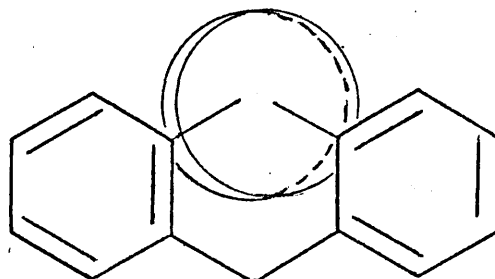
Part 1

The effect of ortho-methyl substituents.

The benzhydryl halides suffer hydrogen-hydrogen steric interactions due to overlap between the two phenyl rings at the ortho-positions. The model (Figure 1) shows that this compression is alleviated but not removed by forming the corresponding carbonium ion.

On placing substituents in the ortho-position of this chloride two distinct effects can be recognised.

(1) Changes in the extent of coplanarity of the carbonium ionic intermediate and of the ground state will cause corresponding changes in the free energy of activation and hence of the observed rate of solvolysis relative to benzhydryl chloride.

FIGURE 1Diphenylmethane and the Benzhydryl Carbonium Ion

Scale: 1 cm represents 1 Å

Overlap of hydrogen atoms in the ortho-position is denoted by partial circles, (van der Waals radius of hydrogen = 1.2 Å).

(2) The electronic effects of the ortho-substituents will be affected by the changes in coplanarity of the system and will show an altered contribution proportional to and in parallel with the change in stabilisation due to the changed contributions of the aryl group.

The second factor applies to all substituents regardless of their position in the aryl rings, whether they are electron donating or electron withdrawing. Williams⁷² has shown that the effects of some para-substituents are diminished by a constant factor when acting in a more crowded system. Further, the extent of this diminution of effect was greatest in the systems where the carbonium ionic intermediate was most removed from coplanarity. The variation in the Hammett reaction constant, ρ , was taken as a measure of these effects and the ratio of ρ values for different ortho-substituted benzhydryl systems was taken as a measure of a "transmission coefficient".

The values of these transmission coefficients found by Williams are listed in Table 7.

Table 7

Transmission Coefficients in ortho-Substituted Benzhydryl Systems

Me Substituents	Transmission Coefficient
0	1.00
2,6-Me ₂	0.90
2,2',6-Me ₃	0.80
2,2',6,6'-Me ₄	0.50*

* Derived from rates measured in 1:1 EtOH/Me₂CO

Para-Substituents in the 2,6-Dimethylbenzhydryl System.

In the present work the nine para-substituted derivatives of 2,6-dimethylbenzhydryl chloride synthesised showed in general a lower susceptibility to substituent effects than their benzhydryl analogues. First order rates of solvolysis of the former compounds at 25° are quoted in Table 8, these give a Hammett plot of $\rho = -3.56 \pm 0.16$ (Graph 5).

Williams noticed that the para-methyl and para-t-Bu substituents showed a remarkably regular decrease in their efficiency as the aryl system to which they were attached became less able to conjugate with the attached α -carbon atom. The results now obtained suggest that this regularity is to some extent fortuitous. While the transmission coefficient of 0.90 deduced by Williams agrees well with the value (0.85) found at present by comparing the Hammett reaction constants associated with benzhydryl chloride and with the 2,6-dimethyl analogue, individual measurements of this factor showed considerable scatter. Similarly, the mean value for the transmission coefficient could not be used successfully to calculate accurate rates of solvolysis.

Deviations between the calculated and experimental rates of solvolysis of the 2,6-dimethylbenzhydryl chlorides are greatest in those chlorides containing two more substituents (f - j in Table 9). Except for the 2,4,4',6-tetramethylbenzhydryl chloride, the calculated rates are all greater than those obtained experimentally.

Nishida^{73,74} has measured the rates of solvolysis in various solvents of various mono- and di-substituted benzhydryl chlorides and obtained a reaction constant, $\rho = -4.17 \pm 0.05$. His calculated rates of solvolysis of disubstituted chlorides agreed to within 10% of the experimental value except for the 4,4'-dimethylbenzhydryl chloride which solvolysed slower than expected by a factor of 0.6. In subsequent work⁷⁵, Nishida showed that the ρ -value for polysubstituted derivatives was not the same

as that for the mono-substituted series and that a saturation of electronic effect was occurring. A modified Hammett equation was suggested:

$$\log k/k_0 = \alpha \rho \Sigma \sigma^+ + \beta \quad (22)$$

where α and β are constants characteristic for the principal substituent.

The present results do not parallel Nishida's observations. The ρ -value for the 2,6-dimethylbenzhydryl chloride system ($\rho = -3.6$) is certainly significantly different from the mono-substituted benzhydryl chloride system ($\rho = -4.36$) but this is explained as a steric effect. A satisfactory Hammett plot is obtained using the usual Hammett equation for electrophilic side-chain reactions:-

$$\log k/k_0 = \rho \Sigma \sigma^+ \quad (23)$$

The discrepancies between the calculated and experimental values probably reflects large variations in the derived rate constant arising from comparatively small errors in the calculated changes in free energy. The calculation method involves small differences in relatively large energies because allowance must be made for the effect of changing the transmission coefficient between the α -carbon atom and the aryl rings from which the bulk of the resonance stabilisation arises. The derived substituent effects, being small second-order perturbations, will contain a relatively high degree of error. Calculated and experimental values of the rate constant for the solvolysis of the substituted 2,6-dimethylbenzhydryl chlorides agree to an average error of $\pm 20\%$, although a value of 80% was obtained in one case. The calculation used a mean transmission coefficient of 0.90, and attempted to allow for the effect of substituents in the ortho-position both electronically and sterically.

Table 8

The Rates of Solvolysis of Some Substituted
2,6-Dimethylbenzhydryl Chlorides

Substituent	$k_1(25^\circ)(\text{sec}^{-1})$	σ^+
4-Hydrogen	0.184×10^{-4}	0
4-Methyl	3.36×10^{-4}	-0.316
4'-Methyl	3.57×10^{-4}	-0.316
4-t-Butyl	2.60×10^{-4}	-0.256
4'-Chloro	9.12×10^{-6}	-0.114
4'-Fluoro	0.32×10^{-4}	-0.0706
4'-Fluoro-4-t-Butyl	2.08×10^{-4}	-0.335
4'-Chloro-4-t-Butyl	4.34×10^{-5}	-0.142
4'-Methyl-4-t-Butyl	2.37×10^{-3}	-0.568
4'-Fluoro-4-Methyl	4.28×10^{-4}	-0.395
4,4'-Dimethyl	3.23×10^{-3}	-0.632

GRAPH 5A Hammett Plot for the 2,6-DimethylbenzhydrylChloride System

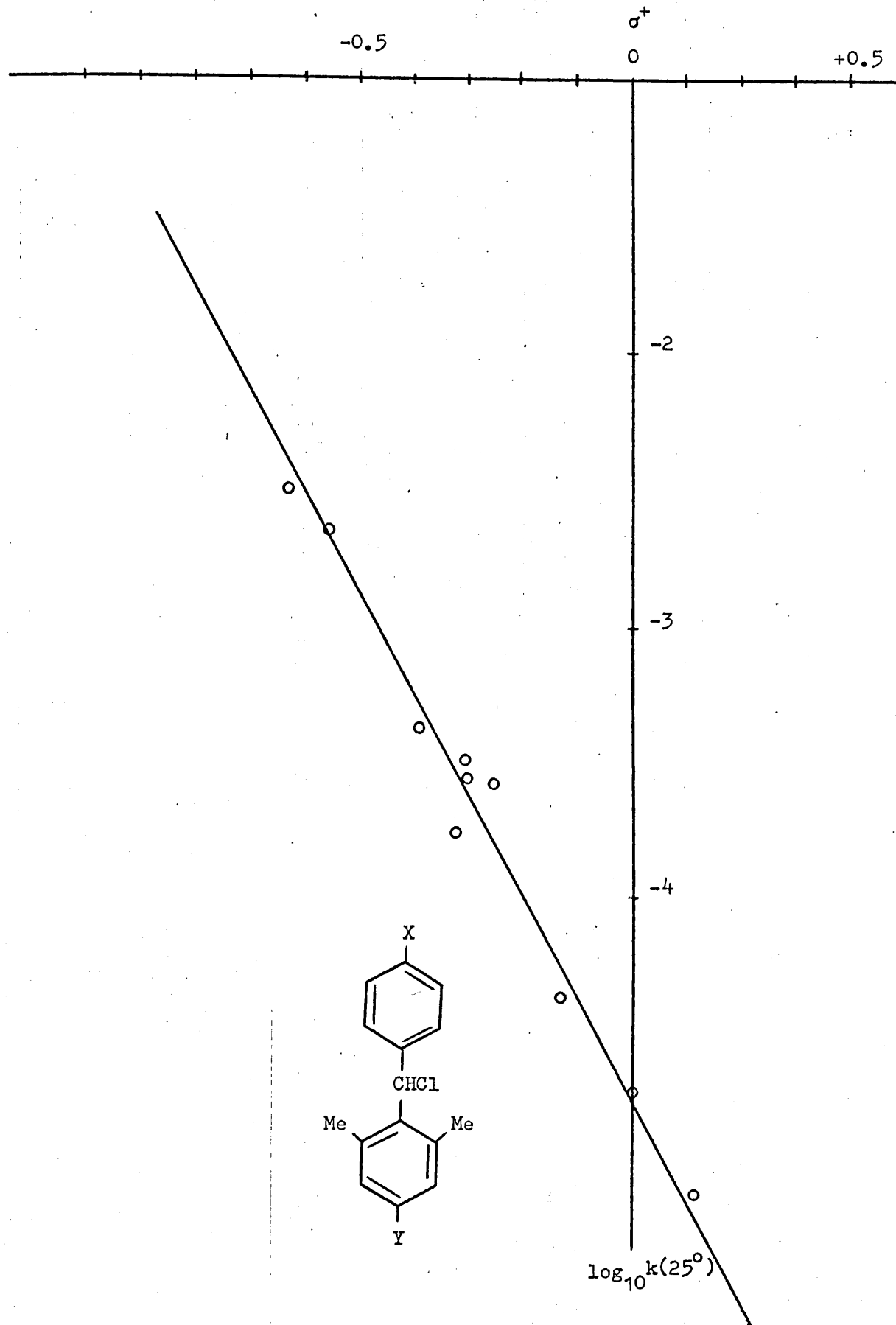
$$\log_{10} k_1(25^\circ) \text{ vs. } \sigma^+$$

$$\rho = -3.56 \pm 0.16$$

k_1 = first-order rate constant at 25° for the solvolysis of substituted 2,6-dimethylbenzhydryl chlorides.

σ^+ = Brown-Okamoto substituent constant.

ρ = Reaction constant.



GRAPH 5

The free energy of reaction of a 4-substituted-2,6-dimethylbenzhydryl chloride (ΔG_1) differs from that of the parent dimethylbenzhydryl chloride (ΔG_2) by a term reflecting the diminished transmission of the incremental free energy of reaction due to the substituent ($m\Delta G_x$).

$$\Delta G_2 = \Delta G_1 - m\Delta G_x \quad (24)$$

The corresponding free energy difference with the same substituent in the benzhydryl system itself, would be ΔG_x . The effect of the two ortho-methyl groups in 2,6-dimethylbenzhydryl chloride is to alter both the stabilisation due to these groups and that due to the aryl system by this factor, m . If the free energy difference arising from ortho-methylation without diminution of transmission is ΔG_{o-Me} and that of the aryl group is ΔG_{Ar} , the free energy difference between benzhydryl chloride (ΔG_o) and the 2,6-dimethyl analogue (ΔG_2) is:

$$\begin{aligned} \Delta G_2 - \Delta G_o &= m(2\Delta G_{o-Me}) - (1 - m) \Delta G_{Ar} \\ &= 2m\Delta G_{o-Me} - (1 - m) (\Delta G_{Ar}) \end{aligned} \quad (25)$$

In the solvolysis of 2-methylbenzhydryl chloride only two of the four possible extreme configurations involve methyl-hydrogen interactions with the attendant possibility of diminished planarity. As a necessary approximation, we may take the free energy difference due to the ortho-methyl substituent in this compound, relative to benzhydryl chloride, as a measure of ΔG_{o-Me} . Values of ΔG_x may be obtained from the effects of substituents upon the solvolysis of benzhydryl chloride and m has already been given the value of 0.9. The difference in free energy of reaction resulting from two ortho-methyl substituents (25) allow ΔG_{Ar} to be estimated.

The free energy of solvolysis of any derivative of 2,6-dimethylbenzhydryl chloride (ΔG_Z) is, in principle, measurable through the equation:

$$\Delta G_Z = \Delta G_O - (1 - m)\Delta G_{Ar} + 2m\Delta G_{O-Me} + m \sum \Delta G_x \quad (26)$$

Table 9 compares calculated and experimental rate coefficients at 25° for some derivatives of 2,6-dimethylbenzhydryl chloride.

Table 9

Substituents	Calc k_1	Exp k_1
(a) 4-Me	3.16 3.16×10^{-4}	3.49×10^{-4}
(b) 4-t-Bu	2.52×10^{-4}	2.51×10^{-4}
(c) 4 ^o -Me	3.16 3.16×10^{-4}	3.57 3.57×10^{-4}
(d) 4 ^o -Cl	7.55 7.55×10^{-6}	9.23×10^{-6}
(e) 4 ^o -F	2.60 2.60×10^{-5}	2.35 2.35×10^{-5}
(f) 4,4 ^o -Me ₂	3.12×10^{-3}	3.23 3.23×10^{-3}
(g) 4-t-Bu, 4 ^o -Me	4.36 4.36×10^{-3}	2.39×10^{-3}
(h) 4-t-Bu, 4 ^o -F	3.60 3.60×10^{-4}	2.11×10^{-4}
(i) 4-t-Bu, 4 ^o -Cl	6.10 6.10×10^{-5}	4.38×10^{-5}
(j) 4-Me, 4 ^o -F	4.56 4.56×10^{-4}	4.34×10^{-4}

Average discrepancy = ± 0.13 kcal mole⁻¹

There are few independent checks which can be applied to the results, but they give a value of 8.7 kcal mole⁻¹ as the change in the free energy of solvolysis of an alkyl halide by replacing an α -hydrogen atom by a phenyl group. This result is appropriate only when both solvolyses take

place by the S_N1 mechanism. Only the reactions of benzhydryl chloride and triphenylmethyl chloride may be compared within this limitation and here it is thought that steric acceleration may intervene. The experimental difference in free energies of the solvolysis of these two species by the S_N1 mechanism in 9:1, ethanol:acetone, is, however, $6.8 \text{ kcal mole}^{-1}$ (ref. 76), and is in fair agreement with the derived value considering the differences in the systems.

C. A General Mechanism of Transmission Across Aryl Systems

Although the solvolytic reaction is one of high selectivity compared with other reactions involving biphenyl in which substituent effects have been studied, i.e. the ionization of ~~benzoic~~^{aric} acids $\rho = 0.5^{70}$, the selective transmission of component electronic effects of a substituent is not observed. Apparently inductive and mesomeric effects of the substituent suffer equal attenuation during transmission across either the biphenyl (fluorene) or the phenyl system. This in turn suggests that the total electronic effects make their way across the phenyl system mesomerically even in a simple mono-substituted benzene. A para-substituted benzyl halide evidently loses some p- π interaction between C_1 and C_α when the bond is rotated; this arises from the observations in 2,6-dimethylbenzhydryl system. This either means that C_1 (adjacent to C_α) or C_4 (adjacent to X) are the carbon atoms bearing the full composite electronic effect of the substituent. Where this effect is predominantly inductive, relay through four carbon atoms would virtually obliterate such an inductive effect by analogy with comparable aliphatic systems. Since no such relative dampening of the inductive effect is found, it follows that it is the electronic perturbation of C_4 which is responsible, presumably through

mesomeric transmission, for all transmitted electronic effects by the substituent within the entire molecule, including the ring to which it is attached.

These deductions, if correct, suggest that the transmission of substituent effects across aromatic systems proceeds entirely through mesomeric relay of a basic perturbation by the substituent of the carbon atom attached to it. They offer a mechanism by which necessary and considerable dipolar effects ($\pm I$) make themselves felt at relatively remote positions of an aromatic system. This is most convincingly demonstrated in the present work by the fact that methyl and t-butyl groups, both with low inductive contributions, and fluorine and chlorine, both with considerable I-effects have their total substituent effect proportionately diminished by rotation of the $C_{\alpha} - C_1$ bond.

D. Discussion of the Preparative Problems

General Modifications

Most of the chlorides studied in this work are new compounds which have been prepared by standard techniques. In general the preparative scheme involved the initial synthesis of the mono-substituted hydrocarbon from which the corresponding benzoyl compound was then obtained using benzoyl chloride and aluminium chloride as the Perrier complex. Reduction of the ketone by sodium borohydride or lithium aluminium hydride yielded the corresponding alcohol from which the chloride was obtained by treatment with thionyl chloride or hydrogen chloride.

In some instances alterations to the experimental scheme had to be made. These are detailed in the Experimental Section. Thus, 4-benzoyl-4'-bromobiphenyl was obtained in higher yield by brominating 4-benzoyl biphenyl

than by benzoylating 4-bromobiphenyl. However, the preparation of the electronically analogous 4-benzoyl-4'-nitrobiphenyl was more successfully achieved by benzoylating 4-nitrobiphenyl.

Similarly the reduction of 3-nitro-4'-benzoylbiphenyl to the corresponding amine compound and its subsequent conversion to the 3-fluoro- and 3-methoxy-4'-benzoylbiphenyls was more successful than the same scheme involving the reduction of 3-nitrobiphenyl and the benzoylation of the resulting 3-fluoro- and 3-methoxybiphenyls. The benzoylation of 3-substituted-biphenyls could result in either 3-X-4'-benzoylbiphenyl or 3-X-4-benzoylbiphenyl depending upon the size and reactivity of the substituent X. The possibility of benzoylation occurring at the 4-, rather than the 4'-, position is greater for 3-fluoro- and 3-methoxybiphenyl than for 3-nitrobiphenyl. This is exemplified in the preparation of α -(3-methyl-4'-biphenyl)benzyl chloride whose synthesis necessitated the benzoylation of 3-methylbiphenyl.

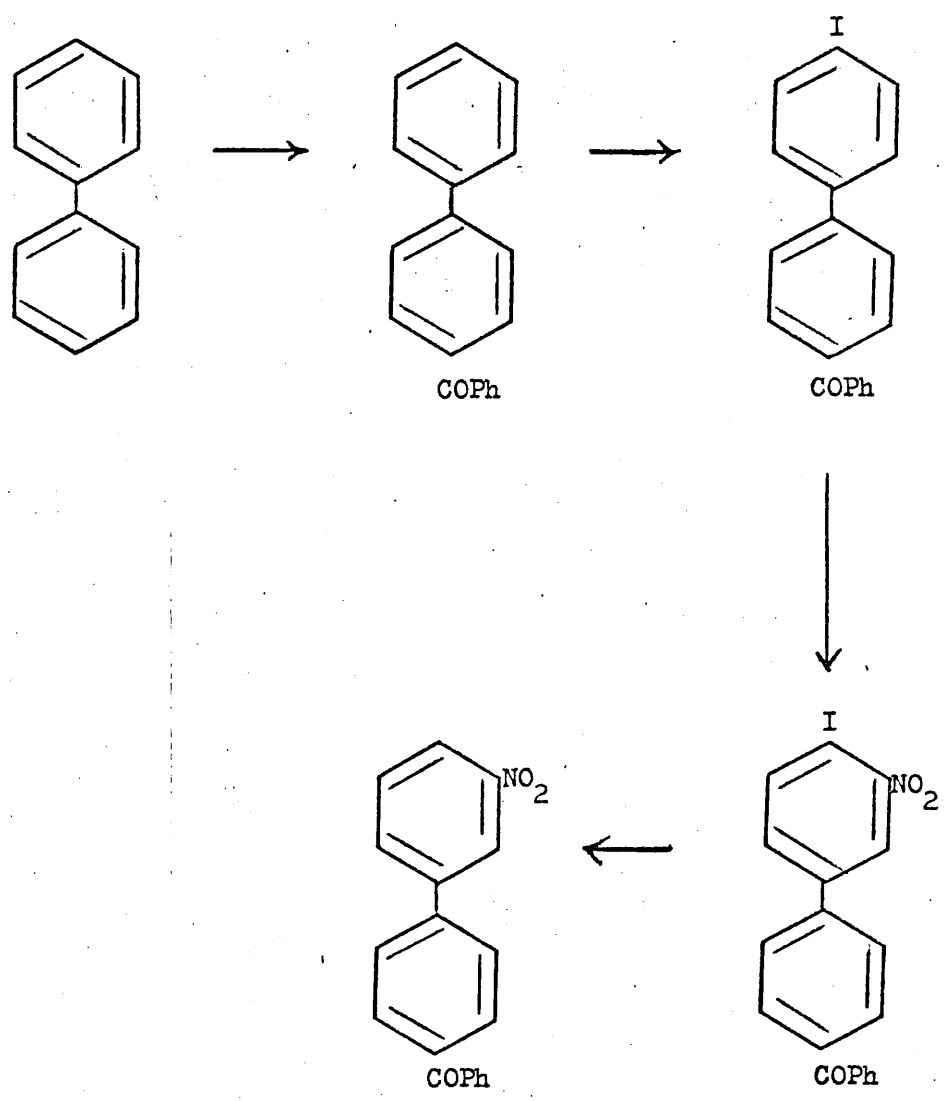
The attempted preparation of (3-methyl-4'-biphenyl)benzyl chloride gave a product whose first-order rate constant at 25^o in ethanol - acetone (9:1 v/v) was $11.6 \times 10^{-4} \text{ sec}^{-1}$, which is unexpectedly fast for a 3-substituted alkyl substituent. The preparation was repeated and an identical product obtained. The orientation of the chloride is most probably (3-methyl-4-biphenyl)benzyl chloride. This conclusion is confirmed by the activating effect of the methyl substituent in the chloride. In comparison with the parent or unsubstituted chloride, this halide reacts at over twice the rate; a similar acceleration is found when an ortho-methyl group is substituted into benzhydryl chloride.⁷²

In both cases the 3-methylbiphenyl was prepared using a modified Gomberg reaction. The attempted preparation of a solid dinitro-derivative of this 3-methylbiphenyl, to confirm its identity, failed to give a crystalline product. An alternative route to 3-methylbiphenyl, using cyclohexanone and m-bromotoluene, was abandoned due to the low yield.⁷⁷

The preparation of a number of the chlorides involved long and tedious syntheses. Instances are the α -(6-X-2-fluorenyl)-benzyl chlorides and the α -(3-X-4'-biphenylyl)-benzyl chlorides. In some cases the preparation of the chlorides had to be abandoned due to low yields of the initial aromatic substrate. For example, 4-t-Bu-biphenyl and 3-nitrofluorene could not be prepared in sufficient yield to warrant their further study. This was disappointing since the failure to obtain 3-nitrofluorene meant that neither α -(6-fluoro-), nor α -(6-methoxy-2-fluorenyl)-benzyl chloride could be studied. Much time was spent trying to find a satisfactory synthetic route to both 2-benzoyl-6-nitrofluorene and 3-nitrofluorene.

The Attempted Preparation of 2-Benzoyl-6-Nitrofluorene

The benzylation of 3-nitrofluorene appeared to be the simplest route to this compound. However, the two reported preparations of 3-nitrofluorene involve the large-scale use of carcinogenic intermediates. An investigation of a possible alternative route was undertaken. Preliminary experiments were carried out on the analogous biphenyl system since products in the latter system are more easily identified. The proposed scheme was:



The reduction of the ketone and treatment of the resulting carbinol with thionyl chloride would yield α -(3-nitro-4'-biphenyl)-benzyl chloride. In an analogous scheme, the precursor of α -(6-nitro-2-fluorenyl)-benzyl chloride, and a number of α -(6-X-2-fluorenyl)-benzyl chlorides, could be prepared.

The benzylation of biphenyl presented no problems. A recent publication⁷⁹ reported the iodination of biphenyl and of bibenzyl with acetyl hypoiodite. This method was followed but failed, probably because 4-benzoylbiphenyl is deactivated toward iodination compared with biphenyl and thus more forcing conditions are required to accomplish its substitution.

The conditions used for the iodination of fluorenone-4-carboxylic acid⁷⁹, which may more closely parallel this system, were then employed on 4-benzoylbiphenyl. The crude product obtained, m.p. 168-72°, showed some darkening and prior decomposition at ca. 120°. An infrared absorption spectrum demonstrated 1:4-disubstitution.

From a study of the literature it seemed that the nitration of 4-bromo-4'-nitrobiphenyl to 4-bromo-3,4'-dinitrobiphenyl represented the system most similar to 4-benzoyl-4'-iodobiphenyl. The nitrating conditions were first tested on 4-bromo-4'-benzoylbiphenyl. The product obtained was a semi-solid which failed to crystallise from petroleum ether, alcohol or benzene. The infrared absorption spectrum did not define the substitution pattern or show the presence of nitro-groups. (Qualitative elemental analysis showed the absence of nitrogen in the compound). Longer reaction times failed to give an improved product.

Despite the failure to obtain 4-benzoyl-3'-nitro-4'-bromobiphenyl, the procedure was applied to 4-benzoyl-4'-iodobiphenyl. Qualitative elemental analysis and infrared analysis showed that no nitration had occurred. Only 4-benzoyl-4'-iodobiphenyl was recovered.

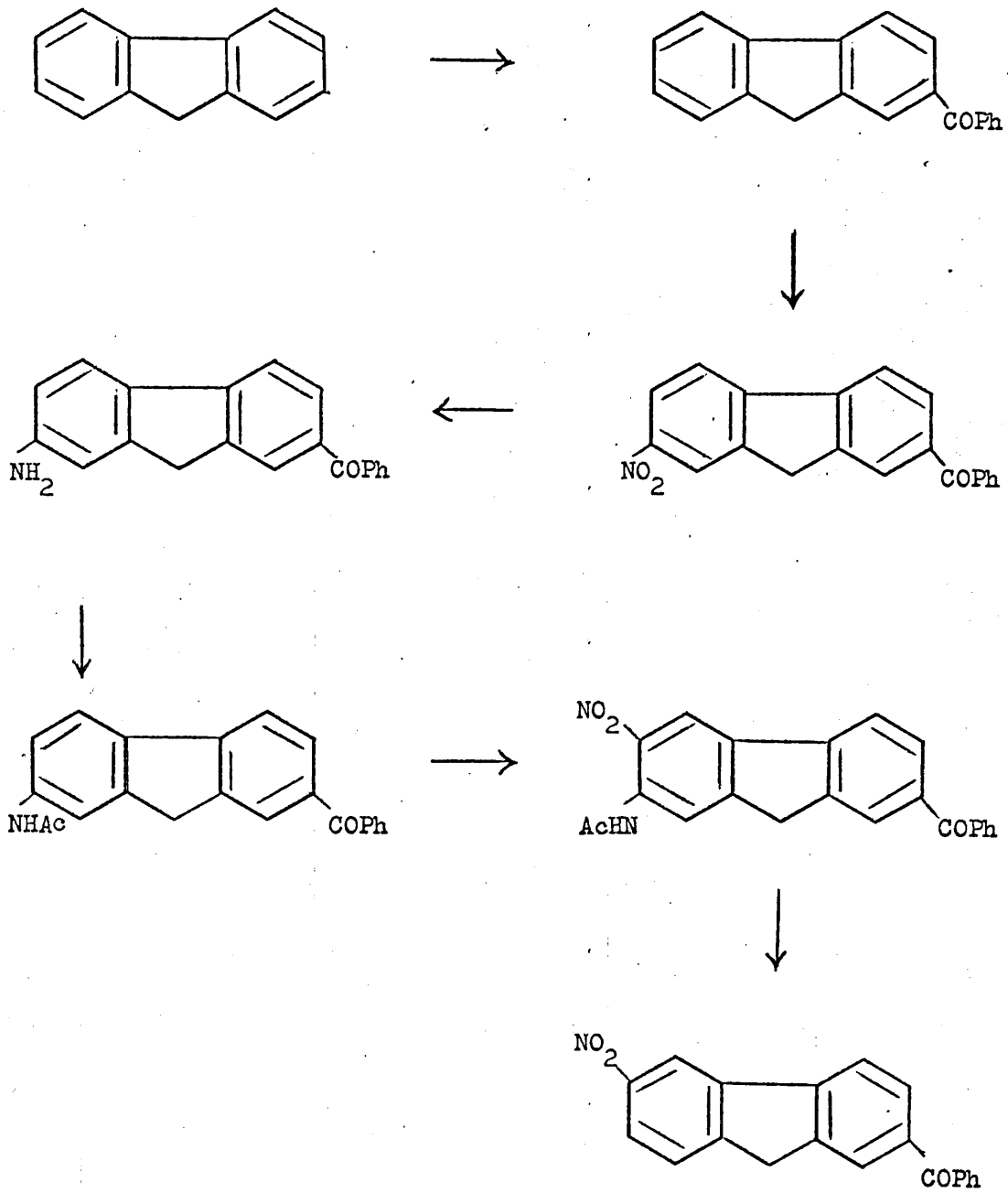
Before searching for alternative nitrating procedures, it was decided to apply the conditions to the more reactive fluorene analogue. 2-Benzoyl fluorene was prepared and iodination was attempted using the method of Novikov. Quantitative elemental analysis of the product showed a discrepancy of 4.73% on the expected formula. (Obtained: C, 55.64%; H, 2.81%; I, 22.80%; O, 14.02%. 2-Benzoyl-7-iodofluorene requires, C, 60.6%; H, 3.28%; I, 32.07%; O, ~~14.04%~~^{14.04%}). A subsequent qualitative elemental analysis on the product showed nitrogen to be present.

Since the iodination reaction was done in the presence of nitric acid ($d = 1.4$) and glacial acetic acid, it is inferred that some concurrent nitration occurred yielding a mixture of products. Repeated recrystallisation from ethanol failed to improve the purity of the product.

A mass spectrum of this product gave a pattern suggesting the presence of 2-iodo-7-benzoylfluorene, 2-nitro-7-benzoylfluorene and dinitro-7-benzoylfluorene.

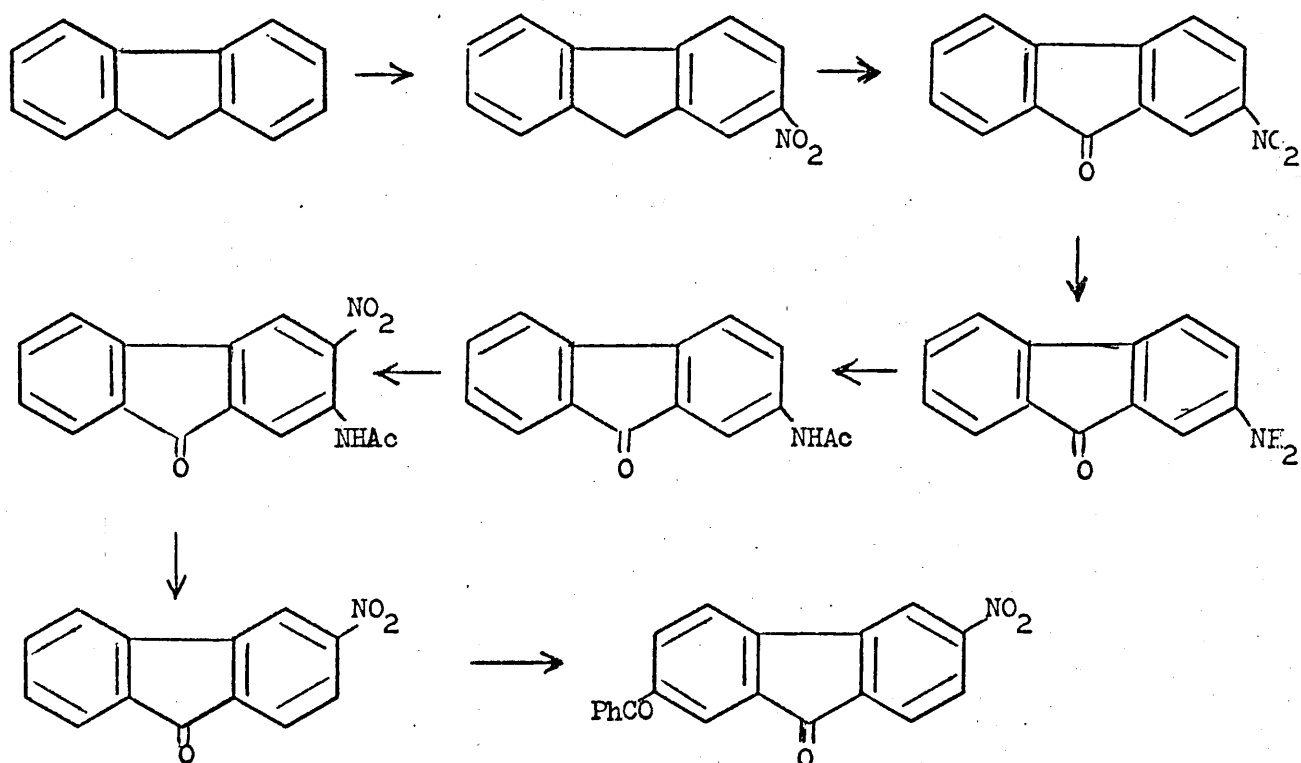
Since the results of quantitative elemental analysis showed the product to be 90% 2-iodo-7-benzoylfluorene it was decided to nitrate this crude product according to the method of ^{Le}Fevre, Moir and Turner⁸⁰, and after a subsequent deiodination using hydriodic acid, to attempt to separate the 3-nitro-7-benzoylfluorene from any 2-nitro-7-benzoylfluorene. However, the crude nitro-compound (obtained: C, 45.90%; H, 1.86%; I, 14.62%; N, 11.4%; O, 26.23%) could not be deiodinated by refluxing with excess aluminium chloride in ethanol or by treatment with hydriodic acid in glacial acetic acid.

Since this route to 3-nitro-7-benzoylfluorene was not immediately successful, two attempts were then made to prepare 3-nitro-7-benzoylfluorene via conventional routes. The first of these involved the following synthetic scheme:



The benzylation and subsequent nitration of fluorene to 2-nitro-7-benzoylfluorene presented no problems. The only method reported in the literature for the reduction of a nitrofluorene is that using sodium bisulphite. This was followed but an investigation of the residue showed no reduction to have occurred. The reduction was then attempted using stannous chloride-concentrated hydrochloric acid. Although successful, the yield of amine was low (20%). Likewise the yield from the subsequent acetylation of 2-amino-7-benzoylfluorene to 2-acetamido-7-benzoylfluorene was too low to warrant further investigation.

The third and final synthetic route to 6-nitro-7-benzoylfluorene to be investigated was the following:



The nitration of fluorene, the oxidation of 2-nitrofluorene to 2-nitrofluorenone and the reduction and acetylation of the latter to 2-acetamidofluorenone, presented no difficulty.

2-Acetamidofluorenone was nitrated in an 80% yield to 2-acetamido-3-nitrofluorenone. Deacetylation of the latter in both concentrated sulphuric acid and 70% sulphuric acid failed. However, boiling 2-acetamido-3-nitrofluorenone in an ethanol-concentrated hydrochloric acid mixture (1:1) was successful yielding 2-amino-3-nitrofluorenone.

The deamination of 2-amino-3-nitrofluorenone to give 3-nitrofluorenone proved extremely difficult. Many modifications to the reported method were attempted. Such included changes in the temperature of the reaction, the length of reaction time, the concentration of nitrous acid, performing the diazotisation in the presence of amyl nitrite and ethanol and finally the inclusion of copper catalysts.

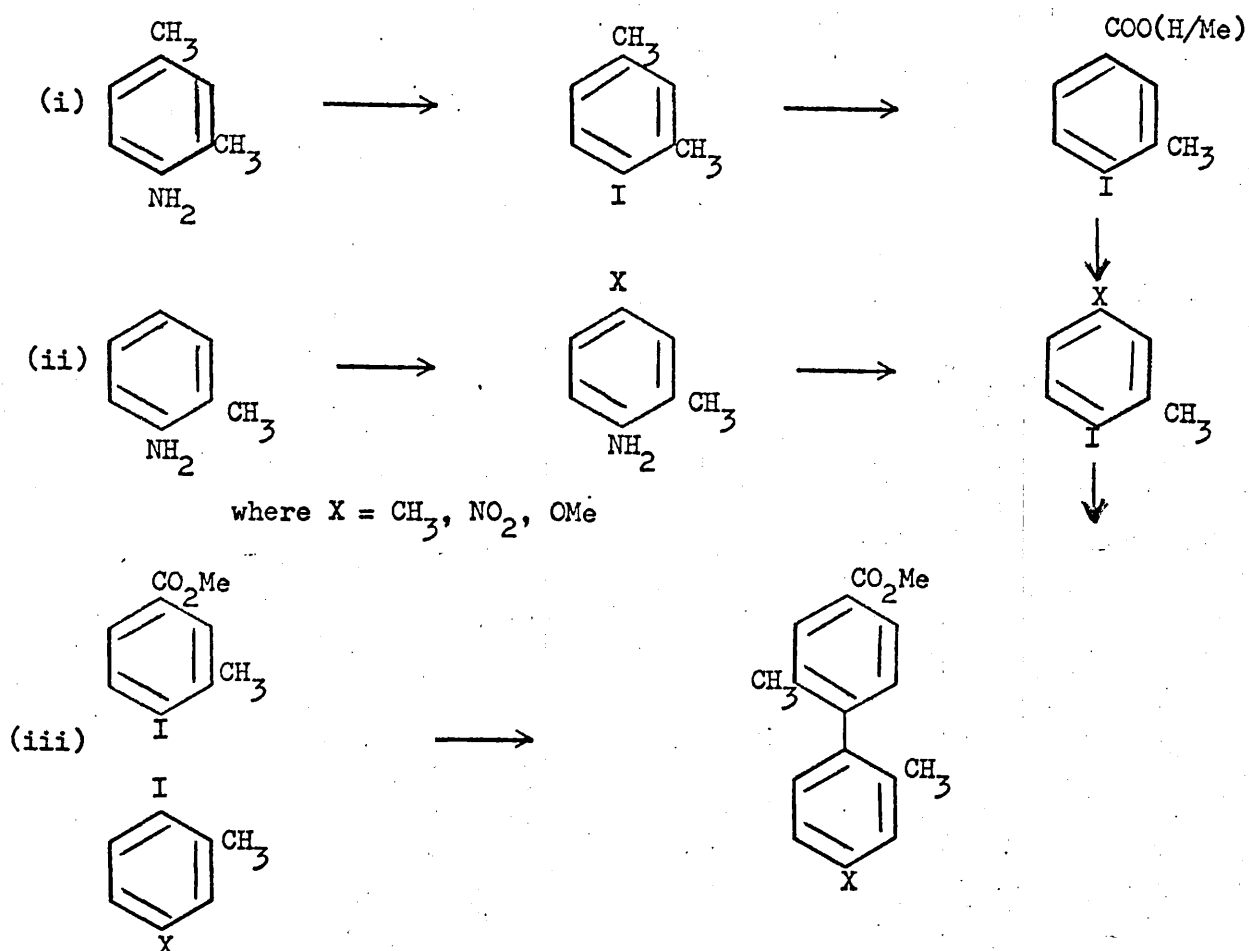
Although a specimen of 3-nitrofluorenone was obtained by the repeated recrystallisation of the crude product obtained by the original method, the yield was too low (< 3%) to be of any use in the required synthesis of the α -(substituted-2-fluorenyl)-benzyl chlorides.

The three reaction sequences studied, although probable, did not represent feasible sources of 3-nitrofluorene and other 3-fluorenyl analogues. This meant that other and more tedious routes were necessary to synthesise individual 3-substituted fluorenes, none of which was successfully convertible into another. Although individual preparations of 1- and 3-methylfluorene and of 3-chlorofluorene were achieved, the disappointing results encouraged the abandoning of this facet of the work for more productive aspects.

The α -(2,2'-Dimethyl-4'-X-4-Biphenylyl)-Methyl Chloride System

The α -(2,2'-dimethyl-4'-X-4-biphenylyl)-methyl chloride system is one in which the interplanar angle between the two phenyl rings is expected to be ca. $70^{\circ 54}$. The kinetic data from the solvolysis of such chlorides should, when compared with the α -(4-X-4'-biphenylyl)-benzyl chloride system reflect the diminished extent of possible mesomeric stabilisation of the resulting carbonium ion.

The general synthetic scheme proposed involved the preparation of (i) methyl 4-iodo-3-methyl benzoate and (ii) a number of 4-substituted 2-methyliodobenzenes. These preparations were achieved with ease. Careful analysis of the reaction products from (iii) a mixed Ullman reaction between (i) and (ii) should result in the isolation of the appropriate 2,2'-dimethyl-4-X-biphenyl-4-carboxylic acid.



A trial Ullman reaction was successfully performed on iodobenzene and methyl o-iodo benzoate, in the presence of a copper catalyst. The same conditions, used in an Ullman reaction involving methyl 4-iodo-3-methyl benzoate and o-iodo toluene gave only 4-iodo-2-methyl benzoic acid indicating that no reaction had occurred.

The same reaction was repeated using a six-molar excess of o-iodo toluene and increasing the reaction time (15 hours). 2-Methyl benzoic acid was once again the only isolable product.

Similarly, using the same experimental conditions no reaction occurred between methyl 4-iodo-3-methyl benzoate and 4-methoxy-2-methyliodobenzene.

Having failed to find the correct experimental conditions for the successful preparation of derivatives in the 2,2'-dimethylbiphenyl system, it was decided that the similar 2,6-dimethylbenzhydryl system should be investigated, where no real synthetic problems were encountered.

CHAPTER IIIEXPERIMENTALAryl Alkyl HalidesPreparation

- (i) The corresponding carbinol in petroleum ether (b.p. 40-60°) was treated with re-distilled thionyl chloride in equimolar proportions and the mixture was heated under reflux until the evolution of hydrogen chloride ceased. A drying tube was used to prevent the entrance of moisture. Excess thionyl chloride was removed by distillation and the crude chloride was purified.
- (ii) The corresponding carbinol was boiled under reflux with an excess of acetyl chloride until the evolution of hydrogen chloride ceased. Excess acetyl chloride was then removed by distillation under reduced pressure and the crude chloride was purified.
- (iii) The method of Hughes and Ingold⁸¹ was used whereby the carbinol in ether (containing a little calcium chloride) was treated for ca. 2 hours with a stream of dry hydrogen chloride. After removing the solvent under reduced pressure, the crude chloride was purified.

Purification

- (a) Fractional distillation under reduced pressure.
- (b) Recrystallisation from a suitable solvent.
- (c) If an uncrystallisable oil, the product was taken up repeatedly in petroleum ether and the solvent removed under reduced pressure. This was carried out until the last traces of thionyl chloride were removed.

Combustion analysis was not always used to establish the purity of the chloride, because isomeric chlorides with different rates of solvolysis would be undetectable. Similarly, the incomplete purification of a chloride could cause poor analyses although the product was suitable for kinetic studies. Ultimately, the only criterion of purity which is appropriate is the kinetic behaviour of the sample. Trace amounts of acidic impurities (e.g. HCl) and of rapidly solvolysed compounds (e.g. SOCl_2) appeared as appreciable "zero time" titration readings; however, all the samples used in this study gave good, linear, first order kinetic plots, often to more than 90% completion. The identity of the solvolysing species could usually be deduced from its approximate equivalent weight.

Chloride	Chlorination Method	Purification Procedure	m.p.
A. <u>α-(X-7-fluorenyl)-benzyl chloride:</u>			
X = 2-ethyl	(i)	(b)*	94° - 5°
= 3-methyl	(i)	(c)	oil
= 1-methyl	(i)	(b)*	64° - 5°
= 3-chloro	(i)	(c)	oil
B. <u>α-(X-4-biphenyl)-benzyl chloride:</u>			
X = 4-fluoro	(i)	(c)	
= 4-bromo	(i)	(c)	
= 4-nitro	(i)	(b)**	115° - 115.5°
= 3-bromo	(i)	(c)	
= 3-methyl	(i)	(c)	
= 3-methoxy	(i)	(c)	
= 3-fluoro	(i)	(c)	
= 3-nitro	(i)	(c)	

Chloride	Chlorination Method	Purification Procedure	m.p.
C. <u>α-(X-4-biphenyl)-isopropyl chloride:</u>			
X = H	(iii)	(b)*	109° - 110°
= 4-methoxy	(ii)	(b)*	132° - 5°
= 4-bromo	(ii)	(b)*	125° - 6°
= 4-chloro	(ii)	(b)*	116° - 7°
= 4-methyl	(ii)	(b)*	120° - 121°
D. <u>X-benzhydryl chloride:</u>			
X = 4-methoxy	(i)	(b)*	140-2/1 mm***
= 4-fluoro	(ii)	(b)*	125-7/1 mm***
= 4-chloro	(ii)	(b)*	159-60/2 mm***
E. <u>X-2,6-dimethylbenzhydryl chloride:</u>			
X = 4'-fluoro	(i)	(a)	130/1 mm***
= 4'-chloro	(i)	(a)	182-3/5 mm***
= 4'-methyl	(i)	(c)	-
F. <u>X-2,4,6-trimethylbenzhydryl chloride:</u>			
X = 4'-fluoro	(i)	(a)	200°/30 mm***
= 4'-chloro	(i)	(a)	130°/1 mm***
= 4'-methyl	(i)	(a)	157-9°/1 mm***

Chloride	Chlorination Method	Purification Procedure	m.p.
G. <u>X-2,6-dimethyl-4-t-butylbenzhydryl chloride:</u>			
X = 4'-fluoro	(i)	(b)	58° - 9°
= 4'-chloro	(i)	(b)*	77° - 8°
= 4'-methyl	(i)	(b)*	68° - 9°

* Recrystallised ex petroleum ether (b.p. 60° - 80°)

** Recrystallised ex petroleum ether (b.p. 60° - 80°)/benzene

*** Boiling point degree/pressure (mm)

The yields obtained in the above chlorinations were in the range 70 - 80%.

Aryl ChloridesCombustion Analysis Results

	Calc.			Found		
	% C	% H	% Cl	% C	% H	% Cl
<u>α-(X-7-fluorenyl)-benzyl chloride:</u>						
X = 2-ethyl	82.87	6.00	11.12	82.8	6.0	11.0
X = 1-methyl	82.8	5.6	11.6	86.7	6.3	-
<u>α-(X-4-biphenylyl)-benzyl chloride:</u>						
X = 4'-nitro	70.2	4.6	10.9	70.4	4.7	10.7
<u>α-(X-4-biphenylyl)-isopropyl chloride:</u>						
X = 4'-bromo	58.2	4.5	-	59.2	4.6	-
X = 4'-chloro	67.92	5.28	-	67.1	5.3	-
X = 4'-methoxy	73.7	6.53	-	72.6	6.50	-
<u>X-2,6-dimethyl-4-t-Bu-benzhydryl:</u>						
X = 4'-fluoro	73.9	7.5	6.5*	75.7	7.1	6.2*
= 4'-chloro	69.9	7.1	22.2	70.8	6.8	22.3
= 4'-methyl	79.6	8.6	12.3	78.6	8.2	12.7
<u>X-2,6-dimethylbenzhydryl:</u>						
X = 4'-fluoro	72.4	5.6	-	73.6	5.9	-
= 4'-chloro	67.9	5.3	-	68.9	5.6	-
<u>X-2,4,6-trimethylbenzhydryl</u>						
X = 4'-fluoro	73.2	6.1	7.2*	74.8	6.2	6.8*
X = 4'-chloro**	68.8	5.7	-	74.7	6.8	-
X = 4'-methyl	78.9	7.4	-	80.2	7.4	-

* Fluorine percentage

** The kinetic data from this chloride were not utilized.

Aryl Alcohols

The ketone was reduced to the corresponding alcohol by one of the following methods.

(i) Sodium Borohydride

The ketone in isopropanol was stirred for 30 mins. with an aqueous solution of the calculated amount of sodium borohydride. The alcohol was isolated by ether extraction, and purified.

(ii) Lithium Aluminium Hydride

The ketone was added as an ethereal solution to an excess of lithium aluminium hydride in sodium-dried ether and stirred for 30 mins. The excess of reagent was destroyed (ethyl acetate) and the product was liberated by adding an excess of dilute acid. On removing the solvent, the product was purified.

(iii) Aluminium Isopropoxide

The ketone (0.07 mole) in isopropanol and aluminium isopropoxide (2.5 g) were heated gently under reflux. Using a Hahn fractionating column acetone was removed slowly. Distillation was continued until a negative test with 2,4-dinitrophenylhydrazine was obtained. The reaction mixture was then cooled, acidified with dilute hydrochloric acid and the alcohol isolated by ether extraction. The extract was washed with dilute hydrochloric acid and water, and was dried. The solvent was then removed and the alcohol was purified.

(iv) Zinc Dust and Alcoholic Sodium Hydroxide

The ketone (0.04 mole), zinc dust (10 g) and sodium hydroxide (10 g) were heated in methylated spirit (150 ml) to 70°. The mixture was stirred until all the sodium hydroxide had dissolved (~ 1.1/2 hours). The mixture was then filtered and the filtrate poured on to crushed ice containing concentrated hydrochloric acid and extracted with ether-benzene

mixture. After drying the organic extract with anhydrous magnesium sulphate and removing the organic solvents, the residual alcohol was purified.

(v) The Grignard Reagent

The ketone (0.02 mole) in sodium-dried ether was added to an excess of Grignard reagent which had been prepared in the usual way (magnesium (7 g), methyl iodide (20 ml) in 100 ml sodium dried ether). An exothermic reaction ensued, and refluxing was maintained for 1 hour. The mixture was then cooled and poured on to a mixture of crushed ice (500 g), concentrated sulphuric acid (20 ml) and ammonium chloride (20 g). Benzene was added to aid dissolution of the alcohol. The organic layer was separated, washed with water, sodium bicarbonate solution (5%) and water again. The extract was then dried and after removing the organic solvents, the alcohol was purified.

Purification of the Aryl Alcohols

(a) Recrystallisation from a suitable solvent, the most generally used being alcohol (methylated spirits).

(b) The oil was heated in a water bath at 15 mm pressure for 1/2 hour, to ensure complete separation from any organic solvent. The oil was then stirred with twice its volume of light petroleum (b.p. 40° - 60°) at room temperature and removed under reduced pressure. An infrared spectrum showed the absence of a ketonic component indicating complete reduction. This alcohol was then used in the preparation of the corresponding chloride.

(c) The oil was treated as in (b), solidification occurring upon trit^{er}ation under light petroleum. The solid was filtered and recrystallised from a suitable solvent, generally alcohol.

The yields obtained in the above reductions were in the range, 60-70%.

Alcohol	Reduction Method	Purification Procedure	m.p.
A. <u>α-(X-7-fluorenyl)-benzyl alcohol:</u>			
X = 2-ethyl	(ii)	(a)	86° - 90°
2-bromo	(i) failed (ii) failed	-	-
3-chloro	(ii)	(a)	164.5 - 105°
3-methyl	(ii)	(a)	99 - 101°
1-methyl	(ii)	(a)	115 - 116°
B. <u>α-(X-4-biphenyl)-benzyl alcohol:</u>			
X = 4'-fluoro	(ii)	(c) ¹	61 - 3°
= 4'-bromo	(i)	(a) ¹	115 - 6°
= 4'-nitro ³	(i)	(a) ²	110 - 111°
= 3'-bromo	(i)	(c)	semi-solid
= 3'-methyl	(ii)	(b)	-
= 3'-fluoro	(ii)	(a)	62 - 5°
= 3'-nitro ³	(i)	(b)	-
= 3'-methoxy	(ii)	(b)	-
C. <u>α-(X-4-biphenyl)-isopropanol:</u>			
X = H	sample obtained		
= 4'-methoxy	(v)	(a)	125 - 6°
= 4'-bromo	(v)	(a)	111 - 112°
= 4'-chloro	(v)	(a)	95 - 6°
= 4'-methyl	(v)	(a)	108 - 9°

	Alcohol	Reduction Method	Purification Procedure	m.p.
D.	X-benzhydrol = H	(iii)	(a)	68°
	X = 4-methoxy	(ii)		67°- 9°
	= 4-fluoro	(ii)	(b)	41°- 2°
	= 4-nitro	(i) and (ii)		failed
	= 4-chloro	(ii)		60°- 1°
E.	<u>X-2,6-dimethylbenzhydrol</u>			
	X = 4'-fluoro	(ii)	(a)	80° - 82°
	= 4'-chloro	(ii)	(b)	-
	= 4'-methyl	(ii)	(b)	-
F.	<u>X-2,4,6-trimethylbenzhydrol</u>			
	X = 4'-fluoro	(ii)	oil	-
	= 4'-chloro	(iv)	oil	-
	= 4'-methyl	(iv)	oil	-
G.	<u>X-2,6-dimethyl-4-t-bu-benzhydrol</u>			
	X = 4'-fluoro	(ii)	(a)	89°- 91°
	= 4'-chloro	(ii)	oil	-
	= 4'-methyl	(ii)	oil	-

¹ Recrystallised ex light petroleum (b.p. 60-80°)

² Recrystallised ex light petroleum (b.p. 60-80°)/benzene

³ Not the most suitable reduction technique.

Aryl Alcohols
Analysis Results

	Calc.			Found		
	% C	% H	% Cl	% C	% H	% Cl
<u>α-(X-7-fluorenyl)-benzyl alcohol:</u>						
X = 3-methyl	88.1	6.3	5.6*	88.0	6.4	5.7*
X = 3-chloro	78.6	4.6	11.6	78.3	4.7	11.6
= 1-methyl	89.5	6.3	5.6*	88.0	6.3	5.6
<u>α-(X-4-biphenyl)-benzyl alcohol:</u>						
X = 3'-fluoro	82.2	5.5	6.7†	82.2	5.4	6.8†

* Percentage oxygen present

† Percentage fluorine present

Aryl Ketones

- (i) The aromatic substrate (0.02 mole) in dichloromethane was heated under reflux with a solution (20 ml) of the Perrier complex from aluminium chloride (0.05 mole) benzoyl chloride (5 ml) and dichloromethane (50 ml), until evolution of hydrogen chloride gas ceased. The mixture was then cooled, poured into cold water, acidified with hydrochloric acid and heated until all the dichloromethane was removed. The initially oily ketone solidified on cooling, when it was filtered and purified.
- (ii) The benzylation was performed exactly as in (i) but substituting carbon disulphide as the solvent instead of dichloromethane. Carbon disulphide was also used in the preparation of the Perrier complex.
- (iii) The aromatic substrate (0.12 mole) in nitrobenzene was heated with the Perrier complex (0.15 mole) for 12 hours to give a deep red reaction mixture. On cooling, the reaction mixture was poured into water and acidified with concentrated hydrochloric acid. Chloroform (30 ml) was added and the organic layer was separated and dried over calcium chloride. Chloroform and nitrobenzene were removed under reduced pressure and the resulting ketone purified.
- (iv) Aluminium chloride (0.02 mole) was dissolved, by gentle warming, in an excess of benzoyl chloride (10 ml). The aromatic substrate (0.02 mole) was added to the amber solution and the deep red mixture was heated under reflux to an internal temperature of 95° - 105° , when a steady stream of hydrogen chloride was evolved. When bubbling subsided, the internal temperature was raised to 115° and held there until no further hydrogen chloride was evolved and then raised to 130° .

The mixture was poured into water, stirred until the red colour of the semi-solid organic phase was discharged, and then treated with 2N-sodium hydroxide (200 ml) and heated with stirring until all of the benzoyl chloride had hydrolysed. The residue was filtered and purified.

(v) The aromatic acid chloride (0.02 mole) in an excess of benzene was heated with aluminium chloride (0.02 mole) in a water bath until evolution of hydrogen chloride gas ceased. The benzene was removed by distillation under reduced pressure.

Water was added to the residue which resulted in an exothermic evolution of hydrogen chloride gas. The crude ketone was filtered and purified.

(vi) To a solution of the aromatic substrate (0.02 mole) and aluminium chloride (0.02 mole) in carbon disulphide, acetyl chloride (excess) was added. When the evolution of hydrogen chloride had ceased, the reaction mixture was poured on to ice. Carbon disulphide was removed by gentle heating and the resulting crude ketone was purified.

(vii) To aluminium chloride (0.2 mole) in nitrobenzene (150 ml), a mixture of aromatic substrate (0.2 mole; xylene; t-butyl-, m-xylene, or mesitylene) and the acid chloride (0.2 mole) was added, with stirring, at 5° - 10°. Stirring was continued for 5 hours at 35°. The reaction mixture was hydrolysed by pouring it on to crushed ice (750 g) containing concentrated hydrochloric acid (150 ml) and stirring vigorously. The organic layer was then separated and washed with water, 6% sodium hydroxide and water acidified slightly with acetic acid. After drying the organic extract over calcium chloride, the nitrobenzene was distilled leaving the crude ketone which was purified.

Purification of the Aryl Ketones

Purification of the crude ketone was performed by recrystallisation ex alcohol (a), by distillation (b), or (c) the oil was heated in a water bath at 15 mm pressure for 1/2 hr to ensure complete separation from any organic solvent. The oil was then stirred with twice its volume of light petroleum (b.p. 40° - 60°) at room temperature and removed by distillation under reduced pressure. Occasionally, (d), when the oil was

heated as in (c), solidification occurred upon trituration under light petroleum. The solid was then filtered and recrystallised ex alcohol.

Ketone	Preparation	Purification Procedure	m.p.
A. <u>X-7-Benzoylfluorene</u>			
X = 2-ethyl	(i)	(a)	108°-109°
= 2-bromo	(i)	(a)	126°-126.5°
= 3-chloro	(i)	(a)	
= 3-methyl	(i)	(a)	65°-7°
= 1-methyl	(i)	(a)	115°-7°
B. <u>4-X-4'-benzoylbiphenyl</u>			
unsubstituted	(v) ¹	(a)	100-100.5° (lit. 100-102 ¹)
X = 4 ¹ -fluoro	(ii)	(a)	110°-112°
= 4 ¹ -bromo	(iii)	(a) ²	155°-7°
= 4 ¹ -nitro	(iii)	(a)	154°-6° (lit. 154-6 ¹)
= 3 ¹ -bromo	(ii)	(d)	87°-88.5°
= 3 ¹ -methyl	(ii)	(c)	-
= 3 ¹ -fluoro ⁸	-	(a) ³	76°-7°
= 3 ¹ -nitro	(iv)	(a) ⁴	135°-136.5°
= 3 ¹ -methoxy ⁹	-	-	oil

Ketone	Preparation	Purification Procedure	m.p.
C. <u>X-4-acetylbiphenyl</u>			
X = 4-methoxy	(vi)	(a) ⁵	147°-9°
= 4-bromo	(vi)	(a)	124°-5°
			(lit. 129-130)
= 4-chloro	(vi)	(a)	86°-7°
			(lit. 103-104)
= 4-methyl	(vi)	(a)	121°-2°
D. <u>X-benzophenone:</u>			
X = 4-methoxy ⁶			65°-6°
= 4-fluoro ⁷			130°-2°
= 4-nitro	(v)	(a) ⁵	138°
E. <u>X-2,6-dimethylbenzophenone</u> ¹⁰			
X = 4'-fluoro		(b)	128°/2 mm
= 4'-chloro		(c)	-
= 4'-methyl		(a)	61°-3°
F. <u>X-2,4,6-trimethylbenzophenone:</u>			
X = 4'-fluoro	(vii)	(b)	200°/30 mm
		(a)	36°-7°
= 4'-chloro	(vii)	(a)	56-8°
= 4'-methyl	(vii)	(c)	-

Ketone	Preparation	Purification Procedure	m.p.
G. <u>X-2,6-dimethyl-4-t-Bu-benzophenone:</u>			
X = 4'-fluoro	(vii)	(a)	124°-5°
= 4'-chloro	(vii)	(a)	164°-164.5°
= 4'-methyl	(vii)	(a)	138°-9°

- 1 The method of D.H. Hey and E.P.B. Jackson, J.C.S., 1936, 803 was followed. Benzoyl chloride (0.4 mole) and aluminium chloride (0.2 mole) were refluxed with a solution of biphenyl (0.2 mole) in benzene (70 ml).
- 2 The ketone was recrystallised ex ethanol/benzene.
- 3 The ketone was recrystallised ex petroleum ether (b.p. 60°-80°)/chloroform.
- 4 The ketone was recrystallised ex ethyl acetate.
- 5 The ketone was recrystallised ex glacial acetic acid.
- 6 4-Methoxybenzophenone was obtained by the methylation of 4-hydroxybenzophenone (Experimental, p. 96)
- 7 4-Fluorobenzophenone was obtained by the reduction and subsequent diazotisation of 4-nitrobenzophenone.
- 8 α -(3'-Fluoro-4-biphenyl)-benzophenone was prepared by the reduction and subsequent diazotisation of the corresponding nitro-ketone.
- 9 α -(3'-Methoxy-4-biphenyl)-benzophenone was prepared by the methylation of the corresponding hydroxy-ketone.
- 10 These ketones were obtained by the debutylation of the corresponding 2,6-dimethyl-4-t-Bu-4'-X-benzophenones.

Aryl KetonesAnalysis Results

	Calc.		Found	
	% C	% H	% C	% H
X-7-benzoylfluorene				
X = 1-methyl	88.7	5.6	88.6	5.6
X = 3-methyl	88.7	5.6	88.6	5.5
X-4-benzoylbiphenyl				
X = 3'-fluoro	82.6	4.7	82.4	4.8 6.6*

* = F

Preparations of the Aromatic Substrates2-BromofluoreneMethod⁸².2-Ethylfluorene

2-Acetylfluorene⁸³ was prepared (pg. 87 (vi) using dichloromethane as the solvent) and reduced with excess hydrazine hydrate in diethylene glycol⁸². The crude product was purified by codistillation with ethylene glycol. A white crystalline solid was obtained in 80% yield. m.p. 93.5° - 94° (Lit. 99°⁸⁴).

1-Methyl-; 3-methyl-; and 3-chlorofluorene

These three fluorenes were obtained by the reduction of the corresponding fluorenones using zinc dust and ethanolic alkali. 3-Methyl- and 3-chlorofluorene were prepared from toluene or from chlorobenzene through

ring-closure of the 2-amino-4'-substituted benzophenones⁸⁵ arising from Friedel-Crafts acylations using N-(p-toluenesulphonyl)-anthranilic acid⁸⁶.

1-Methylfluorene was similarly prepared from 2-amino-2'-methylbenzophenone^{85,86}.

3-methylfluorene ex ethanol m.p. 87.8° (Lit. 88° (a))

3-chlorofluorene ex methanol m.p. 94.5° (Lit. 95° (b))

1-methylfluorene ex ethanol m.p. 87° (Lit. 87° (c))

(a) Sieglitz, A., and Schatzkes, J., Ber., 1921, 54, 2071.

(b) Bell, F., and Gibson, J.A., J. Chem. Soc., 1955, 3560.

(c) Pinck, L.A., and Hilbert, G.E., J. Amer. Chem. Soc., 1946, 68, 751.

4-Fluorobiphenyl⁸⁷

4-Fluorobiphenyl was obtained in 50% yield by the standard diazotisation of 4-aminobiphenyl (0.1 mole) in the presence of sodium borofluoride. The borofluorate salt was decomposed by gentle heat under petroleum ether (b.p. > 110°) until the evolution of boron trifluoride gas had ceased. The crude product was recrystallised ex alcohol. m.p. 68°-71° (Lit. 74.2°).⁸⁸

4-Aminobiphenyl was itself prepared by the reduction of 4-nitrobiphenyl (0.2 mole) by Raney nickel and hydrazine hydrate (1.2 mole) in 40% yield.

The crude 4-aminobiphenyl was recrystallised ex aqueous ethanol.

m.p. 51°-2°⁸ (Lit. 50°-2°).

4-t-Bu-biphenyl⁷⁰

t-Butylchloride (0.16 mole), biphenyl (0.16 mole) and ferric chloride (7.4 g) in carbon disulphide (100 ml) were kept at 25° for two hours.

The reaction mixture was then poured into water (800 ml) and the carbon disulphide removed. The aqueous mixture remaining was ether extracted and the organic extract washed with sodium bicarbonate (5%), water and dried

over anhydrous magnesium sulphate. The solvent was removed under reduced pressure and the remaining product distilled. Three fractions were obtained:

- (i) white solid b.p. $160^{\circ}/30$ mm
- (ii) yellow solid b.p. $180^{\circ}/30$ mm
- (iii) yellow liquid b.p. $185^{\circ}-190^{\circ}/30$ mm

Fractions (i) and (ii) were recrystallised ex alcohol to give white plates with m.p. $125^{\circ}-126.5^{\circ}$ and $115^{\circ}-116^{\circ}$ respectively. Fraction (iii) solidified when cooled in ethanol. When recrystallised ex alcohol only a semi-solid was obtained. Fractions (i) and (ii) showed a 1:4-di-substitution pattern upon infrared analysis and were presumed to be 4-4'-di-t-Bu-biphenyl (m.p. $128^{\circ}-9^{\circ}$)⁹⁰.

The preparation was repeated, the temperature being kept at 15°C for a reaction time of 30 minutes. The crude product was obtained as before, distilled at $140^{\circ}-6^{\circ}/2$ mm, and recrystallised ex alcohol m.p. $33^{\circ}-8^{\circ}$. A second crop was obtained with a m.p. $51^{\circ}-2^{\circ}$ (Lit. $49^{\circ}-50^{\circ}$)⁷⁰. Recrystallisation of the first crop failed to improve the melting point. The yield, < 5%, was too low to warrant further investigation.

3-Bromobiphenyl

3-Bromobiphenyl was obtained by a modified procedure of that of H.A. Scarborough and W.A. Waters⁹³.

2-Aminobiphenyl was obtained commercially and converted in a 75% yield to 2-acetamidobiphenyl m.p. $120^{\circ}-1^{\circ}$ (Lit. 121°)⁹³ which was brominated to 5-bromo-2-acetamidobiphenyl m.p. $129^{\circ}-30^{\circ}$ (Lit. 130°)⁹² in 60% yield.

The 5-bromo-2-acetamidobiphenyl was hydrolysed in a 10% alcoholic solution of hydrobromic acid by boiling for 3 hours. Addition of concentrated

hydrochloric acid precipitated some of the amine salt which was filtered and dried. The remaining acidic mixture was extracted with benzene and ether and the organic extract separated. Concentrated ammonium hydroxide solution (.880) was added to the alcoholic hydrobromic acid solution when the amine was liberated as an orange-brown oil. This was separated and converted to the sulphate-salt by the addition of 4N sulphuric acid. Yield 30%.

2-Phenyl-4-bromoaniline sulphate was diazotised in the presence of hypophosphorous acid in the standard way⁹³ to give 3-bromobiphenyl $145^{\circ}/2 \text{ mm}$ ($169^{\circ}-73^{\circ}/17 \text{ mm}$)⁹⁴ n_D^{25} 1.6390 (Lit. 1.6390)⁹⁴.

3-Methylbiphenyl

(a) 3-Methylbiphenyl was made in 20% yield from m-toluidine (0.1 mole), amyl nitrite (1.5 mole) and benzene (5 mole) by the standard aryl homolytic reaction⁹⁶. (Lit. $148^{\circ}-50^{\circ}/20 \text{ mm}$). The colour was improved by treatment with zinc dust and dilute acid in ethanol.

(b) 3-Methylbiphenyl was prepared as above and was fractionally distilled. Three fractions were obtained:

- (i) b.p. $< 70^{\circ}/2 \text{ mm}$
- (ii) b.p. $70^{\circ}-83^{\circ}/2 \text{ mm}$
- (iii) b.p. $84^{\circ}-115^{\circ}/2 \text{ mm}$

G.l.c. analysis of fractions (ii) and (iii) showed the presence of more than one component. These fractions were combined and eluted from an alumina column using methylated spirit as eluent. G.l.c. analysis showed the purity to have improved. The eluted 3-methylbiphenyl was distilled from zinc dust ($119^{\circ}-121^{\circ}/4 \text{ mm}$).

3-Nitrobiphenyl

3-Nitrobiphenyl was made from m-nitroaniline by the standard aryl homolytic reaction (25%) b.p. $160^{\circ}-170^{\circ}/3 \text{ mm}$ ⁹⁵. (Lit. $206^{\circ}-5^{\circ}/20 \text{ mm}$)⁹⁶,

recrystallised ex aqueous alcohol m.p. $61^{\circ}-2^{\circ}$ (Lit. $58^{\circ}-9^{\circ}$ ⁹⁶, $58.5^{\circ}-59.5^{\circ}$ ⁹⁷).

3'-Fluoro-4-Benzoylbiphenyl

3'-Nitro-4-benzoylbiphenyl (0.05 mole) was reduced with stannous chloride (0.20 mole), concentrated (0.50 mole) hydrochloric acid, in glacial acetic acid, ^{93b} to give 3'-amino-4-benzoylbiphenyl in 60% yield, m.p. $165-8^{\circ}$. The amine was liberated from its salt by stirring in a 60% sodium hydroxide solution. Since the free amine was found to be only slightly soluble in benzene, the solid obtained upon neutralising the salt was filtered and then exhaustively extracted with benzene, using a soxhlet apparatus. The benzene was then removed under reduced pressure.

3'-Amino-4-benzoylbiphenyl ($165-8^{\circ}$) was diazotised in the presence of sodium borofluoride in the standard way ^{93c} and 3'-fluoro-4-benzoylbiphenyl was obtained by decomposing the resulting borofluorate salt under petroleum ether (b.p. $> 110^{\circ}$) and xylene. The crude ketone was recrystallised ex petroleum ether ($60^{\circ}-80^{\circ}$)/chloroform. m.p. $74^{\circ}-6^{\circ}$.

4-Fluorobenzophenone was prepared in an identical way from 4-nitrobenzophenone in 40% yield. m.p. $48^{\circ}-9^{\circ}$. Lit. $48.2^{\circ}-48.7^{\circ}$ ⁹⁹.

3'-Methoxy-4-Benzoylbiphenyl

3'-Amino-4-benzoylbiphenyl (0.01 mole) was diazotised according to the method of Gray, Hartley and Ibbotson ⁹⁹ to give 3-hydroxy-4'-benzoylbiphenyl as a yellow solid, m.p. 143° . Yield 65%.

3'-Hydroxy-4-benzoylbiphenyl (0.05 mole) was stirred with an excess of dimethyl sulphate (0.1 mole) in methylated spirits at room temperature. A concentrated solution (50%) of sodium hydroxide was added and the reaction

mixture kept below 50° until all the phenol was in solution. Excess sodium hydroxide was used so that any unreacted phenol stayed in solution as the sodium salt. When the reaction mixture became homogeneous the temperature was raised to 70° for 30 minutes. On cooling, a dark red oil was obtained. The coloured azo impurities were removed by boiling with stannous chloride. 3'-Methoxy-4-benzoylbiphenyl was extracted with ether and obtained as an uncrystallisable oil in a 20% yield.

4-Methoxybiphenyl and 4-Methoxybenzophenone

4-Methoxybiphenyl and 4-methoxybenzophenone were each obtained in 60% yield from commercially available 4-hydroxybiphenyl and 4-hydroxybenzophenone respectively. The procedure used was the same as that for the preparation of 3'-methoxy-4-benzoylbiphenyl.

4-methoxybiphenyl ex ethanol m.p. 89° - 90° ¹⁰⁰

4-methoxybenzophenone ex petroleum ether (b.p. 40° - 60°)
m.p. 65° - 6° (Lit. 65° - 6°)¹⁰¹.

Benzoyl Chlorides

The substituted benzoyl chlorides were obtained in 70% yield from the corresponding benzoic acids (0.4 mole) by heating with an excess of thionyl chloride (23 ml) until evolution of hydrogen chloride gas ceased. Excess thionyl chloride was removed by distillation and the substituted benzoyl chloride obtained by distillation.

4-fluorobenzoyl chloride b.p. 185° - 192° (193°)⁸⁸

4-chlorobenzoyl chloride b.p. $111^{\circ}/18$ mm ($111^{\circ}/18$ mm)⁸⁸

4-methylbenzoyl chloride b.p. 214° - 16° (214° - 16°)⁸⁸

2,6-Dimethyl-4'-X-Benzophenones (X = F, Cl, Me)

The 2,6-dimethyl-4'-X-benzophenones were obtained by boiling the corresponding 2,6-dimethyl-4-t-Bu-4'-X-benzophenone (0.66 mole) with

aluminium chloride (1.0 mole) in benzene at 75° for 8 hours^{102, 103}. The reaction mixture was hydrolysed by pouring on to crushed ice and acidifying with concentrated hydrochloric acid. The organic layer was separated, washed with dilute hydrochloric acid and water and finally dried over anhydrous sodium sulphate. Benzene and t-Bu-benzene were removed under reduced pressure.

- (a) 2,6-Dimethyl-4'-fluorobenzophenone b.p. $128^{\circ}/2$ mm.
- (b) 2,6-Dimethyl-4'-methylbenzophenone ex alcohol m.p. $61^{\circ}-3^{\circ}$.
- (c) 2,6-Dimethyl-4'-chlorobenzophenone was obtained as an oil. Infrared analysis showed the same substitution pattern as that obtained for (a) and (b).

3-Nitro-4-Bromo-4'-Benzoylbiphenyl

4-Bromo-4'-benzoylbiphenyl (0.05 mole) was treated with potassium nitrate (8 g) and concentrated sulphuric acid (50 ml) according to the method of Le Fevre, Moir and Turner⁸⁰. The crude product, when crystallised from glacial acetic acid, gave a semi-solid which failed to crystallise from petroleum ether, chloroform or benzene. An infrared spectrum was inconclusive. On triturating in water a yellow solid was obtained. m.p. $60^{\circ}-85^{\circ}$. This preparation was abandoned.

4-Iodo-4'-Benzoylbiphenyl

(a) The procedure of Novikov⁷⁸ was successful. To a mixture of 4-benzoylbiphenyl (0.025 mole), iodine (0.025 mole), concentrated sulphuric acid (17 ml) and glacial acetic acid (150 ml) was added concentrated nitric acid ($d = 1.4$, 4 ml) at 80° . The colour of the iodine solution immediately paled and the mixture was stirred continuously for 3.1/2 hours. On cooling, the pale yellow precipitate was filtered and

dried. m.p. 168° - 172° , darkened at 120° with slight decomposition.

An infrared spectrum showed 1:4-disubstitution.

(b) An attempt to iodinate 4-benzoylbiphenyl according to the method of Ogata, Urasaki and Ishibashi⁷⁹ failed. An acetic acid solution (10 ml) of peracetic acid (0.02 mole) was slowly added to a stirred solution of 4-benzoylbiphenyl (0.04 mole) and iodine (0.02 mole) in glacial acetic acid (130 ml) at 60° during 4 hours. The reaction mixture was cooled, filtered and the precipitate washed with sodium bicarbonate (5%). Only iodine and 4-benzoylbiphenyl were recovered.

3-Nitro-4-Iodo-4'-Benzoylbiphenyl

An attempt to nitrate 4-iodo-4'-benzoylbiphenyl according to the method of Le Fevre, Moir and Turner failed⁸⁰.

2-Iodo-7-Benzoylfluorene

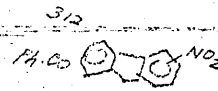
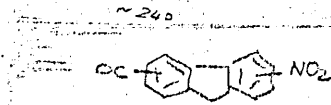
2-Benzoylfluorene was treated with iodine and nitric acid by Novikov's method⁷⁸. The resulting pale yellow solid was recrystallised ex alcohol, m.p. $150 - 152^{\circ}$.

(Required: C, 66.6%; H, 3.3%; I, 32.1%; O, 4.0%; obtained C, 55.6%; H, 2.8%; I, 22.8%; O, 14.0%). The analysis accounts for only 95.2% of the compound. A subsequent qualitative elemental analysis showed nitrogen to be present.

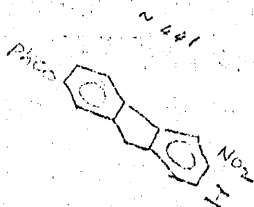
The mass spectrum of the compound was obtained and is reproduced here.

FIGURE 2

The mass spectrum of the product obtained by iodinating 2-benzoylfluorene in nitric acid.



no classification (357)



Peaks:	105	benzoyl (not in diagram)
	240	X-carbonyl-X-nitrofluorene
	312	X-benzoyl-X-nitrofluorene
	~ 440	X-benzoyl-X-nitro-X-iodofluorene

Since the iodination was performed in the presence of nitric acid and glacial acetic acid some nitration also occurred.

The product was estimated to be 90% 2-iodo-7-benzoylfluorene.

2-Iodo-3-Nitro-7-Benzoylfluorene

2-Iodo-7-benzoylfluorene (10 g) was added gradually to a mixture of concentrated sulphuric acid (40 ml) and concentrated nitric acid (40 ml). There was no obvious rise in temperature. The solid dissolved to give an orange solution which was heated on a water bath at 50°-60° for 45 minutes. The solution became viscous and a lower oily layer separated. The mixture was poured into cold water (750 ml) and the solid which separated was filtered, washed and dried.

(Required: C, 55.7%; H, 2.8%; I, 29.5%; N, 3.3%; O, 11.1%; obtained: C, 45.9%, H, 1.9%; I, 11.6%; O, 26.2%; N (by difference), 14.4%).

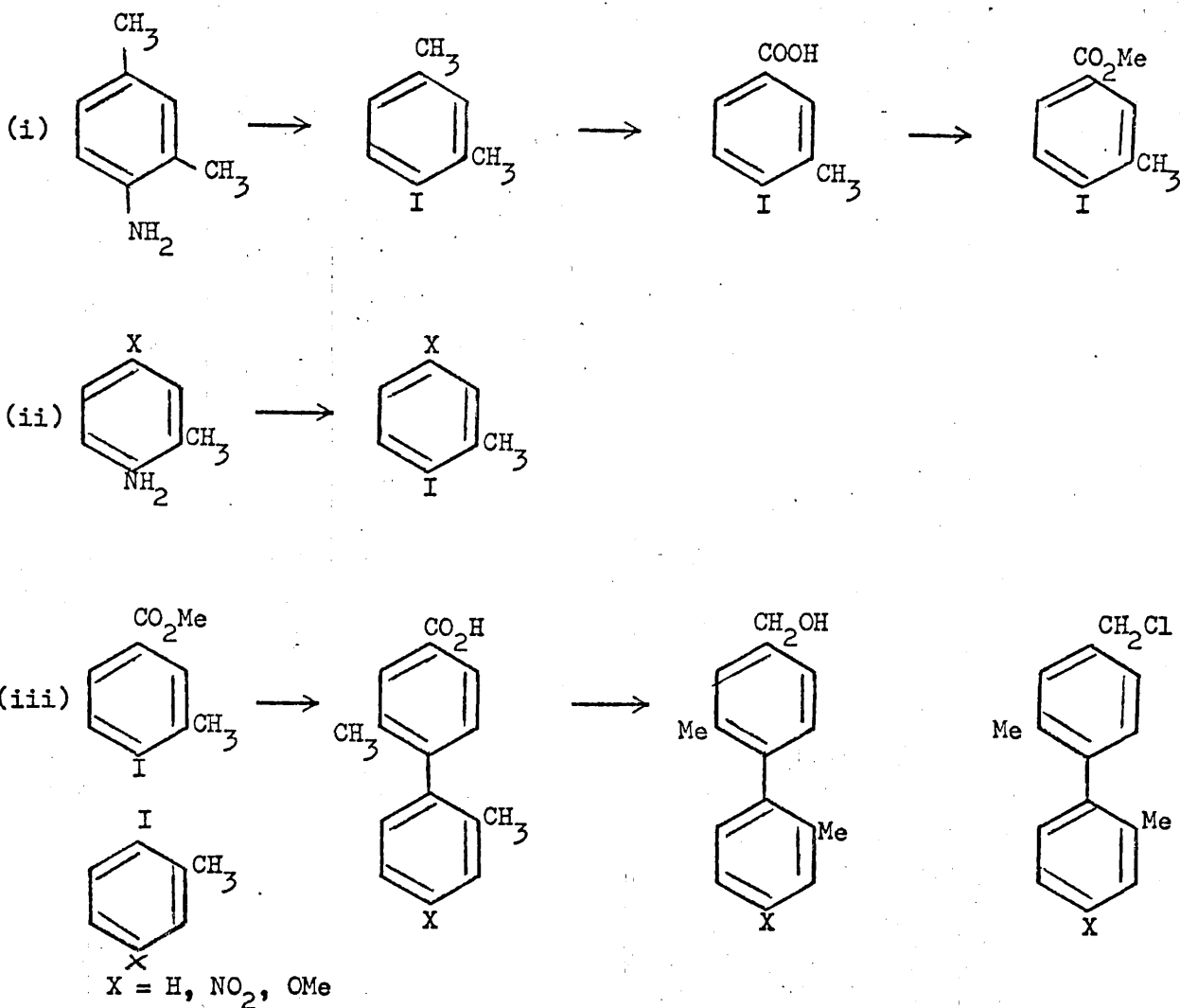
De-iodination of the Crude 2-Iodo-3-Nitro-7-Benzoylfluorene

(a) 3-Nitro-2-iodo-7-benzoylfluorene (4 g) and aluminium chloride (9 g) were boiled under reflux in toluene (250 ml) for one hour. The solvent was then removed by distillation but no iodine co-distilled. The residue was poured into water and a deep brown oily layer separated. Addition of sodium metabisulphite and warming failed to remove the brown coloration. The organic product was extracted with ether, dried (Na_2SO_4) and on removal of the ether a dark brown, uncrystallisable oil was obtained. The yield was too low (< 10%) to warrant further investigation.

(b) De-iodination of 2-iodo-3-nitro-7-benzoylfluorene (0.2 mole) in hydriodic acid (80 ml) and glacial acetic acid (75 ml) was attempted according to the method of Jorgensen and Reid¹⁰⁴. The crude product recovered m.p. 115° - 135° was recrystallised ex ethyl acetate-ethanol. The product was taken up in ethyl acetate and precipitated by the addition of ethanol, m.p. 242° - 245° (darkened at 200°). Qualitative elemental analysis showed iodine to be still present.

The Attempted Preparation of Some Substituted-2,2'-Dimethylbiphenyls

The proposed synthesis involved three series of reactions.



The Preparation of Iodo-Compounds

These were prepared from the corresponding amine by diazotisation and decomposing the diazonium salt with potassium iodide.

The amine (0.50 mole) was dissolved in 5N hydrochloric acid (250 ml) and diazotised at 5°-7° by the slow addition of sodium nitrite solution (0.52 mole). On completion of the diazotisation the solution was filtered from undissolved solids and slowly poured into a well-stirred solution of potassium iodide (0.50 mole) in water (100 ml) at room temperature. During the vigorous decomposition oxides of nitrogen were evolved, iodine was liberated, and a brown unstable precipitate was formed in the solution. The reaction mixture was allowed to stand for 15 minutes at room temperature and was then warmed on the steam bath until gas evolution ceased.

The cooled solution was shaken with ether (250 ml) and the organic layer was separated and was washed with 2N sodium hydroxide, 2N sodium metabisulphite and water. After drying the solution (K_2CO_3) the solvent was removed.

Iodo-Compounds

Compound	b.p.	lit. b.p.	Yield
2-iodotoluene	72°-4°/1 mm	212°/760 mm ¹	70%
4-iodo-m-xylene	86°/20 mm	215°/760 mm ²	65%
2-methyl-4-nitroiodobenzene	99°-99.5° *	103°-5° ³	65%
2-methyl-4-methoxyiodobenzene	220°/8 mm 43°-4° *	44°-5° ⁴	68%

* m.p. ex alcohol

- 1 Datta, R.L., and Chatterjee, N.R. J. Amer. Chem. Soc., 1917, 39, 437
- 2 Grahl, A. Ber., 1895, 28, 85
- 3 Carlin, R.B. and Foltz, G.E. J. Amer. Chem. Soc., 1956, 78, 1997
- 4 Sletzinger, M., and Dawson, C.R. J. Org. Chem., 1949, 677

3-Methyl-4-Iodobenzoic Acid

4-Iodo-m-xylene (0.08 mole) was refluxed for 36 hours with a mixture of nitric acid ($d = 1.4$, 950 g) and water (2 l). The solid was filtered to give 3-methyl-4-iodobenzoic acid, m.p. $214^{\circ}-5^{\circ}$ ¹⁰⁵ (35%) (requires C, 36.7%; H, 2.7%; I, 48.4% obtained C, 33.7%; H, 2.2%; I, 51.0%).

Methyl-4-Iodo-3-Methylbenzoate

3-Methyl-4-iodobenzoic acid (0.05 mole) was refluxed for 15 hours with excess methanol and concentrated sulphuric acid (5 ml). The ester was isolated in the standard way in 80% yield.

The conditions required for the proposed Ullman reactions were first investigated using iodobenzene and methyl-o-iodobenzoate.

(a) Iodobenzene (0.10 mole) and methyl-o-iodobenzoate (0.10 mole) were heated in a metal bath at 220° (two thermometers were employed; one was placed in the metal bath, the second in the reaction mixture). Copper bronze (0.60 mole) was added in small quantities with stirring. No exothermic reaction was evident.

(b) Iodobenzene (0.10 mole), methyl-o-iodobenzoate (0.10 mole) and copper bronze (0.60 mole) were heated together ¹⁰⁶. Boiling occurred at 215° . After 30 mins. the temperature rose to $230^{\circ}-235^{\circ}$ and was accompanied by a colour change from black through to beige-brown. The mixture was boiled under reflux for 5 hours.

The reaction mixture was then cooled to 150° , chlorobenzene (50 ml) added, and the mixture was stirred so that all the organic material was dissolved. The inorganic residue was filtered, washed with chlorobenzene and discarded. The solvents were removed on the steam bath at 15 mm. leaving a residual, orange oil.

A solution of sodium hydroxide (30%) was added to an ethanolic solution of the organic residue and the mixture boiled under reflux for 1.1/2 hours before pouring into water (700 ml). The aqueous mixture was

extracted twice with ether (125 ml) and the remaining aqueous layer was run on to crushed ice (500 g) containing concentrated sulphuric acid (60 ml) and stirred. An orange oil separated. This was extracted with ether, dried (MgSO_4) and the ether removed by distillation to leave a yellow solid (m.p. 160° - 180°). This residue, a mixture of diphenic acid and biphenyl-2-carboxylic acid was boiled with aqueous methanol (50%) and filtered hot. The solid residue when dry had a m.p. 228° - 230° (softened at 195°); diphenic acid m.p. 229° - 230° ¹⁰⁷. The filtrate, on cooling and scratching gave a precipitate, m.p. 110° - 125° and was presumed to be predominantly biphenyl-2-carboxylic acid.

2,2'-Dimethyl-4-Carboxylic Acid

The procedure detailed above was employed for an Ullman reaction between methyl-4-iodo-3-methyl benzoate (0.03 mole) *o*-iodotoluene (0.10 mole) and copper bronze (0.60 mole). A large excess of *o*-iodotoluene was used so as to lower the yield of 2,2'-dimethylbiphenyl-4,4'-dicarboxylic acid. 2,2'-Dimethylbiphenyl is easily removed from the reaction mixture.

After hydrolysis with sodium hydroxide a reddish-yellow semi-solid was obtained which was dissolved in sodium hydroxide solution (10%) and re-precipitated with dilute hydrochloric acid. When filtered and air-dried it gave a m.p. 130° - 160° . Recrystallisation ex aqueous ethanol (75%) failed to improve the m.p. of the product.

The filtrate from the last recrystallisation was evaporated down. The residue was extracted with petroleum ether and benzene to remove any non-carboxylic acid products. The remaining residue was recrystallised ex aqueous ethanol (75%) m.p. 217.5° - 219° (shrinkage at 214°). Quantitative elemental analysis showed this to be 4-iodo-3-methyl benzoic acid.

The Ullman reaction was repeated on the same scale but boiling was maintained for 15 hours. The time of hydrolysis by sodium hydroxide solution was also lengthened to 8 hours. However, only unreacted 4-iodo-3-methyl benzoic acid was ultimately isolated.

The Ullman reaction between methyl-4-iodo-3-methyl benzoate and 4-methoxy-3-methyl iodobenzene was attempted using the above procedure. The mixture boiled at 270° and was maintained at the boil for 18 hours. Again, only unreacted 4-iodo-3-methyl benzoic acid was isolated.

2-Benzoyl-7-Nitrofluorene

2-Benzoylfluorene (2.8 mole) was nitrated in glacial acetic acid (1 l) by the slow addition of fuming nitric acid ($d = 1.5$, 250 ml), the temperature of the exothermic reaction being kept below 55° during this addition. On stirring, the suspension dissolved with a slight rise of temperature and the reaction mixture was kept between 60° - 65° for 10 minutes when precipitation of the yellow 2-benzoyl-7-nitrofluorene occurred. This was filtered, washed with glacial acetic acid and water and recrystallised from nitromethane, m.p. 208° (Lit. 206°)¹⁰⁸.

2-Benzoyl-7-Aminofluorene

(a) 2-Benzoyl-7-nitrofluorene (0.3 mole) was suspended in glacial acetic acid (600 ml) and heated to 60° . A solution of stannous chloride (200 g) in hydrochloric acid (36%, 250 ml) was added slowly, whilst the reaction mixture was stirred and gently heated. The reaction was initially mildly exothermic. A brown product was precipitated. This was filtered and on suspension in 2N sodium hydroxide some yellow fluorescent amine (20% yield) was deposited, and was recrystallised ex alcohol m.p. 153° - 5° (Lit. 155°)¹⁰⁸.

(b) The method of Ishikawa and Hayashi¹⁰⁹ was followed. 2-Benzoyl-7-nitrofluorene (95 g, 0.3 mole) was boiled in fifty volumes of ethanol with sodium bisulphite (4 mole) for 8 hours. The solvent was removed by distillation and the product was precipitated by the addition of water. The product was then extracted with hot 2N hydrochloric acid. No amine salt was obtained and the investigation of the residue showed it to be 2-benzoyl-7-nitrofluorene.

2-Benzoyl-7-Acetamidofluorene

2-Benzoyl-7-aminofluorene (0.05 mole) was stirred in glacial acetic acid (250 ml). Acetic anhydride (400 ml) was added slowly. A mildly exothermic reaction ensued accompanied by a change in colour of the reaction mixture from yellow through to green. The mixture was boiled under reflux for 1 hour and the resulting suspension was filtered hot. Water (100 ml) was added to the filtrate but very little 2-benzoyl-7-acetamidofluorene was obtained in this way. The yield was < 10%.
m.p. $227^{\circ}-8^{\circ}$ ex alcohol (Lit. 228°)¹⁰⁸.

2-Nitrofluorene

Commercial fluorene (0.8 mole) was nitrated in glacial acetic acid (1 l) by the slow addition of concentrated nitric acid (166 ml). 2-Nitrofluorene was recrystallised ex glacial acetic acid $155^{\circ}-6^{\circ}$.
(Lit. $155^{\circ}-6^{\circ}$)¹¹⁰.

2-Nitrofluorenone

2-Nitrofluorene (0.5 mole) was oxidised with sodium dichromate (400 g) in glacial acetic acid (1300 ml) to 2-nitrofluorenone according to the method of Ishikawa and Hayashi¹¹¹. The red colour of the solution deepened on heating and at 102° the exothermic oxidation reaction began, the temperature rising to 115° . 2-Nitrofluorene dissolved and the

solution was boiled under reflux at 105° for 1 hour. The yellow 2-nitrofluorenone was precipitated. The product was filtered, washed with acetic acid, hot water and dried. The yield was quantitative. 2-Nitrofluorenone was recrystallised ex glacial acetic acid. m.p. 218° - 220° (Lit. 219° - 20°)¹¹¹.

2-Aminofluorenone

2-Nitrofluorenone (0.5 mole) was boiled vigorously for 4 hours with sodium sulphide (320 g) in water (2 l) according to the method of Ishikawa and Hayashi¹⁰⁹. The boiling was accompanied by a change in colour from orange through to deep red. The solid product was filtered and extracted with warm hydrochloric acid (1%, 1.5 l). The amine salt was then precipitated by the addition of concentrated hydrochloric acid (300 ml). This was filtered, suspended in concentrated ammonium hydroxide (0.880) and the purple amine filtered. The crude product was recrystallised ex ethanol m.p. 157° - 158° (Lit. 157° - 8°)¹⁰⁹. The yield was 40%.

2-Acetamidofluorenone¹⁰⁹

To 2-aminofluorenone (0.4 mole) in glacial acetic acid (500 ml), acetic anhydride (250 ml) was added until no further exothermic reaction occurred. The reaction mixture was then boiled for 4 hours, during which there was a change in colour from reddish-brown through to greenish-brown. The reaction mixture was then poured into water (1.5 l) and the resulting biscuit-coloured precipitate filtered. The crude product in 40% yield was recrystallised ex glacial acetic acid. 2-Acetamidofluorenone m.p. 224° - 7° (Lit. 227° - 8°)¹⁰⁹.

2-Acetamido-3-Nitrofluorenone

2-Acetamidofluorenone (0.04 mole) was nitrated in an 80% yield according to the method of Ishikawa and Hayashi¹⁰⁹. The crude product was recrystallised ex chlorobenzene to give orange needles. m.p. 246°-8° (Lit. 246°-7°).

2-Amino-3-Nitrofluorenone

(a) 2-Acetamido-3-nitrofluorenone (0.03 mole) was heated with concentrated sulphuric acid (40 ml) according to the method of the same authors¹⁰⁹.

Charring occurred and no product was isolable.

(b) The procedure as in (a) was repeated using 70% sulphuric acid. Boiling was maintained for 20 minutes, after which the reaction mixture was poured into water, and the precipitated product filtered, washed with water dried and recrystallised ex pyridine. The melting point was very vague 200°-260° and the yield < 10%.

(c) 2-Acetamido-3-nitrofluorenone (0.03 mole) was boiled in an ethanol: concentrated hydrochloric acid (1:1) mixture (100 ml) for 1 hour. The initial orange suspension gradually assumed a dark violet colour. The reaction mixture was poured into water and the violet precipitate filtered, washed with water, dried and recrystallised ex pyridine m.p. 284°-5° (Lit. 283°-4°)¹⁰⁹. The yield was 60%.

3-Nitrofluorenone

(a) The method of Ishikawa, Okazaki and Hayashi¹¹¹ was followed. 2-Amino-3-nitrofluorenone (0.02 mole) was diazotised with sodium nitrite (1.5 g) and concentrated sulphuric acid (10 ml). Brown nitrous fumes were observed. The reaction mixture was left at room temperature for 4 hours before being poured on to crushed ice. 95% Ethanol (200 ml) was added and the resulting bright yellow precipitate was filtered and dried. m.p. 150°-165° (Lit. 230°).

Infrared analysis showed strong absorption at 3500 - 3460 cm⁻¹.

Recrystallisation ex toluene-petroleum ether (b.p. 80° - 100°) gave a small amount of a yellowish-brown precipitate m.p. 212° - 220° which showed no absorption at $3500 - 3400 \text{ cm}^{-1}$ in the infrared region.

From the filtrate a second crop of crystals was obtained m.p. 216° - 220° . Quantitative elemental analysis showed deamination to have occurred.

(Required: C, 69.4%; H, 3.1%; N, 6.8%;

Obtained C, 69.0%; H, 2.9%; N, 7.2%)

The yield was very low $< 5\%$.

(b) Repetition of the above procedure failed to give a higher yield of 3-nitrofluorenone.

(c) The reaction was repeated keeping the temperature of the diazotising mixture below 30° . The reaction mixture was stirred for 3 hours. Some evolution of nitrogen occurred when the mixture was poured on to ice and stirred. After gentle heating, the precipitate was filtered, washed with water and recrystallised ex ethanol. m.p. 150° - 165° . This product was not the required 3-nitrofluorenone.

(d) To a paste of 2-amino-3-nitrofluorenone (0.02 mole) in glacial acetic acid, concentrated sulphuric acid (10 ml) was added, the temperature being kept within the range 0° - 5° . A saturated solution of sodium nitrite was added until a positive reaction with potassium iodide paper was noted. The mixture was then poured into an equivolume quantity of S.V.R. ethanol and a little copper powder added. Bubbles of nitrogen were observed when the mixture was gently heated, the mixture finally being left at room temperature for 8 hours. On pouring this ethanolic solution on to ice, a dark brown product was precipitated and found to be identical to that obtained in (c) above.

(e) The diazotisation was performed in the presence of cuprous oxide. This also failed to give the required product.

(f) Diazotisation with deamination of 2-amino-3-nitrofluorenone was attempted using amyl nitrite and absolute alcohol. No change in colour was observed when the amine was suspended in the alcoholic amyl nitrite mixture. Addition of concentrated sulphuric acid caused a deepening of the red colour, due presumably to the protonation of the amino group.

The following hydrocarbons were obtained commercially. The solids were recrystallised from a suitable solvent, but the liquids were not redistilled. The melting points are in agreement with literature values⁸⁸.

4-Chlorobiphenyl	m.p. 77° (<u>ex</u> ethanol)
4-Bromobiphenyl	m.p. 89° (<u>ex</u> ethanol)
4-Methylbiphenyl	m.p. 49°-50° (<u>ex</u> methanol)
4-Nitrobenzoyl chloride	m.p. 75° (<u>ex</u> petroleum ether b.p. 60°-80°)
4-Chlorobenzoic acid	m.p. 243° (<u>ex</u> water)
4-Fluorobenzoic acid	m.p. 185° (<u>ex</u> water)
p-Toluic acid	m.p. 181° (<u>ex</u> water)
Mesitylene	b.p. 164.5°-165°

CHAPTER IVRESULTS1. Kinetic Procedure(a) Apparatus

'A' grade standard burettes and pipettes were used but were not calibrated since all the reactions followed were kinetically first order, and thus the velocity coefficients were independent of concentration units.

(b) Technique of following reactions

A 100 ml, three-necked flask was equipped with a magnetic stirrer, a thermometer dipping into the body of the flask, and an inlet for a 10 ml burette containing standard sodium ethoxide solution in ethanol. The flask was charged with pure ethanol (90 ml) to which two drops of bromothymol blue indicator had been added, and the apparatus was immersed in a conventional thermostat.

The chloride (ca. 10^{-2} mole) was dissolved in pure acetone (100 ml) and the solution was immersed in the thermostat and allowed to reach constant temperature. The reaction was started by adding the acetone solution (10 ml) to the ethanol in the reaction flask, zero time being taken at the half-point of addition. Sufficient sodium ethoxide solution was run in to change the colour of the internal indicator from yellow to blue. The time at which the blue/yellow colour change occurred was taken, and a further quantity of ethoxide solution was added. This procedure was repeated as often as possible.

By this technique the reactions could be studied from 0% to over 90% completion without difficulty, and with more accuracy (due to the larger number of points comprising the graph) than that given by the normal sampling technique.

The success of this method depends on the following factors. Firstly, the reaction studied must be a unimolecular (S_N1) reaction; that is, the varying amounts of ethoxide ion in solution should have no effect upon the reaction rate. Secondly, the total volume of titrant should be small (less than 10%) compared with the initial volume of solution. Definite deviations in the slope of the kinetic plot were detected when the total volume of titrant exceeded that of the initial solution, but small volumes of titrant were used to ensure that no great change in the nature of the solvent occurred during the reaction.

2. Detailed Summary of Rate Coefficients

Solvolysis Reactions in 90% Ethanol - 10% Acetone

 α -(2-Ethyl-7-fluorenyl)benzyl chloride

Temperature: 2.0°C	k_1 (sec ⁻¹)	$2.13 \times 10^{-3} \pm 0.02$
7.5°		$4.30 \times 10^{-3} \pm 0.13$
12.7°		$7.95 \times 10^{-3} \pm 0.05$
14.0°		$9.66 \times 10^{-3} \pm 0.21$
20.7°		$1.93 \times 10^{-2} \pm 0.02$
21.5°		$2.18 \times 10^{-2} \pm 0.02$

Activation energy: 20.09 kcal/mole \pm 0.2 $\log_{10} A$: 13.32 ΔS : -2.0 eu α -(6-Chloro-2-fluorenyl)benzyl chloride

Temperature: 25.0°C	k_1 (sec ⁻¹)	$9.68 \times 10^{-4} \pm 0.08$
30.0°		$1.55 \times 10^{-3} \pm 0.02$
34.0°		$2.06 \times 10^{-3} \pm 0.03$
39.5°		$3.57 \times 10^{-3} \pm 0.04$
44.0°		$5.09 \times 10^{-3} \pm 0.03$

Activation energy: 16.76 kcal/mole \pm 0.32 $\log_{10} A$: 9.27 ΔS : 16 eu

α -(4-Fluoro-4'-biphenyl)benzyl chloride

Temperature:	24.8°C	$k_1(\text{sec}^{-1})$	$3.93 \times 10^{-4} \pm 0.06$
	38.3°		$1.78 \times 10^{-3} \pm 0.10$
	49.5°		$4.83 \times 10^{-3} \pm 0.18$
	54.5°		$5.70 \times 10^{-3} \pm 0.06$

Activation energy: 18.70 kcal/mole \pm 0.10

$\log_{10} A$: 10.41

ΔS : 2.1 eu

 α -(4-Bromo-4'-biphenyl)benzyl chloride

Temperature:	25.0°C	$k_1(\text{sec}^{-1})$	$2.80 \times 10^{-4} \pm 0.02$
	30.8°		$4.41 \times 10^{-4} \pm 0.02$
	39.0°		$1.04 \times 10^{-3} \pm 0.01$
	47.0°		$2.16 \times 10^{-3} \pm 0.03$
	51.0°		$2.68 \times 10^{-3} \pm 0.08$
	57.0°		$4.58 \times 10^{-3} \pm 0.04$
	62.8°		$6.14 \times 10^{-3} \pm 0.04$

Activation energy: 17.4 kcal/mole \pm 0.5

$\log_{10} A$: 9.21

ΔS : 16 eu

 α -(4-Nitro-4'-Biphenyl)benzyl chloride

Temperature:	36.2°C	$k_1(\text{sec}^{-1})$	$7.56 \times 10^{-5} \pm 0.15$
	40.3°		$2.89 \times 10^{-4} \pm 0.11$
	46.6°		$4.90 \times 10^{-4} \pm 0.08$
	50.8°		$7.33 \times 10^{-4} \pm 0.14$
	56.5°		$1.36 \times 10^{-3} \pm 0.02$
	63.0°		$2.15 \times 10^{-3} \pm 0.05$

Activation energy: 20.80 kcal/mole \pm 1.26

$\log_{10} A$: 10.92

ΔS : 9 eu

α -(3-Bromo-4'-biphenyl)benzyl chloride

Temperature:	28.5°C	k_1 (sec ⁻¹)	$9.29 \times 10^{-5} \pm 0.21$
	40.0°		$2.47 \times 10^{-4} \pm 0.09$
	48.0°		$5.67 \times 10^{-4} \pm 0.14$
	54.0°		$9.93 \times 10^{-4} \pm 0.10$
	60.5°		$1.39 \times 10^{-3} \pm 0.12$
	64.0°		$2.01 \times 10^{-3} \pm 0.03$

Activation energy: 17.68 kcal/mole \pm 0.32

$\log_{10} A$: 9.12

ΔS : 17 eu

 α -(3-Fluoro-4-biphenyl)benzyl chloride

Temperature:	25.6°C	k_1 (sec ⁻¹)	$8.18 \times 10^{-5} \pm 0.25$
	38.0°		$2.58 \times 10^{-4} \pm 0.04$
	41.0°		$3.29 \times 10^{-4} \pm 0.04$
	46.0°		$5.58 \times 10^{-4} \pm 0.05$
	51.0°		$9.20 \times 10^{-4} \pm 0.13$
	58.0°		$15.75 \times 10^{-4} \pm 0.01$

Activation energy: 18.19 kcal/mole \pm 0.06

$\log_{10} A$: 10.56

ΔS : 10

 α -(3-Methoxy-4-biphenyl)benzyl chloride

Temperature:	25.2°C	k_1 (sec ⁻¹)	$1.98 \times 10^{-4} \pm 0.03$
	30.0°		$3.24 \times 10^{-4} \pm 0.14$
	34.0°		$5.23 \times 10^{-4} \pm 0.09$
	40.0°		$9.11 \times 10^{-4} \pm 0.09$
	42.5°		$12.52 \times 10^{-4} \pm 0.20$
	45.0°		$14.71 \times 10^{-4} \pm 0.33$
	49.0°		$21.24 \times 10^{-4} \pm 1.04$

Activation energy: 19.17 kcal/mole \pm 0.35

$\log_{10} A$: 10.70

ΔS : 10

α -(3-Methyl-4'-biphenyl)benzyl chloride

Temperature:	24.0°C	$k_1(\text{sec}^{-1})$	$5.056 \times 10^{-4} \pm 0.04$
	27.3°		$8.15 \times 10^{-4} \pm 0.09$
	30.0°		$1.04 \times 10^{-3} \pm 0.03$
	35.9°		$1.51 \times 10^{-3} \pm 0.03$
	40.0°		$2.02 \times 10^{-3} \pm 0.03$
	49.5°		$4.79 \times 10^{-3} \pm 0.09$

Activation energy: 15.75 kcal/mole \pm 0.84

$\log_{10} A$: 8.7

ΔS : 18 eu

 α -(3-Nitro-4'-biphenyl)benzyl chloride

Temperature:	24.5°	$k_1(\text{sec}^{-1})$	$2.52 \times 10^{-5} \pm 0.05$
	27.0°		$3.83 \times 10^{-5} \pm 0.33$
	30.0°		$5.97 \times 10^{-5} \pm 0.07$
	34.0°		$7.85 \times 10^{-5} \pm 0.08$
	40.5°		$1.41 \times 10^{-4} \pm 0.02$
	49.5°		$2.98 \times 10^{-4} \pm 0.03$
	54.5°		$4.86 \times 10^{-4} \pm 0.20$

Activation energy: 18.30 kcal/mole \pm 0.9

$\log_{10} A$: 9.26

ΔS : 16 eu

2,4,6-Trimethyl-4'-fluoro-benzhydryl chloride

Temperature	25°C	$k_1(\text{sec}^{-1})$	$4.28 \times 10^{-4} \pm 0.05$
	37°		$1.24 \times 10^{-4} \pm 0.02$

Apparent Activation energy: 16 kcal/mole

2,4,6-Trimethyl-4'-chlorobenzhydryl chloride

Temperature:	20°C	$k_1(\text{sec}^{-1})$	$2.79 \times 10^{-4} \pm 0.07$
	30.5°		$3.78 \times 10^{-4} \pm 0.07$

Apparent Activation energy: 10 kcal/mole

2,6-Dimethyl-4'-methylbenzhydryl chloride

Temperature:	25.0°C	$k_1(\text{sec}^{-1})$	$3.57 \times 10^{-4} \pm 0.04$
	25.0		$3.48 \times 10^{-4} \pm 0.20$
	27.4°		$4.93 \times 10^{-4} \pm 0.05$
	33.7		$8.65 \times 10^{-4} \pm 0.20$

2,6-Dimethyl-4'-fluorobenzhydryl chloride

Temperature:	52.0°C	$k_1(\text{sec}^{-1})$	$3.54 \times 10^{-4} \pm 0.04$
	55.0°		$5.36 \times 10^{-4} \pm 0.20$
	57.0°		$7.46 \times 10^{-4} \pm 0.42$
	45.0°		$2.24 \times 10^{-4} \pm 0.05$
	49.0°		$3.29 \times 10^{-4} \pm 0.02$

Activation energy: $21.14 \text{ kcal mole}^{-1} \pm 0.06$

2,6-Dimethyl-4'-chlorobenzhydryl chloride

Temperature:	52.0°C	$k_1(\text{sec}^{-1})$	$1.23 \times 10^{-4} \pm 0.02$
	57.0°		$1.88 \times 10^{-4} \pm 0.05$
	61.0°		$2.53 \times 10^{-4} \pm 0.22$
	60.0°		$3.05 \times 10^{-4} \pm 0.07$
	64.0°		$3.32 \times 10^{-4} \pm 0.11$
	67.0°		$4.16 \times 10^{-4} \pm 0.15$

Activation energy: $18.80 \text{ kcal mole}^{-1} \pm 0.02$

4-Chloro-benzhydryl chloride

Temperature:	25.0°C	$k_1(\text{sec}^{-1})$	$7.86 \times 10^{-6} \pm 0.12$
	33.6°		$2.21 \times 10^{-5} \pm 0.05$
	43.5°		$6.98 \times 10^{-5} \pm 0.09$
	48.8°		$1.19 \times 10^{-4} \pm 0.02$
	53.0°		$1.96 \times 10^{-4} \pm 0.01$
	59.0°		$3.37 \times 10^{-4} \pm 0.05$
	62.0°		$4.41 \times 10^{-4} \pm 0.08$

Activation energy: 21.81 kcal/mole \pm 0.20

$\log_{10} A$: 10.88

ΔS : 9 eu

4-Methoxy-benzhydryl chloride

Temperature:	-9.0°C	$k_1(\text{sec}^{-1})$	$4.67 \times 10^{-3} \pm 0.20$
	-11.5°		$3.94 \times 10^{-3} \pm 0.03$
	-14.5°		$2.47 \times 10^{-3} \pm 0.09$
	-20.0°		$1.80 \times 10^{-3} \pm 0.04$

Activation energy: 14.0 kcal/mole \pm 1.5

$\log_{10} A$: 9.24

ΔS : 16 eu

4-Fluoro-benzhydryl chloride

Temperature:	51.0°C	$k_1(\text{sec}^{-1})$	$6.21 \times 10^{-4} \pm 0.16$
	55.2°		$8.56 \times 10^{-4} \pm 0.13$
	58.5°		$11.04 \times 10^{-4} \pm 0.08$
	62.0°		$14.50 \times 10^{-4} \pm 0.03$

Activation energy: 16.75 kcal/mole \pm 0.39

The rate constants for the following chlorides were determined at only one temperature (25°C).

<u>Chloride</u>	$10^4 k_1 (\text{sec}^{-1})$
2,4,6-Trimethylbenzhydryl chloride	3.34 ± 0.02
2,4,4',6-Tetramethylbenzhydryl chloride	32.3 ± 0.5
4-t-Butyl-4'-chloro-2,6-dimethylbenzhydryl chloride	0.434 ± 0.013
4-t-Butyl-2,4',6-trimethylbenzhydryl chloride	23.7 ± 0.2
4-t-Butyl-4'-fluoro-2,6-dimethylbenzhydryl chloride	2.13 ± 0.02
α -(4-Methyl-4'-biphenyl)isopropyl chloride	277 ± 9
α -(4-Bromo-4'-biphenyl)isopropyl chloride	8.53 ± 0.10
α -(4-Methoxy-4'-biphenyl)isopropyl chloride	118 ± 1
α -(4-Chloro-4'-biphenyl)isopropyl chloride	9.48 ± 0.3
α -(4-Biphenyl)isopropyl chloride	14.4 ± 0.2

Results in a Typical Solvolysis Experiment

The ethanolysis of α -(6-chloro-2-fluorenyl)benzyl chloride
in ethanol-acetone (9:1 v/v) at 34°.

Titant. Ethanolic sodium ethoxide (0.01 M)

Time	V_{OEt^-}	% Reaction	$\log_{10} \left[\frac{a}{a-x} \right]$	$k_1 (\text{sec}^{-1})$
Zero	(from the graph)		0.02	
5 (sec)	0.28	9.76	0.0446	
70	0.93	32.40	0.1701	2.151
83	1.03	35.89	0.1930	2.084
119	1.31	45.64	0.2647	2.056
150	1.52	52.96	0.3275	2.050
184	1.70	59.23	0.3896	2.010
203	1.82	63.41	0.4366	2.052
247	2.00	69.69	0.5185	2.018
280	2.14	74.56	0.5945	2.052
320	2.27	79.10	0.6799	2.062
	2.87	-	-	

$$\text{Mean } k_1 = 2.059 \times 10^{-3} \text{ sec}^{-1} \pm 0.033$$

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