A STUDY OF THE MECHANISM OF AROMATIC CYCLODEHYDRATION

BY

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A Thesis
Submitted To The Faculty Of
The Virginia Polytechnic Institute
In Partial Fulfillment Of The Requirements
For The Degree

DOCTOR OF PHILOSOPHY

Accepted:

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VIRGINIA POLYTECHNIC INSTITUTE
DEPARTMENT OF CHEMISTRY
DECEMBER 1950

TO MY PARENTS

AND

TO MY WIFE

THIS THESIS IS

AFFECTIONATELY DEDICATED

ACKNOWLEDGEMENTS

The author wishes to thank Dr. Frank A. Vingiello for his many suggestions in directing this work, and for the critical discussions in the analysis of the experimental results. Thanks are also extended to Mr. Robert A. Kasey and particularly to Mr. H. Hayden Hanabass for the preparation of some of the compounds used in this investigation. This work was made possible by the financial aid given by the Virginia Polytechnic Institute in the form of fellowships and an instructorship, and by generous grants from the Research Corporation; these are gratefully acknowledged.

J. G. V. O.

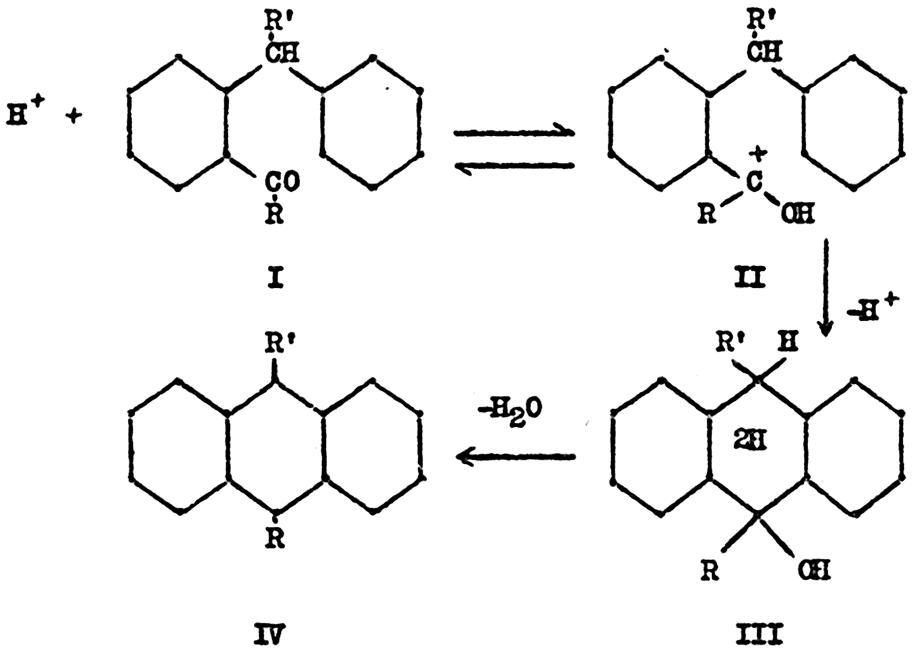
TABLE OF CONTENTS

Page

INTRODUCTION

Recently, Bradsher and Vingiello (1,2) published information concerning the mechanism of aromatic cyclodehydration, with particular reference to the cyclization of _o_-benzylphenones. This mechanism is diagrammed in Chart I.

CHART I*



R is alkyl, phenyl, and _p_-substituted phenyl.

R' is hydrogen, methyl, and phenyl.

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*Unless otherwise indicated in this thesis, all rings are fully aromatic.

This reaction is postulated as proceeding through three steps: the addition of the proton to the carbonyl oxygen, this being a reversible step; the attack of the conjugate acid (carbonium ion) thus formed on the ortho position of the ring into which cyclization takes place; and finally the rapid elimination of water to form the fully aromatic anthracene derivative. A study of the rate of cyclization of various ketones of type I led to the conclusions that "for similar experimental conditions, the rate of cyclization of o-benzylphenones depends upon several factors, the most important of which appear to be: (1) the steric nature of R and perhaps also of R', (2) the position of the equilibrium between ketone and conjugated acid ($I \rightleftharpoons II$), (3) the effective positive character of the central carbon atom of the conjugate acid, (4) the electron density at the ortho position of the benzene ring into which cyclization takes place, and (5) the number of such positions available." (1).

The investigation reported in this thesis has produced new experimental evidence bearing on this question; a critical discussion of the mechanism of aromatic cyclodehydration is offered in the light of these new facts.

HISTORICAL

Since several reviews (See for example Ref. 2 and 3) concerning the mechanism of the cyclization of ortho-benzylphenones have been published, it is not necessary to repeat that material here. Rather, these established facts will be brought forth as needed in the general discussion of the reaction. Because the interpretation of the experimental results reported in this thesis and the work which immediately preceded it (1, 2) requires a rather intimate knowledge of the electronic effects of the halogens, and because there still is controversy among chemists concerning these effects, it is considered pertinent to present a review of the more outstanding papers on this subject. This review will serve as a basis for a number of conclusions reached in this thesis.

The electronic theory of the English school is set forth in some detail by Remick in his book (4). Here, the modern, most widely accepted views concerning the electronic effects of the halogens are enumerated. The halogens are considered to have a strong inductive ($-I_s$) effect (a strong permanent electron attractive effect, along the valence bond) diminishing in intensity from fluorine to iodine. They are considered to have an I_d effect (the inductomeric effect, a polarizability effect along the valence bond, brought into play only at the moment of reaction at the demand of the attacking reagent) but in the reverse order, diminishing from iodine to fluorine. The halogens are also considered to have a +T effect (a tautomeric electron release, where the unshared electrons on the halogen atoms shift their octet affiliations). This tautomeric effect manifests itself in two ways: a permanent polarization of the molecule (M), and a polarizability effect (E) brought into play only at the moment of reaction, and then only at the demand of the attacking reagent. These tautomeric effects are considered at the present time to diminish in intensity from fluorine to iodine. This conclusion was reached after the mass of experimental evidence required it, but with some hesitation, since it is difficult to see how fluorine, with its high electronegativity would release its electrons with less difficulty than the more electropositive iodine atom. This fact has been the source of much controversy among chemists, particularly in the years when the electronic theory of the English school was just beginning to take shape. It is the main purpose of this review to outline the data and arguments of chemists who have contributed to this aspect of the electronic theory.

When the phenomenon of the electronic shift, now known as the electromeric effect, was first postulated by Lowry (5), there was no detailed discussion of the relative magnitude of the effect among the different atoms. Later chemists, in extending these ideas, proposed on theoretical grounds, that the polarizability of the halogen-carbon bonds diminished in the order $I > Br > Cl > F$, the order which would be predicted from Fajans' rules (6), and indeed the order now ascribed to the inductomeric polarizabilities.

Christopher K. Ingold, probably the most influential contributor to the English theory, was the first to distinguish the permanent, mesomeric, polarization of the molecule from the dynamic electromeric, polarizability effect, and classed the two as the tautomeric effect (7). In the first consolidated statement of the principles of the electronic theory of the English school (8), he stated that the E and M effects decreased in the order I > Br > Cl > F, and based his statement, aside from the logical thought that iodine would have the greatest polarizability and the weakest hold on its electrons, on the work of Sutton (9). In this work, Sutton measured the effective mesomeric moment of a substituent (X), by taking the difference in the dipole moments of a tertiary aliphatic-X and a phenyl-X. Sutton pointed out that since the mesomeric effect would not be present in the saturated aliphatic compound, but would operate in the aromatic ring, the differences in these two dipole moments would give a comparative value of the M effect for a series of substituents. Sutton's values for these differences (i.e., mesomeric moments) were as follows:

I	Br	Cl	(NO_2)
0.86	0.69	0.59	(-0.88)

This series confirmed the order among the halogens which was assigned by Ingold. Later work in 1937 by Groves and Sugden (10) showed that if a correction for the moment <u>induced</u> by the measuring field be introduced, the order among the halogens was reversed. Their values for the mesomeric moments follow:

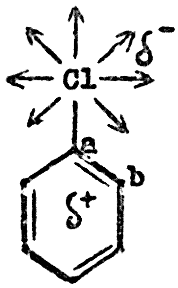
(OH)	F	Cl	Br	I	(NO_2)
(1.12)	1.00	0.97	0.89	0.87	(-0.29).

These corrected values place fluorine closer to the electron releasing groups than iodine. As will be shown later, this and other chemical evidence required Ingold to acknowledge that the M effect diminished in the order F > Cl > Br > I, but he still maintained in 1938 (30) that the polarizabilities (E) were in the opposite order.

The first paper to show that chemical evidence required the tautomeric effect to diminish in intensity from fluorine to iodine was published in 1933 by Baddeley and Bennett (11). In this paper, they studied the rate of reaction of substituted aromatic β-chloroethylsulfides ($Ar-S-CH_2-CH_2-Cl$) with iodide ion (Reaction I) and with water (Reaction II). The variation in the velocities in Reaction I was found to be *p*-anisyl < *p*-tolyl < phenyl < *p*-halogenophenyl < *p*-nitrophenyl < 2,4-dinitrophenyl. The order for Reaction II was just the reverse. Reaction I being accelerated by the nitro group made it probable that the rate determining step was the attack on the carbon holding the chlorine by the iodide ion: the withdrawal of electrons by the nitro group would facilitate the attack by the negative ion. Likewise, the presence of the nitro group in Reaction II retarded the reaction, and the rate determining step was thought to be the ionization of the chlorine atom, this being facilitated by the presence of electron releasing groups in the phenyl ring. The influence of the halogen atom in the *para* position was found to be in the order $Cl > Br > I$ for Reaction I (Rate constants, 0.197; 0.150; 0.116 resp.). This is the order which would be expected from a consideration of the inductive effect alone, i.e., the same order of strengths of the halogen acetic acids. In Reaction II, however, while the order in the overall series was the reverse of that of Reaction I, the order among the halogens themselves was the same, and not reversed: Cl, 0.613; Br, 0.507; I, 0.426. Since Reaction II has been shown to be accelerated by electron releasing groups, it follows that the electron release (i.e. the +T effect) of the halogens must be in the same order as the rates: $Cl > Br > I$. It is unfortunate that this side chain reaction was chosen to prove the point in question: in order for the T effect originating in the ring to have any influence upon the side chain halogen, it is necessary to infer that the T effect is relayed inductively along the single bonds of the side chain. This has been the source of criticism of this paper (see below), and is one of the weak points in the arguments of Baddeley and Bennett.

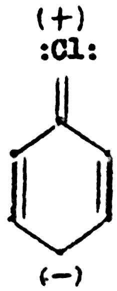
In order to further substantiate their statement that this unusual order of electron release was actually the case, Baddeley and Bennett in the same paper (11) stated that the same results could have been obtained by other chemists from their published data, but the significance of their results was apparently not noticed. It was pointed out that in a reaction where the -I effect of the halogens would retard, the +T effect would accelerate from the *para* position; the T effect would be almost inoperative from the *meta* position. (They stated here that the I effect would be weaker in the *meta* position than it is in the *para*, which is the reverse of the accepted fact today (Ref. 4, p. 48) but this statement does not appreciably alter their conclusions). It follows then, that the relative magnitudes of the electromeric effect were indicated by the variation in the ratio of velocities *para/meta*, or by the order of velocities of the *para* isomerides. Thirteen reactions from fifteen sources of both type I and type II were quoted here to support their arguments; in all cases the T effect would have to diminish in the order F > Cl > Br > I.

With the experimental evidence requiring that this order be accepted, Baddeley and Bennett in the same paper (11), and Bennett in a subsequent paper (12), offered an explanation of the fact that fluorine apparently released its electrons with greater ease than the other halogens. They rejected the idea that in this case, the T effect involved an increase in covalency of the halogens. They stated, without elaboration, that there was no tendency for the halogens to form quinonoid links; further they could not see how the inductive effect could persist when the nature of the carbon-halogen bond is changed. As an alternative to the covalency increase, they suggested that the electromeric effect of the halogens could be considered to be ethenoid or butadienoid changes in the nucleus promoted by the electrical fields of the halogens. Thus in chlorobenzene, the net negative charge (δ^-) in the field around the



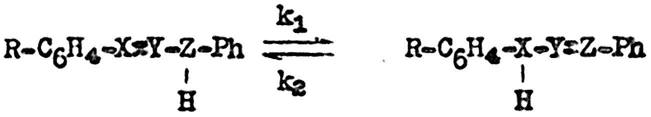
chlorine atom has its positive equivalent charge (δ^+) distributed through the nucleus (deactivation); the electron repelling field (the direct effect, operating in every direction in space) may control at least the outer electrons of the bond a-b to a point of initiating the electromeric change: ethenoid for ortho activation, butadienoid for <u>para</u> activation. Since this electron repelling field, although opposite in sign, is parallel in magnitude to the I effects, the order among the halogens for electromeric electron release would be F > Cl > Br > I.

These novel ideas concerning the cause of the electromeric effect of the halogens were not well received by many chemists. Among the chief dissenters was Robert Robinson (13), whose rebuttal included the following points. First, this mechanism could not be extended to explain the electromeric effect of other atoms in the -I, +T category, such as nitrogen and oxygen. These atoms activate the ring, and hence the electron density in the ring is increased, and not decreased as in the case of the halogens; the same mechanism, therefore, cannot apply to nitrogen and oxygen. If this new mechanism is to apply, then why do the four unshared electrons of oxygen initiate so much more powerful an electromeric effect than the six similar electrons of the halogens? Secondly, the new view of Baddeley and Bennett repudiated the idea of a covalency increase for the halogens, and, therefore, would not be able to explain the stability of aryl halides to hydrolysis,



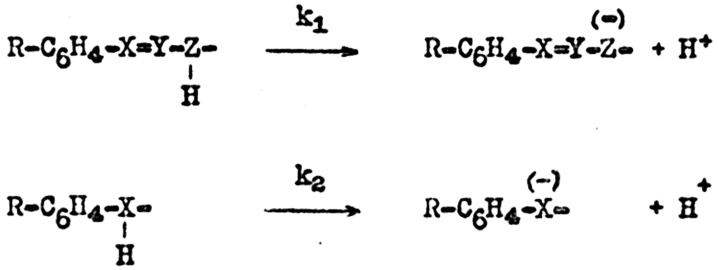
generally attributed to the contribution to the resonance hybrid of forms of the type shown on the left. Thirdly, they did not present any reactions where the E effect enters directly--all of the reactions are side chain reactions where the E effect initiates strains which are relayed inductively. And finally, Robinson argued that even if the M effect is in the order F > Cl > Br > I, the <u>polarizabilities</u> of the carbon-halogen bond should be in the order I > Br > Cl > F.

The proceding two papers (12, 13) were presented at a discussion of "Substitution in Organic Compounds" held at Leeds University in May, 1933. At the same meeting, Shoppee (14) presented an example where there was no inversion among the halogens. The effect of nuclear substitution on the mobility (i.e., the velocity of interconversion, $K_1 + K_2$) on simple triad prototropic systems of the type



$$R\text{-}C_6H_4\text{-}X{=}Y\text{-}\underset{\displaystyle H}{\underset{|}{Z}}\text{-}Ph \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R\text{-}C_6H_4\text{-}\underset{\displaystyle H}{\underset{|}{X}}\text{-}Y{=}Z\text{-}Ph$$

is that the mobility is increased by variants R which are strongly electron attractive. Thus, R, in either the <u>m</u> or the <u>p</u> position, increases the mobility in the series: $NMe_2 < Me < OMe < I < Br < Cl < NO_2$, which is also the order of the dipole moments of the compounds $R\text{-}C_6H_5$. This sequence shows that the processes

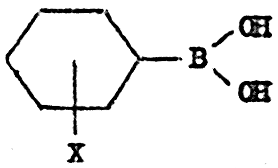


$$R-C_6H_4-X=Y-\underset{H}{\underset{|}{Z}}- \xrightarrow{k_1} R-C_6H_4-X=Y-\overset{(-)}{Z}- + H^+$$

$$R-C_6H_4-\underset{H}{\underset{|}{X}}- \xrightarrow{k_2} R-C_6H_4-\overset{(-)}{X}- + H^+$$

are both facilitated by electron recession from the seat of ionization. The effect of the same substituents on the equilibrium constant for the reaction given above shows, however, that the order of the halogens is reversed: $Me > Cl > Br > I > NO_2$. Shoppee reasoned from these facts that the mechanism (s) for aromatic side-chain reactions may involve two rate-affecting phases, each phase being of opposite polar requirements (one being retarded, the other accelerated, by electron attracting groups, and vice versa). Then the relative reaction rates could vary among the substituents in the -I, +T category, depending upon which phase was predominant. Further details of this unique paper are not included here, for the ideas presented there are now considered for the most part erroneous. It is worth noting, however, that these ideas received some support (15).

The next rather significant paper in the development of the theory of the English school is to be found in the Journal of the American Chemical Society. In this paper (16) Bettman, Branch and Yabroff published the strengths of the meta and para substituted halogenphenyl boric acids, measured in 25% ethanol at 25°:



		meta	*para*
F	-	1.10×10^{-9}	3.66×10^{-10}
Cl	-	1.35	6.30
Br	-	1.46	7.26

It is to be noted that the acid strength for both positions falls from bromine to fluorine. The -I effect operating alone would increase the strength of the acid, whereas a +T effect would decrease the strength. If the +T order is assumed to be I > Br > Cl > F, then the order of the acid strength would be F > Cl > Br; experimentally the reverse is the fact. In this case the differences in strength are greater than the experimental error; this is not the case with the corresponding benzoic acids, where (17) the differences in strengths are not great enough to be excluded from inaccuracy in measurement:

For benzoic acids:	*m*-F	*m*-Cl	*m*-Br	*m*-I
- log Ka	3.85	3.81	3.86	3.80.

The fact that the *meta* acids showed the same order of strengths as the *para* acids, (although the differences are small) was attributed to secondary resonance interactions between the halogen atom and the benzene ring. (This same idea is expressed by Remick (Ref. 4, p. 66) as follows: "...a halogen atom in the *meta* position can stimulate a mesomeric displacement, the effect of which is relayed by an inductive mechanism..." This statement is based on a similar statement by Dippy and Lewis (18), who measured the thermodynamic dissociation constants of the meta-halogenated benzoic acids, and found that the order of strengths (outside the limit of experimental error) for the fluoro, chloro, and bromo acids was the reverse of the order anticipated from the I effects alone.)

In 1935, Baddeley and Bennett, with Glasstone and Jones, present a carefully argued paper (19) in which they repeat most of the arguments of their previous papers (11, 12). This extensively annotated paper showed unequivocally that the T effect of the halogens must decrease from fluorine to iodine. However, it failed to give a credible explanation as to why this must be the case, other than explaining it on the basis of a "nuclear ethenoid or butadienoid polarization" which they had postulated earlier. Their argument began with quotations from various papers showing the effect of halogens in the meta position, or their effect transmitted through a side chain. Some of these are tabulated here:

A. The strengths of m-halogenophenols in 30% ethanol (20):

	F	Cl	Br	I
$K_a \times 10^{-10}$	1.51	4.90	4.37	3.89

B. The strengths of m-halogenoanilines in 30% ethanol (20):

	F	Cl	Br	I
$K_b \times 10^{-12}$	10.5	8.51	7.94	7.59

C. The reaction velocity constant for the reaction of *m*-halogenobenzyl chlorides (21):

	F	Cl	Br	I	H
With iodide at 20°	1.84	2.17	2.47	2.34	1.32
With water at 70°	0.0159	0.0156	0.0132	0.0143	0.0671

D. The reaction of *p*-halogenophenylethyl chlorides with iodide (21):

	F	Cl	Br	I	H
K	1.55	1.65	1.63	1.40	0.735

E. The strengths of *m*-halogenobenzoic acids (17):

	F	Cl	Br	I
$-\log K_a$	3.85	3.81	3.86	3.80

Since in all of these cases the electronic effects of the halogens are transmitted from the *meta* position, or through a side chain, the results show an apparent inductive effect. In all cases the differences are small, but in most of the cases, there is shown an *apparent* inductive effect in the order Br > Cl > F. This fact must be due to some modification of the inductive effect by the E or M effect, even when relayed from the *meta* position or through a side chain, since there are numerous well established facts which point to the decrease in magnitude of inductive effects in the order

$F > Cl > Br > I$ in aromatic compounds. Some of these facts are quoted here:

A. First, the relative strengths of the halogen acetic acids reported by Scudder (23):

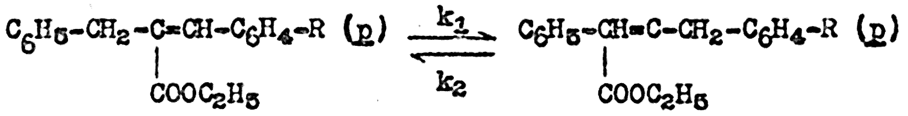
	F	Cl	Br	I
Dissociation constants	2.17	1.55	1.38	0.71 x 10^{-3}

B. The rates of reaction of p-halogenophenyl β-chloroethyl sulfides (p-$X-C_6H_4-S-CH_2-CH_2-Cl$) (11):

	Cl	Br	I
K	0.197	0.150	0.116

Here a direct or relayed E effect would not facilitate the reaction and hence would not be called into play.

C. The effect of R on the velocity of interconversion of the system:



$$C_6H_5-CH_2-\underset{\displaystyle COOC_2H_5}{\underset{|}{C}}=CH-C_6H_4-R\ (\underline{p}) \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C_6H_5-CH=\underset{\displaystyle COOC_2H_5}{\underset{|}{C}}-CH_2-C_6H_4-R\ (\underline{p})$$

R (para):	OCH_3	I	Br	Cl
$k_1 + k_2$:	0.058	0.39	0.64	1.02

(This and other work of Shoppee (14, 24) was quoted in the paper of Baddeley *et al.* (19) to show the -I effect decreases from fluorine to iodine).

D. And finally, the work of Fluerscheim and Holmes (25) and also that of the Ingolds (26) who gave the percentage of <u>meta</u> derivative formed when benzyl halides are nitrated (the percentages drop from fluorine to bromine).

If all of the above facts are to be interpreted as proving that the -I effects of the halogens drop in the order F > Cl > Br > I, then the conclusion must be reached that the magnitudes of the M effects must decrease in the same order in order to account for the approximate equality (or slight inversion of the "normal" order among the halogens) in the <u>apparent</u> inductive effects mentioned above.

But, it is pointed out, there is even a greater necessity for explaining the much larger variations among the data relating to similar properties among the <u>para</u> halogenated substances.

For example, the dissociation constants of <u>p</u>-halogenated benzoic acids and phenylacetic acids are (27):

<u>para</u>	F	Cl	Br	I
Benzoic	7.22	10.55	10.7	---
Phenylacetic	5.68	6.45	6.49	6.64

The chloro and bromo acids are close together here, but the general sequence is clear, and the reverse of that to which the I effects alone would lead.

Consider also the dissociation constants for the para-halogenoanilines, and the para-halogenophenols in 30% ethanol (19):

	F	Cl	Br	I	H
p-halogenoanilines: $K_b \times 10^{-12}$	120	28.8	21.9	15.1	126
p-halogenophenols: $K_a \times 10^{-10}$	0.26	1.32	1.55	2.19	0.32

In the case of the anilines, the -I effect alone (Cl > Br) should make the chloro base the weaker. If the +M effect were Br > Cl, then this should make the chloro base even weaker than this. The fact that the chloro base is actually stronger shows that the +M effect counteracts the -I effect, and may even outweigh it.

But even more striking are the facts concerning the strengths of these compounds in aqueous solutions. The fluorine in the meta position of aniline and phenol reveals the large inductive effect of fluorine (19):

$K_b \times 10^{-11}$:	aniline 400;	m-F-aniline	25.7
$K_a \times 10^{-10}$:	phenol 1.2;	m-F-phenol	5.25

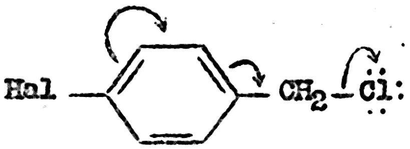
When the fluorine is in the para position, however, the strengths are equal to the parent substances:

p-F-aniline:	444;	p-F-phenol	1.12

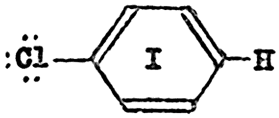
The comparative data for the velocities of hydrolysis of the halogenated benzyl chlorides also bear on this point. Thus the velocity coefficients at 70°C for the hydrolysis of halogenobenzyl chlorides are (19):

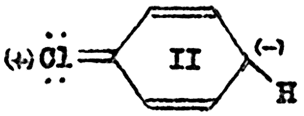
	F	Cl	Br	I	H
meta	0.0159	0.0156	0.0132	0.0143	0.0671
para	0.114*	0.0394	0.0310	0.0296	

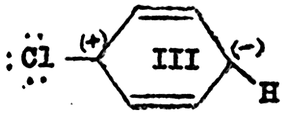
The figures for the _meta_ substituted compounds show the presence of the retarding inductive effects; but in addition there is an influence which facilitates the reaction for the _para_ halogenated benzyl chlorides relatively (to the _meta_) in all cases, and absolutely in comparison with the parent benzyl chloride itself in the case of the fluoro compound. (Note that the _para_ fluoro compound (*) is not only faster than the _para_ chloro, but is approximately twice as fast as the parent H compound). This influence falls in a pronounced manner from fluorine to iodine as shown by the _para_/_meta_ velocity ratios: F, 7.17; Cl, 2.53, Br, 2.35; I, 2.07. The hydrolysis might be expected to be facilitated by the shift:



All of the above data, compiled in the paper of Baddeley, _et al._, (19), inevitably indicate an M or E effect, or both, in the order F > Cl > Br > I. In line with their novel explanation for this fact, the authors are careful to point out that the electronic shift shown above doesn't necessarily require complete conjugation of the halogen with the benzene nucleus by an increase in covalency. Such an increase in covalency would be indicated by (I ⟷ II), and the fall in magnitude of the effect from F to I would be "hard to explain".



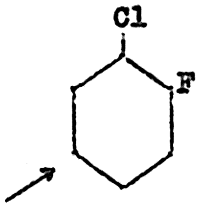


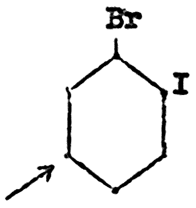


If the origin of the M effect is in the controlling field of the halogen atom (Ref. 11 and 12) (I ⟷ III), "the observed order is exactly that which would be expected". (III is described as a "nuclear butadienoid polarization").

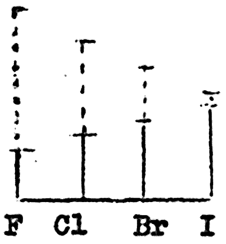
One of the significant conclusions to which this paper comes is one based on analogy: if the M effect decreases from fluorine to iodine in intensity, then the E effect should do likewise, since the two effects are intimately related and have a common origin. The argument is as follows: if the M effect in *p*-fluorobenzyl chloride facilitates the reaction, then it must develop into a true E effect in the actual reaction. The *para* fluoro compound is the fastest on hydrolysis of all the compounds given, including the unsubstituted compound, and hence the E effect is highest for fluorine among the halogens.

Further comment concerning the polarizability effect is made in this same paper (19). The *ortho-para* directive power of the methyl group in toluene is customarily ascribed to the +I effect, but this cannot be extended to $-CH_2CN$ and $-CH_2Cl$ which must have a -I effect. The *ortho-para* orientation in these cases must be ascribed to the polarizability of the bond from the carbon of the nucleus to the substituent. In the halogens, the polarizability (I_d) effect drops in the order $I > Br > Cl > F$. Thus it may be a combination of the M effect and the polarizability factor which can account for the fact that *o*-chlorofluorobenzene substitutes *para* to the fluorine, but *o*-bromoiodobenzene substitutes *para* to the iodine (both by electrophilic reagents):



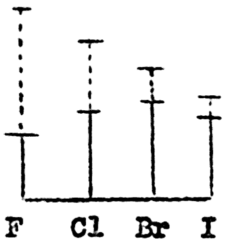


By this time, it was fairly generally agreed that the -I effect and the +T effect of the halogens decreased in magnitude from fluorine to iodine, but there were still several bits of conflicting evidence which puzzled the chemists. For example, the order of the strengths of the *p*-halogenophenylacetic acids (A) is $I > Br > Cl > F$, while the order of strengths of the *m*-halogenobenzoic acids (B) is $Br > Cl > I > F$, and the tautomeric mobilities of the *p*-halogeno-α,γ-diphenylpropenes (C) (Ref. 24a) fall in the order $F > Cl > Br > I$. In 1936, Dippy and Lewis (18) showed qualitatively how these conflicting orders might be explained. They pointed out that the two effects of the halogens are of opposite electrical nature (-I, +T), and until more quantitative data could be obtained concerning those effects, one effect might be expected to predominate under one set of conditions, while the other effect might become more pronounced under other conditions. Thus in the diagrams below, there is shown three examples given just above. The total line represents the electron attraction of the halogens due to the -I effect alone; the dotted portion of the line represents the opposing +T effect -- both effects decreasing in the order F > Cl > Br > I. The solid line will then represent the observed order, which is in each case overall electron attracting (-I > +T).



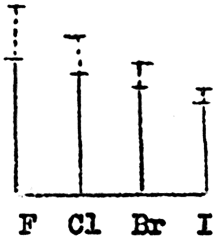
(A)

I > Br > Cl > F



(B)

Br > Cl > I > F



(C)

F > Cl > Br > I

The rates of reaction of the halogenated benzyl bromides with pyridine in dry acetone (28) gives some interesting information concerning the electronic effects of the halogens. The rate constants are given here:

R-C_6H_4-CH_2-Br

R:		K x 10^{-4} 1/g. mol. sec.		R:		K x 10^{-4}	
		20°	40°			20°	40°
	H	1.22	4.82				
para	F	1.48	5.78	meta	F	0.95	3.62
"	Cl	1.27	5.10	"	Cl	1.08	4.07
"	Br	1.30	5.19	"	Br	1.07	3.77
"	I	1.48	5.43	"	I	1.14	4.13

It is to be noted that the velocity of all the *meta* halobenzylbromides is less than that of the unsubstituted parent, so that the total effect is an electron attraction, and the order I > Br ≈ Cl > F shows that the E and M effects are of minor importance from the *meta* position, particularly in this side-chain reaction. In addition it is to be noted that the rates of the *para* substituted compounds are greater than the unsubstituted parent; hence here, the total polar effect is an electron release by the halogen. The order is F ≈ I > Br > Cl. The ratio of the *para* velocities to the *meta* give an idea as to the extent to which the T effect operates (since it is of minor importance in the *meta* position). The *p/m* velocity ratios are:

	F	Cl	Br	I
at 20°	1.56	1.18	1.19	1.22
40°	1.59	1.25	1.38	1.32

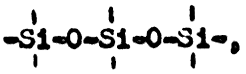
Baker, however, in interpreting these values, accepts the order F>Cl>Br>I for the M effect only. (Also the same order for the I effect, as shown from the K values for the meta compounds). Further, he states that the above data are consistent with the order I>Br>Cl>F for the E effect; that is, the polarizability varies in that order. The fact that the rate constant for the para iodo compound approximately equals that for the fluoro compound indicates that the polarizability of the iodo compound is high, while the polarization of the fluoro compound is high.

The statement that the M effect decreases while the E effect increases in magnitude from fluorine to iodine is supported by Bird and Ingold (29). They measured the rates of nitration of the halobenzenes by acetyl nitrate in acetic anhydride at 18°, and found the following relative values (benzene = 1): (Ph is C_6H_5)

PhF, 0.15; PhCl, 0.033; PhBr, 0.030; PhI, 0.18

These values were confirmed qualitatively by Benford and Ingold (30) using a different experimental method. The fact that the rates go through a minimum is explained by a greater polarization of the fluoro compound (high M value), and by the greater polarizability of the iodo compound (high E value). With reference to Bennett's statement (19), that the E and M effect "have a common origin", Ingold replies that he "does not see that common origin necessitates common behaviour". (29)

The present reviewer was unable to find any papers subsequent to this (1938) dealing directly with the order of the E effect among the halogens. It is apparent, however, that the most recent authorities (i.e., Remick, Ref. 4) ascribe the same order for both the E and M effects, decreasing in magnitude from fluorine to iodine. This conclusion was reached because the mass of the experimental data required it; the opinion of the authors whose papers indicate the reverse order is now considered erroneous.

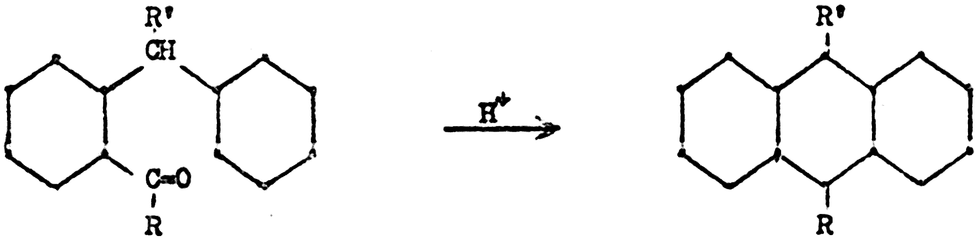
Although ample evidence has been presented in this historical review to support the conclusion that the T effect falls in the order F>Cl>Br>I, there has been given here only one explanation as to why this should be so (19) and this explanation has been widely criticized by many chemists (13, 29). At the present time, there is still no good explanation. A suggestion by Lewis (31) might have a bearing on the subject (See Ref. 4, p. 57). When the halogens exhibit the +T shift of electrons, they form a double bond with the carbon atom; and fluorine, being an element in the first period of the periodic table, is, according to Lewis, better able to form double bonds than the other halogens, which are further down in the periodic table. Thus fluorine is better able to form double bonds, and, therefore, gives up its electrons in a +T shift with more ease than the other halogens. (Compare the oxides of carbon and silicon: in the former we have double bonds from oxygen to carbon, resulting in a discrete covalent molecule, a gas. In silicon oxide, we have a space lattice of  $-\overset{|}{\underset{|}{Si}}-O-\overset{|}{\underset{|}{Si}}-O-\overset{|}{\underset{|}{Si}}-$, etc., forming a hard solid, because presumably of silicon's inability to form double bonds.) The fact that iodine can form more than one bond to carbon (iodinium compounds) was used as evidence that the +T effect for iodine would be greater, but this argument would be invalid since these are not double bonds.

In conclusion, it might be said that, while there is no satisfying explanation for the observed fall in magnitude of the +T effect in the halogens with increasing atomic weight, this is an experimental fact, and can be used to advantage by the theoretical chemist. The utility of this aspect of the English theory is not impaired by the lack of explanation for it, and its application has found constant use in the elucidation and prediction of reaction mechanisms and in the interpretation of experimental data.

THEORETICAL
AND
DISCUSSION OF RESULTS

A study of the mechanism of aromatic cyclodehydration was recently made by Bradsher and Vingiello (1, 2) who studied the rates of cyclization of ketones of the o-benzylphenone type to give 9-substituted anthracenes. The values for some of the rate constants of the ketones which they investigated are given in Table I.

TABLE I

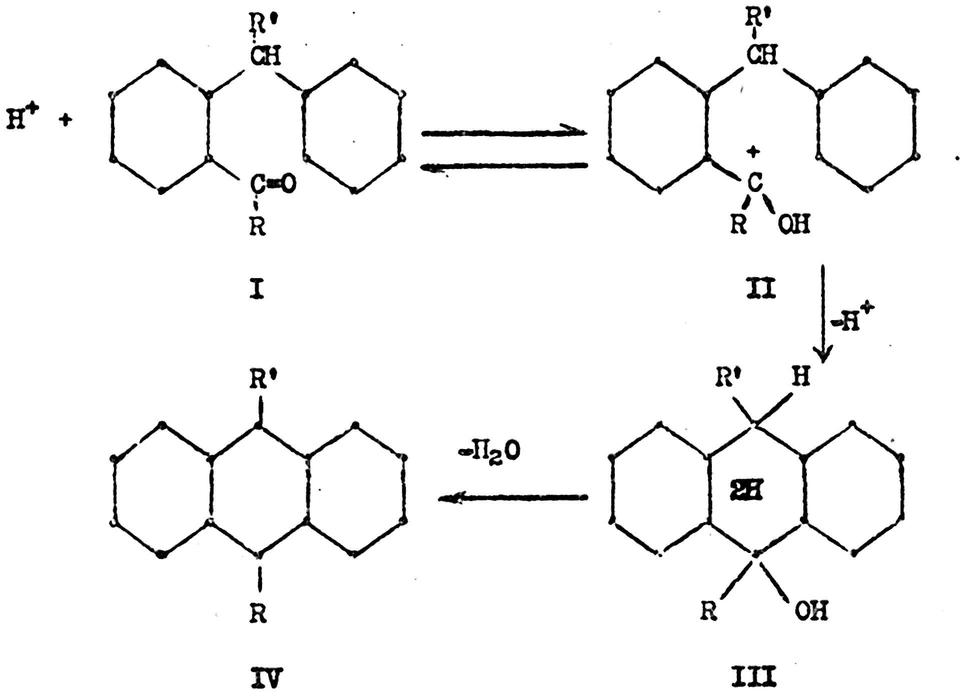


R:	R':	K (hr.$^{-1}$) x 10^{-2}
p-Methylphenyl	Hydrogen	4.2
p-Bromophenyl	"	4.2
p-Chlorophenyl	"	4.1
p-Fluorophenyl	"	2.8
Phenyl	"	4.4
Phenyl	Methyl	13.
Phenyl	Phenyl	13.

A comparison of the rates of the *para*-substituted phenyl ketones showed that regardless of whether an electron attracting or an electron releasing group be present in the *para* position, the rates were the same, within the probable experimental error, as the parent unsubstituted phenyl ketone. The lone exception to this was the *p*-fluoro ketone which cyclized at a significantly slower rate; this will be discussed in more detail later.

The fact that both electron releasing and electron attracting substituents gave essentially the same rate led these investigators to the conclusion that the overall rate of the reaction was controlled by two rate determining steps of opposing electrical requirements.

CHART I



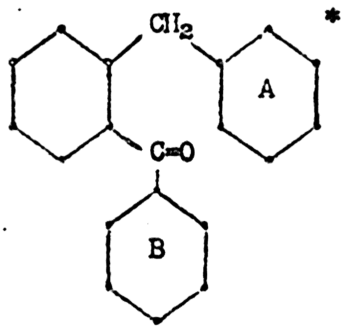
Thus they indicated "that a decrease in the effective positive character of the central carbon atom of the conjugate acid (II) would lead to a lower rate of cyclization of that acid (II → IV)." (1). Such a decrease in the positive character of the central carbon atom would be effected by an electron releasing group in the phenyl ring. This conclusion was also reached by Berliner (33), who, however, failed to recognize the following fact. An electron releasing group would, however, also increase the electron density of the carbonyl oxygen, and so the equilibrium (I ⇄ II) would shift to the right (34), thus increasing the concentration of the conjugate acid (II) and accelerating the overall rate (I → IV). The dependence of the overall rate on the hydrogen ion concentration (33) showed that this rate was dependent on the position of the equilibrium (I ⇄ II), thus supporting this latter postulate. An electron attracting substituent would have just the opposite effect on these two steps (i.e., shift the equilibrium in step one to the left and thus decreasing the concentration of the conjugate acid, but at the same time increasing the positive character of the carbonium ion, and thus facilitating its attack on the ortho position of the upper benzene ring.) If the opposing electrical requirements of these two steps were exactly compensating, then the overall rate would be independent of the nature of the substituent on the phenyl group, providing, of course, all other factors are held constant. As it has been pointed out, this was true experimentally with the outstanding exception of the para-fluorophenyl ketone. As Bradsher and Vingiello stated (1): "The significance of the lower rate shown by the fluorophenyl ketone is not clear, for the decreasing order of the electron release of the various substituent groups, as indicated by the ionization of the para-substituted benzoic acids (35) appears to be $CH_3 > H > F > Cl > Br$."

In considering an extension of this investigation in order to clarify some of the problems involved, the following reasoning was applied. Since the halogens fall into the electronic category -I, +T, and since the T effect operates strongly from the para position but only weakly from the meta position, it was thought that valuable information could be obtained if the rates of the corresponding meta substituted ketones could be studied. Any change in the rate of cyclization of these ketones would be principally due to the I effect only, divorced from the complicating opposing +T effect. Further, if it were possible to prepare ketones with very strongly electron releasing, or electron attracting properties in either the para or the meta position, a study of the effect those extreme properties might shed some light on the mechanism of the reaction. Vingiello (Ref. 2, p. 63) prepared 2-benzyl-4'-methoxybenzophenone, but could not isolate any solid material from the attempted cyclization of this compound in the standard acid mixture (hydrobromic-acetic acids). For this reason it seemed unwise to attempt the preparation and cyclization of the corresponding meta methoxy ketone. A consideration of the various possible strongly electron attracting or releasing substituents with regard to the practicability of synthesis and compatibility with the method of rate measurement seemed to eliminate all but the trifluoromethyl group for purposes of study.

The major portion of this investigation, therefore, was devoted to the syntheses of and rate measurements on 2-benzyl-3'-substituted benzophenones, where the substituent is methyl, fluoro, chloro, bromo, and trifluoromethyl; and also 2-benzyl-4'- trifluoromethylbenzophenone.

Among the other ketones whose rates were studied by Bradsher and Vingiello (1, 2) were o-benzoyltriphenylmethane and o-benzoyl-1,1-diphenylethane (Formula I, Chart I: R is C_6H_5 and R' is C_6H_5 and CH_3, resp.). Both of these ketones had a rate constant of 13×10^{-2} $hrs.^{-1}$ which is an increase in the rate over that of the ketone where R' is H (o-benzylbenzophenone, K is 4.4×10^{-2} $hrs.^{-1}$). This increase in the rate was explained on the basis of an increased electron density at the ortho position at which cyclization takes place, or, alternatively, in the case of the triphenylmethane derivative, on a statistical basis, since there are four ortho positions (instead of two) in this compound, leading to an increase in the probability of the reaction. It should further be noted that the steric factors in these compounds are not the same as in the remainder of the compounds studied, and this might also alter the rates somewhat. As a result, it was concluded that in these cases the rate of cyclization depended upon the steric nature of R and R', the electron density at the *ortho* position of the benzene ring into which the conjugate acid cyclizes, and the number of such *ortho* positions.

The obvious way to test these conclusions would be to prepare ketones of the following type with substituents in ring A:



Thus for example, a methyl group *ortho* or *para* to the methylene bridge would be *meta* to the point of cyclization, and hence in both of these compounds the methyl group would presumably have the same electronic effect upon the point of cyclization. However, with the methyl group *para* to the methylene bridge, there are two *ortho* positions into which cyclization can take place; whereas with the methyl group in the *ortho* position, we find that there is only one *ortho* position available for cyclization. Hence it would be predicted that on a statistical basis, the latter (*ortho*) would cyclize slower than the former (*para*). When the methyl group is *meta* to the bridge, it is

---

*Hereafter in the discussion, ring A will be referred to as the "upper" ring, while ring B will be called the "lower" ring.

para (also ortho) to the point of cyclization, and hence should increase the electron density on that ortho position to an even greater extent so that cyclization should take place more rapidly. If, however, a trifluoromethyl group, or some other strongly electron attracting group, should be placed in this position, or in any position in the upper ring for that matter, the rate of cyclization should be markedly lowered.

Having decided upon the ketones to be studied, attention was turned to methods of synthesis. Since none of the ketones, and few of the intermediates leading to these ketones, had been prepared before, the problem of synthesis was a very real one. For the syntheses of the ketones with substituents in the lower ring the two paths used by Vingiello (2) proved satisfactory. Thus for the syntheses of 3'-R'-2-benzylbenzophenones where R' is methyl, m- (and p-) chloro-. m- and p-trifluoromethyl and hydrogen, the sequence of reactions diagrammed in Chart II (R is H) was used.

The Grignard reagent of bromobenzene was allowed to react with o-chlorobenzaldehyde to give o-chlorobenzhydrol (V)*, in 87.3% yield. This hydrol was reduced to the corresponding diphenylmethane (VI) in 90% yield, by the use of red phosphorus and iodine in acetic acid. By the use of a von Braun reaction (cuprous cyanide in anhydrous pyridine at 250°C) the chloro compound was converted to o-cyanodiphenyl-

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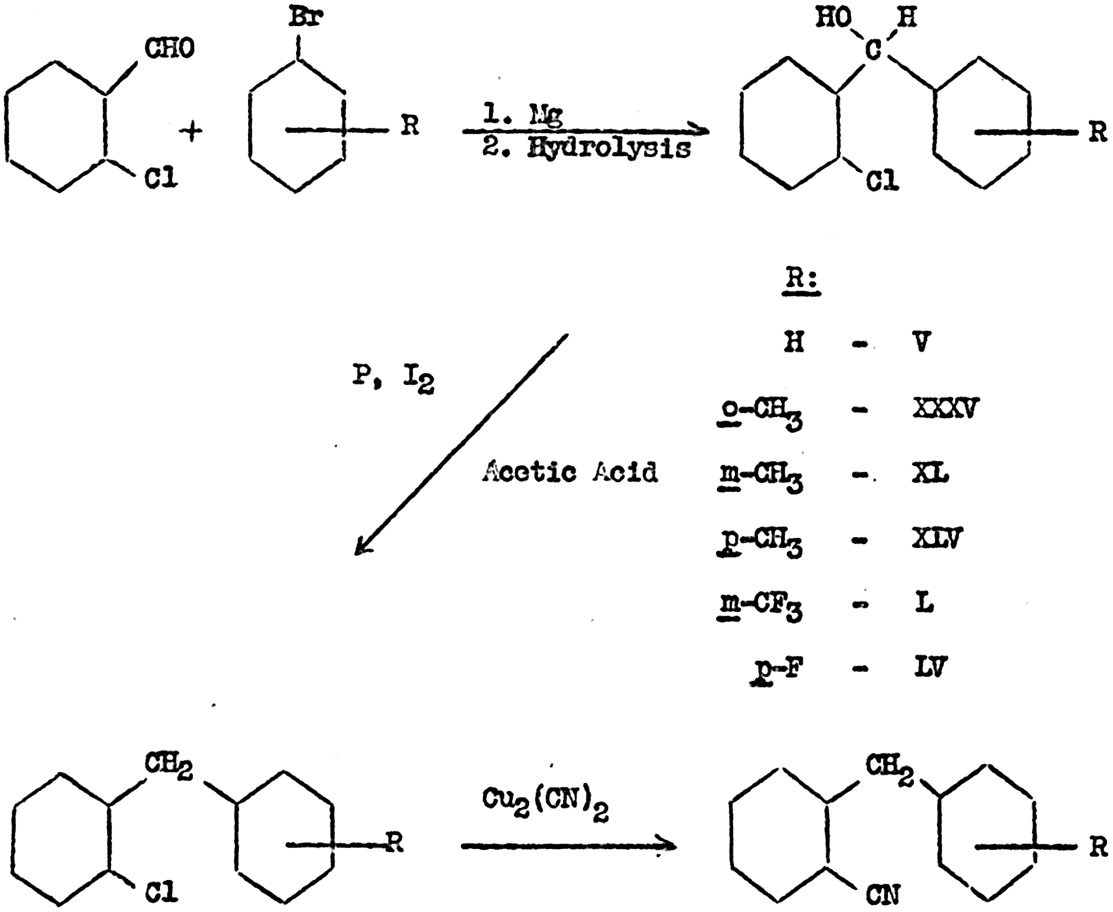
*The Roman numerals refer to the compounds listed, in order, in the experimental section.

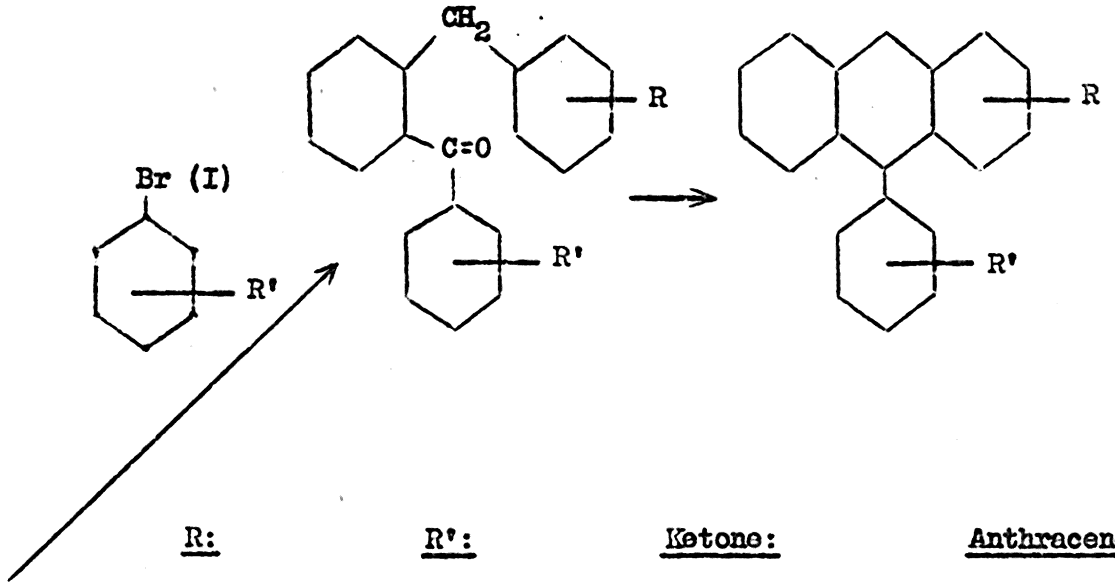
CHART II



R:	
H	V
o-CH$_3$	XXXV
m-CH$_3$	XL
p-CH$_3$	XLV
m-CF$_3$	L
p-F	LV

R:	
H	VI
o-CH$_3$	XXXVI
m-CH$_3$	XLI
p-CH$_3$	XLVI
m-CF$_3$	LI
p-F	LVI

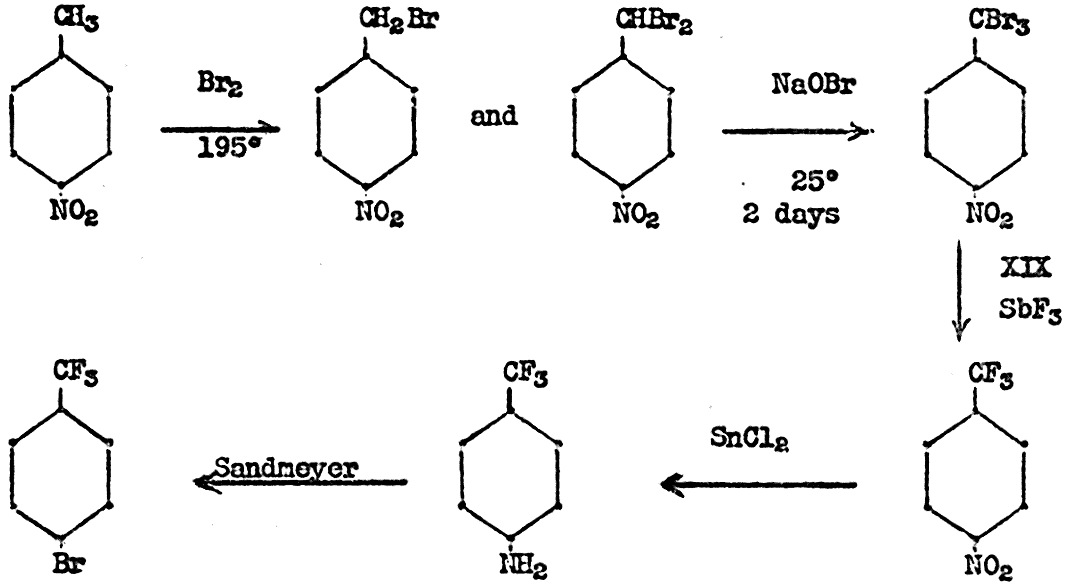
R:	
H	VII
o-CH$_3$	XXXVII
m-CH$_3$	XLII
p-CH$_3$	XLVII
m-CF$_3$	LII
p-F	LVII



R:	R':	Ketone:	Anthracene:
H	H	VIII	IX
o-CH_3	H	XXXVIII	XXXIX
m-CH_3	H	XLIII	XLIV
p-CH_3	H	XLVIII	XLIX
m-CF_3	H	LIII	LIV
p-F	H	LVIII	LIX
H	*m*-Cl	XII	XIII
H	*p*-Cl	X	XI
H	*m*-CH_3	XIV	XV
H	*m*-CF_3	XVII	XVIII
H	*p*-CF_3	XXIII	XXIV

methane (VII) in 71 % yield. The reaction of this nitrile with the appropriate Grignard reagent (in three molar excess) gave a ketimine, which was hydrolyzed to the corresponding ketone by heating under reflux with dilute (2 N) hydrochloric acid. The Grignard reagent prepared from m-iodotoluene and this nitrile gave the 3'-methylphenyl ketone (XIV) in 49.5 % yield. The meta-chlorophenyl ketone (XII) was prepared by Hannabass (36) in 59 % yield, and the para-chlorophenyl ketone (X) was prepared by Kasey (37) in 80 % yield, following the directions of Vingiello (2) using this method. The m-trifluoromethylphenyl ketone (XVII) was obtained in 96 % yield, and the p-trifluoromethylphenyl ketone (XXIII) was obtained in 61 % yield from the corresponding m- and p-bromobenzotrifluoride through the Grignard reaction. The syntheses of these intermediates was accomplished in the following manner. m-Aminobenzotrifluoride was obtained from the Hooker Electrochemicals Company, and was converted into the bromo compound by means of the Sandmeyer reaction, based upon the method worked out by Shields and Wallerstein (38). For the preparation of the para analog, the process was more lengthy. The sequence of reactions was that given by Jones (39) and is diagrammed in Chart III. Difficulty was had in attempting to repeat the work of Jones, particularly in the first step, the direct bromination. In several of the runs, the reaction mixture polymerized near the end of the reaction, generally with the development of heat. Very poor yields of the product were obtained in these cases (0-5%). It

CHART III



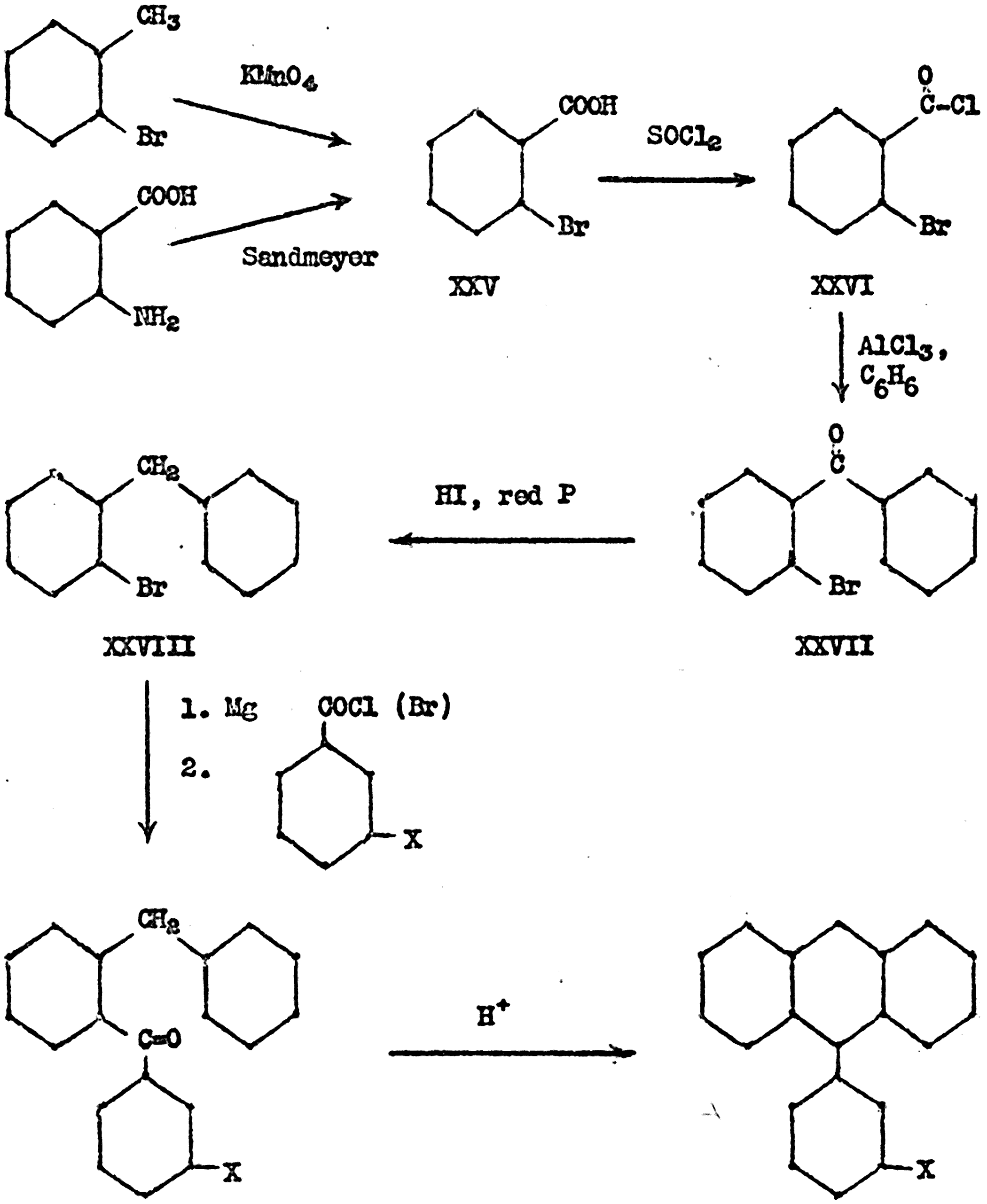
XXII XXI XX

was found, however, that the reaction proceeded rather smoothly if a large electric light were placed near the flask. With this modification, and the careful purification of the *p*-nitrotoluene and the use of a reaction temperature about five degrees less than that employed by Jones, a yield (46.5%) of the *p*-nitrobenzotribromide approaching that of Jones (58%) was obtained. In the treatment of this latter compound with antimony trifluoride it was found necessary to have pure starting materials in order to obtain a reasonable yield (61%). The quality of the antimony trifluoride is said to have a pronounced effect upon the yield (40); here the technical grade was used. The reduction of the nitro group with stannous chloride, and the replacement of the resulting amino group with bromine through the diazonium reaction was accomplished in

87.5% and 60% yields respectively, to give p-bromobenzotrifluoride.

A different route to the 3'-bromo and 3'-fluoro-2-benzylbenzophenones was required since the above route would require the formation of the mono-Grignard reagent of m-dibromobenzene (or m-iodobromobenzene), and because the required bromo (or iodo) fluorobenzene was not easily available. This method (See Chart IV) was also developed by Vingiello (2) and used by Hannabass (36) for the preparation of the bromo ketone which was used in this investigation. The method starts with the preparation of o-bromobenzoic acid from either o-bromotoluene by permanganate oxidation, or from anthranilic acid through the Sandmeyer reaction. This acid is then converted to the acid chloride and this used in a Friedel-Crafts reaction with benzene to give o-bromobenzophenone. The reduction of this ketone by means of red phosphorus and hydroiodic acid will produce o-bromodiphenylmethane, which can be used for the syntheses of a number of ketones. In the preparation of 3'-bromo-2-benzylbenzophenone, Hannabass (36) used m-bromobenzoyl bromide, (Eastman Kodak Company) which when allowed to react with the Grignard reagent prepared from o-bromodiphenylmethane, will give this ketone directly. The preparation of the corresponding fluoro ketone proceeded in the same manner: m-fluorobenzoyl chloride was allowed to react with the same Grignard reagent to give 3'-fluoro-2-benzylbenzophenone in 43.5% yield. In this case, the acid chloride was obtained from the acid by the action of phosphorus pentachloride, and the acid was in turn obtained by the alkaline permanganate oxidation of m-fluorotoluene. The o-bromodiphenylmethane

CHART IV



X:

Br - XXIX

F - XXXIII

X:

Br - XXX

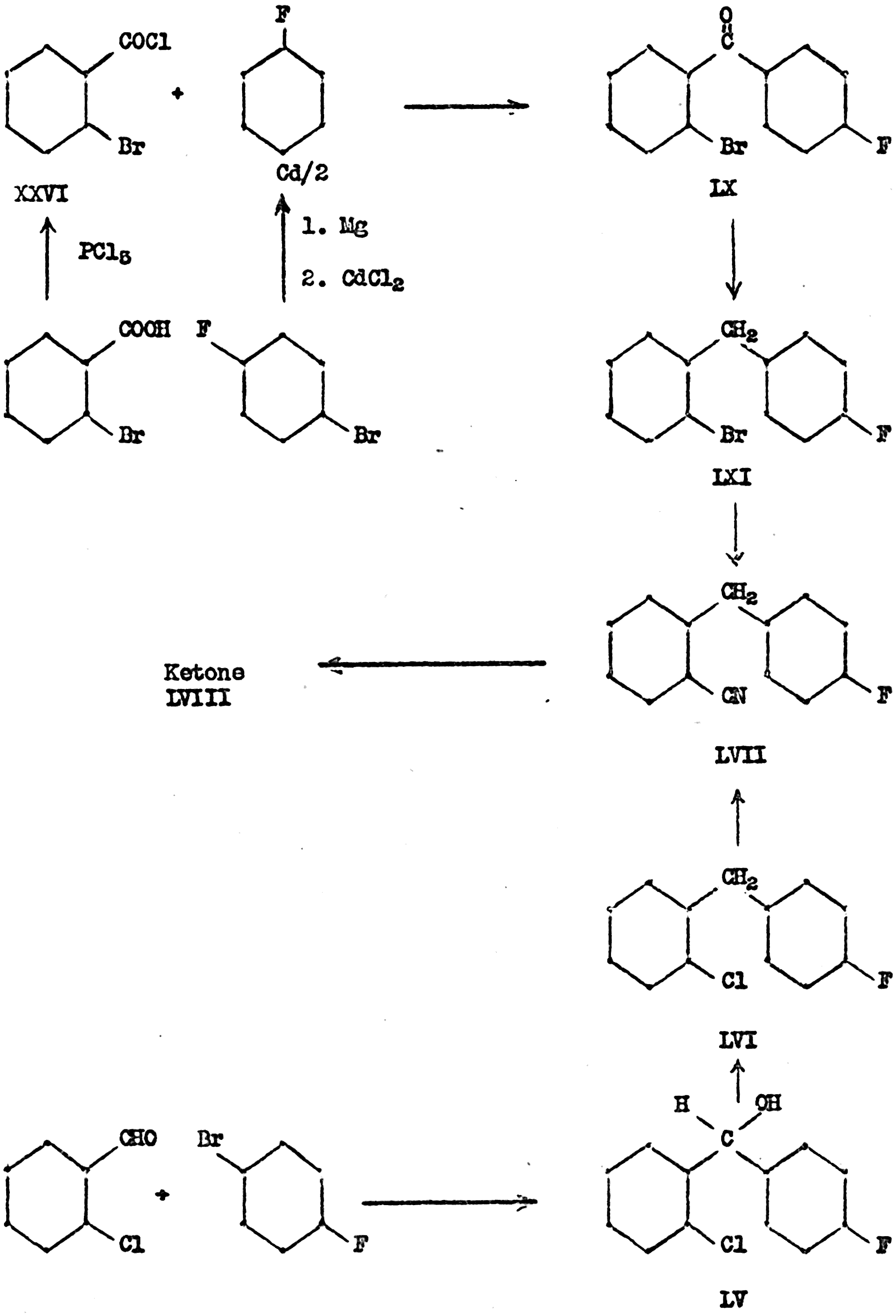
F - XXXIV

was obtained from Hannabass.

The first sequence of reactions above is also applicable for the preparation of ketones with substituents in the upper ring, providing that these substituents will not interfere with either the Grignard reaction, the reduction step, or the von Braun reaction. These restrictions immediately eliminate chloro, bromo, nitro, amino, carboxyl, and carbonyl groups. But the fluoro, methyl and trifluoromethyl groups would not be affected, and can, therefore, be used in the syntheses. By beginning the sequence of reactions with the reaction between o-chlorobenzaldehyde and the Grignard reagent from the appropriately substituted bromobenzene (or iodobenzene), this series (Chart II) of reactions will give 2-cyano-o', m', or p'-substituted-diphenylmethanes, from which the phenyl ketone can be obtained easily. This series of reactions was, therefore, carried through five more times giving the ketones substituted in the upper ring with o-methyl (XXXVIII) m-methyl (XLIII), p-methyl (XLVIII), m-trifluoromethyl (LIII), and p-fluoro (LVIII). In nearly all cases the yields were greater than 75%; the details of these experiments are given in the experimental section. It is interesting to note, however, that the trifluoromethyl group was not harmed by the rather vigorous treatment of the von Braun reaction (250° for 24 hours): 2-cyano-3'-trifluoromethyldiphenylmethane was obtained in 78.5% yield.

The preparation of 2-cyano-4'-fluorodiphenylmethane warrants closer examination. Since this compound was prepared in 63.5% yield from 2-chloro-4'-fluorodiphenylmethane, it became apparent that the action of the cuprous cyanide in the von Braun reaction was largely on the chlorine atom, and not on the fluorine. This fact could not have been predicted with certainty before the reaction had actually been run. The preparation of this compound was carried out through a different sequence of reactions involving an aryl cadmium reagent in order to test the applicability of this sequence in syntheses of this type, and also incidentally to give further proof (beyond that of the elemental analysis) of the structure of the compound. This new sequence is diagrammed with the first sequence in Chart V. The Grignard reagent from p-bromofluorobenzene was prepared by the usual reaction with magnesium turnings in ether, and the magnesium compound then converted to bis-(p-fluorophenyl) cadmium simply by the addition of anhydrous cadmium chloride to the reaction mixture. The aryl cadmium was then allowed to react with o-bromobenzoyl chloride (XXVI) prepared as described above, in benzene solution to give 2-bromo-4'-fluorobenzophenone (IX) in 51% yield. The use of the cadmium reagent here was indicated, because cadmium reagents are reported (41) to be less reactive than magnesium aryls towards carbonyl groups, and, therefore, generally give higher yields of ketones when allowed to react with acid chlorides. This same benzophenone has been prepared in 45% yield (44) by the action of p-fluorophenylmagnesium bromide on

CHART V


COCl
Br
XXVI
PCl$_5$
COOH
Br
F
Cd/2
1. Mg
2. CdCl$_2$
F
Br
O
C
Br
F
LX
CH$_2$
Br
F
LXI
CH$_2$
CN
F
LVII
Ketone
LVIII
CH$_2$
Cl
F
LVI
H
OH
C
Cl
F
LV
CHO
Cl
Br
F

o-bromobenzonitrile, followed by the hydrolysis of the resulting ketimine, and could presumably also be prepared by the Friedel-Crafts reaction between *o*-bromobenzoyl chloride and fluorobenzene. The use of the Friedel-Crafts reaction in syntheses of the type involved here, however, where the position of the substituent must be unequivocally known, is unsatisfactory. Further the Friedel-Crafts method would be of no use in the preparation of, for example, 2-bromo-*3'*-fluorobenzophenone, whereas the synthetic route through the cadmium reagent could be used. The cadmium reagent thus has several advantages, and has been used subsequent to the above preparation, by other members of the present research group (42).

The 2-bromo-4'-fluorobenzophenone was then reduced to 2-bromo-4'-fluorodiphenylmethane (47% on a 10 g. run) and when this compound was subjected to the von Braun reaction, the bromine atom was replaced by the cyano group to give 2-cyano-4'-fluorodiphenylmethane (62%) shown to be identical to the same material prepared from 2-chloro-4'-fluorodiphenylmethane (63.5%) by refractive index measurements. The obvious extension of this series of reactions, not undertaken in the present work, would be the preparation of *o*-benzylbenzophenones substituted in the upper ring with fluorines in the *ortho* and *meta* positions, and perhaps chlorine in the *ortho*, *meta* and *para*. The preparation of these chloro compounds would be contingent upon the question of whether, in a von Braun reaction, the cyano group would replace the bromo atom to the exclusion of the chloro atom. Although when a molecule with chlorine and fluorine is subjected to the reaction, the chlorine is removed preferentially, there is less reason to believe that this would hold correspondingly in the case of chlorine and bromine, since there is less difference in reactivity between chlorine and bromine than there is between fluorine and chlorine. This remains to be seen, however.

After the syntheses of the ketones had been accomplished, a small amount of each (about one gram) was converted to the anthracene by heating it under reflux in the acetic-hydrobromic acid mixture for periods varying from a few hours to several days, depending upon the ease of conversion of the particular ketone. The anthracene generally separated out when the solution was cooled, and was filtered off, purified and characterized.

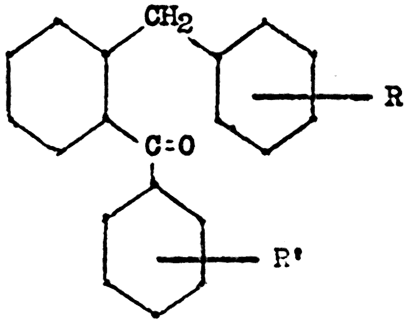
The rate measurements were then undertaken. An exact description of the apparatus used, the materials, and methods of measurement is given in the experimental part of this thesis, but a brief account of the method is in order here. A small amount of the ketone was weighed into the reaction tubes, a measured quantity of the acid mixture then pipetted into the tube, the ketone brought into solution by gentle heating to the boiling point. The time was taken, the tube capped and placed in the constant temperature bath. At the end of an appropriate time interval, the tubes were cooled to about 100° and opened, the contents poured into a small beaker, the crystallization of the anthracene induced by scratching the beaker, and the beaker placed in a constant temperature cold room for a period of several hours. The anthracene was then filtered off, washed with water, and dried to constant weight. A correction for the solubility of the anthracene in the cyclizing mixture was made by putting the anthracene itself through the same process, and determining the loss in weight by difference. The corrected yield of anthracene was then used in conjunction with the time interval to calculate the rate constant from the usual first order equation. Details for each ketone are given in the experimental section, and the results are summarized in Table II.

These results have substantially verified the conclusions reached in the earlier research into the problem. Let us first examine the effects of substituents in the upper ring on the rate of cyclization. From Table II, we can see that the introduction of a methyl group into the upper ring causes an activation of that ring to the electrophilic carbonium ion by the increase of electron density in the ring. In all of the methyl compounds, the rate of cyclization is greater than that of the unsubstituted o-benzylbenzophenone. This is to be expected from the known +I effect of the methyl group. When the methyl group is para to the point of cyclization, moreover, we note that there is a very great increase in the rate. This is in line with the known +T effect of the methyl group causing ortho-para direction in electrophilic substitution in the benzene ring.

It was thought that since the para methyl compound above had two ortho positions into which cyclization could take place, that it would cyclize at a faster rate than the ortho methyl compound above,

TABLE II

Rate of Cyclization of Some Substituted o-Benzylbenzophenones.



R:		R':		K x 10^{-2} hrs.$^{-1}$
H	-	H	-	4.4
H	-	m-CH_3	-	4.4
H	-	m-F	-	5.3
H	-	m-Cl	-	5.3
H	-	m-Br	-	5.0
H	-	m-CF_3	-	6.4
H	-	p-CF_3	-	9.3
o-CH_3	-	H	-	15.4
m-CH_3	-	H	-	200.
p-CH_3	-	H	-	13.8
m-CF_3	-	H	-	Does not cyclize in 10 days.
p-F	-	H	-	Does not cyclize in 3 days.

which has only one such ortho position. An examination of the results shows, however, that the ortho compound cyclizes at a slightly faster rate than the para. With the present information available, it is only possible to surmise that there must be some preferred orientation in the molecule which would aid the reaction, due to the ortho methyl group. The fact that the ortho methyl ketone is a solid, while the para ketone is a liquid, shows that there is some difference in the intramolecular forces in the two compounds. If the probable error in the measurement of the rates is taken into consideration, there is a difference between the rates for these two ketones which is less than one hundredth of a reciprocal hour. This small difference, compared to the difference between these ketones and the meta substituted ketone (two reciprocal hours) is insignificant, and does not overshadow the electronic interpretation of the reaction given above.

In line with the fact that electron releasing groups in the upper ring accelerate the rate of reaction is the fact that electron attracting groups retard the reaction. The substitution of the very powerful electron attracting trifluoromethyl group para to the point of cyclization reduced the rate of reaction to such an extent that no cyclization product could be isolated from the reaction mixture after more than ten days heating. The material obtained from the reaction mixture at the end of this time was identified as unchanged ketone. Likewise, the substitution of an electron attracting fluorine atom meta to the point of cyclization also strongly inhibits the reaction. In this case no anthracene could be isolated from the reaction mixture after heating for over three days; again the material was identified as unchanged ketone.

In order to prove that the latter two ketones actually did not cyclize, it was necessary to identify the material isolated from the reaction mixture at the end of the reaction time. Since both of these ketones were liquids, this identification was best accomplished through the preparation of derivatives. By this means, a rather rough determination of the amount of ketone remaining after the reaction was also possible. Because of the highly hindered nature of the carbonyl group, the preparation of the usual carbonyl derivatives either proceeded in very poor yields, or failed entirely. (See for example, Bachmann, (43) who, in order to prepare the oxime of o-tolyl p-biphenyl ketone, which is less hindered than the ketones here, required 48 hours of heating under reflux, to obtain at best only a 75% yield.) It has been shown by Kasey (37) that o-benzylbenzophenones could be oxidized in almost quantitative yield to the diketones, derivatives of o-dibenzoylbenzene. The oxidation of the ketones in question was carried out by means of acid dichromate, and gave the diketones in yields of about 95%. The material obtained from the reaction mixture after treatment for several days (by neutralizing the acid, extracting the organic matter with ether, drying the ether solution and recovering the organic matter by evaporation of the ether) was oxidized in the above manner, and the product so obtained compared (mixed melting point) with the diketone obtained by oxidizing the pure ketone. The structures of these diketones were proved by preparing them through a different route: the oxidation of 3'-trifluoromethyl-2-benzylbenzophenone gave the same diketone as the oxidation of 2-(3-trifluoromethylbenzyl)-benzophenone; likewise, the oxidation of 4'-fluoro-2-benzylbenzophenone (37) gave the same diketone as the oxidation of 2-(4-fluorobenzyl)-benzophenone.

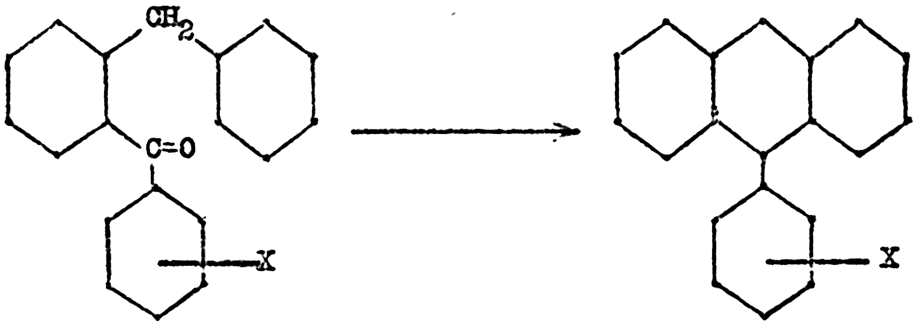
The above evidence thus supports the conclusion of Vingiello and Bradsher, who stated that the rate of cyclization of ketones of this type would depend upon the electron density at the ortho position in the benzene ring into which cyclization takes place.

Let us now examine the effects of the various substituents in the lower ring on the rate of cyclization. The values obtained in the present work are compared with the values obtained in the earlier work in Table III. The fact that these two sets of data are comparable was established by the redetermination of the values for the rates of cyclization of two of the ketones which were reported in the earlier work. The values for the rates of o-benzylbenzophenone and 4'-chloro-2-benzylbenzophenone agreed with the values previously obtained for these rates (2).

One of the outstanding features of this series of rate constants is that there is very little numerical difference in the rate constants when substituents with such widely differing electronic effects as the trifluoromethyl group and the methyl group are present. (In the upper ring, it will be remembered, these groups

TABLE III

Rates of Cyclization of Some 3'- and 4'-Substituted-2-benzylbenzophenones.



X:		$K \times 10^{-2} hrs.^{-1}$
p-F	-	2.8*
p-Cl	-	4.1*#
p-Br	-	4.2*
$p-CH_3$	-	4.2*
$m-CH_3$	-	4.4
H	-	4.4*#
m-Br	-	5.0
m-Cl	-	5.3
m-F	-	5.3
$m-CF_3$	-	6.4
$p-CF_3$	-	9.3

*Values from the earlier work (1, 2).

#Redetermined for comparison in this work.

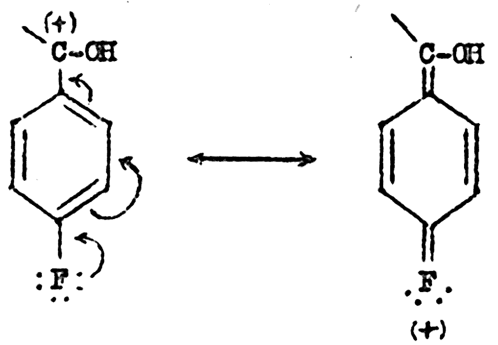
cause a tremendous retarding and accelerating effect, respectively, on the rate.) This fact corroborates the statement of Bradsher and Vingiello that the overall rate of the reaction was dependent on two rate determining steps of opposing electrical requirements. The electrical effect of any substituent which would accelerate one step in the reaction would retard the other; the compensating effects of these two steps would serve to nullify any retardation or acceleration, and the rate of the overall reaction would remain essentially unchanged.

There is, however, a general trend in the reaction rates of the ketones studied in the present work which shows that perhaps the second step in the reaction is slightly more susceptible to the effects of the substituents than the first step is. As we change from the unsubstituted ketone to the ketones containing the halogens in the meta position, we find a slight increase in rate. This can be interpreted as being caused by the -I nature of the substituent. With the meta trifluoromethyl group, there is a stronger -I effect, and correspondingly a slight increase in the overall rate of cyclization. When this trend was noted, it was predicted that the para trifluoromethyl group which exerts not only a strong -I effect, but also a strong -T effect (45) would cause a larger jump in the rate of reaction; this prediction was borne out by experiment. It is also to be noted that the rates for ketones in which a +T effect can operate are slower than those cases where this effect cannot operate. Now it must be pointed out that these differences are indeed small, whereas the differences in the electrical effects of the substituents are by comparison quite large. This point emphasizes again that it is the compensating nature of the two steps in the reaction which is the major factor; otherwise the following fact would be difficult to explain: the unsubstituted ketone, the ketone with strongly electron attracting substituents (chlorine and bromine in the *para* position) and the ketone with an electron releasing group (methyl) all cyclize at the same rate.

When the work (1, 2) which preceded the present investigation was done, the significance of the lower rate shown by the *para*-fluorophenyl ketone was not clear. If the criterion for the order of decreasing electron release of the various substituents were the strengths (35) of the corresponding *para* substituted benzoic acids, then fluorine would be found in the middle of the series: $CH_3 > H > F > Cl > Br$.

In the light of the facts presented in the present work, this value for the fluoro ketone is not out of line. The results of the present work show that fluorine in the *meta* position, with its large -I effect, actually increases the rate of cyclization slightly. Since the tautomeric effect does not operate significantly from the *meta* position, it follows that the presence of the tautomeric effect operating from the *para* position would seem to be the cause of the slower rate. The objection to this argument is, of course, that if the +T effect slowed the second step, why then does it not correspondingly speed the first step (i.e., shift the equilibrium to the right) and nullify any change in rate?

The answer to this question may be found in a closer analysis of the problem. It is to be noted here that step two might be considered a nucleophilic attack by the ortho position of the upper benzene ring on the carbonium ion, and hence the +E effect of the fluorine would not be called into play since it would not aid the reaction. The +M effect, being a permanent polarization of the molecule, would, however, serve to impede this step (Ref. 4, p. 59). The +M effect of the fluorine atom is larger than that of any of the other halogens in a neutral molecule. Moreover, in the present case, we find that there is a full positive charge on the carbonium ion, and the +M effect of the halogens is undoubtedly considerably enhanced by this charge. This would result in a relatively significant contribution of the form on the right below to the resonance hybrid of the carbonium ion:



It can be plainly seen that any contribution of such a form would lower the electropositive character of the central carbon atom, and hence slow the rate at which it would attack the upper benzene ring. The fact that fluorine is better able to donate its electrons in such a shift as shown above than any of the other halogens, coupled with the experimental fact that the fluoro ketone cyclizes slower than the other halogenated ketones, would indicate that only in the case of fluorine is this above resonance form strong enough to overcome the compensating nature of the two steps in the reaction.

The statement that the slower rate of cyclization of the fluoro ketone is due to its large +M effect might be objected to on the basis that normally fluorine exerts a predominant electron attraction, and not an electron release. This objection can be met, it is felt, with the argument that here the +M effect is magnified by the presence of the positive charge of the carbonium ion, and the increase in the +M effect in this case would reverse the normal electronic nature of the fluorine atom by overshadowing the inductive effect. There are cases comparable to this quoted by Alexander (47) where it was necessary to postulate that the M effect appeared to outweigh the inductive (I_s) effect.

Several examples showing the extreme degree which the +T effect of fluorine has on the properties and reaction velocities of its compounds have already been given in the historical section. The outstanding example given there is the effect of the halogen atoms in the para and meta position on the rate of hydrolysis of benzyl chlorides (p. 18). In all cases, the rates of the halogenated compounds are slower than that of the unsubstituted compound, with the exception of the para fluoro compound. Here the rate is almost twice as fast as that of the parent compound. Since the hydrolysis is thought to be facilitated by a +T shift, these figures show that only in the case of fluorine in the <u>para</u> position is the T effect strong enough to speed this reaction so that the rate is faster than that of the unsubstituted compound.

It may be possible that this same factor (increase in the +M effect) is partially responsible for the similarity in rates of the <u>para</u>-chloro, <u>para</u>-bromo, methyl and unsubstituted ketones, by acting in the halogenated ketones to nullify the large -I effect.

Since the M effect of the methyl group is of hyperconjugative origin, its magnitude is quite small by comparison to that of the halogens. This fact, and the fact that the +E effect is not called into play in the second step of the reaction, may be the reasons why no difference is noted in the rates for the <u>m</u>- and <u>p</u>-methyl ketones. Any small difference here, and between these ketones and the unsubstituted ketone are not noticed presumably because of the compensating action of the two steps in the reaction.

In conclusion, we may say that the present investigation (a) confirms the statement of Bradsher and Vingiello that the rate of cyclization of the ketones is dependent upon the electron density at the ortho position in the upper ring into which cyclization takes place, (b) corroborates their statement that the rate is dependent upon two rate determining steps of opposing electrical requirements, but shows that these two opposing factors are not exactly compensating, (c) explains why 4'-fluoro-2-benzylbenzophenone cyclizes at a slower rate than the other ketones studied by showing that the magnification of the +M effect of the fluorine by a full positive charge serves to slow the reaction by acting in step two of the reaction, and finally (d) indicates that the steric requirements of the reaction are important.

EXPERIMENTAL[a,b]

o-Chlorobenzohydrol. (V)[c] A Grignard reagent was prepared from 37 g. (1.54 moles) of magnesium, 242 g. (1.54 moles) of bromobenzene in ca. 400 ml. of ether, using a crystal of iodine as catalyst. When the magnesium had gone into solution after about an hour of heating with stirring, the solution was cooled and a solution of 109 g. (0.78 moles) of o-chlorobenzaldehyde in ca. 100 ml. of ether was added dropwise with stirring. After the addition, the mixture was heated under reflux with stirring for about an hour, was then cooled in an ice bath, and decomposed with the equivalent amount of ice-cold 20% ammonium chloride. The ethereal solution was poured off, and the residue extracted twice with fresh ether, the combined ether solutions then were dried over calcium chloride. The ether was then evaporated and the residue distilled, the fraction coming over at 179-180°/8 mm. being collected (Lit.(48) 163-176°/5 mm.). The viscous, colorless liquid solidified almost immediately; yield 146.5 g., 87.3%.

(a) All melting points are corrected.

(b) All the analyses reported here were done by the MicroTech Laboratories, Skokie, Illinois except the ones marked with an asterisk, which were done by the Oakwold Laboratories, Alexandria, Va.

(c) Roman numerals I-IV refer to formulas in Chart I.

o-Chlorodiphenylmethane. -- (VI) A slurry of 139 g. (0.64 moles) of o-chlorobenzohydrol, 23.2 g. (0.75 moles) of red phosphorus, and 23.2 g. of iodine in ca. 1400 ml. of glacial acetic acid and 200 ml. of water was heated with stirring under reflux for thirty hours. The mixture was then cooled to room temperature and the phosphorus filtered off. The filtrate was then poured into twice its volume of water, and the acid neutralized with sodium carbonate. The organic matter was extracted with ether, and the ether solutions combined and washed with 10% aqueous sodium hydroxide until the iodine color was removed, washed with water, and then dried over calcium chloride. The ether was removed by distillation at atmospheric pressure, and the residue fractionated. The fraction coming over at 141-143°/5 mm. was collected (Lit. (48, 2) 138-142°/5 mm.; 144°/5 mm.). Some mechanical losses incurred lowered the yield to 90.0 g. (70%).

o-Benzylbenzonitrile. -- (VII) A mixture of 90.0 g. (0.445 moles) of o-chlorodiphenylmethane, 48 g. (0.54 moles) of cuprous cyanide, a few crystals of anhydrous cupric sulfate and approximately 50 ml. of pyridine which had been dried and distilled from barium oxide, was heated in a metal bath for 24 hours at 250°. The pyridine was allowed to distil off slowly thru a tall air condenser. At the end of this heating time, the flask was equipped with a von Braun distilling head and a crude distillation of the product was made at 4 mm. pressure. The distillate was cooled and poured into dilute ammonium hydroxide. This mixture was extracted with ether, and the combined ether extracts washed with 2 N HCl twice, and then with water twice, and finally dried over calcium chloride and concentrated. The residue was distilled, and the fraction coming over at 146-154°/2 mm. (Lit. (48) 160-164°/4 mm.; (36) 153-154°/3 mm.) was collected. The yield was 61.2 g. (71.4%).

o-Benzylbenzophenone. -- (VIII) A Grignard reagent was prepared in 200 ml. of ether from 29.4 g. (0.187 moles) of redistilled bromobenzene and 4.55 g. (0.187 moles) of magnesium. After the magnesium had gone into solution, the ether was distilled off and replaced with dry benzene. When the temperature of the vapors reached 70°, 12 g. (0.0623 moles) of o-benzylbenzonitrile in 200 ml. of dry benzene was added in one portion. The solution was heated under reflux with stirring for 18 hrs., cooled and hydrolyzed with 20% ammonium chloride solution. The benzene solution was poured off, and the residues extracted with fresh benzene. The combined benzene solutions were heated under reflux with 200 ml. of 2 N HCl for 20 hrs. The layers were separated, washed with 10% NaOH, twice with water, and then dried over $CaSO_4$. The ether was distilled off, and the residue fractionated, the portion coming over at 212-214°/4 mm. weighing 13.9 g. (82.2%). This material was recrystallized from ethanol, and had a melting point of 55-56° (Lit. (2) 51-52°).

9-Phenylanthracene. -- (IX) Five tenths of a gram of the above ketone (VIII) was heated in the standard acid mixture for 27 hours. On cooling, 0.32 g. of the anthracene crystallized out (68%). The crystals were filtered off, recrystallized from ethanol, and had a melting point of 152-153° (Lit. (2) 151-152°).

4'-Chloro-2-benzylbenzophenone. — (X) This compound was obtained from R. A. Kasey (37). It had a melting point of 72-73° and was used in Control Run #2, cyclizing to 9-(4-chlorophenyl)-anthracene (XI).

3'-Chloro-2-benzylbenzophenone. — (XII) This compound was obtained from Hannabass (36) who prepared and purified it for this investigation. It boiled at 222-224°/5 mm.

9-(3-Chlorophenyl)-anthracene. — (XIII) The above ketone (0.45 g.) was heated in the standard acid mixture for 24 hours. When the solution was cooled, 0.25 g. of the anthracene crystallized out. (71.2%) Recrystallized from ethanol, it had a melting point (133-134°) which agreed with that found by Hannabass (36).

3'-Methyl-2-benzylbenzophenone. — (XIV) A Grignard reagent was prepared from 51 g. (0.234 moles) of redistilled m-iodotoluene and 5.6 g. of magnesium in dry ether. In this run, a rather considerable amount of magnesium did not go into solution after two hours of reflux. Then 15 g. (0.078 moles) of the o-benzylbenzonitrile in ca. 200 ml. of dry benzene was added. The ether was allowed to distil off, and the solution heated under reflux with stirring for fourteen hours. It was then decomposed with dilute hydrochloric acid and then placed in a flask with 200 ml. of 2 N HCl and heated under reflux with stirring for 9.5 hrs. The benzene was distilled off, and the residue fractionated. The fraction coming over at 212-215°/3.5 mm. (Lit. (36) 205-206°/3 mm.) was a viscous yellow oil, and weighed 10.6 g. (49.5%).

9-(3-Methylphenyl)-anthracene. — (XV) Considerable difficulty was experienced in the cyclization of the above ketone in order to obtain a crystalline product. Several attempts to crystallize the oil obtained from the usual cyclization procedure (varying lengths of reflux time) were unsuccessful. The use of phosphoric acid in acetic acid gave no crystalline product. Chromatography on alumina using hexane gave a colorless fluorescent oil from which no crystalline material could be obtained. The successful attempt is described here. Two grams of the ketone (XIV) was heated in 125 ml. of the standard acid mixture for a total of 49 hours. On cooling this solution slowly, a heavy black oil separated. This oil was thick enough to filter off; it was washed once with water, taken up in ethanol, and the solution charcoalled to a light yellow color. The solution was concentrated, and then cooled in a dry-ice acetone bath. This treatment precipitated a tan material which, when it warmed up to room temperature, was quite gummy. The mother liquor from this treatment, standing at room temperature overnight deposited amber crystals, which melted at ca. 85°. Using these crystals as seed, no subsequent difficulty was had in getting the anthracene to crystallize directly from the cyclization mixture. Recrystallized four times from a mixture of formic acid and ethanol, the anthracene melted at 97-98.5°.

Anal. Calc'd. for $C_{21}H_{16}$: C, 93.99; H, 6.01.

Found: C, 93.84; H, 6.10

m-Bromobenzotrifluoride. --- (XVI) This compound was prepared by the method used by Shields and Wallerstein (38), a Sandmeyer reaction on the corresponding amine. The procedure is as follows: Into a solution of 40 g. of copper sulfate pentahydrate and 33 g. sodium bromide in 264 ml. of 48% hydrobromic acid in a one l. round bottom flask was placed 22.5 g. of copper turnings, and the solution was boiled for thirty minutes. Then 75 ml. of water was added, and the boiling continued until all the copper dissolved. This solution was then filtered through glass wool into a boiling solution of 75 g. (0.465 moles) of m-aminobenzotrifluoride, 197 ml. of 48% HBr in 1150 ml. water, contained in a three liter round bottom flask which could be equipped with a reflux condenser or a stirrer as needed. Then to this solution there was added a solution of 64.5 g. of sodium nitrite in 320 ml. of water, dropwise and cautiously with stirring. The reflux condenser was then attached, and the solution allowed to cool to room temperature and then put into the refrigerator at 0°. The organic layer was separated, taken up in ether, and the aqueous layer extracted twice with ether and then discarded. The combined ether solution was washed with 10% NaOH, and then with water, and then dried over calcium chloride. The ether was distilled off and the residue fractionated. The bromo compound was collected at 151-154°/710 mm. (Lit. (38) 151-152°). It weighed 71.1 g. (67.5%).

3'-Trifluoromethyl-2-benzylbenzophenone. --- (XVII) The exploratory work on this compound was done by Hannabass (36). A Grignard reagent was prepared in ether from 38.3 g. (0.17 moles) of m-bromobenzotrifluoride and 4.1 g. (0.17 moles) of magnesium. The reaction started in within two minutes, and required only half an hour of heating under reflux before all the magnesium had disappeared. A solution of 11 g. (0.057 moles) of o-cyanodiphenylmethane in benzene was added rather rapidly and the ether allowed to distil off. The benzene solution was heated under reflux with stirring for 15 hrs. The solution turned dark red soon after the addition of the nitrile and remained that way overnight, with no sign of a precipitate. The solution was then cooled and decomposed with the theoretical amount of cold ammonium chloride. The benzene solution was poured off, and the residue extracted twice with fresh benzene, and the combined benzene solutions heated under reflux with stirring, in contact with 200 ml. of 2 N HCl for 22 hrs. The benzene layer was then separated, washed with 10% NaOH, then with 2N HCl, finally twice with water and dried over $CaSO_4$, concentrated and fractionated. The material coming over at 195-198°/3 mm. weighed 18.7 g., which corresponds to 96.5% of the theoretical amount.

Anal. Calcd. for $C_{21}H_{15}OF_3$: C, 74.11; H, 4.44.
Found: C, 74.16; H, 4.63.

/ 9-(3-Trifluoromethylphenyl)-anthracene. -- (XVIII) The above ketone was cyclized in the usual manner, 0.42 g. of the ketone yielding 0.27 g. of the anthracene (66.9%) after 16.25 hours of heating. The anthracene, when crystallized from ethanol melted at 116-117° (Lit. (36) 116-117°).

Anal. Calcd. for $C_{21}H_{13}F_3$: C, 78.18; H, 4.07.

Found: C, 78.45; H, 4.08

p-Nitrobenzotribromide. — (XIX) In a 500 ml. three necked flask, equipped with a dropping funnel, stirrer, and an air condenser with efficient gas trap, was placed 96 g. (0.70 moles) of redistilled p-nitrotoluene. The flask was about one half immersed in a metal bath maintained at 190-195°, and a 200 watt uncoated tungsten filament bulb clamped into position so that it was about 0.5 cm. from the flask. The stirrer was started and 280 g. (1.75 moles) of bromine added over the course of two hours. At the beginning, dropping the bromine in at the rate of about two drops a second resulted in half of the bromine being added during the first 45 min., leaving an hour and fifteen minutes for the second half of the bromine to be added. The rate of addition of the bromine during the second half of the reaction was necessarily slower, since it was not taken up as rapidly. Within two minutes after the addition of the last of the bromine, the brown vapors in the top half of the flask had disappeared, and there was only a very small amount of hydrogen bromide detected coming from the reaction mixture. The melt, a dark amber thin oil, was then poured into a porcelain pan, and allowed to cool. It was then dissolved in about three liters of ligroin (or petroleum ether) (65-105°), leaving about ten grams of a brown solid undissolved. The solvent was then distilled off until about 800 ml. of the solution remained. This was cooled to 5°, and the greenish white solid filtered off and dried. It weighed 172 g. This material was dissolved in 500 ml. of warm methanol and poured slowly with rapid stirring into one liter of ice water. The white precipitate was collected, and washed with water, being careful not to allow the solid to form a cake by being sucked dry. The wet solid was then added to a solution of sodium hypobromite prepared by adding 180 g. of bromine to a solution of 180 g. of sodium hydroxide in 1500 cc. of water. As the material stood at room temperature for two to three days, it became more crystalline and flocculent. The solid was then filtered off, and recrystallized twice from methanol, yellow flakes, m.p. 87-88°, 120 g., yield, based on the nitrotoluene, 46.5% (Lit. (39) m.p. 86-87°, 58%).

p-Nitrobenzotrifluoride. — (XX) An intimate mixture of 85 g. (0.23 moles) of pure p-nitrobenzotribromide and 50 g. (0.275 moles) of antimony trifluoride (technical grade, not sublimed) was placed in a small flask to which was attached a large-bore air condenser set for distillation, and this connected to a small flask with side arm so that a vacuum could be applied. The receiving flask was cooled by means of a stream of cold water, and a gas trap cooled in an ice-salt bath placed between this flask and the vacuum system. The mixture was warmed gently with a free flame at atmospheric pressure; a gentle exothermic reaction took place. When this reaction had subsided, the flask was heated again so that some of the material distilled over. The pressure was then reduced to about 30 mm., and the remaining material in the flask distilled over. The distillate was then dissolved in a mixture of ether and 6 N hydrochloric acid, the ether layer separated and washed with a large excess of 6 N sodium hydroxide solution. A large amount of antimony salt came out of solution with this treatment, and then most of it redissolved as the antimonate salt. The ether solution was then dried over magnesium sulfate, concentrated, and the residue distilled. The material coming over at 80-82°/10 mm. was collected; it weighed 26.8 g. (61%). Lit. (39) 81-82°/10 mm.

p-Aminobenzotrifluoride. — (XXI) A solution of 20.9 g. (0.129 moles) of p-nitrobenzotrifluoride in 82 ml. of concentrated hydrochloric acid and 55 ml. of ethanol was heated to about 60° on the water bath. Then there was added 110 g. of stannous chloride dihydrate in portions over the course of 30 minutes. There was a slight exothermic reaction and the solution turned yellow. The solution was allowed to remain at 60° for another half hour, after which it was poured onto a mixture of 400 g. of ice, and 250 ml. of 36% sodium hydroxide solution. This amount of base was just sufficient to dissolve all of the tin as the stannite. The organic matter was extracted with ether, and the ether solution dried over magnesium sulfate, concentrated, and the residue distilled. The amine distilled at 82°/11 mm. (Lit. (39) 83°/12 mm.) **The yield was 15.3 g. (87%).**

p-Bromobenzotrifluoride. — (XXII) Forty and two tenths grams (0.25 moles) of p-aminobenzotrifluoride in 75 ml. of 48% hydrobromic acid (0.67 moles) was cooled to 0° in an ice-salt bath. Then a solution of 17.5 g. of sodium nitrite in 30 ml. of water added rather rapidly until near the end point, which was detected by means of starch-iodide paper. Because the amine hydrobromide was in the form of lumps, it was necessary to break these up before the reaction was complete. The temperature during the diazotization was kept below 10° by the addition of small pieces of ice. Meanwhile, 19.8 g. of cuprous bromide (prepared by the method of Snyder and Wicks (50)) in 20 ml. of 48% hydrobromic acid was heated to boiling in a one liter 3-necked flask, equipped with dropping funnel, stirrer and condenser set for distillation. About 2 g. of sodium bisulfite was added to ensure the complete reduction of the copper. When diazotization was complete, a portion of the diazo solution was added to the dropping funnel, the remainder of the solution being kept cold until needed. The product steam distills off and is collected. In this run, it appeared that some of the amine hydrobromide had not been diazotized, and so a solution of 1 g. of sodium nitrite in 10 ml. of water was added to the boiling mixture; more product distilled over. Water was added through the dropping funnel to replace that lost as steam, and the solution boiled until no more organic matter came over (about 800 ml. was collected). The distillate was cooled, and the heavy organic matter separated. The aqueous portion extracted with ether, and the ether and organic matter combined, washed with water, twice with 10% sodium hydroxide, twice with water, dried over calcium sulfate, the ether distilled off, and the residue fractionated. The portion coming over at 152-155°/713 mm. (Lit (39) 160-160.5/745 mm.) weighed 32.2 g., 60% of the theoretical. About 10 g. of high boiling material remained; this was not starting material.

2-Benzyl-4'-trifluoromethylbenzophenone. — (XXIII) A Grignard reagent was prepared from 32.2 g. of p-bromobenzotrifluoride (0.144 moles) and 3.5 g. (0.144 moles) of magnesium in 150 ml. of dry ether. The ether was replaced by dry benzene, and when the temperature of the distilling vapors reached 70°, 10 g. (0.052 moles) of o-benzylbenzonitrile in 50 ml. of benzene was added in one portion. The solution was heated under reflux for 26.5 hours. The solution was reddish brown when the Grignard reagent was formed; this did not change color until the final product was isolated. The solution was cooled, and hydrolyzed with ice cold 20% ammonium chloride solution to the end point. The benzene solution was poured into a liter flask. The residue was extracted with fresh benzene, but this was apparently not sufficient to remove all the color from the residue, so the residue was dissolved in dilute hydrochloric acid, and this solution extracted with benzene. The combined benzene solutions were heated with 200 ml. of 2 N HCl for 22 hours, with stirring. The layers were separated after cooling, and the benzene layer washed four times with water, then with 5% sodium carbonate, and then twice with water. Washing with stronger base caused the formation of an emulsion. The benzene layer was then dried over $CaSO_4$, and concentrated. After a solid fore-run, the portion from 175-182°/1.7 mm. was collected, nearly all of the material coming over at 182°. It weighed 10.8 g., 61% of the theoretical amount. Redistilled in a smaller flask, the ketone came over at 169-170°/0.9 mm.

Anal. Calc'd. for $C_{21}H_{15}OF_3$: C, 74.11: H, 4.44

Found: C, 74.20; H, 4.52

9-(4-Trifluoromethylphenyl)-anthracene. -- (XXIV) The cyclization of the above ketone was carried out in the usual manner with no difficulty at all. A 61% yield of the anthracene is obtained in 10 hours in the standard acid mixture. Recrystallized from ethanol, the anthracene melts at 205-206°.

Anal. Calc'd. for $C_{21}H_{13}F_3$: C, 78.18; H, 4.07.
Found: C, 78.50; H, 4.13

o-Bromobenzoic acid. -- (XXV) Thirty-one grams (0.18 moles) of *o*-bromotoluene was placed in a 2 l. flask, in which there was a solution of 57 g. (0.36 moles) of $KMnO_4$ and 10 ml. of 10% NaOH in one liter of water. The mixture was heated with stirring under reflux for four hours. The reflux condenser was set downward for distillation and the excess toluene distilled off; about 20% of the toluene was recovered. The hot solution was filtered, the filtrate acidified, cooled and the acid filtered off, washed with water and dried. It weighed 19.4 g., or 54% of the theoretical yield, based on the original amount of toluene used. The melting point was 145-147° (Lit. (49) 149°). The first filtrate above was still colored, indicating incomplete reaction. The amount of acid produced was adequate for the purpose and so the reaction was not repeated.

o-Bromobenzoyl chloride. -- (XXVI) A mixture of the above acid (19.4 g., 0.0967 moles) and phosphorus pentachloride (21 g., 1.008 moles) were warmed gently in a small flask. When the exothermic reaction had subsided, the liquid now in the flask was heated with a small free flame under reflux for one hour. The phosphorus oxychloride was distilled off at atmospheric pressure, and the residue distilled under reduced pressure; 16.4 g. of the acid chloride distilled at 116-117°/9 mm. (Lit. (32) 125°/20 mm.) This amounts to 78% of the theoretical amount.

o-Bromobenzophenone. — (XXVII) The preparation of this compound and its conversion to o-bromodiphenylmethane (XXVIII) was done by Hannabass (36).

3'-Bromo-2-benzylbenzophenone. -- (XXIX) This compound was obtained from Hannabass (36) who prepared and purified it for use in this investigation. It boiled at 220-221°/3 mm.

9-(3-Bromophenyl)-anthracene. -- (XXX) The above ketone was cyclized in the usual manner without difficulty, 17 hrs. of heating giving a 54% yield. Recrystallized from ethanol, the anthracene appeared to be a mixture of two crystalline forms, needles and plates. After about four recrystallizations, the needles were the only form, and these had a double melting point: 128-130° and 138-140°. (Lit. (36) 135-137°)

Anal. Calc'd for $C_{20}H_{13}Br$: C, 72.08; H, 3.93.
Found: C, 72.37; H, 3.96

3-Fluorobenzoic acid. -- (XXXI) The permanganate oxidation of m-fluorotoluene was the method of Holleman and Slothouwer (51) as modified by Cohen (52), further modified by the addition of 2 ml. of 1 N NaOH to the reaction mixture. This gave an 80% yield, based on the amount of toluene actually used (15% of the toluene was recovered), of the acid melting at 123.5° (Lit. 124°) without recrystallization.

3-Fluorobenzoyl chloride. -- (XXXII) Into a flask containing dry m-fluorobenzoic acid, and equipped with a reflux condenser with drying tube and HCl trap, was added quickly an equimolecular amount of solid PCl_5. The reaction proceeded at once, and within a few minutes a clear yellow liquid was left. This was heated in a water bath for about thirty minutes, and then allowed to stand for two hours. On fractionally distilling phosphorus oxychloride came over around 100°, and the fraction distilling at 179-180°/720 mm. was collected. The highest yield of the acid chloride was 84%. The method was used by Cohen (52) who gave no experimental details.

3'-Fluoro-2-benzylbenzophenone. -- (XXXIII) A Grignard reagent was prepared from 45.7 g. (0.185 moles) of o-bromodiphenylmethane and 4.6 g. of magnesium. The flask had been baked out over a free flame with dry nitrogen passing in, and a crystal of iodine sublimed over the magnesium. The reaction started quickly and within 1.5 hours most of the magnesium had disappeared, contrary to the usual rate of reaction reported for this compound. Refluxing the mixture overnight did not appreciably change the amount of unreacted magnesium. The Grignard solution was siphoned into a separatory funnel with nitrogen pressure and the flask rinsed twice with dry benzene, and this added to the Grignard solution. The excess magnesium was then washed out of the flask with dry benzene, and 26.3 g. (0.166 moles) of m-fluorobenzoyl chloride in 200 ml. of benzene placed in the same flask. The Grignard was then added rather rapidly, the ether distilling out of the flask during addition (the temperature of the flask was 40-50° during the addition). The mixture was heated under reflux with stirring overnight, and then cooled in an ice bath and hydrolyzed with saturated, ice-cold ammonium chloride solution to the equivalence point. The solution was poured off, and the residues extracted with fresh benzene until white. The combined solutions were washed with 10% NaOH twice, then with water, and then dried over Drierite. The benzene was removed at atmospheric pressure and the residue fractionated, the material coming over at 170-180°/1 mm. amounted to 23.3 g. (43.5% of the theoretical). On redistillation, 19.3 g. (36%) came over at 174-176°/1 mm. An analytical sample was taken at 174°/1 mm.

Anal. Calc'd. for $C_{20}H_{15}OF$: C, 82.735; H, 5.21.
Found*: C, 82.78; H, 5.53.

9-(m-Fluorophenyl)anthracene. -- (XXXIV) Two and three tenths grams of 3'-fluoro-2-benzylbenzophenone was weighed into a 200 ml. flask and 100 ml. of "acid mixture" added. The mixture was heated under reflux for 66 hours. The ketone went into solution at the start of reflux to give a clear yellow solution, which darkened at the end of the reflux time, with the formation of black solid particles. The flask was cooled to room temperature and then put into the ice-box. Long needles and flat plates crystallized out. These were filtered off and washed with water and recrystallized from 95% ethanol (charcoal). The yield of pale yellow parallelopipids was 1.3 g. (60%) and when recrystallized twice more, melted at 143.5-144.5°.

Anal. Calc'd. for $C_{20}H_{13}F$: C, 88.21; H, 4.81.
Found*: C, 88.22; H, 4.78.

2-Chloro-2'-methyldiphenylcarbinol. -- (XXXV) A Grignard reagent was prepared from 17.1 g. (0.1 moles) of o-bromotoluene and 2.4 g. (0.1 moles) of magnesium in ca. 200 ml. of ether. When the magnesium had disappeared a solution of 14.1 g. (0.1 moles) of o-chlorobenzaldehyde in 100 ml. of ether was added dropwise. The mixture was then heated under reflux overnight, then cooled and decomposed with cold ammonium chloride solution. The ether solution was poured off, and the residues extracted with fresh ether. The combined ether solutions were dried and concentrated, and the residue distilled. The portion coming over at 179-184°/4.8 mm. (mostly at 183°) weighed 15.4 g. (66.5%). This material solidified almost immediately, and when recrystallized from 50% ethanol-water, melted at 113.5-114.5°.

Anal. Calc'd. for $C_{14}H_{13}OCl$: C, 72.25; H, 5.63.
Found: **C, 72.84; H, 5.73**

2-Chloro-2'-methyldiphenylmethane. -- (XXXVI) A slurry of 96.5 g. (0.412 moles) of the above carbinol, 14 g. (0.45 moles) of red phosphorus, and 14 g. of iodine in ca. 1000 ml. of glacial acetic acid was heated under reflux with stirring for 39 hours. The mixture was then poured into twice its volume of water, and the acid neutralized with sodium carbonate. The organic matter was extracted from the water and inorganic material with ether, and the combined ether extracts washed with 10% sodium hydroxide to remove the free iodine, and then with water, and finally dried over calcium chloride. The ether was removed at atmospheric pressure, and the residue distilled. The fraction coming over at 159-159.5°/9 mm. on the first distillation amounted to 68.4 g. (76.6%). An analytical sample was taken at 159°/9 mm. on a third distillation.

<u>Anal.</u> Calc'd for $C_{14}H_{13}Cl$: C, 77.59; H, 6.05.
Found: C, 77.87; H, 6.13

<u>2-Cyano-2'-methyldiphenylmethane.</u> -- (XXXVII) A mixture of 23.3 g. (0.1075 moles) of 2-chloro-2'-methyldiphenylmethane, 11.7 g. (0.13 moles) of cuprous cyanide, a trace of anhydrous cupric sulfate and about 50 ml. of dry pyridine was heated at 250° for 22 hours, allowing the pyridine to evaporate from the air condenser. The mixture was then subjected to a crude separation by a von Braun distillation at 1 mm. The distillate was poured into 100 ml. of 1:1 ammonia, and the ammonia then extracted with ether. The ether extracts were combined and washed with 2N HCl, twice with water, and finally dried over calcium chloride. The ether was evaporated and the residue fractionated, the material coming over at 171-175°/6 mm. (most of the material came over at 174-175°) being collected. The colorless liquid was viscous and highly fluorescent, and weighed 17.2 g. (77%).

<u>Anal.</u> Calc'd. for $C_{15}H_{13}N$: C, 86.91; H, 6.32.
Found: C, 86.86; H, 6.42.

<u>2-(2-Methylbenzyl)-benzophenone.</u> -- (XXXVIII) A Grignard reagent was prepared from 27.3 g. (0.174 moles) of bromobenzene in 200 ml. of ether and 4.18 g. (0.174 moles) of magnesium. Most of the ether was

evaporated off, and a solution of 12 g. (0.058 moles) of 2-cyano-2'-methyldiphenylmethane in 100 ml. of benzene was added dropwise. There was no immediate evidence of reaction, but the clear solution gradually became cloudy, and after about two hours, insoluble particles could be seen. There was no apparent change in the appearance of the mixture after four hours, but the mixture was heated under reflux and stirred overnight (about 17 hours.). The mixture was hydrolyzed with the theoretical amount of cold ammonium chloride solution, and the benzene solution poured off. The residue was extracted twice with fresh benzene, and the combined benzene solutions heated with stirring, under reflux, for sixty hours, until the imine hydrochloride which had appeared and was insoluble in the benzene layer, had disappeared. The benzene layer was separated, washed with water, dried over calcium chloride, concentrated, and the residue fractionated. A pale yellow, very viscous oil, came over at 228-230°/5 mm., and solidified almost immediately. It weighed 14.0 g. (84.3%). The solid was recrystallized from hexane, m.p. 85-86°.

Anal. Calc'd. for $C_{21}H_{18}O$: C, 88.08; H, 6.33.
Found: C, 88.48; H, 6.31.

1-Methyl-10-phenylanthracene. -- (XXXIX) The above ketone was cyclized in the usual manner in the standard acid mixture. (0.51 g. of the ketone in 20 ml. of acid mixture for 15 hours gave 0.43 g. of the anthracene (90.1%). The anthracene, crystallized from ethanol, melted at 104-104.5°.

Anal. Calc'd. for $C_{21}H_{16}$: C, 93.99; H, 6.01.
Found: C, 93.70; H, 6.14.

2-Chloro-3'-methyldiphenylcarbinol. -- (XL) A Grignard reagent was prepared in the usual manner from 65.4 g. (0.3 moles) of m-iodotoluene and 7.2 g. (0.3 moles) of magnesium in 600 ml. of ether. A small amount of magnesium was left after 3 hours of reflux. To this solution was added dropwise a solution of 28.2 g. (0.2 moles) of o-chlorobenzaldehyde in 200 ml. of ether. The reaction was exothermic, and a sediment was formed as the reaction progressed. The mixture was heated with stirring for three hours, and then allowed to stand overnight. Decomposition was accomplished with ammonium chloride solution (less than the theoretical amount was required). The ether extract was washed with 10% sodium hydroxide and then water, the ether was concentrated, and the residue distilled. After 5.5 g. of a fore-run, 35.2 g. of amber liquid was collected at 161-163°/2 mm. amounting to 76% of the theoretical amount. The liquid solidified and was crystallized from hexane, m.p. 56.5-57.5°.

Anal. Calc'd. for $C_{14}H_{13}OCl$: C, 72.25; H, 5.63.
Found: **C, 72.36; H, 5.76**

2-Chloro-3'-methyldiphenylmethane. -- (XLI) A slurry of 23.3 g. (0.1 moles) of 2-chloro-3'-methyldiphenylcarbinol, 4.3 g. (0.14 moles) of red phosphorus, and 4.3 g. of iodine in 250 ml. of glacial acetic acid was heated under reflux with stirring for 30 hours. The phosphorus was then filtered off, the filtrate poured into 1500 ml. of water and the acid neutralized with a concentrated solution of sodium hydroxide. The iodine color disappeared and a flocculent white precipitate formed. The organic matter was extracted with ether, the ether solution was washed twice with water, and finally dried over calcium chloride. The ether was distilled off, and the residue distilled, the portion coming over at 155-156°/7.4 mm. being collected. This amounted to 16.8 g., or 78% of the theoretical. On redistillation, the boiling point of the colorless oil was 151-153°/7.5 mm. An analytical sample was taken at 152°/7.5 mm.

Anal. Calc'd. for $C_{14}H_{13}Cl$: C, 77.59; H, 6.05.
Found: C, 77.80; H, 6.10.

2-Cyano-3'-methyldiphenylmethane. -- (XLII) To 12.8 g. (0.059 moles) of 2-chloro-3'-methyldiphenylmethane in a 50 ml. flask, there was added 7.0 g. (0.078 moles) of cuprous cyanide, a trace of anhydrous cupric sulfate, and 10 ml. of pyridine freshly distilled from barium oxide. The flask was equipped with an air condenser, and placed in a metal bath maintained at 250° for 21 hours, allowing the pyridine to evaporate from the top of the condenser. A crude von Braun distillation was carried out on the mixture, and the distillate poured into dilute ammonium hydroxide, extracted with ether, washed with water, dried over calcium sulfate and concentrated. The residue yielded 8.2 g of viscous liquid boiling at 167-169°/5 mm. which is 67.1% of the theoretical amount. On redistillation, a boiling range of 165-165.5°/ 4.5 mm. was obtained.

Anal. Calc'd. for $C_{15}H_{13}N$: C, 86.91; H, 6.32.
Found: C, 87.05; H, 6.27.

2-(3-Methylbenzyl)-benzophenone. -- (XLIII) A Grignard reagent from 15.2 g. of bromobenzene and 2.3 g. of magnesium (0.0972 moles each) was prepared in 200 ml. of ether. Most of the ether was distilled off and 6.7 g. of 2-cyano-3'-methyldiphenylmethane (0.0324 moles) in 100 ml. of benzene was added rather rapidly (5 min.), to give a clear amber solution. The mixture was stirred and heated under reflux for 28 hours, after which it was cooled and hydrolyzed with the theoretical amount of 20% ammonium chloride solution. The benzene solution was decanted to a 1 liter flask, the white precipitate washed three times with fresh benzene, and the combined benzene solutions was heated under reflux with 200 ml. of 2 N. hydrochloric acid for 18 hours. The layers were separated, and the benzene layer washed with 10% sodium hydroxide, then twice with water, and then dried over calcium chloride. The benzene was then distilled off at atmospheric pressure, and the residue fractionated. The portion coming over at 193-196°/1.2 mm. was a yellow oil with a green fluorescence, and weighed 7.9 g. (85.5%). On redistillation, 5.5 g. of material distilled at 191-191.5°/1.5 mm.

Anal. Calc'd. for $C_{21}H_{18}O$: C, 88.08; H, 6.33.

Found: C, 87.98; H, 6.47.

2-Methyl-10-phenylanthracene. — (XLIV) The above ketone (0.39 g.) when heated for 80 minutes in the standard acid mixture gave a 93% yield (0.34 g.) of the anthracene, which when crystallized from ethanol, melted at 119°. This agrees with the melting point reported in the literature (53).

2-Chloro-4'-methyldiphenylcarbinol. — (XLV) A Grignard reagent was prepared from 6 g. (0.25 moles) of magnesium and 42.7 g. (0.25 moles) of p-bromotoluene in 600 ml. of dry ether. The yield was considerably improved when the flask was baked out before the reaction over a free flame with a stream of dry nitrogen passing through the system, and the amount of coupling was reduced by using the dilute solution above. After the heat of reaction had subsided, the Grignard solution was heated under reflux for one hour, then cooled to room temperature. A solution of 28 g. (0.2 moles) of o-chlorobenzaldehyde in 300 ml. of dry ether was added rather rapidly, thus maintaining a vigorous rate of refluxing. The mixture was then heated under reflux for sixteen hours, and then cooled in an ice bath, and decomposed to the equivalence point with ice-cold 20% ammonium chloride solution. The ether solution was poured off, the residue extracted once with fresh ether, and the combined ether solution evaporated off, and the residue fractionated. After a fore-run of 8 g. which consisted mostly of solid coupling product, the colorless viscous oil boiling* at 173-175°/ 6 mm. was collected. Yield 29.8 g. (64%).

2-Chloro-4'-methyldiphenylmethane. -- (XLVI) A slurry of red phosphorus (6.4 g., 0.16 moles), iodine (6.4 g.), 2-chloro-4'-methyldiphenylcarbinol (29.8 g., 0.128 moles) in 300 ml. of glacial acetic acid was heated under reflux, with stirring, for 36 hours. The cooled mixture was filtered, the flask and filter rinsed with fresh acid, the solution diluted with 800 ml. water, and the acid neutralized with solid sodium carbonate. The solution was extracted with ether, and the ether solution washed twice with 10% NaOH, twice with water, and finally dried over $CaSO_4$. The ether was removed by distillation, and the residue fractionated, the colorless liquid coming over at 146-147°/ 6 mm. being collected. The yield was 16.4 g. (59.2%). An analytical sample was taken on a subsequent distillation of a sample combined from two runs at 146°/ 5 mm.

Anal. Calc'd. for $C_{14}H_{13}Cl$: C, 77.59; H, 6.05.
Found: C, 77.85; H, 6.01.

2-Cyano-4'-methyldiphenylmethane. -- (XLVII) In a 200 ml. flask was placed 25.5 g. (0.1178 moles) of the corresponding 2-chloro compound, ca. 13 g. of cuprous cyanide and a small crystal of anhydrous cupric sulfate, with about 25 ml. of dry pyridine. This mixture was

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* Cohen (ref. (54)) prepared this carbinol by reducing the corresponding ketone with aluminum amalgam, and gave a melting point of 67°. The attempt made here to crystallize the oil was unsuccessful.

heated in a metal bath maintained at 250° for 22 hours, with an air cooled condenser to allow the slow evaporation of the pyridine. The reaction mixture was then cooled and subjected to a crude distillation in a von Braun flask at 4 mm. The distillate was poured into ca. 150 ml. of 1:1 NH_4OH, stirred well and extracted with ether. The combined ether extracts were washed twice with 2N HCl, then with water, and then dried over Drierite. The ether was distilled off, leaving a clear fluid liquid which was fractionated. The portion coming over at 165-171°/4.5 mm. with the greater portion coming over at 170° was collected on the first distillation. Yield 14.7 g., 60%.

Anal. Calc'd. for $C_{15}H_{13}N$: C, 86.91; H, 6.32.
Found*: C, 87.20; H, 6.28.

2-(4'-Methylbenzyl)-benzophenone. -- (XLVIII) A Grignard reagent was prepared from 23.6 g. (0.15 moles) of bromobenzene and 3.6 g. (0.15 moles) of magnesium in approximately 100 ml. of ether. Most of the ether was distilled off, and to the cooled solution was added 10.6 g. (0.0512 moles) of 2-cyano-4'-methyldiphenylmethane in 100 ml. of dry benzene. The mixture was heated under reflux with stirring for about 18 hours. It was then cooled and decomposed with the equivalent amount of cold 20% ammonium chloride solution. The benzene solution was poured off and the residue extracted with fresh benzene until the residue was white. The combined benzene solutions were heated with ca. 250 ml. of 2N hydrochloric acid with stirring, and under reflux, for 17 hours. The layers were separated, the benzene layer washed with 10% sodium hydroxide solution, then with water, and then dried over calcium chloride. The benzene was removed at atmospheric pressure, and the residue fractionated, the portion distilling at 194-196°/1 mm. being collected. The greenish yellow oil was fluorescent, and weighed 13.6 g. (95%). An analytical sample was taken at 181°/0.3 mm.

Anal. Calc'd. for $C_{21}H_{18}O$: C, 88.08; H, 6.33.
Found: C, 88.42; H, 6.36

3-Methyl-10-phenylanthracene. — (XLIX) The above ketone (0.50 g.) was cyclized in the usual manner, 14.5 hours giving 0.41 g. of the anthracene (87.7%). Recrystallized from ethanol the anthracene melted at 117-118°.

Anal. Calc'd. for $C_{21}H_{16}$: C, 93.99; H, 6.01.
Found: C, 93.86; H, 6.05.

2-Chloro-3'-trifluoromethyldiphenylcarbinol. — (L) The reaction between 49.5 g. (0.22 moles) of m-bromobenzotrifluoride (XVI) and 5.35 g. (0.22 moles) of magnesium in 300 ml. of ether commenced immediately, and all of the magnesium had disappeared in 1.5 hours. A solution of 28.1 g. (0.2 moles) of o-chlorobenzaldehyde in 250 ml. of ether was added as fast as the strong exothermic reaction would allow. The solution was brownish red. It was allowed to reflux overnight (9.5 hours), and in the morning was a tan material, insoluble in the ether. The mixture was cooled, and hydrolyzed with the theoretical amount of ice cold ammonium chloride solution to the end point. The ether solution was poured off and the residue was extracted twice with dry ether. The combined ether solutions were further dried with calcium sulfate, the ether distilled off, and the residue fractionated. After 1.4 g. of fore-run, there was collected 52.4 g. (92.9%) of material boiling at 174-176°/5.8 mm. The colorless viscous oil did not crystallize on standing at 0° overnight, and attempts to crystallize it from ethanol and hexane were unsuccessful. An analytical sample was taken at 164°/5 mm.

Anal. Calc'd. for $C_{14}H_{10}OClF_3$: C, 58.65; H, 3.52.
Found: C, 58.20; H, 3.59.

2-Chloro-3'-trifluoromethyldiphenylmethane. — (LI) A slurry of 46.0 g. of the above carbinol (0.162 moles), 7.4 g. (0.23 moles) of red phosphorus and 7.4 g. of iodine in 450 ml. of glacial acetic acid to which about 50 ml. of water was added, was heated under reflux with stirring for 24.5 hours. The phosphorus was filtered off, and washed with fresh acetic acid. The filtrate was diluted with water, and the acid neutralized with a concentrated solution of sodium hydroxide in water. The slightly basic solution was colorless and clear, with a cream colored oil separating out on the bottom. The organic matter was extracted with ether, and the ether solution washed, dried, and the ether distilled off. Fractionation of the residue yielded only one fraction: after three drops of fore-run there was collected 34.8 g. (80%) of a slightly amber liquid at 134-135°/3.6 mm. An analytical sample was taken at 125°/3.5 mm.

Anal. Calc'd. for $C_{14}H_{10}ClF_3$: C, 62.12; H, 3.72.
Found: C, 62.00; H, 3.82.

2-Cyano-3'-trifluoromethyldiphenylmethane. -- (LII) In a 100 ml. flask was placed 27.0 g. (0.1 moles) of 2-chloro-3'-trifluoromethyldiphenylmethane, 13.5 g. (0.12 moles) of cuprous cyanide, about 0.01 g. of anhydrous cupric sulfate, and then about 20 ml. of pyridine was distilled from barium oxide directly into the flask. The contents were well mixed, an air condenser was attached, and the flask placed in a metal bath maintained at 250° for 35.5 hours. The flask was cooled slightly, and then attached to a von Braun distilling head; a crude distillation was made at 3 mm. The distillate was poured into dilute ammonia and extracted with ether. On washing the ether solution with 2 N hydrochloric acid, a small amount of white, partially insoluble material was evident; this partially disappeared when washed with 10% sodium hydroxide. The ether solution was then washed with water and dried. The ether was distilled off, and the residue fractionated. After five drops of fore-run 20.4 g. (78.5% of the theoretical) of the cyano compound was obtained as a colorless liquid with a strong fluorescence in ultra violet light, and distilling at 135.5-136°/1 mm. An analytical sample was taken at 134°/0.6 mm.

Anal. Calc'd. for $C_{15}H_{10}F_3N$: C, 68.96; H, 3.86.
Found: C, 69.08; H, 3.98.

2-(3-Trifluoromethylbenzyl)-benzophenone. — (LIII) A Grignard reagent was prepared from 25.2 g. of bromobenzene and 3.9 g. of magnesium (0.16 moles each) in 200 ml. of ether. The magnesium disappeared in 1.5 hours. The ether was mostly distilled off, and replaced with benzene. About half of this was distilled off, and then 14 g. (0.0537 moles) of 2-cyano-3'-trifluoromethyldiphenylmethane in 100 ml. of benzene was added rapidly. The solution gradually turned orange-red in the first ten hours, after which there was little change. The mixture was heated under reflux with stirring for 22 hours, after which it was cooled and hydrolyzed with 20% ammonium chloride solution. The benzene solution was poured off, and the residue extracted once with fresh benzene. Since the residue still had a color to it, it was dissolved in water and extracted once with fresh benzene. The combined benzene extracts were heated under reflux with stirring with 300 ml. of 2N hydrochloric acid for 44.5 hours. The benzene layer was separated, washed with water, dilute sodium carbonate, again with water, and then dried by azeotropic distillation. The benzene was all distilled off, and the residue fractionated. After the fore-run of diphenyl, there was obtained 15.3 g. (84%) of greenish, viscous liquid distilling at 185-186.5°/1 mm. An analytical sample was taken at 170°/0.4 mm.

Anal. Calc'd. for $C_{21}H_{15}OF_3$: C, 74.11; H, 4.44.
Found: C, 73.74; H, 4.55.

2-Trifluoromethyl-10-phenylanthracene. -- (LIV) Although several cyclizing media were tried in the attempt to prepare this compound from the above ketone, no crystalline product could be obtained from the reaction mixtures. (Concentrated sulfuric acid, sulfuric acid-acetic acid mixture, 85% phosphoric acid, and phosphoric-acetic acid mixtures were tried.)

2-Chloro-4'-fluorodiphenylcarbinol. -- (LV) A Grignard reagent prepared in 200 ml. of ether from 47.2 g. (0.27 moles) of p-bromofluorobenzene and 6.6 g. (0.27 moles) of magnesium turnings was allowed to react with 35.2 g. (0.25 moles) of o-chlorobenzaldehyde in 200 ml. of ether which was added dropwise over the course of 3 hrs. The mixture was stirred overnight, and then heated to reflux temperature for one hour. It was then cooled to ice temperature and hydrolyzed with the theoretical amount of 20% ammonium chloride solution. The ether solution was dried, concentrated, and the residue distilled. The portion which came over at 175-178°/6.8 mm. (nearly all at 178°) weighed 42.3 g., 71.5% of the theoretical amount. An analytical sample was taken at 170°/6.5 mm.

Anal. Calc'd for $C_{13}H_{10}OClF$: C, 65.97; H, 4.26.
Found: C, 66.00; H, 4.18.

2-Chloro-4'-fluorodiphenylmethane. -- (LVI) A slurry of 36.2 g. (0.153 moles) of the above carbinol, 6.7 g. (0.224 moles) of red phosphorus and 6.7 g. of iodine in 400 ml. of glacial acetic acid was heated under reflux with stirring for 27 hours. At the end of this time, the phosphorus was filtered off and washed with fresh acetic acid. The acid solution was poured into 2 l. of water and neutralized with a slurry of sodium hydroxide in water. The solution was cooled with ice during the process, and the temperature was not allowed to exceed 40° during the neutralization process. A total of two liters of ether was used to extract this solution, and the ether extract was washed with 10% sodium hydroxide solution to remove the pink iodine color, and then washed twice with water, and finally dried over calcium chloride. The ether was distilled off, and the residue distilled. The portion distilling at 149-154°/11 mm. was collected. This amounted to 22.2 g. (66%). An appreciable residue was left. An analytical sample was taken at 150°/10.5 mm.

<u>Anal.</u> Calc'd. for $C_{13}H_{10}ClF$: C, 70.75; H, 4.57.
Found: C, 70.75; H, 4.55.

<u>2-Cyano-4'-fluorodiphenylmethane</u>. -- (LVII) (A) <u>From 2-Bromo-4'-fluorodiphenylmethane</u> (LXI). Four and seven-tenths grams of the bromo compound (0.0177 moles) was treated with 1.8 g. (0.02 moles) of cuprous cyanide in the usual von Braun reaction. (Trace of anhydrous $CuSO_4$, 12 ml. of pyridine dried over barium oxide, air condenser, 250° for 24 hours.) A crude distillation was made at 4 mm., and the distillate taken up in ether, washed sucessively with concentrated ammonium hydroxide, 2N HCl, and then with water, and finally dried over calcium sulfate. The ether was distilled off, and the residue fractionated: 171-173°/8.2 mm. 2.3 g., 62%. The refractive index of this liquid was 1.5682.

(B) From 2-Chloro-4'-fluorodiphenylmethane (LVI). The exact same procedure as above was repeated with the chloro compound: 17 g. (0.077 moles), and 8.5 g. (0.095 moles) of cuprous cyanide. The product distilled in the larger Spitz flask at 169-173°/4 mm. and weighed 10.3 g. (63.5%). The refractive index was 1.5683.

Anal. Calc'd. for $C_{14}H_{10}NF$: C, 79.60; H, 4.77.
Found: C, 80.00; H, 4.73

2-(4-Fluorobenzyl)-benzophenone. -- (LVIII) A Grignard reagent was prepared from 17.9 g. (0.114 moles) of bromobenzene and 2.75 g. (0.114 moles) of magnesium in 200 ml. of ether. The ether was replaced with 100 ml. of dry benzene, and a solution of 8 g. (0.0379 moles) of 2-cyano-4'-fluorodiphenylmethane in 100 ml. of benzene was added rapidly. The solution was heated with stirring under reflux for 23 hours, was then cooled and hydrolyzed with ammonium chloride solution. The benzene solution was transferred to another flask, and the residue in the first flask extracted with fresh benzene until white. The combined benzene solution was heated under reflux with 200 ml. of 2N HCl for 33 hours. The benzene layer was separated, washed with water, 5% sodium bicarbonate, and then twice with water. The benzene solution was then dried by azeotropic distillation, and the residue fractionated. After a fore-run of diphenyl, there was obtained a viscous greenish-yellow oil at 193-195°/2 mm. The yield was 9.8 g., or 89% of the theoretical amount.

Anal. Calc'd. for $C_{20}H_{15}OF$: C, 82.74; H, 5.21.

Found: C, 83.07; H, 5.14

3-Fluoro-10-phenylanthracene. -- (LIX) Although several cyclizing media were tried in the attempt to prepare this compound from the above ketone, no crystalline product could be obtained from the reaction mixtures. (Concentrated sulfuric acid, sulfuric acid-acetic acid mixture, 85% phosphoric acid, and phosphoric-acetic acid mixtures were tried.)

2-Bromo-4'-fluorobenzophenone. -- (LX) A 500 ml. three necked flask equipped with a dropping funnel, reflux condenser, and mercury sealed stirrer, containing 2.4 g. (0.1 moles) of magnesium and a crystal of iodine, was baked out over a free flame, with a stream of dry nitrogen passing through. The flask was allowed to cool, maintaining the system dry by means of calcium chloride tubes. The magnesium was covered with dry ether, and then 17.5 g. (0.1 moles) of p-fluorobromobenzene in 100 ml. ether was added slowly. The magnesium practically all disappeared in an hour, at which time the solution was cooled in an ice bath. Cadmium chloride, (Ref. 41) 9.2 g. (0.05 moles) which had been previously treated as described below, was added in one batch. (The hydrated cadmium chloride had been dehydrated by heating with a free flame in a large evaporating dish, had been kept overnight in a drying oven maintained at 103°, ground to a fine powder in a mortar and stored over anhydrous calcium chloride in a desiccator.) Within 15 minutes, the solution had turned brown, and the Gilman test (46) was negative. The ether was distilled off until the residue was nearly dry, and 50 ml. of dry benzene was added, and 25 ml. of this distilled off. Then 100 ml. of benzene was added and the solution heated to boiling. 16.4 g. of o-bromobenzoylchloride in 50 ml. of benzene was added rapidly (2-3 min.) as fast as the refluxing from the exothermic reaction would allow. External heat was applied to maintain the refluxing for one hour. The solution was then poured onto ice and dilute sulfuric acid. The benzene layer was separated, washed with 10% NaOH, and then with water, and finally dried with calcium chloride. After distilling off the benzene, the residue was fractionated. The portion which came over at 166-168°/4.8 mm. weighed 10.6 g. (51% of the theoretical) solidified in the flask. Its melting point was 47-49° (Lit. (44) 49.5-50°).

2-Bromo-4'-fluorodiphenylmethane. — (LXI) A mixture of 10.6 g. (0.038 moles) of 2-bromo-4'-fluorobenzophenone, 10 g. of red phosphorus, and 10 ml. of hydroiodic acid (ca. 47%) was heated under reflux, with stirring, for 44 hours. The mixture was then cooled, extracted with ether, the phosphorus filtered off, and washed with ether. The combined ether solutions were washed with 10% sodium hydroxide, and then two times with water, and finally dried over calcium sulfate. The ether was distilled off, and the residue distilled. The portion coming over at 135-138°/2.5 mm. weighed 4.7 g. which is 47% of the theoretical amount.

3-Trifluoromethyl-2'-benzoylbenzophenone. -- (LXII) (A) From 2-(3'-Trifluoromethylbenzyl)-benzophenone. — This ketone (0.415 g.) was placed in a 50 ml. Erlenmeyer flask, 10 ml. of glacial acetic acid, and 0.5 g. of sodium dichromate added. The mixture was warmed to effect solution, and then cooled. Then one milliliter of conconcentrated sulfuric acid was added, and a small reflux condenser attached. When the exothermic reaction subsided, the mixture was heated to reflux temperature for about tem minutes, with occasional shaking. The mixture was then cooled and poured onto ice and 200 ml. of water, and allowed to stand for about 15 minutes. The gummy precipitate was filtered off, washed with water, and recrystallized from dilute ethanol (about 50% water); 0.350 g., of crystalline material was formed, and on concentrating the mother liquor, another 0.055 g. of crystals was obtained: total yield 0.405 g. (94%) of white needles, melting point 107.5-108°.

Anal. Calc'd. for $C_{21}H_{13}O_2F_3$: C, 71.19; H, 3.70.
Found: C, 71.20; H, 3.77

(B) From 3'-Trifluoromethyl-2-benzylbenzophenone.-- An identical procedure as the above with this ketone gave the same diketone: m.p. and mixed m.p. were the same.

(C) From 2-(3-Trifluoromethylbenzyl)-benzophenone.-- after the cyclization attempt. Two grams of this ketone was heated under reflux in 80 ml. of the standard acid mixture for 246 hours, then cooled and poured into 200 ml. of water, and the acid neutralized with 30% NaOH. The organic matter was extracted with ether, clarified with a minimum of charcoal, dried over calcium chloride, and the ether evaporated to leave an amber oil. This oil was oxidized by the same procedure as that described above, 0.967 g. of it giving a total of 0.872 g. of the diketone from a crystallization from ethanol and including the material obtained from the mother liquors. This is an 86.5% yield, and this material gave no depression in melting point when mixed with the authentic sample prepared above.

2-Benzoyl-4'-fluorobenzophenone. -- (LXIII) (A) From 2-(4-fluorobenzyl)-benzophenone. -- To a solution of 0.875 g. of 2-(4-fluorobenzyl)-benzophenone and 1.00 g. of sodium dichromate in 20 ml. of glacial acetic acid was added 1 ml. of concentrated sulfuric acid. When the exothermic reaction had subsided, the mixture was heated under reflux for about ten minutes with occasional shaking. The mixture was then cooled slightly, and poured onto 100 g. of ice and 200 ml. of water. After standing about 15 minutes, the white solid was filtered off, washed with water, and recrystallized from dilute ethanol (about 50% water). The crystalline material from this solution plus the material obtained from the mother liquors weighed a total of 0.867 g., which is 95% of the theoretical amount. The melting point of this material was 97-98°, and after four more crystallizations, this was raised to 99-100°. Kasey (37) reported a melting point of 101-102° for this compound, which he prepared by the oxidation of 4'-fluoro-2-benzylbenzophenone, but a mixed melting point of his sample and the above compound melted at 100-101°.

(B) From 2-(4-Fluorobenzyl)-benzophenone after cyclization attempt.- This compound (monoketone) was heated under reflux in the standard acid mixture for 72 hours. The solution was then cooled and poured into water, and the acid neutralized with 30% NaOH. The organic matter was extracted with ether, the ether solution dried and concentrated to leave an amber oil. This oil (0.811 g.) was oxidized in the above manner to give a total of 0.805 g. (94.7%) of the dry unrecrystallized diketone (2-benzoyl-4'-fluorobenzophenone), which when recrystallized gave the same m.p. and mixed m.p. as the above compound.

Another sample of the mono ketone was heated in the standard acid mixture for 8 days, and a considerable quantity (about 80%) of the diketone was obtained in this run. This experiment was invalidated by a slight mechanical loss during the recrystallization.

RATE MEASUREMENTS

Apparatus: The apparatus used to measure the rates consisted of Pyrex glass reaction tubes of about 18 mm. internal diameter and about 40 ml. capacity, equipped at the upper end with a 24/40 standard taper female joint and two glass hooks, which could be used to secure (by means of rubber bands) a glass stopper similarly equipped. The constant temperature bath was well insulated and contained mineral oil maintained thermostatically at 117.5 ± 0.2°. The tubes were supported in the oil simply by placing them in holes drilled in the cover of the bath especially prepared for the purpose; the larger diameter of the ground glass joints over the diamter of the rest of the tube supported the tube so that the portion of it which contained the cyclizing mixture was well below the surface of the oil in the bath.

Materials: The liquid ketones used in this investigation were carefully fractionated so that they had a distilled over a range of one degree or less. The solid ketones were recrystallized to constant melting point. A stock solution of the cyclizing medium was prepared by adding 700 ml. of redistilled glacial acetic acid to a mixture of 166.4 ml. of 48% hydrobromic acid and 43.6 ml. of distilled water. This stock solution and the temperature employed are those of Bradsher and Vingiello (1) so that the rates found here could be compared to the previously found values for the other ketones.

Description of Runs: In making an actual run, a sample of the ketone (300 to 500 mg.) was weighed into one of the tubes, and then

20 ml. of the stock acid mixture was added. Thirty milliliters of the acid mixture was used if the solubility of the ketone gave a non-homogeneous mixture in 20 ml. at the cyclizing temperature. The mixture was then heated to a gentle boil over a Bunsen Burner, capped immediately, and placed in the constant temperature bath. The time was noted when the solution began to boil and after sufficient time had elapsed for the particular ketone to be from 25 to 90% converted to the anthracene (determined approximately by preliminary runs), the tube was removed from the bath and the contents poured into a 50 ml. beaker, where crystallization of the anthracene was induced by scratching the beaker and cooling in a cold water bath. After crystallization had started, the beaker was covered with a watch glass and placed in a cold room maintained at 15 ± 1° and allowed to remain there for a least five hours. The crystals were then transferred quantitatively to a previously weighed sintered glass funnel, the tube and beaker being rinsed out with the mother liquor and this filtered through the same filter. The crystals were then sucked as dry as possible and then washed three times by covering them with about 10 ml. of distilled water and allowing the water to be sucked through the filter before the next addition. The filter and crystals were then dried in a vacuum desiccator over calcium chloride to constant weight. The melting points were determined in each case. These weights were corrected for the solubility of the anthracene in the cyclizing medium by putting a weighed quantity (ca. 0.2 g.) of the anthracene through the same procedure used in the cyclization, in triplicate, and determining the dissolved portion by difference. From

the corrected weight of anthracene, the rate constant was determined using the following first order rate equation:

$$K = \frac{2.303}{t} \log \frac{100}{100 - x}$$

where:

K = rate constant ($hrs.^{-1}$)

x = percent yield

t = time in hours.

At least five different time intervals were used for each ketone. The case of the cyclization of 3'-methyl-2-benzylbenzophenone to 9-(3-methylphenyl)-anthracene required seeding of the cooled reaction mixture with crystals of the anthracene, and cooling the mixture in a refrigerator at about 5° C. Solubility measurements were made under the same conditions.

TABLE IV

Rate of Cyclization of o-Benzylbenzophenone to 9-Phenylanthracene

Control Run 1.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	$K \times 10^{-2}$ hrs.$^{-1}$
1	0.4663	0.1141	6.5	26.2	4.64
2	0.4981	0.1651	10.0	35.4	4.35
3	0.4492	0.1426	10.5	34.0	3.94
4	0.4492	0.2558	22.0	61.0	4.28
5	0.5093	0.3247	26.67	68.4	4.31
			Average		4.3
			Average Deviation		0.2

20 ml. of the acid mixture was used.

The solubility of the anthracene in 20 ml. of the acid mixture is 0.02 g., according to Vingiello (Ref. 2., p. 86).

The rate constant reported by Vingiello is $4.4 \pm 0.2 \times 10^{-2}$ hrs.$^{-1}$

TABLE V

Rate of Cyclization of 4'-Chloro-2-benzylbenzophenone to 9-(4-Chlorophenyl)-anthracene.

Control Run 2.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	K x 10^{-2} $hrs.^{-1}$
1	0.4812	0.1347	9.0	29.8	3.91
2	0.5100	0.1710	11.17	35.6	3.94
3	0.5407	0.2411	16.0	47.5	4.01
4	0.4969	0.2716	20.5	58.0	4.22
5	0.5080	0.3179	25.5	66.5	4.27
			Average		4.1
			Average Deviation		0.1

30 ml. of acid mixture was used.

The solubility of the anthracene in 30 ml. of acid mixture is 0.006 g. according to Vingiello (Ref. 2, p 89).

The rate constant reported by Vingiello is 4.1 ± 0.1 x 10^{-2} $hrs.^{-1}$

TABLE VI

Rate of Cyclization of 2-(2-Methylbenzyl)-benzophenone to 1-Methyl-10-phenylanthracene.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	K x 10^{-2} hrs.$^{-1}$
1	0.4874	0.3983	12.0	85.0	15.8
2	0.5006	0.3899	12.5	83.3	14.3
3	0.5045	0.4166	14.0	88.4	15.4
4	0.4793	0.3964	14.0	88.5	15.4
5	0.4176	0.3662	14.5	93.8	16.3
6	0.5146	0.4335	15.0	90.1	15.9
7	0.4315	0.3626	15.5	89.8	14.7
			Average		15.4
			Average deviation		0.5

20 ml. of acid mixture was used.

The solubility of the anthracene in 20 ml. of the acid mixture at 15° is 0.058 g.

TABLE VII

Rate of Cyclization of 2-(3-Methylbenzyl)-benzophenone to 2-Methyl-10-phenylanthracene.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	$K \times 10^{-2}$ hrs.$^{-1}$
1	0.3000	0.2208	0.75	78.7	206
2	0.2968	0.2392	1.0	86.0	196
3	0.3011	0.2502	1.084	88.8	202
4	0.3915	0.3310	1.184	90.4	198
5	0.3963	0.3449	1.333	93.0	199
			Average		200.
			Average deviation		3.

20 ml. of the acid mixture was used.

The solubility of the anthracene in 20 ml. of acid mixture at 15° is 0.032 g.

TABLE VIII

Rate of Cyclization of 2-(4-Methylbenzyl)-benzophenone to 3-Methyl-10-phenylanthracene.

Run	Weight ketone	Weight. anthracene	Time Hours	Yield %	K x 10^{-2} hrs.$^{-1}$
1	0.5420	0.4113	12.0	81.0	13.8
2	0.4907	0.3760	12.5	81.8	13.6
3	0.5175	0.4068	13.0	84.0	14.1
4	0.5037	0.3997	13.5	84.1	13.5
5	0.5310	0.4214	14.0	84.6	13.4
6	0.5003	0.4109	14.5	87.7	14.4
7	0.4671	0.3828	15.0	87.3	13.7
			Average		13.8
			Average deviation		0.3

20 ml. of the acid mixture was used.

The solubility of the anthracene in 20 ml. of the acid mixture at 15° is 0.05 g.

TABLE IX

Rate of Cyclization of 3'-Methyl-2-benzylbenzophenone to 9-(3-Methylphenyl)-anthracene.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	$K \times 10^{-2}$ hrs.$^{-1}$
1	0.4416	0.2475	21.5	59.9	4.25
2	0.4422	0.2564	22.0	61.9	4.38
3	0.5154	0.3141	23.0	65.0	4.56
4	0.7335	0.4622	24.0	67.2	4.63
5	0.4554	0.2717	25.0	63.6	4.04
			Average		4.4
			Average deviation		0.2

20 ml. of acid mixture was used.

The solubility of the anthracene in 20 ml. of acid mixture at 5° C. is 0.036 g.

TABLE X

Rate of Cyclization of 3'-Fluoro-2-benzylbenzophenone to 9-(3-Fluorophenyl)-anthracene.

Run	Weight ketone	Weight anthracene	Time Hours	Yield %	$K \times 10^{-2}$ $hrs.^{-1}$
1	0.4857	0.1307	7.0	28.65	4.84
2	0.5250	0.2225	10.0	45.25	6.03
3	0.5043	0.1978	10.833	41.95	5.01
4*	0.4747	0.2046	11.0	47.1	5.80
5	0.4523	0.2004	12.0	47.2	5.31
6	0.4959	0.2321	13.0	49.9	5.30
7	0.4755	0.2468	15.0	55.4	5.37
8*	0.5033	0.2630	16.0	55.7	5.10
9	0.4915	0.2678	17.0	58.0	5.10
10*	0.5114	0.3253	23.75	67.7	4.76
			Average		5.3
			Average deviation		0.3

*20 ml. of acid mixture was used in these runs. 30 ml. of acid mixture was used in all unstarred runs.

The solubility of the anthracene in 30 ml. of acid mixture at 15° is 0.093 g.

TABLE XI

The Rate of Cyclization of 3'-Chloro-2-benzylbenzophenone to 9-(3-Chlorophenyl)-anthracene.

Run	Weight Ketone	Weight Anthracene	Time Hours	Yield %	K x 10^{-2} hrs.$^{-1}$
1	0.4478	0.1615	9.0	38.3	5.35
2	0.4448	0.1915	11.5	46.2	5.38
3	0.4252	0.1916	12.33	47.8	5.27
4	0.4395	0.2413	17.0	58.4	5.15
5	0.4370	0.2607	19.5	63.4	5.15
6	0.4491	0.3009	24.0	71.2	5.19
			Average		5.3
			Average deviation		0.1

30 ml. of the acid mixture was used.

The solubility of the anthracene in 30 ml. of acid mixture at 15° is 0.054 g.

TABLE XII

Rate of Cyclization of 3'-Bromo-2-benzylbenzophenone to 9-(3-Bromophenyl)-anthracene.

Run	Weight Ketone	Weight Anthracene	Time Hours	Yield %	K x 10^{-2} hrs.$^{-1}$
1	0.5571	0.2206	10.0	41.75	5.40
2	0.4621	0.1994	11.5	45.5	5.29
3	0.5352	0.2408	12.5	47.4	5.12
4	0.5757	0.2876	15.75	52.6	4.75
5	0.5471	0.2821	17.0	54.45	4.61
			Average		5.0
			Average deviation		0.3

30 ml. of the acid mixture was used.

The solubility of the anthracene in 30 ml. of the acid mixture at 15° is 0.066 g.

TABLE XIII

Rate of Cyclization of 3'-Trifluoromethyl-2-benzylbenzophenone to 9-(3-Trifluoromethylphenyl)-anthracene.

Run	Weight Ketone	Weight Anthracene	Time Hours	Yield %	K x 10^{-2} Hrs.$^{-1}$
1	0.4320	0.2182	11.75	53.4	6.49
2	0.4300	0.2459	14.5	60.4	6.37
3	0.4085	0.2472	15.5	62.3	6.29
4	0.4215	0.2670	16.25	66.9	6.70
5	0.4235	0.2629	17.0	65.6	6.26
			Average		6.4
			Average deviation		0.1

20 ml. of the acid mixture was used.

The solubility of the anthracene in 20 ml. of the acid mixture at 15° is 0.119 g.

TABLE XIV

Rate of Cyclization of 4'-Trifluoromethyl-2-benzylbenzophenone to 9-(4-Trifluoromethylphenyl)-anthracene.

Run	Weight Ketone	Weight Anthracene	Time Hours	Yield %	K x 10^{-2} $hrs.^{-1}$
1	0.4485	0.1803	6.0	42.5	9.20
2	0.4240	0.1912	7.0	47.7	9.28
3	0.4516	0.2210	8.0	51.6	9.10
4	0.4425	0.2377	9.0	56.8	9.34
5	0.4684	0.2712	10.0	61.0	9.41
			Average		9.3
			Average deviation		0.1

20 ml. of the acid mixture was used.

The solubility of the anthracene in 20 ml. of the acid mixture at 15° is 0.039 g.

SUMMARY

1. The rates of cyclodehydration of nine ketones have been measured; two additional ketones were shown not to cyclize under the same conditions.

2. The rate of acid catalyzed cyclization of ketones of the o-benzylbenzophenone type to 9-phenylanthracenes has been shown to be dependent upon several factors postulated by Bradsher and Vingiello (1): (a) the electron density of the ortho position in the ring into which cyclization takes place, (b) two rate controlling steps of opposing electrical requirements, and (c) the steric nature of the molecule.

3. The apparently anomalous rate of cyclization of 2-benzyl-4'-fluorobenzophenone (1) has been explained.

4. The syntheses of twenty-seven compounds not previously reported in the literature have been described.

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