A STUDY OF THE AROMATIC CYCLODEHYDRATION OF 2-(2-NAPHTHYLMETHYL)-2'-CHLORO-5'-METHYLBENZOPHENONE

by

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THIS THESIS IS AFFECTIONATELY

DEDICATED TO MY WIFE AND PARENTS

ACKNOWLEDGEMENTS

The author wishes to express his deepest and most sincere appreciation to for his assistance and the encouragement he has shown in this investigation. The privilege of working under him has been of inestimable value and will be long remembered.

The author also wishes to express his gratitude to the other faculty members and graduate students who have been most helpful in making numerous valuable suggestions.

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Finally, the author wishes to express his appreciation of the encouragement and help provided by his wife which was essential to the successful completion of this work.

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INTRODUCTION

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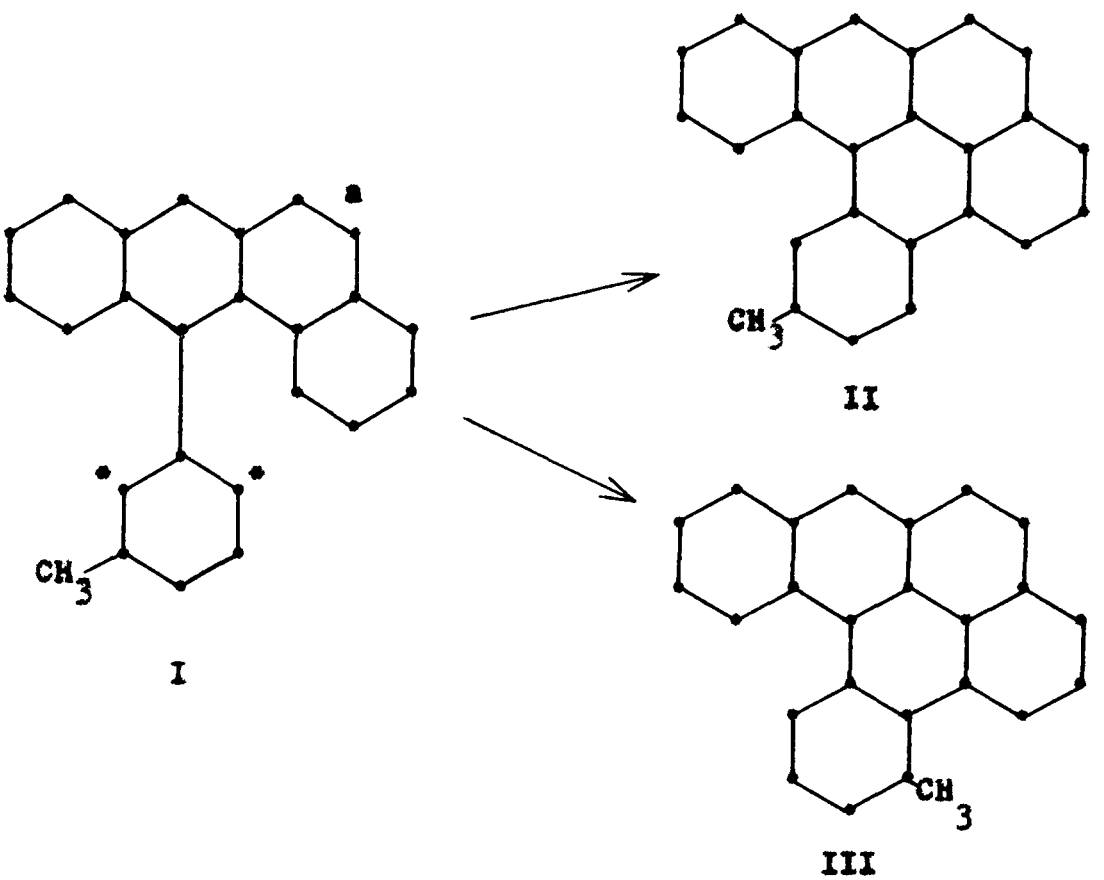
In a recent study of cyclodehydrogenation reactions of potential carcinogenic or carcinolytic hydrocarbons Zajac (1) pointed out that ring closure of 12-(3-methylphenyl)benz [a] anthracene (I) might take place at either of the two ortho positions of the phenyl ring. These positions are not equivalent with respect to the methyl group and ring closure might yield either 2-methyldibenzo [a,l] pyrene (II) or 4-methyldibenzo [a,l] pyrene (III) or both.



[a] In this thesis, all rings are aromatic unless otherwise indicated.

The aluminum chloride-catalyzed cyclodehydrogenation produced only one monomethyldibenzo [a,l] pyrene which could be either of the isomers, II or III. It was hoped that the problem could be solved by synthesizing II using an unequivocal synthesis. Attempts were made to prepare 12-(2-chloro-5-methylphenyl)-benz [a] anthracene which on cyclodehydrohalogenation should produce only one isomer, 2-methyldibenzo [a,l] pyrene (II). However, these attempts were unsuccessful and the results sufficiently variable so that no definite conclusion could be drawn.

Laboratory impressions of other investigators (2,3,4,8,9) have been that ortho substituted ketones, as a class, require different variations in the route of preparation.

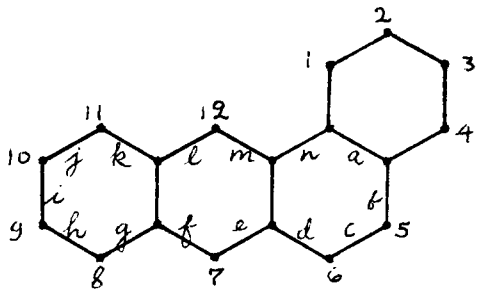
The objectives of the present investigation are to study possibilities and methods to prepare 2-(2-naphthylmethyl-2'-chloro-5'-methylbenzophenone (Xc), as shown in Charts VI and VIII, in a sufficient yield so that a study of the cyclization reaction under a variety of conditions can be made in order to prepare 2-methyldibenzo [a,l] pyrene (II).

NOMENCLATURE

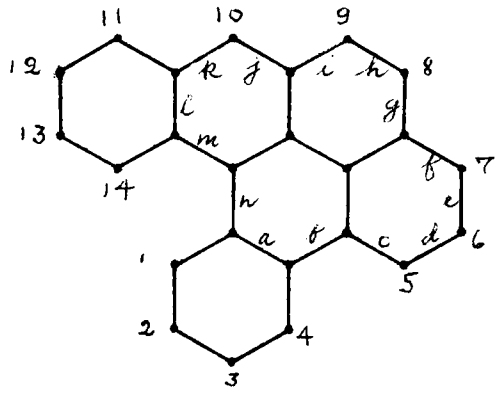
NOMENCLATURE

The nomenclature used throughout this thesis is in accordance with the recommendations presented in the Journal of the American Chemical Society, 82, 5545 (1960).

For example:



Benz [a] anthracene



Dibenzo [a,l] pyrene

HISTORICAL

HISTORICAL

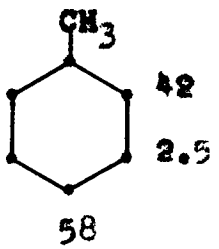
As early as 1872 Victor Meyer (6) and his collaborators were tangling with the problems of the peculiar effects of groups in the ortho position. Meyer emphasized the fact that the ortho-effect does not depend upon the chemical nature of the substituent; thus, ortho-fluoro is not comparable with the other halogens, but appears rather to be governed by the size as measured by the weights of the atoms. There is, however, no definite relationship, even of a qualitative nature, between the influence of a group in the ortho-position and the weight and volume.

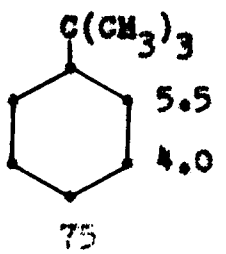
Almost as soon as quantitative data on the dissociation of aromatic acids and bases were available (7) it was recognized that the effect of ortho substituents on the acid strength often differed greatly from the expected behavior. It has been common to attribute any peculiar effect of a substituent in the ortho position to an ortho or proximity effect, these terms remaining free of any physical implications as to the precise nature of the interaction. That the ortho effect is a combination of many different types of interactions is now well recognized.

At this point it seems appropriate to review the available data and theory of the ortho effect as it is recognized at this time and very well presented by Remick (24)

and Ingold (25).

Steric effects at the ortho-position include steric hindrance, steric strain, and steric inhibition of resonance. Steric hindrance, the term associated with a temporary condition of steric interference in a reacting system, may be illustrated by the results of studies of the mononitration of toluene and tert-butylbenzene. The relative rate constants summarized below (the rate for one position in benzene being taken as unity) show that the tert-butyl group is more





activating than the methyl in all positions except the ortho. Apparently, the nitrating species attacks the ortho-position in tert-butylbenzene less readily due to non-bonding interference by the methyl groups.

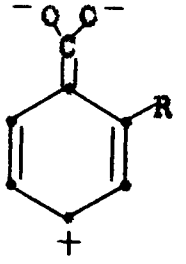
Another aspect of the steric portion of ortho effects is steric inhibition of resonance. This may be illustrated by the influence on acid strength of the introduction of a methyl or tert-butyl group into the para-, meta-, or ortho position of benzoic acid (Table I). The substitution

Table I

Substituted Benzoic Acids

Benzoic Acid	pKa[a]	Benzoic Acid	pKa
H	4.20	p-$C(CH_3)_3$	4.40
p-CH_3	4.34	m-$C(CH_3)_3$	4.28
m-CH_3	4.24	o-$C(CH_3)_3$	3.46
o-CH_3	3.91		

of a methyl or tert-butyl group in the para- or meta-position causes a weakening of the acid strength with the tert-butyl group being slightly more effective. This is due to the weak electron releasing effects of these two groups. However, the ortho groups both cause acid strengthening with the larger group producing the greater effect. This is attributed to steric inhibition of such a resonance structure as IV in the anion.



IV

[a] The pKa value is the negative log of the acid dissociation constant. Increased acid strength produces a decrease in pKa and vice versa.

This resonance form and the two containing ortho quinoid structures are acid-weakening due to the increased electron density in the carboxylate group. Resonance contributions of this type require that the carboxylate group be coplanar with the ring. This occurs when R=H. When $R=CH_3$ there is steric interference between R and the carboxylate group. This crowding is relieved by twisting the carboxylate group out of the plane of the ring, thus reducing the contribution from resonance forms such as IV. It will be necessary to twist the carboxylate group even further when $R=C(CH_3)_3$ causing an even smaller contribution from IV and a further increase in acid strength.

Another important steric aspect of ortho effects is steric strain, that aspect which involves an equilibrium condition in a relatively permanent system. This may be illustrated by means of the base strengths of ortho-substituted N,N-dimethylanilines. The introduction of one methyl group into the ortho-position causes an increase in base strength[a] due to steric inhibition of resonance of the dimethylamino group with the ring. On the other hand, two ortho-substituted

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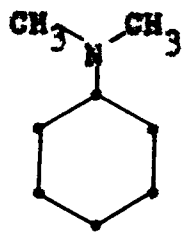
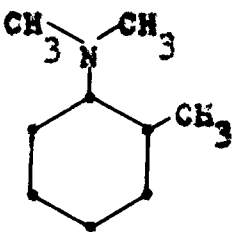
[a] pKa increases with increasing base strength.



pKa 4.09



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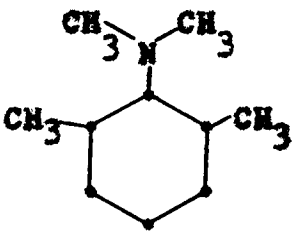
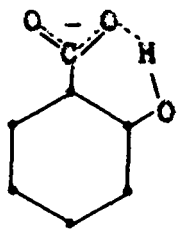


4.69

methyl groups do not produce a further increase in base strength as might be expected but a decrease in base strength as compared to the monomethyl derivative. This decrease is attributed to an increase in steric strain resulting from the addition of a proton to the nitrogen. The change of the group from an approximately planar one to an essentially tetrahedral one when the proton is added increases the steric crowding. This decreases the tendency of the proton to attach itself to the basic center decreasing the base strength. This effect probably operates also in the monomethyl derivative but is outweighed by the base-strengthening effect of the steric inhibition of resonance. As expected, the influence of steric strain becomes more pronounced as the ortho group is made larger, e.g., with iso-propyl and tert-butyl groups.

Another factor which contributes to ortho effects is chelation, particularly that involving hydrogen-bonding. A well known example of this is the strong acidity of salicylic acid in comparison to its meta- and para-isomers. This

appears to be due to hydrogen-bonding in the anion (V) which tends to stabilize the anion and favor ionization of the acid. This effect is even stronger in 2,6-dihydroxy-



V

benzoic acid, a substance which is a stronger acid than phosphoric acid. Intramolecular hydrogen-bonding is effective only between small atoms which are high on the electronegativity scale, e.g., fluorine, oxygen, nitrogen, and when these atoms are at the proper distances from one another.

The direct effect and steric inhibition of solvation may also play a part in ortho effects but their importance does not appear to be as well established as that of the effects reviewed briefly above.

As it was briefly mentioned in the Introduction, it has been observed in this laboratory that ortho effects operate during the course of synthesis and further reactions of ortho-halo ketones.

Kramer reports (8) that 2'-methyl-2-benzylbenzophenone could not be cyclized to the corresponding hydrocarbon using the same conditions that were effective in cyclizing the 3'- and 4'-isomers. He was only able to cyclize this ketone

when the severity of the conditions was increased using the same cyclizing reagents.

In a similar way, the 2'-, 3'-, 2'-, 4'-, and 2',5'-dimethyl-2-benzylbenzophenones of the corresponding ketimine salts cyclized much less readily than the 3',4'- and 3',5'-isomers. Synthetic difficulties became even greater when the methyl groups were both in the ortho-position. Neither 2',6'-dimethyl-2-benzylbenzophenone nor the corresponding ketimine salt could be cyclized under any of the conditions used. The only product that could be isolated was a cleavage product, anthracene.

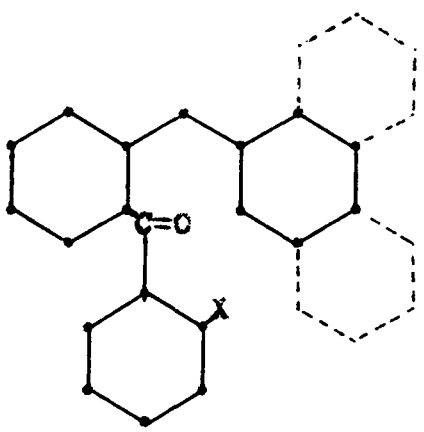
A similar pattern was observed in the preparation of the dimethyl-2-benzylbenzophenones from the corresponding ketimine salts (8). The 3',4'- and 3',5'-isomers were hydrolyzed the most readily, the 2',5'-, 2',3', and 2',4'-isomers less readily, and the 2',6'-isomers with the greatest difficulty.

Similar difficulties were encountered when the preparation and cyclodehydration of 2-(2-naphthylmethyl)-dimethylbenzophenones were undertaken (4,9). Again, the 2',6'-dimethyl-substituted ketimine salts required more severe conditions for hydrolysis than the other isomers (10,11). Cyclodehydration of the ketones was carried out in sealed tubes at 180°. Those ketones having at least one methyl group in the ortho-position required longer heating

periods than those in which both groups were either meta or para (4). The 2-(2-naphthylmethyl)-dimethylbenzophenones generally gave lower yields than the 2-(1-naphthylmethyl)-dimethylbenzophenones as might be expected from steric considerations. Steric hindrance appears to outweigh the effect of the higher electron density at the 1-position (12).

When the cyclization of 2-(1-naphthylmethyl)-2',6'-dimethylbenzophenone and 2-(2-naphthylmethyl)-2',4',6'-trimethylbenzophenone was attempted using the drastic conditions of the sealed tube method none of the desired product could be obtained (13). In each case the cleavage product, benz [a] anthracene, was obtained. This is analogous to the anthracene obtained when attempts were made to cyclize 2',6'-dimethyl-2-benzylbenzophenone.

All attempts so far to prepare and cyclodehydrate 2'-halo-ketones of the type VI were met with difficulties (14,3,15,5). It seems logical to attribute these



VI

X= F, Cl, Br

synthetic difficulties to steric effects.

The ortho effects of alkyl groups provide a relatively simple area of study. The absence of important resonance interactions and relatively small polar contributions of alkyl groups make it possible to estimate the electrical contribution of such groups with considerable precision. Deviations from the predicted behavior can then be interpreted in terms of such concepts as steric inhibition, steric inhibition of resonance, steric strain and, possibly, steric hindrance to solvation.

However, it has not been possible previously to estimate accurately the relative importance of electrical effects and specific ortho effects for strongly polar substituents. Consequently, it is usually not possible to state from the experimental data whether specific ortho effects are present and are playing any significant role in determining the behavior of the substituted compounds.

DISCUSSION OF RESULTS

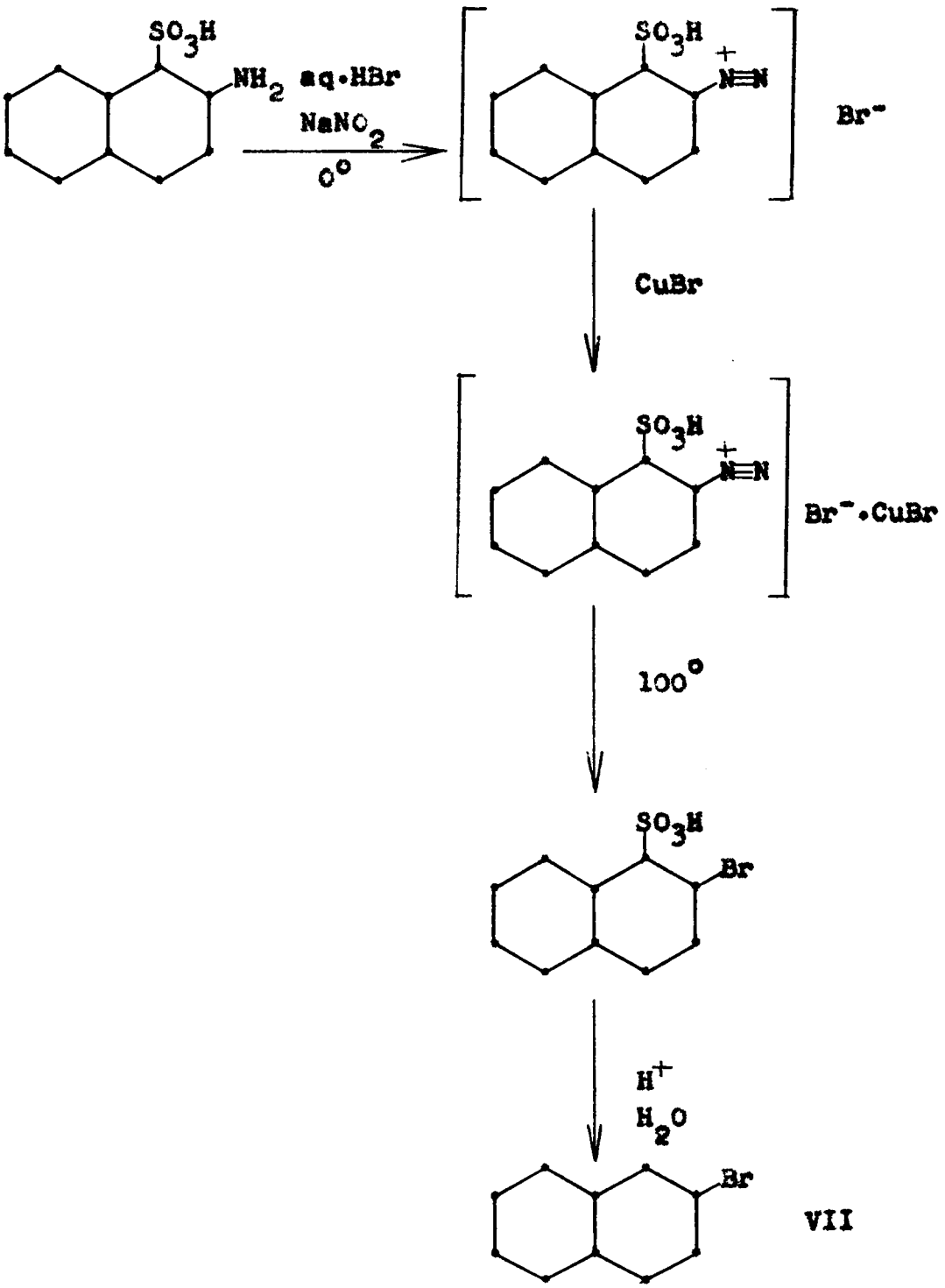
DISCUSSION OF RESULTS

Preparation of 2-Bromonaphthalene (VII).

The utilization of the Grignard reagent of 2-bromonaphthalene would be, perhaps, the most practical direct synthetic route to obtain 2-(2-naphthylmethyl) substituted benzophenones as shown in Charts II and VI. Since 2-bromonaphthalene has proven quite useful as a starting material in this laboratory, and since its cost is prohibitive, an improved synthetic route to this material was desirable.

2-Bromonaphthalene is ordinarily prepared by the diazotization of 2-naphthylamine with sulfuric acid and sodium nitrite, followed by the usual treatment with cuprous bromide (16) and hydrobromic acid (17). In an alternative method, proposed by Newman and Wise (18), 2-naphthylamine was first diazotized with hydrochloric acid and sodium nitrite. A stable complex was then formed with mercuric bromide and this complex decomposed by heating to 90°. Wahl and Basilos (19) have recently reported a more satisfactory method, as shown in Chart I, in which the dye intermediate 2-naphthylamine-1-sulfonic acid was first diazotized. The stable diazonium compound was treated with cuprous bromide and hydrobromic acid to obtain 2-bromo-1-naphthalene-sulfonic acid. The sulfonic acid group was then removed by sulfuric acid hydrolysis and yields of 77

Chart I


SO3H
NH2
aq.HBr
NaNO2
0°
SO3H
+
N≡N
Br⁻
CuBr
SO3H
+
N≡N
Br⁻·CuBr
100°
SO3H
Br
H+
H2O
Br
VII

to 80 per cent of the theoretical value were reported. Wolfe and Doukas (20) have investigated the method of Wahl and Basilos and found it to give yields of 58-65 per cent, when a technical grade of 2-naphthylamine-1-sulfonic acid was used as starting material. They claim that when the product was further purified by passing a normal-hexane solution of this compound through an alumina column 2-bromonaphthalene was obtained which was sufficiently pure for use in Grignard reactions. The improved method by Wolfe and Doukas has been investigated in this laboratory in some detail. It was found to give consistent yields of about 58 per cent when a technical grade of 2-naphthylamine-1-sulfonic acid was used as starting material, but even repeated purifications by chromatography did not give sufficiently pure product for use in Grignard reactions. The yields of Grignard reagents formed were substantiated by the Gilman titration method and varied from 12 to 48 per cent. Only when the procedure of Wolfe and Doukas was altered (21) by using hydrobromic acid instead of hydrochloric acid in the diazotization step, salting out with potassium bromide instead of potassium chloride, and using 20 per cent potassium bromide instead of 20 per cent potassium chloride for washing the crude 2-bromo-1-naphthalene sulfonic acid was a sufficiently pure final product of 2-bromonaphthalene obtained that formed Grignard reagents

in 86-87 per cent yields.

Attempted Preparations of 2'-Halogen Substituted 2-(2-Naphthylmethyl)benzophenones via the 2-(2-Naphthylmethyl)-benzonitrile Intermediate.

Three methods utilizing Grignard reagents were approached in order to prepare ketones necessary for this study:

1) A Grignard reagent in general reacts with a nitrile to give the magnesium salt of a ketimine which may be hydrolyzed with dilute acid to a ketone.

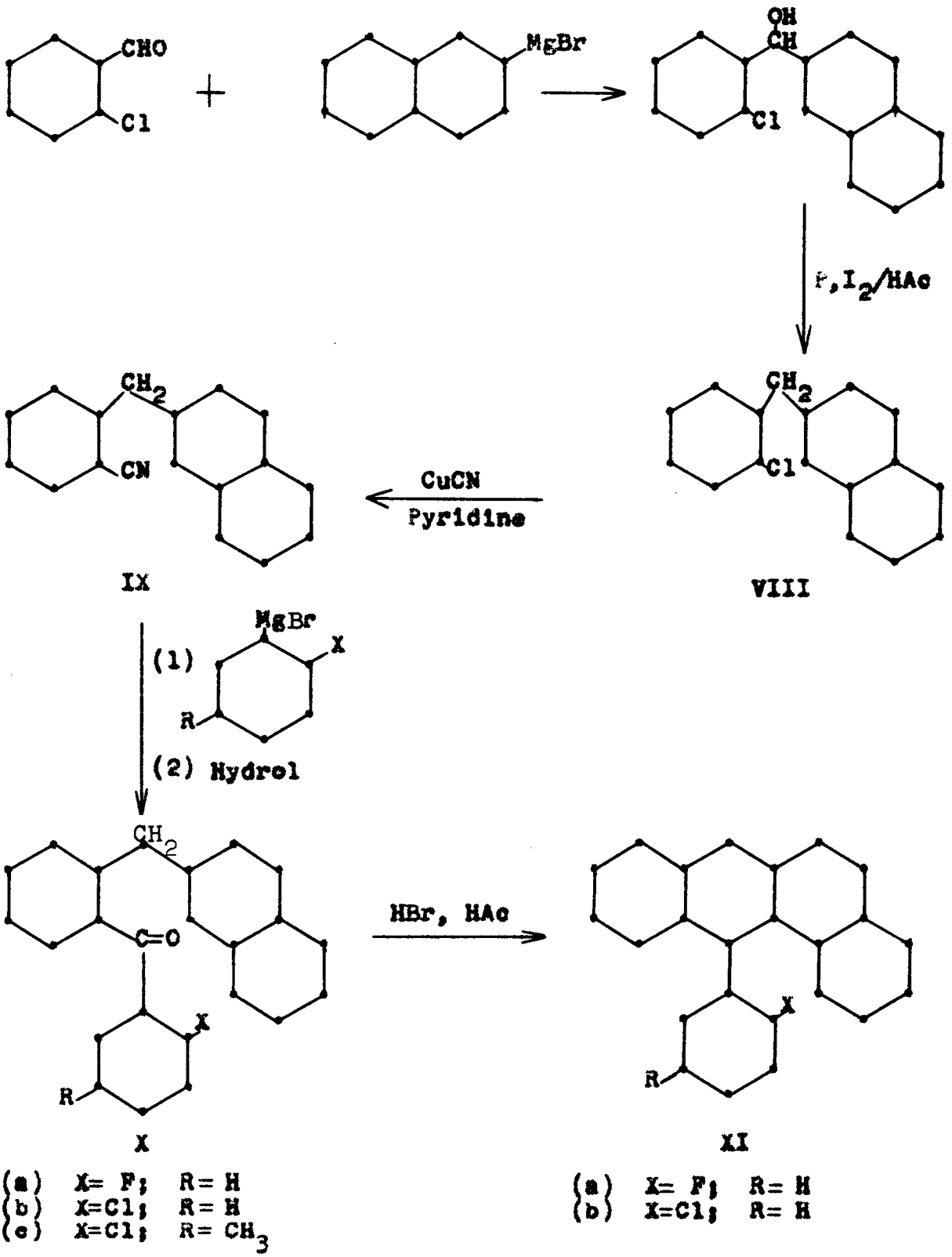
2) An organocadmium reagent, R_2Cd, may be substituted for the Grignard reagent. The acid chloride would then be added to the benzene solution of the organocadmium reagent and hydrolysis carried out in the normal fashion to obtain a ketone.

3) A Grignard reagent in general reacts with an acid halide to give a ketone as the initial product.

However, the first and second methods gave none of the desired ketones and the probable reasons will be discussed.

Previous success (22) in applying the first method listed above for the preparation of related ketones suggested an expansion of this method to the present study. The most convenient route in terms of the yields obtained and the time required to carry out the reactions is outlined

Chart II



(a) X= F; R= H
(b) X=Cl; R= H
(c) X=Cl; R= CH_3

XI

(a) X= F; R= H
(b) X=Cl; R= H

in Chart II (22).

The reaction between the Grignard reagent of 2-bromonaphthalene and the o-chlorobenzaldehyde seemed to proceed quite smoothly. The reduction of the crude carbinol to 2-(2-naphthylmethyl)chlorobenzene by red phosphorus and iodine suffers from a low yield of the expected product. Distillation of the reaction mixture between 181-206° at 1.5 mm. yielded only 33.7 per cent of the expected reduced product and 15.8 per cent of a material boiling between 220-223° at 1.5 mm. An infrared spectrum of this high boiling material possessed a sharp peak at 1664 cm.$^{-1}$ indicative of a carbonyl group. The analysis established that this material could be identified as 2-naphthyl-2-chlorophenyl ketone.

Anal. Calcd. for $C_{17}H_{11}OCl$: C, 76.55; H, 4.16; Cl, 13.29
Found: C, 76.55; H, 4.41; Cl, 13.23.

Furthermore, it was observed that the yields of the reduced material could be increased to about 48 per cent when the procedure is hurried through. By doing this the possibilities of oxidation are decreased. Also keeping the reaction media in all of the reaction stages from direct light and unnecessary exposure to the air seemed to be beneficial.

The 2-(2-naphthylmethyl)chlorobenzene was converted to 2-(2-naphthylmethyl)benzonitrile in 84 per cent yield by the Rosenmund-von Braun reaction using cuprous

cyanide and pyridine.

Zajac (45) reported some success in the preparation of 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone by the sequence of reactions as outlined in Chart II, where the Grignard reagent from 3-bromo-4-chlorotoluene was allowed to react with 2-(2-naphthylmethyl)benzonitrile. Encouraged by this apparent success the procedure was repeated as follows.

The 3-bromo-4-chlorotoluene was prepared from 3-bromo-4-aminotoluene by the Sandmeyer reaction in 65 per cent yield (23). The Grignard reagent from this compound was readily prepared, the nitrile added and the hydrolysis carried out in the usual way. However, the resultant material gave no distinct product upon distillation at reduced pressure. The presence of white fumes in the distillation column indicated that some decomposition was occurring during distillation. A thorough effort to crystallize the very viscous red-colored oil did not succeed. An infrared spectrum of the oil showed the presence of a strong peak at 1664 cm.$^{-1}$. This peak corresponds to the carbonyl frequency. The Beilstein test for halogen was positive. Elemental analysis indicated the presence of the following elements (%): C, 87.95; H, 5.59; Cl, 2.24, showing an appreciable deviation from the calculated values; C, 80.96; H, 5.16; Cl, 9.56. All attempts to

cyclize the red oil, with either acidic or basic cyclizing agents by applying in a total of fourteen different reactions, were unsuccessful.

Considering an extension of this investigation in order to clarify some of the steric problems involved, it was thought that the reaction might be successful by using the Grignard reagent from o-fluorobromobenzene since the bulkier o-chloro-compound might sterically hinder the ketone formation. The action of the Grignard reagent of bromobenzene on 2-(2-naphthylmethyl)benzonitrile followed by subsequent hydrolysis of the resulting ketimine forms 2-(2-naphthylmethyl)benzophenone in good yield. Replacement of o-hydrogen with fluorine will not change the size of the molecule considerably. There is no good steric reason why the Grignard reagent from o-fluorobromobenzene would not react to give the ketone, but all efforts to isolate the product were totally unsuccessful. Only 73 and 98.5 per cent of the starting nitrile from two reactions respectively and a very small amount of a high boiling viscous dark oil were recovered. An infrared absorption spectrum[a] of this dark oil did not show a peak at 1664 cm.$^{-1}$.

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[a] Throughout this thesis the infrared absorption spectra were obtained by using a Beckman Spectrophotometer (Model IR-5). The 2 mg. samples were ground with 400 mg. of potassium bromide and the resulting mixture subjected to pressure to give a clear disc which served in place of a cell.

Therefore it was concluded that none of the desired ketone was present and no further identification of this material was attempted.

The attempted synthesis of 2-(2-naphthylmethyl)-2'-chlorobenzophenone by this method also ended in a complete failure.

Attempts have been made by previous investigators (15, 14, 5) to prepare 2'-chloro-2-benzylbenzophenone by the action of the Grignard reagent from o-iodochlorobenzene and o-chlorobromobenzene on o-benzylbenzonitrile. These attempts have been completely unsuccessful.

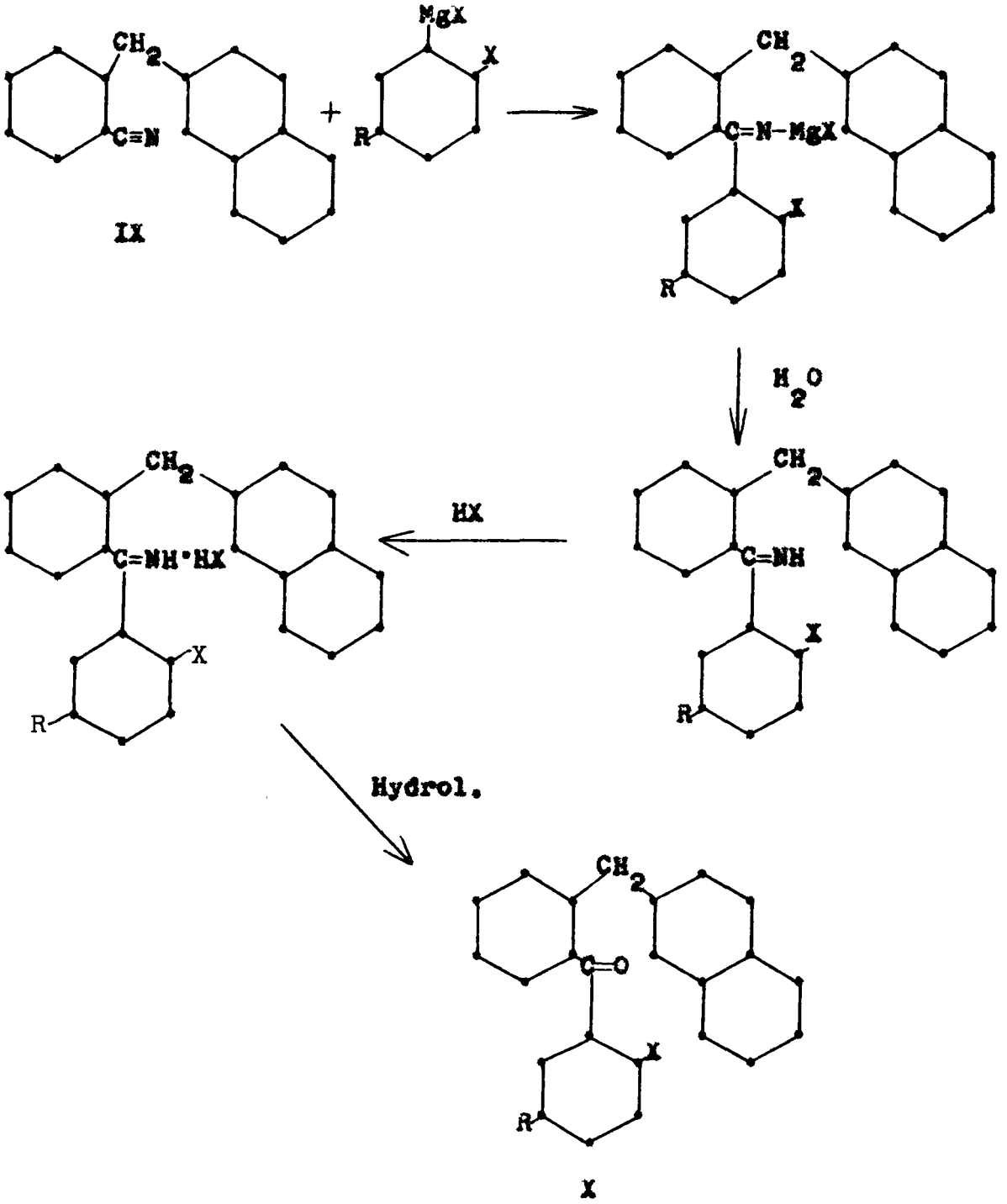
The method, although ideally suited for our purposes, is not feasible in practice.

Culbertson (26), in his study on the hydrolysis of substituted diphenylketimine, and others (8, 4) have found that methyl groups ortho to the ketimine group provide steric hindrance to the reaction and that ortho or para groups, which have important resonance contributions in the ion of the ketimine salt, inhibit the reaction.

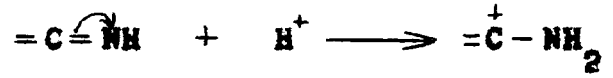
From the detailed scheme of the reaction (Chart III), it can be seen that the hydrolysis of the magnesium complex proceeds in three phases, yielding in each phase quite stable compounds which can be isolated.

The probable mechanism (24) of this acid catalyzed hydrolysis is based on three steps:

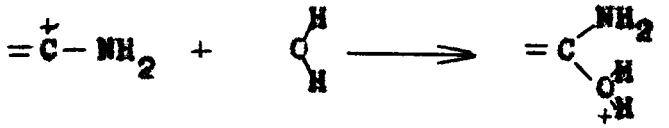
Chart III



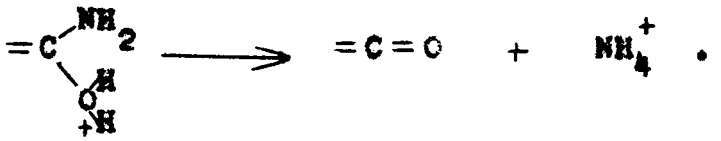
1) Electrophilic attack on the polarized ketimino group which results in the formation of a carbonium ion.



2) Hydration of the carbonium ion, and

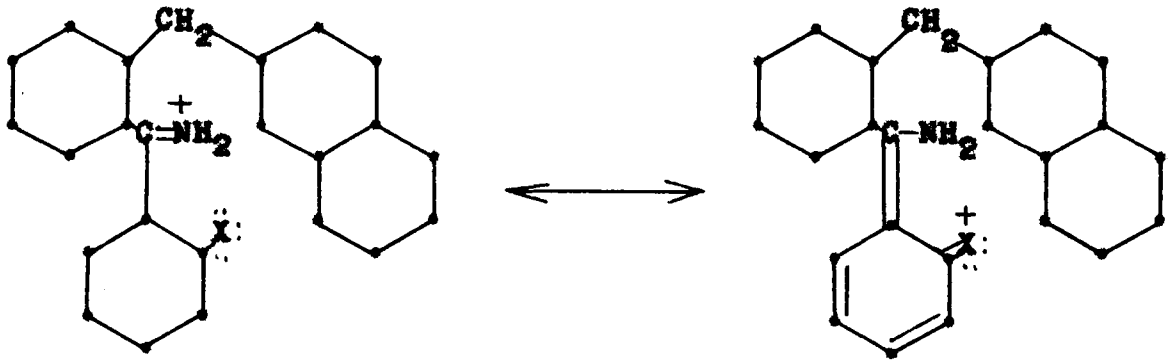


3) Transformation of the unstable oxonium complex to a ketone



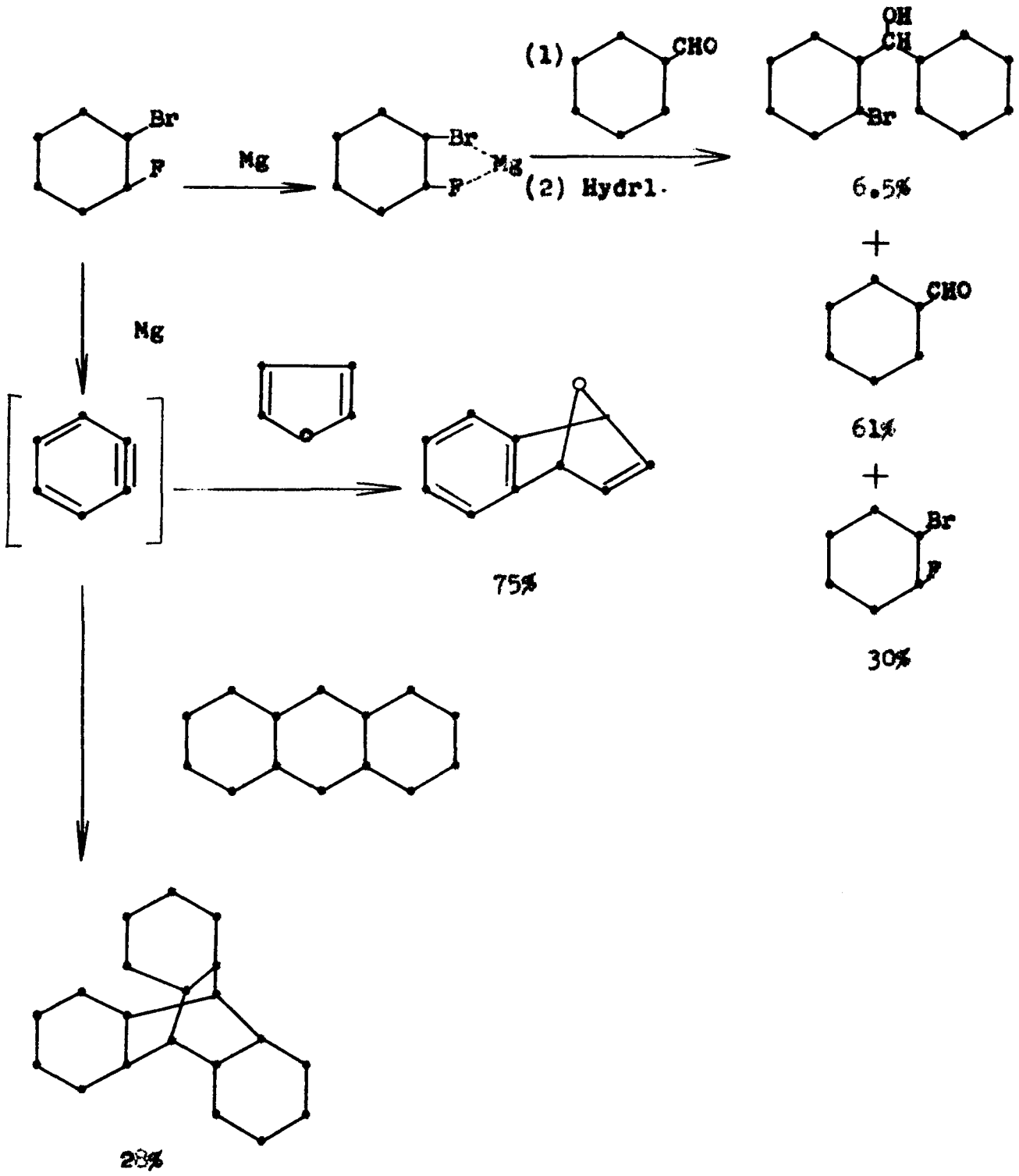
Culbertson (26) shows that in cases where the two benzene rings adjacent to the ketimino group are substituted by a hydroxyl or amino group, the ketimine-enamine tautomerism is possible, and may then largely influence the rate of hydrolysis. However, if the substituents are in the enamine form, the difficulties connected with the hydrolysis of the ketimine could be adequately described by steric hindrance resulting from o-substituents.

Since the halogens fall into the electronic category -I, +T, and since the T effect operates from the ortho position, the ketimine-enamine resonance is possible,



and may greatly influence the rate of hydrolysis. The opinion of G. N. Lewis (24) was that only elements of the first short period are capable of forming double bonds. Modern investigators hold that the tendency to form double bonds persists even with larger atoms, though the π bonds so formed by p orbital overlap are weak because the effectiveness of overlap diminishes as the p orbitals become larger and more diffuse. Thus despite the electronegativity order F > Cl > Br > I the electron releasing order is the same because of the more effective overlap (or greater tendency to form double bonds) of the smaller atom. When Wittig (27, 28) treated the Grignard reagent of o-bromofluorobenzene with benzaldehyde none of the expected o-fluorobenzhydrol was isolated. When o-bromofluorobenzene was treated with magnesium in the presence of furan or anthracene, products were isolated that may be rationalized most easily by assuming a Diels-Alder condensation with benzyne, which, in turn, results from dehalogenation of the starting material. There is a considerable amount of relevant data available in connection with Wittig's proposed mechanism (29,30).

Chart IV



The generation of a benzyne intermediate in the synthesis of our systems was considered as a possibility. While this was not ruled out completely by the experimental work, efforts to isolate addition products were unsuccessful.

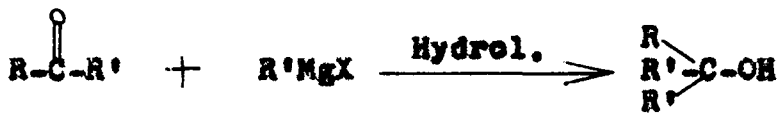
From what has been previously described it could be concluded that this method for producing ketones is handicapped by several factors. Steric hindrance resulting from o-substituents in connection with the hydrolysis of ketimines is certainly adequately described (4). The ketimine-enamine tautomerism and also the possibility of a contributing factor of a benzyne intermediate cannot be ruled out. In addition to that, there are some indications that in the course of hydrolysis with 40-60 per cent sulfuric acid a small amount of the respective hydrocarbons were obtained (4). Although the experimental data were not conclusive, contributions from all of these factors could produce a complex mixture of compounds which would probably be difficult to separate.

Preparation of 2'-Halogen Substituted 2-(2-Naphthylmethyl)benzophenones by the Methods Utilizing Acid Chlorides.

Grignard reactions utilizing acid chlorides give ketones as the initial product.

$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl + R'MgX \longrightarrow R\text{-}\overset{\overset{O\text{-}MgX}{|}}{\underset{R'}{C}}\text{-}Cl \xrightarrow{-MgXCl} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}R'$$

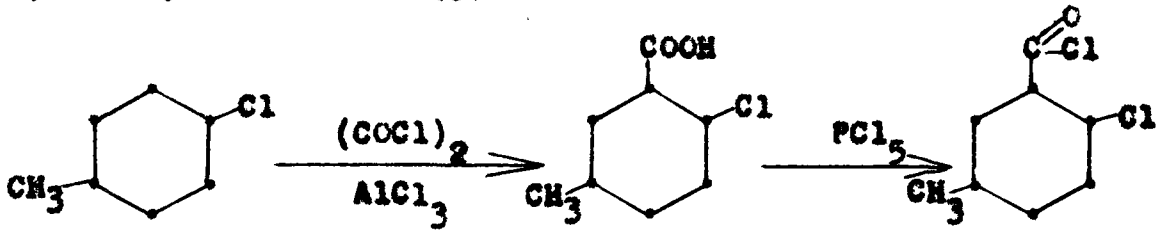
The ketone can, of course, react with more Grignard reagent to give a tertiary alcohol.



According the Cason (31), considerably better results may be obtained in this reaction when an organocadmium reagent, R_2Cd, is substituted for the Grignard reagent. The success of this method, as contrasted with the Grignard method, depends upon the negligible reactivity of the organocadmium reagent toward the ketone function.

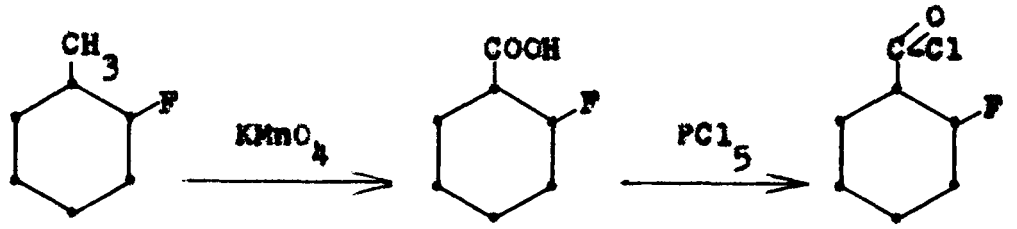
For this reason and because of the successful use of the organocadmium method by previous investigators (23, 3, 2) of related problems, the use of this method was encouraged for the present study.

2-Chloro-5-methyl benzoic acid was prepared from p-chlorotoluene by the Friedel-Crafts reaction (32) in 47.5 per cent yield. The acid was converted to 2-chloro-5-methylbenzoyl chloride in 94.7 per cent yield with phosphorus pentachloride (3).



o-Fluorotoluene was oxidized to o-fluorobenzoic acid

in 64 per cent yield using an alkaline solution of potassium permanganate (33). This acid was converted to the acid chloride in 82 per cent yield using phosphorus pentachloride (3).

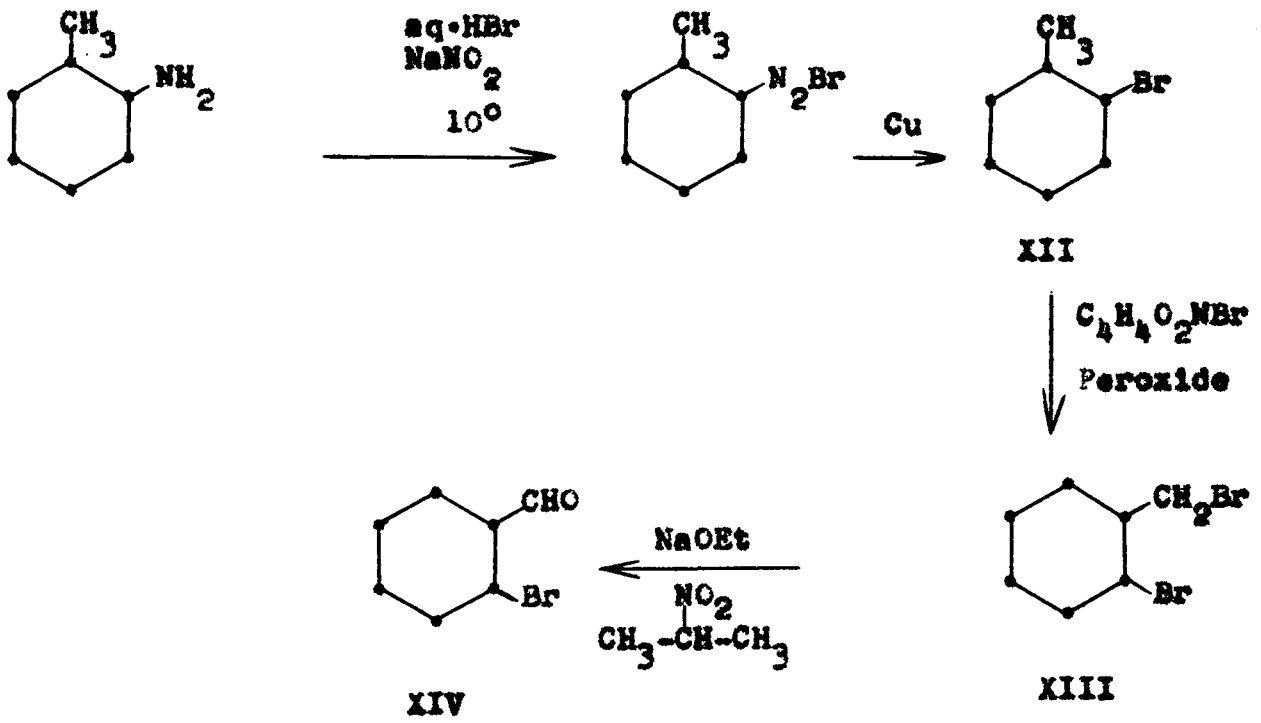


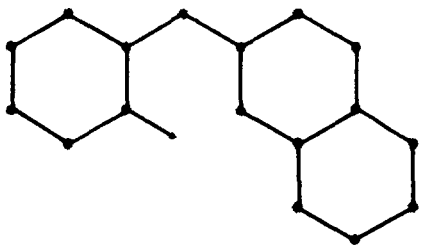
The synthetic route to obtain o-bromobenzaldehyde (XIV) is outlined in Chart V. o-Bromotoluene (XII) was prepared from o-toluidine by a Sandmeyer reaction in 35 per cent yield. o-Bromobenzyl bromide (XIII) was prepared from this compound in 74 per cent yield and on further reaction with 2-nitropropane and sodium ethoxide gave o-bromobenzaldehyde (XIV) in 66.4 per cent yield (41).

The general method for the preparation of 2-(2-naphthylmethyl)bromobenzene (XV) which gave a 47 per cent yield with modifications was the same that was used for the preparation of 2-(2-naphthylmethyl)chlorobenzene (VIII) and is outlined in Chart VI. The cadmium complex was prepared quite simply by adding dry cadmium chloride to the ether solution of the Grignard reagent.

$$2RMgX + CdCl_2 \longrightarrow R_2Cd + 2MgXCl$$

Chart V

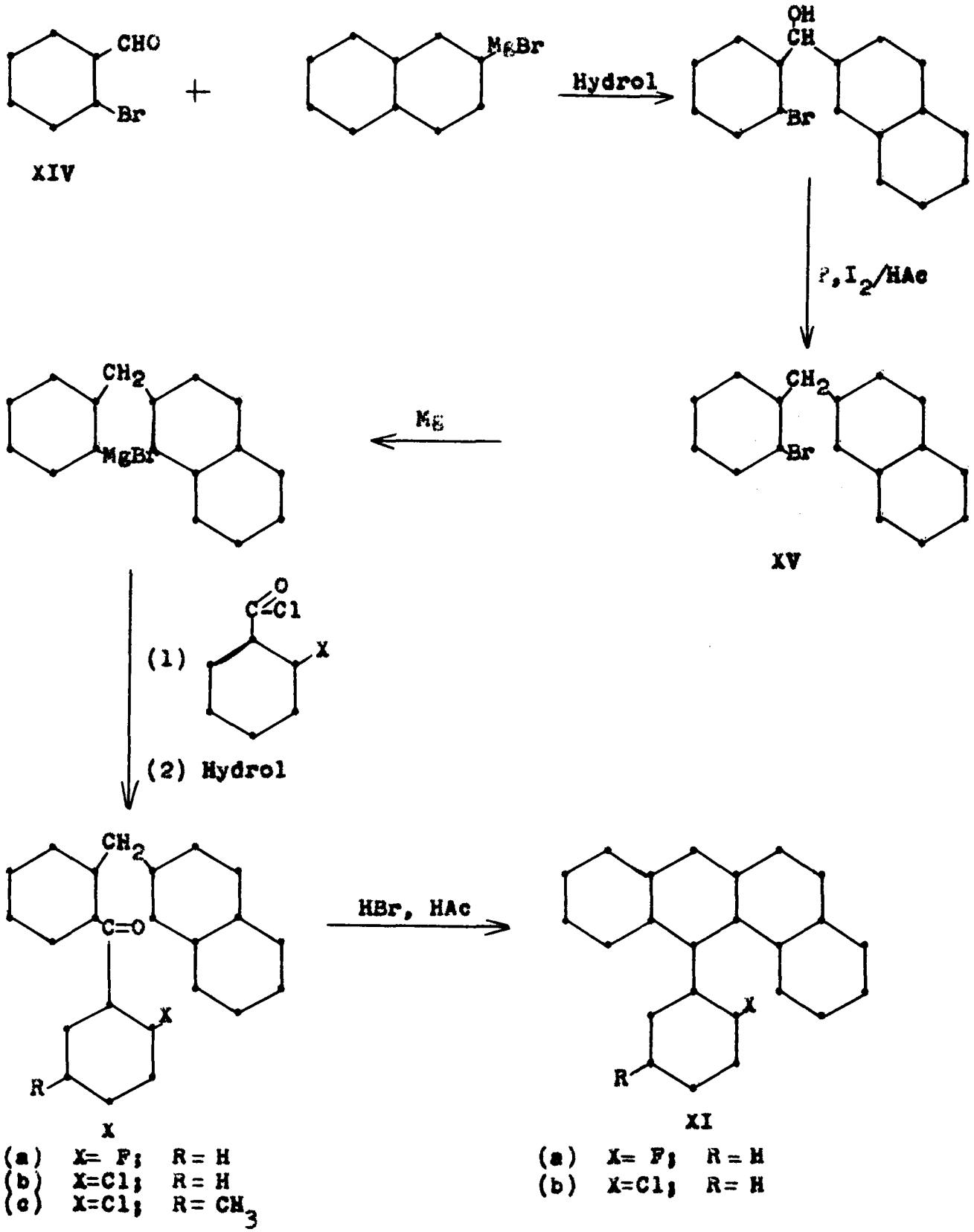

CH3
NH2
aq·HBr
NaNO2
10°
CH3
N2Br
Cu
CH3
Br
XII
C4H4O2NBr
Peroxide
CH2Br
Br
XIII
NaOEt
NO2
CH3-CH-CH3
CHO
Br
XIV

R= 

When the above reaction was complete, as evidenced by a negative Gilman test for RMgX, the ether was distilled and replaced by benzene as solvent. The acid chlorides were then added in the normal fashion to the benzene solution of the organocadmium reagent. However, the failure to secure products was attributed to the fact that reactions of this type are generally greatly affected by steric factors (34).

Next, it became of interest to determine whether the reactions of acid chlorides would yield products with Grignard reagents. The success of the reaction as a preparative method for ketones depends upon the fact that the Grignard reagent reacts somewhat faster with an acid chloride than with the ketone, which has been formed from the reaction between a Grignard reagent and an acid halide. Fairly satisfactory yields of ketones have been reported (34) when an ether solution of the Grignard reagent was added dropwise to the ketone ("inverse" Grignard addition) so that the Grignard reagent was never present in excess (35). This procedure, as shown in Chart VI, was applied to the preparation of the following ketones: 2-(2-naphthylmethyl)-2'-fluorobenzophenone (Xa) in 37.2 per cent yield,

Chart VI


CHO
Br
XIV
MgBr
Hydrol
OH
CH
Br
P, I2/HAc
CH2
Br
XV
Mg
CH2
MgBr
(1)
C=O
Cl
X
(2) Hydrol
CH2
C=O
X
R
X
(a) X= F; R = H
(b) X=Cl; R = H
(c) X=Cl; R = CH3
HBr, HAc
X
R
XI
(a) X= F; R = H
(b) X=Cl; R = H

2-(2-naphthylmethyl)2'-chlorobenzophenone (Xb) in 37.8 per cent yield, and 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone (Xc) in 60.4 per cent yield.

The structures of the above ketones, which had not been previously reported in the literature, were established by elemental analyses and by infrared absorption spectra. The carbonyl group in all of the named ketones exhibits the characteristic infrared absorption band at 1664 cm.$^{-1}$. See Fig. 3 and 4. Because of the intensity of this particular band and the absence of all other bands in the 1600-1800 cm.$^{-1}$ region, its location and classification was made easy.

Cyclodehydration of Some 2'-Halo Substituted Ketones.

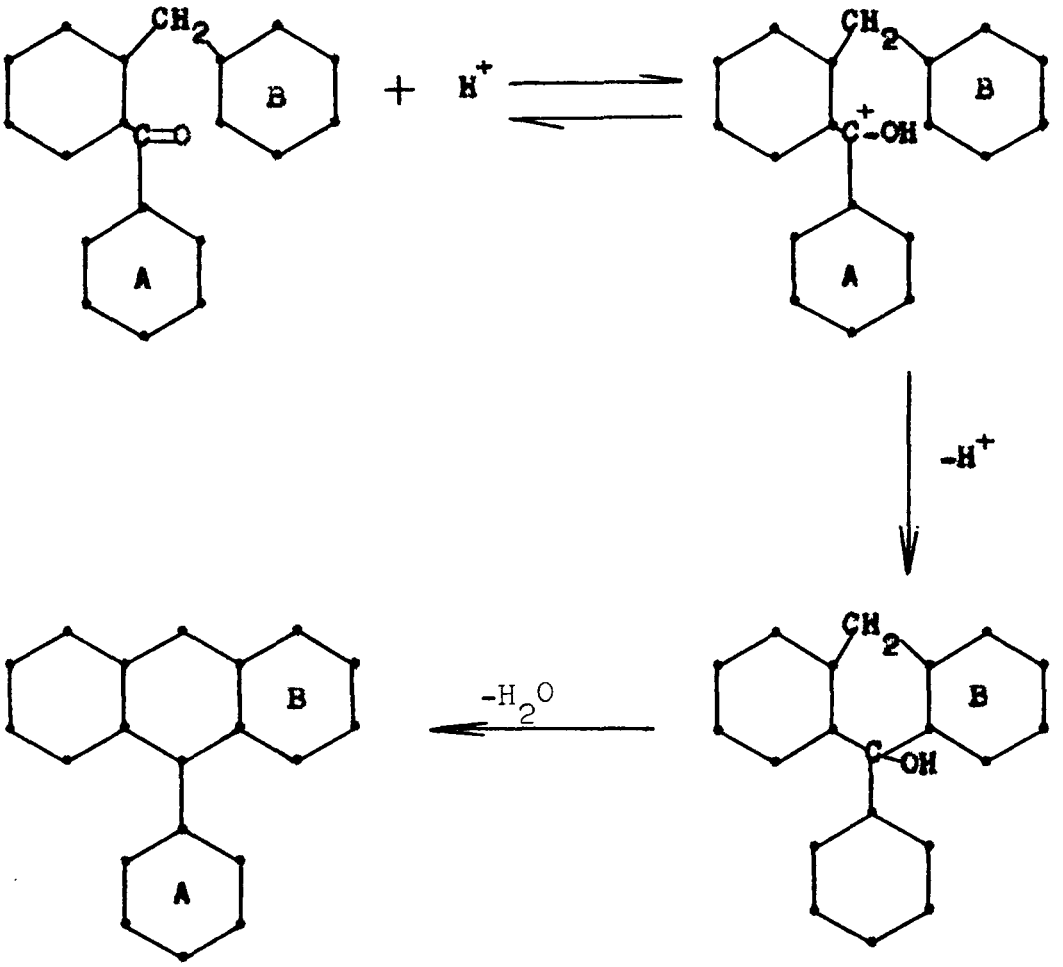
Bradsher and Vingiello (36) and Vingiello and Van Oot (37, 38) have established the mechanism of the aromatic cyclohydration of ketones by the reactions shown in Chart VII. This involves the following steps: (a) the reversible addition of a proton to the carbonyl oxygen, (b) an electrophilic attack of the positively charged carbon atom upon the ortho position of ring B, (c) the elimination of a proton, and (d) transannular elimination of water. It has been observed that one of the most important factors, on which the rate of cyclization depends, appears to be the steric nature of ring A.

Reactions of this type were generally carried out in a homogeneous, strongly acidic medium. For example, a mixture of hydrobromic and acetic acids was quite commonly used.

Previously attempts (14, 3) to cyclize 2'-halo-substituted ketones by heating under reflux with a mixture of hydrobromic and acetic acids had failed. This indicated that more severe conditions would be necessary to effect cyclization in this series of compounds. It was found that cyclization at 150° in a sealed tube with a mixture of hydrobromic and acetic acids gave satisfactory results(2).

Investigation of the sealed tube method revealed that the following three ketones could be cyclized at 180°

Chart VII



with a mixture of hydrobromic and acetic acids in seven hours. Under these conditions 2-(2-naphthylmethyl)-2'-fluorobenzophenone (Xa) gave 12-(2-fluorophenyl)benz [a] anthracene (XIa) in 78 per cent yield, 2-(2-naphthylmethyl)-2'-chlorobenzophenone (Xb) gave 12-(2-chlorophenyl)benz [a] anthracene (XIb) in 90 per cent yield. Under the same conditions after several trials 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone (Xc) gave 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene (XVI) only in about 20 per cent yield. This product was isolated with difficulty due to the formation of low melting by-products. The solid could not be purified by column chromatography or sublimation under reduced pressure. Numerous attempts at crystallization from a great variety of solvents finally gave a pure sample of the dihydrobenz [a] anthracene from 95 per cent ethanol. Further study of the cyclization indicated that the same cyclized product can be obtained in 61 per cent yield when the procedure was altered by using a mixture of hydriodic and acetic acids as outlined in Chart VIII. Spectroscopic data and elemental analysis revealed that the compound was 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene (XVI) instead of a fully aromatized compound. Since hydriodic acid is known to be

a strong reducing agent this result was not entirely suprising. The structures of these new products were established by elemental analyses, by ultraviolet absorption spectra[a] and by infrared absorption spectra.

The elemental analyses of the above named three benz [a] anthracenes were consistent with the structures.

According to Clar (46) the ultraviolet absorption spectrum of benz [a] anthracene has maxima at 222, 227, 267, 280, 290, 316, 329, 344, 359, 385 mμ. These have been divided into two rather distinct parts, one with maxima in the 240-300 mμ range, the other to the higher wavelength range. It has been suggested (47) that these parts are related to different types of electronic excitations. On this theory the 240-300 mμ maxima are associated primarily with electronic shifts, and therefore polarization along the horizontal axis, while the higher wavelength range maxima are related to polarization along the vertical axis of the benz [a] anthracene molecule. The ultraviolet spectra of 12-(2-fluorophenyl)benz [a] anthracene (XIa) and 12-(2-chlorophenyl) benz [a] anthracene (XIb) correspond with the benz [a] anthracene maxima given

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[a] Throughout this thesis ultraviolet absorption spectra were obtained by using a Perkin-Elmer model 3000 Spectracord (1 cm., quartz cell) at a concentration of about 5 mg. per liter in 95% ethanol.

above and were observed at 225, 268, 279, 289, 320, 335, 344, 350, 359 mμ. See Fig. 1.

The spectrum for 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene (XVI) would be expected to exhibit the general features of a spectrum of naphthalene and benzene. The composite curve was completely overshadowed by the naphthalene curve which suggests that the dihydrobenz [a] anthracene spectrum should have the general features of a naphthalene curve. Although a slight bathochromic shift was observed in the dihydrobenz [a] anthracene spectrum the general features were comparable with the naphthalene spectrum which according to Clar (46) have maxima at: 221, 248, 257, 266, 275, 285, 297, 311 and 319 mμ. The maxima of the ultraviolet absorption spectrum of 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene were observed at 235, 265, 269, 273, 280, 291, 306, 313, 321 mμ. See Fig. 2.

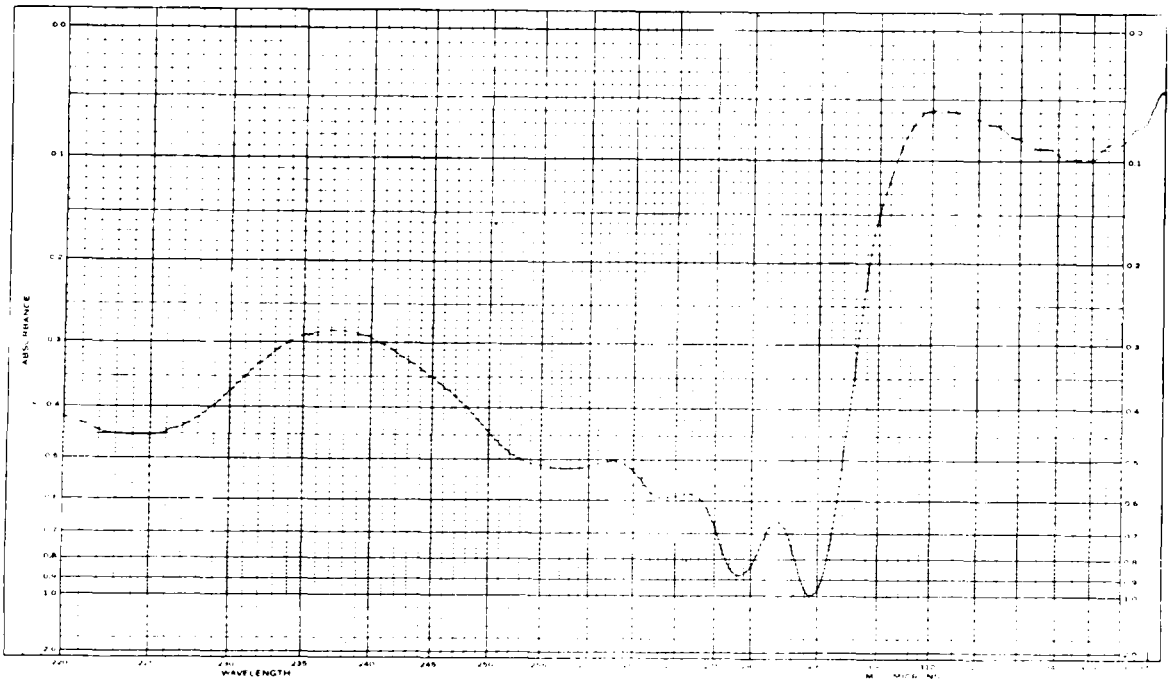
According to Orr and Thompson (47) the general characteristics of the infrared absorption spectra of the benz [a] anthracenes are a number of strong bands between 700 and 900 cm.$^{-1}$, a region of comparative transparency at 900-1200 cm.$^{-1}$, and a complex arrangement of bands between 1200 and 1700 cm.$^{-1}$ The vibrations giving rise to the intense bands at 700-900 cm.$^{-1}$ will include the out-of-plane deformations of carbon-hydrogen bonds in the

SAMPLE 1-(2-Chlorophenyl)bens a Anthracene
SOLVENT 95% Ethyl Alcohol
CONC Qualitative
CELL Quartz

SPECTRACORD
THE PERKIN-ELMER CORP.

SERIAL NO 1
SLIT
SCANNING TIME
DATE May 2nd, 1961

U.V. 1993

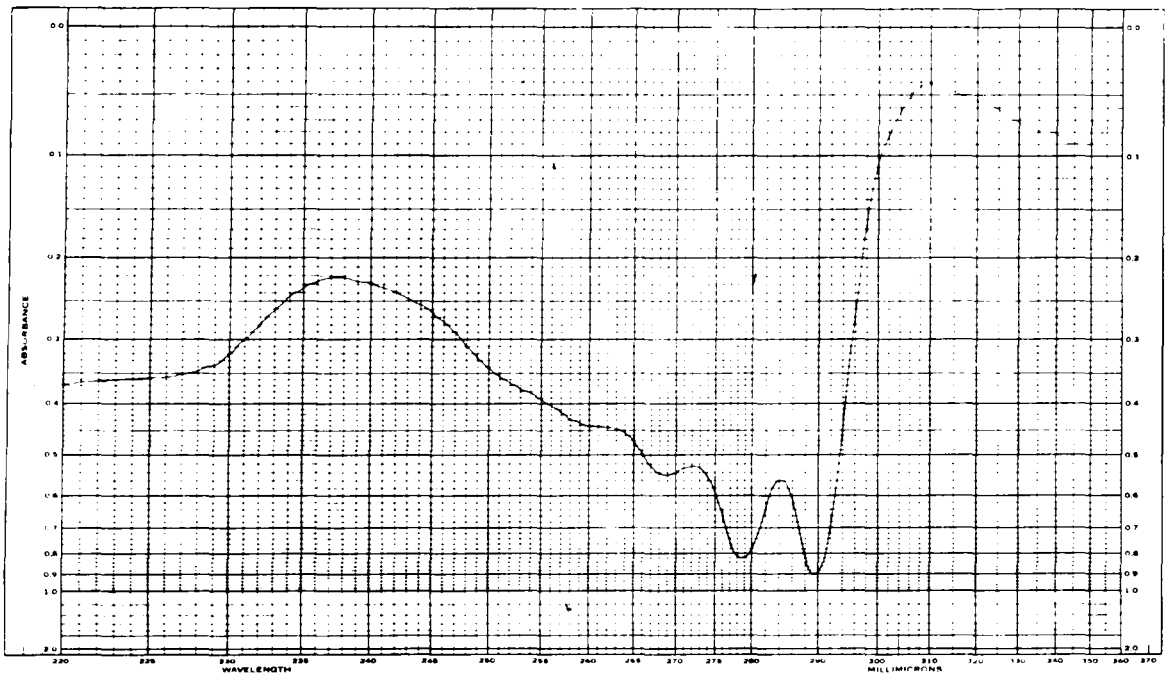


SAMPLE 1-(2-Chlorophenyl)bens a Anthracene
SOLVENT 95% Ethyl Alcohol
CONC Qualitative
CELL Quartz

SPECTRACORD
THE PERKIN-ELMER CORP.

SERIAL NO
SLIT
SCANNING TIME
DATE May 2nd, 1961

U.V. 1993



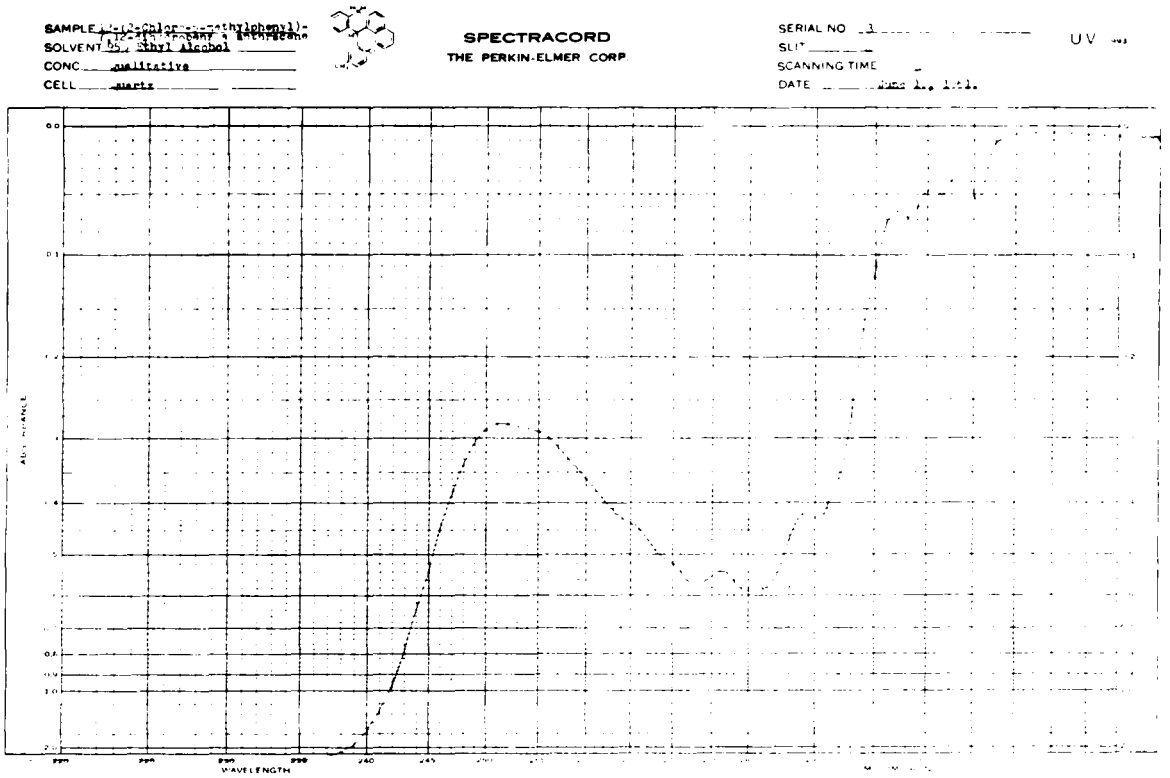
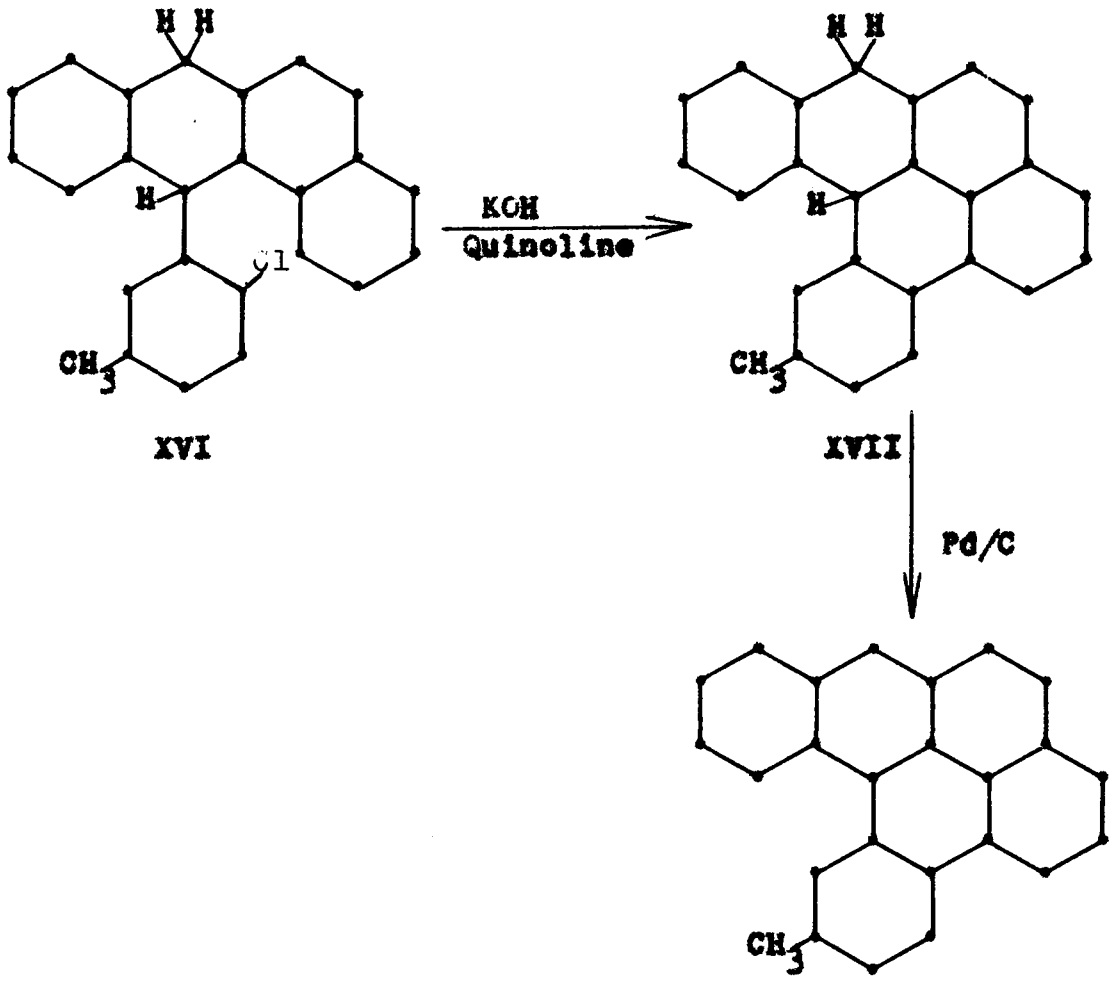

SAMPLE
SOLVENT 95% Ethyl Alcohol
CONC qualitative
CELL quartz
SPECTRACORD
THE PERKIN-ELMER CORP
SERIAL NO
SLIT
SCANNING TIME
DATE
UV
WAVELENGTH

Fig. 11

substituted aromatic rings. Another band which seems to persist throughout the benz [a] anthracenes lies near 1240 cm.$^{-1}$. The infrared absorption spectra of the 12-(2-fluorophenyl)benz [a] anthracene (XIa) and 12-(2-chlorophenyl)benz [a] anthracene (XIb) were consistent with the above described features plus the generally expected result that the aromatic carbon-hydrogen vibrations give bands at 3000-3100 cm.$^{-1}$. Although the general features of the spectrum for the 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene (XVI) were similar, the band near 1240 cm.$^{-1}$ was missing and besides the aromatic carbon-hydrogen vibration band at 3000-3100 cm.$^{-1}$ there was another band at 2850-2950 cm.$^{-1}$ significant for the aliphatic carbon-hydrogen vibrations. See Fig. 4 and 5. Apparently the steric nature is such that the dihydro compound is less hindered and would form more favorably, which suggests the desirability of further studies among a larger series of related compounds.

In order to obtain 2-methyldibenzo [a,l] pyrene (II) from 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz [a] anthracene (XVI) the following sequence of reactions was proposed:

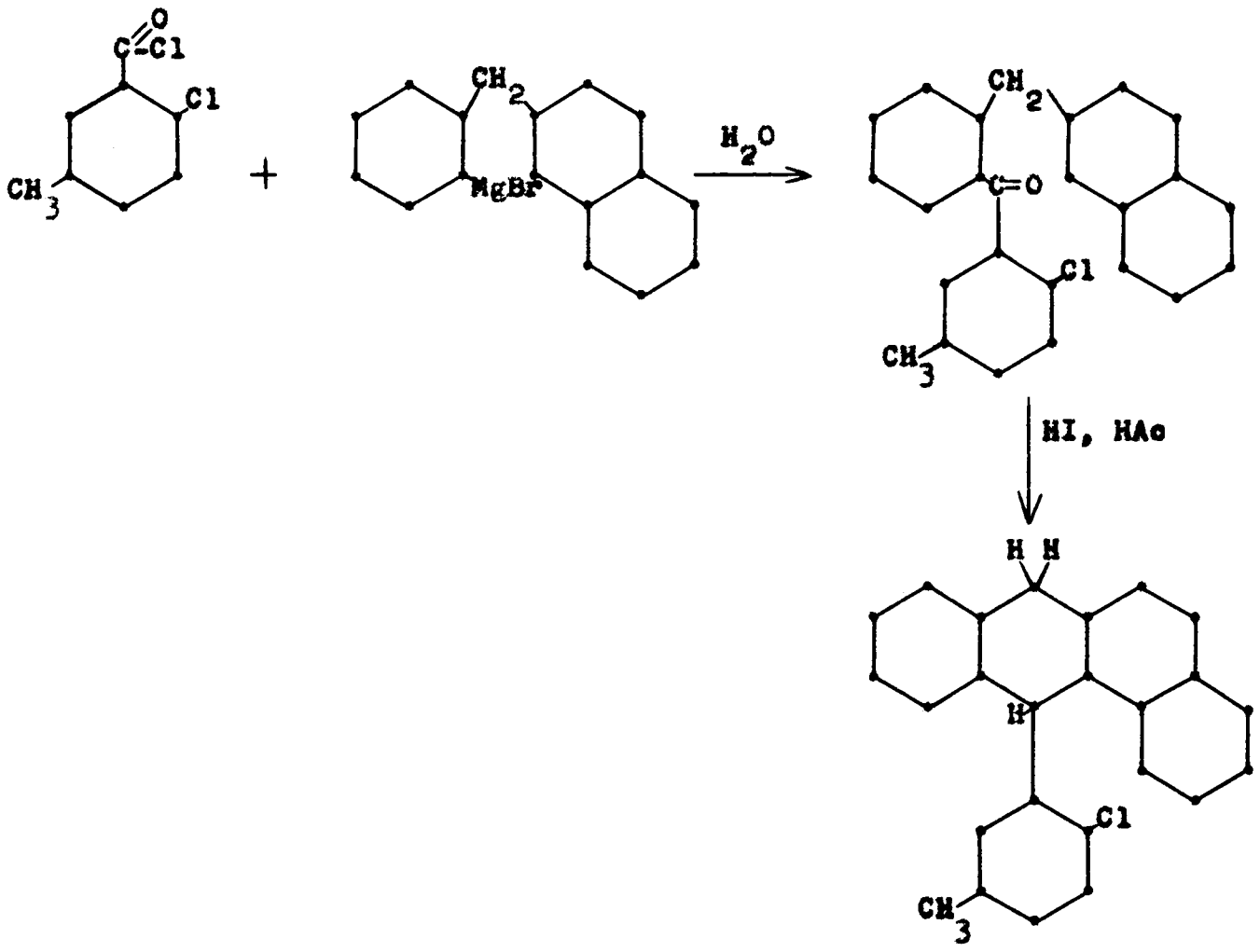


XVI XVII II

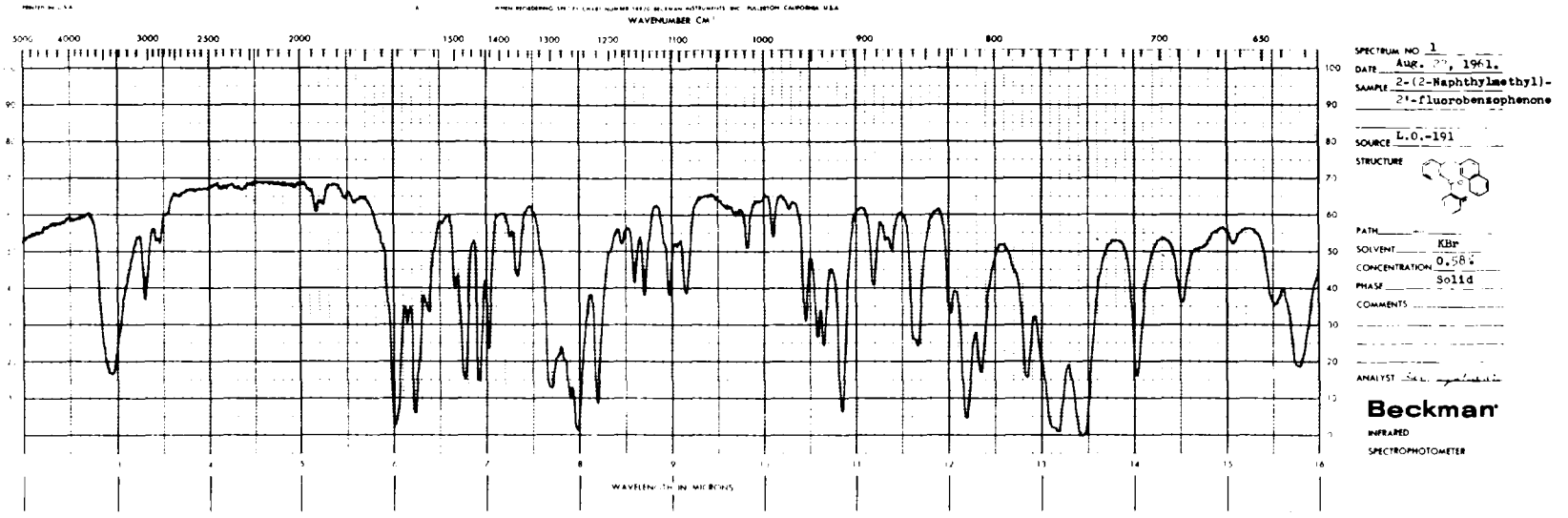
One attempt was made to cyclodehydrohalogenate XVI with potassium hydroxide and quinoline (48). The reaction appeared to be straightforward and proceeded according to expectations. The product was separated from the reaction mixture by chromatography. Although no analytical data was obtained due to the lack of a sufficient amount of the product the preliminary findings appear to suggest the compound XVII. The Beilstein test

for chlorine was negative. Furthermore the changes in the ultraviolet and infrared spectra of the material strongly suggest the structure assigned to the hydrocarbon XVII.

Chart VIII

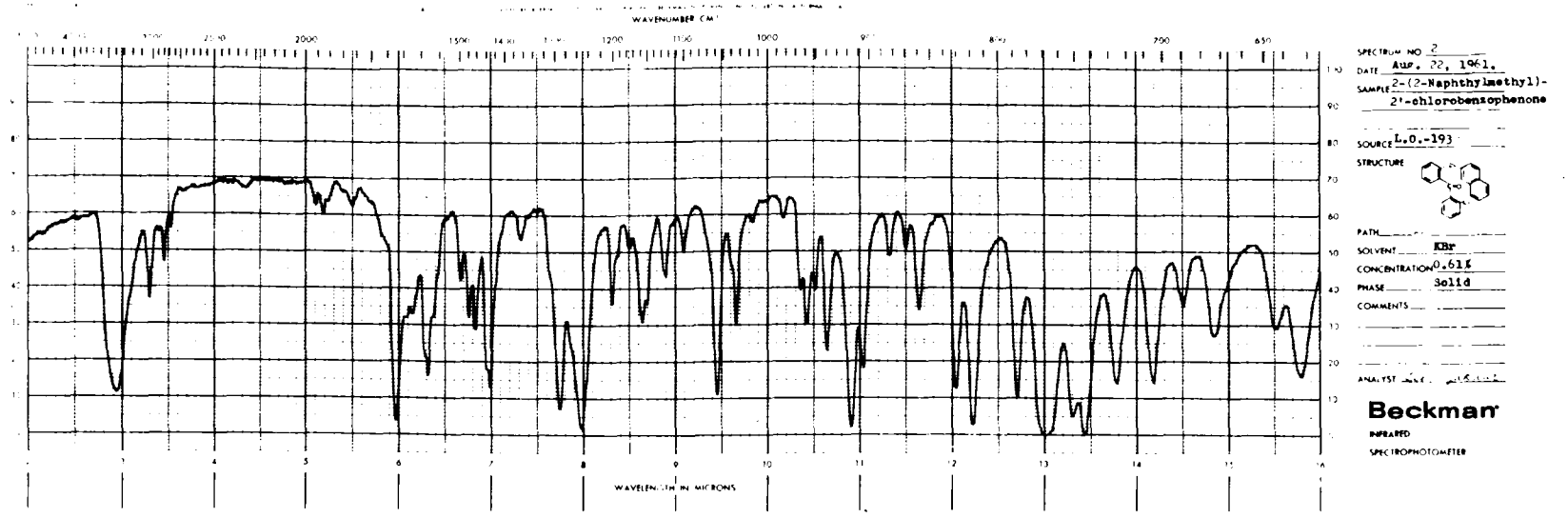


XVI



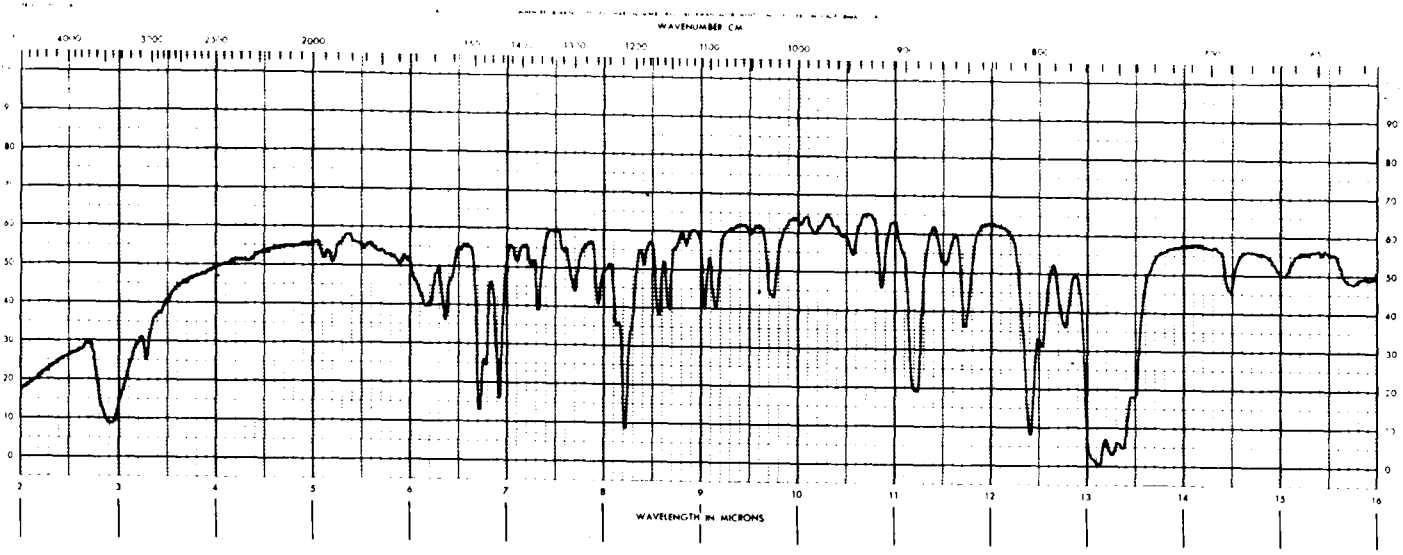
SPECTRUM NO 1
DATE Aug. 22, 1961.
SAMPLE 2-(2-Naphthylmethyl)-2'-fluorobensophenone
SOURCE L.O.-191
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.58%
PHASE Solid
COMMENTS
ANALYST

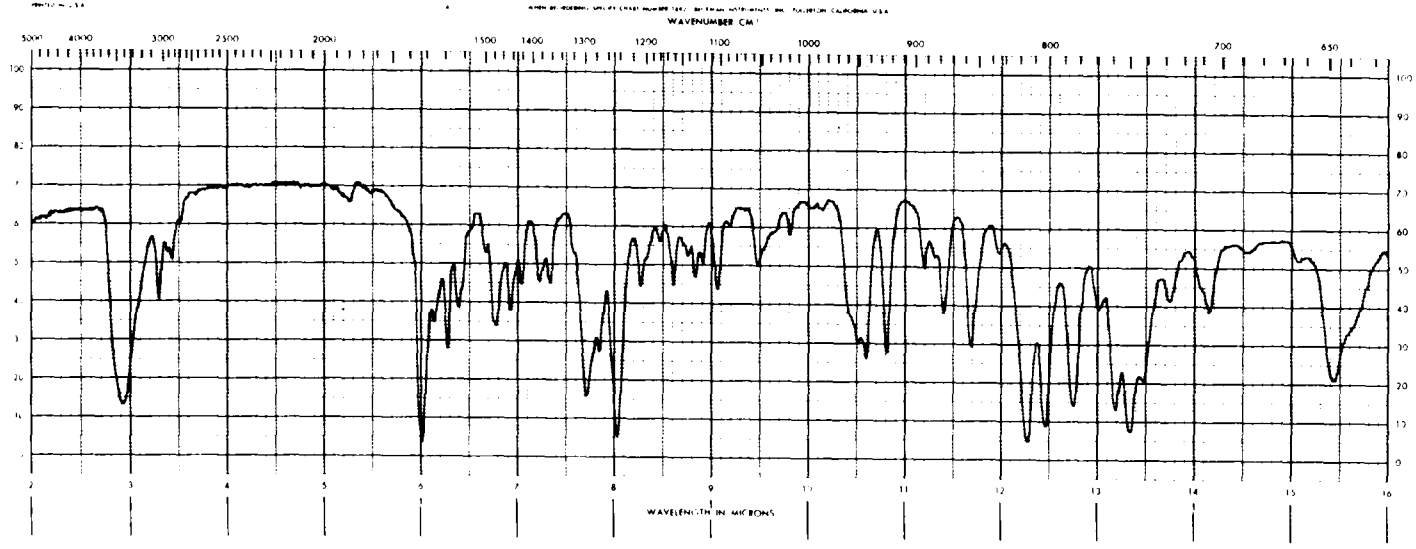
Beckman
INFRARED
SPECTROPHOTOMETER

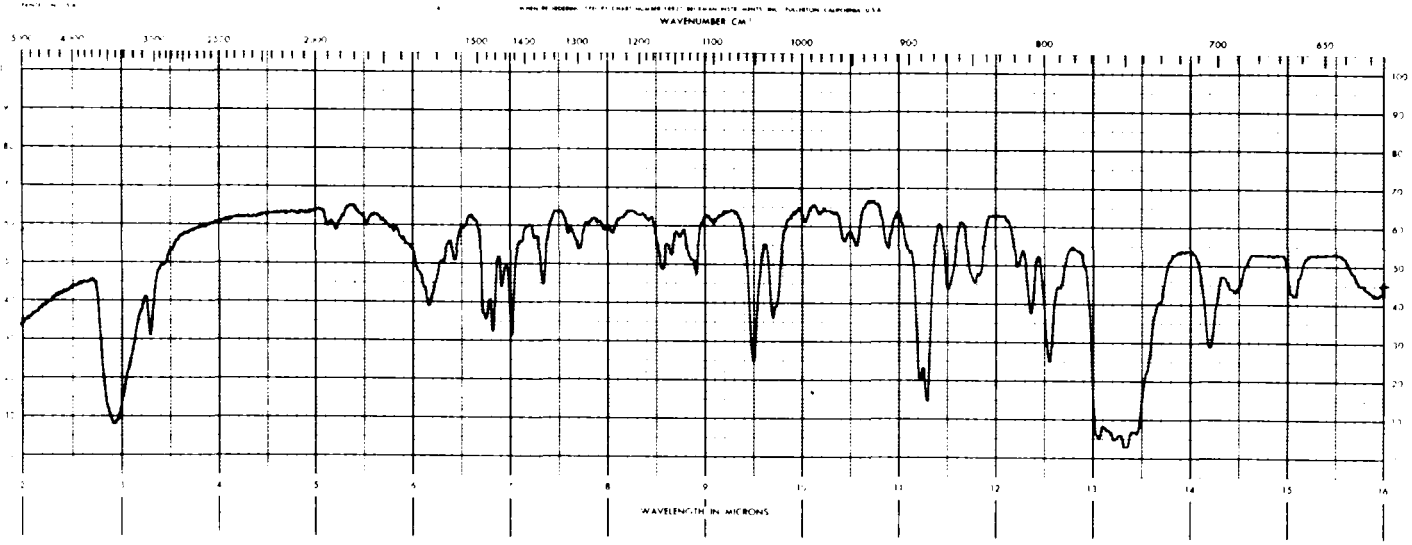


SPECTRUM NO 2
DATE Aug. 22, 1961.
SAMPLE 2-(2-Naphthylmethyl)-2'-chlorobensophenone
SOURCE L.O.-193
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.61%
PHASE Solid
COMMENTS
ANALYST

Beckman
INFRARED
SPECTROPHOTOMETER

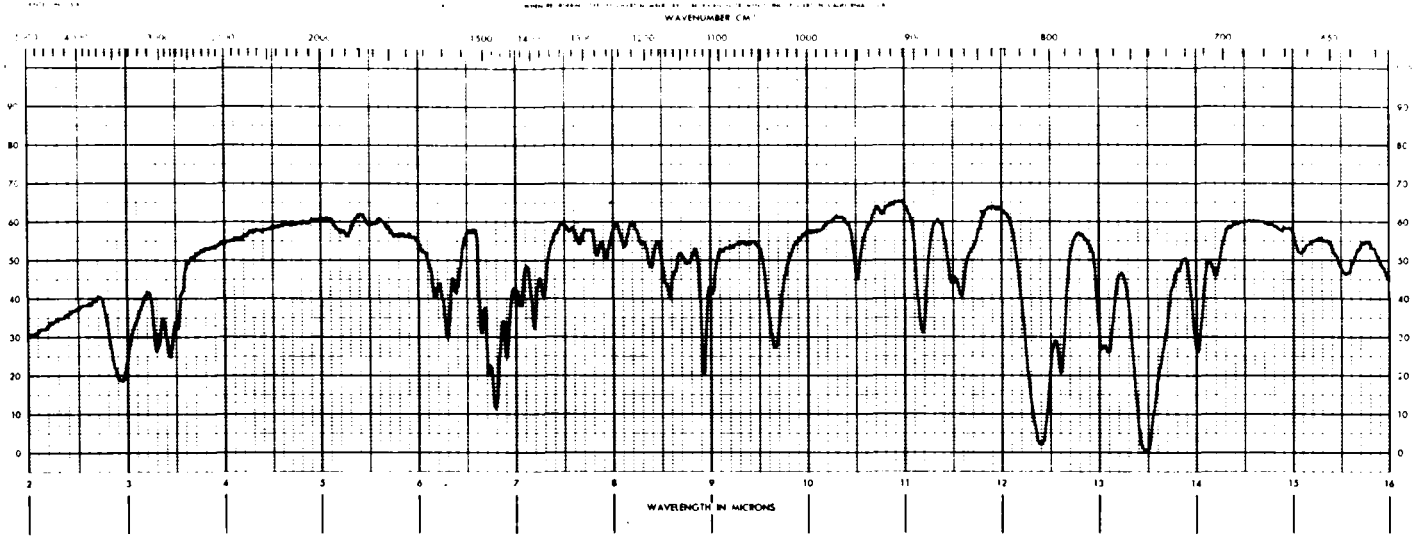

WAVENUMBER CM
WAVELENGTH IN MICRONS
SPECTRUM NO 4
DATE Aug. 22, 1941.
SAMPLE 12-(2-Fluorophenyl)-benz [a] anthracene
SOURCE L.O.-197
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.47
PHASE Solid
COMMENTS
ANALYST
Beckman
INFRARED
SPECTROPHOTOMETER


WAVENUMBER CM
WAVELENGTH IN MICRONS
SPECTRUM NO 3
DATE Aug. 22, 1941.
SAMPLE 2-(2-Naphthylmethyl)-2'-chloro-5'-methylbensophenone
SOURCE L.O.-195
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.50
PHASE Solid
COMMENTS
ANALYST
Beckman
INFRARED
SPECTROPHOTOMETER



SPECTRUM NO 2
DATE Aug. 2, 1961.
SAMPLE 12-(2-Chlorophenyl) benz[a]anthracene
SOURCE L.O.-136
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.49
PHASE Solid
COMMENTS
ANALYST

Beckman
INFRARED
SPECTROPHOTOMETER



SPECTRUM NO
DATE Aug. 2, 1961.
SAMPLE 12-(?-Chloro-?-methyl)-7,12-dihydrobenz[a]anthracene
SOURCE L.O.-202
STRUCTURE
PATH
SOLVENT KBr
CONCENTRATION 0.42%
PHASE Solid
COMMENTS
ANALYST

Beckman
INFRARED
SPECTROPHOTOMETER

EXPERIMENTAL

EXPERIMENTAL[a,b,c]

2-Bromonaphthalene[d] (VII) (20).

In a 4000 ml. beaker fitted with a mechanical stirrer 223 g. (1 mole) of 2-naphthylamine-1-sulfonic acid (tech.) was dissolved with stirring in 1800 ml. of aqueous sodium hydroxide (1.025 mole). An aqueous solution of 69 g. (1 mole) of sodium nitrite was then added with stirring, and the resulting solution was filtered. A 10 l. insulated jar that contained 500 ml. of 37% hydrochloric acid and 200 g. of crushed ice was fitted with a mechanical stirrer, thermometer and a separatory funnel

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[a] All melting points were taken on a Fisher-Johns melting point block and are corrected.

[b] All temperature values are expressed as degrees centigrade.

[c] All microanalyses were carried out by Geller Laboratories, Bardonia, New York.

[d] The method of preparation has been improved by Perry Polss in This Laboratory by the use of 500 ml. of 37% hydrobromic acid instead of 500 ml. of 37% hydrochloric acid in the diazotization step, for the salting out 225 g. of potassium bromide instead of 225 g. of potassium chloride was used and the crude precipitate of 2-bromo-1-naphthalenesulfonic acid was washed with 500 ml. of 20% potassium bromide solution instead of 500 ml. of 20% potassium chloride solution. The modifications in the procedure increased the yield of Grignard reagent formation of 2-bromonaphthalene from a varying 12-47% by the above procedure to 86-87% by the improved procedure. All of the per cent yields were substantiated by titration.

through which the filtered solution of sodium nitrite and the sodium salt of 2-naphthylamine-1-sulfonic acid was added with stirring. The temperature was maintained at 0-5° by adding crushed ice. The reddish-brown precipitate that forms was collected in a large Buchner funnel and washed with about 1 liter of ice water. While the diazotization was in progress, a suspension of cuprous bromide in hydrochloric acid was prepared by dissolving 300 g. (2.4 mole) of cupric sulfate pentahydrate crystals and 350 g. (3.4 mol) of sodium bromide in 2 liters of warm water. The solution was stirred while 151 g. (1.2 mole) of solid sodium sufite was added over a period of 10 minutes. Then some additional sodium sulfite was added until all of the blue color disappeared. The mixture was cooled and the solid collected on a Buchner funnel, washed with water and pressed dry on funnel. The precipitate of cuprous bromide was suspended in a mixture of 150 ml. of concentrated hydrobromic acid and 400 ml. of water. The damp cake of the diazonium compound was added portion wise with stirring to 550 ml. of the cuprous bromide (2.4 mole) suspension contained in a 10 liter jar provided with a stirrer. After the vigorous evolution of nitrogen had subsided, the mixture was heated to 95-100° on a steam bath and filtered hot through a large Buchner funnel. Some cuprous bromide appeared in

the filtrate but this does not interfere with the next step in the preparation. The filtrate was poured back into the 10 liter jar and 225 g. of potassium chloride was added with stirring. The resulting paste was allowed to cool to room temperature, then filtered with suction and washed with 1 liter of 20% aqueous potassium chloride solution. The reddish-brown precipitate of 2-bromo-1-naphthalenesulfonic acid was air-dried overnight. The dried 2-bromo-1-naphthalenesulfonic acid was transferred to a 5 liter round-bottom flask and a mixture of 400 ml. of concentrated sulfuric acid and 400 g. of crushed ice was added with occasional shaking. A reflux condenser was attached to the flask, which was then placed in the heating mantle. The mixture was mildly refluxed for 16 hours, cooled to room temperature and poured onto about 2 kg. of crushed ice contained in a 4000 ml. beaker. The mixture was shaken with 1 liter of benzene in a separatory funnel. The benzene layer was separated, washed with water until the washings were neutral to litmus paper. The benzene was distilled off and the product was distilled under reduced pressure. The fraction distilling between 98-100° at 1.5 mm. was collected as a slightly yellow oil, which solidifies to a light yellow solid, m.p. 55-57°; 238 g. (58%). In order to remove the yellow color the

product was dissolved in 600 ml. of normal hexane and passed through an alumina[e] column[f] wet packed with normal hexane. An additional 600 ml. of normal hexane was used to wash the column. The eluate, after evaporation to dryness, yielded 238 g. (58%) of 2-bromonaphthalene as white flaky crystals, (98% recovery) m.p. 56.5-57°; (Lit. [20] m.p. 56.8-57°).

2-(2-Naphthylmethyl)chlorobenzene (VIII) (22).

A Grignard reagent was prepared from 12.0 g. (0.48 g.-atom) of magnesium turnings and 100 g. (0.48 mole) of 2-bromonaphthalene in 250 ml. of dry ether. When the reaction was completed, a solution of 65.0 g. (0.46 mole) of 2-chlorobenzaldehyde in 250 ml. of anhydrous ether was added dropwise with stirring. A yellow precipitate appeared. The mixture was heated under reflux for two hours and then allowed to stand overnight at room temperature. Then the mixture was decomposed with a 20% aqueous ammonium chloride solution. The etheral layer was decanted from the hard residue and the solution was washed with water and then concentrated. The residual oil was dissolved in 585 ml. of 90% acetic acid, and 14.0 g.

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[e] The alumina used throughout this investigation, if not otherwise indicated, was basic, Brockman Activity I, 80-200 mesh.

[f] The column used throughout this investigation was 28 mm. x 150 mm.

(0.12 mole) of red phosphorus and 14.6 g. (0.06 mole) of iodine were added. This mixture was heated under reflux with stirring for 25 hours. The hot solution was filtered by suction to remove the unreacted phosphorus, allowed to cool and mixed with a large quantity of crushed ice. To this mixture, an iced 40% aqueous sodium hydroxide solution was slowly added with constant stirring until the mixture was just alkaline to litmus. The red oily layer was then separated and dissolved in ether and the aqueous layer was extracted with fresh ether. The combined ether layers were washed with a 20% aqueous sodium hydroxide solution to remove the free iodine and then washed again with water and dried over mangesium sulfate. The dry organic layer was concentrated and distilled under reduced pressure. The fraction distilling between 158-162° at 0.1 mm., (Lit. [22] b.p. 203-204°, 3 mm.) was collected as a nearly colorless oil; yield 50.0 g. (43%).

2-(2-Naphthylmethyl)benzonitrile (IX) (22).

In a 100 ml. round bottom flask furnished with a long air condenser, a mixture of 40.0 g. (0.16 mole) of 2-(2-naphthylmethyl)chlorobenzene, 17.76 g. (0.099 mole) of cuprous cyanide, 0.05 g. of anhydrous cupric sulfate and 15 ml. of dry pyridine was heated in a metal bath maintained between 180-190° for 2 hours and then between

260-270° for additional 20 hours. After that time, the condenser was replaced by a von Braun distilling head and the black material was crudely distilled with a free flame at about 1 mm. pressure. The distillate was then fractionated under reduced pressure. The fraction distilling between 178-180° at 0.4 mm. was collected as a slightly yellow oil which, on standing, crystallized as colorless plates. The solid was recrystallized from ethanol. The yield of 2-(2-naphthylmethyl)benzonitrile was 32 g. (84%) as white crystals; m.p. 85°, (Lit.[22] m.p. 84.5-85.5°).

3-Bromo-4-chlorotoluene (23).

In a 2 liter round-bottom flask a solution of 250 g. (1.00 mole) of cupric sulfate pentahydrate and 70 g. (1.20 mole) of sodium chloride in 800 ml. of hot water was prepared. In a 2 liter beaker a solution of 54 g. (0.52 mole) of sodium bisulfite and 36 g. (0.90 mole) of sodium hydroxide in 400 ml. of water was prepared and this solution was added with swirling to the hot copper sulfate solution over a period of five to ten minutes. The cuprous chloride precipitated as a white powder and was washed by decantation. The cuprous chloride was dissolved in 270 ml. of concentrated hydrochloric acid and 100 ml. of water and the flask was stoppered to minimize oxidation. The cuprous chloride solution was then cooled to 0° (solution tempera-

ture) and set aside.

In a 2 liter beaker equipped with a magnetic stirrer, 125.0 g. (0.6 mole) of 3-bromo-4-aminotoluene was dissolved in 270 ml. of concentrated hydrochloric acid and 1 liter of water. On cooling the solution to 0° the hydrochloride separated as fine crystals. To the stirred suspension, a solution of 45 g. (0.65 mole) of sodium nitrite in 160 ml. of water was added at such a rate that the solution temperature did not rise above 5°. After the diazotization was complete, the cold diazonium slurry was poured slowly with stirring into the cold cuprous chloride solution. The mixture was then allowed to warm slowly to room temperature and the solution was warmed on a steam bath for one-half hour and then steam distilled. From the distillate the halide was separated, washed with 150 ml. of a 10% sodium hydroxide solution, 100 ml. of an 80% sulfuric acid solution and then twice with water, and dried over anhydrous calcium chloride. The halide was purified by distillation under reduced pressure. The yield of 3-bromo-4-chlorotoluene was 80.0 g. (65%), collected between 121-123° at 28 mm. (Lit.[23]; 120-125°, 28 mm.) as a colorless oil.

<u>Attempted Preparation of 2-(2-Naphthylmethyl)-2'-fluorobenzophenone (Xa).</u>

A Grignard reagent was prepared from 2.43 g. (0.10 g.-

atom) of magnesium turnings and 17.5 g. (0.10 mole) of 2-bromofluorobenzene in 100 ml. of anhydrous ether. The reaction was very difficult to start even when a few drops of methyl iodide were used as initiator. When the reaction was completed the titration indicated presence of 20% Grignard reagent. The ether was replaced with 100 ml. of anhydrous toluene and the mixture was heated under reflux for an additional two hours and then cooled to room temperature. To this mixture was added 12.2 g. (0.05 mole) of 2-(2-naphthylmethyl)benzonitrile in 150 ml. of anhydrous toluene in one portion. Heating under reflux was continued for 30 hours after which the reaction mixture was cooled to ice temperature and 5.6 ml. concentrated sulfuric acid solution in 50 ml. of water was added dropwise. The whole was transferred into a 1000 ml. three-necked round-bottom flask which contained 40 ml. of concentrated sulfuric acid and 200 ml. of water and heated under reflux for 46 hours. The mixture was cooled. The organic layer was separated, washed with water and dried over anhydrous magnesium sulfate. The solvent was removed and the residual oil was fractionated under reduced pressure. The first fraction (b.p. 179-181° at 0.2 mm.) was unreacted nitrile (8.9 g.; 73%). The second fraction (boiled at 203-220° at 0.2 mm., 0.9 g.) was a dark oil. An infrared spectrum of the oil did not possess the

expected peak at 1664 cm.$^{-1}$ which is indicative of a carbonyl group. No further identification of this material was attempted.

Using the same quantities of reagents as described above, the reaction was performed in 80 ml. of anhydrous tetrahydrofuran. When the reaction was completed the titration indicated presence of 27.6% Grignard reagent. Again, there was a recovery of 98.5% of the starting nitrile and no expected ketone.

Attempted Preparation of 2-(2-Naphthylmethyl)-2'-chlorobenzophenone (Xb).

A Grignard reagent was prepared from 1.22 g. (0.05 mole) of magnesium turnings and 7.65 g. (0.04 mole) of o-chlorobromobenzene in 30 ml. of anhydrous ether. After all of the halide solution had been added, heating was continued for 30 minutes. Titration of this mixture indicated the presence of 100% Grignard reagent. To the cool mixture 4.86 g. (0.02 mole) of 2-(2-naphthylmethyl)-benzonitrile in 30 ml. of dry toluene was added in one portion. Heating under reflux was continued for 44 hours after which the reaction mixture was cooled to ice temperature and 2.8 ml. of concentrated sulfuric acid solution in 25 ml. of water was added dropwise. The whole was transferred into a 500 ml. three-necked round-bottom flask which contained 20 ml. of concentrated sulfuric

acid and 100 ml. of water and heated under reflux for 46 hours. The mixture was cooled. The organic layer was separated, washed with water and dried over anhydrous magnesium sulfate. The solvent was removed and the residual oil fractionated under reduced pressure. The fraction boiling between 237-245° at 0.2 mm. was a red viscous oil which hardens on cooling and weighed 3.5 g. All of this material was redistilled boiling between 241-245° at 0.2 mm. Although an infrared spectrum of the oil possessed a peak at 1664 $cm.^{-1}$ indicative of a carbonyl group, further purifications and attempted crystallizations did not give a distinct pure crystalline material.

Attempted Synthesis of 2-(2-Naphthylmethyl)-2'-chloro-5'-methylbenzophenone (Xe).

A Grignard reagent was prepared from 7.3 g. (0.30 mole) of magnesium turnings and 61.5 g. (0.30 mole) of 3-bromo-4-chlorotoluene in 300 ml. of anhydrous ether. After the reaction was completed the ether was replaced with 300 ml. of anhydrous toluene and 25.5 g. (0.105 mole) of 2-(2-naphthylmethyl)benzonitrile in 150 ml. of anhydrous toluene was added in one portion. Heating under reflux was continued for one day. The mixture was cooled to room temperature and 750 ml. of a 25% sulfuric acid solution was added dropwise. The whole was then heated under reflux for 57 hours. The mixture was cooled. The organic layer was separated, washed twice with water and

dried over anhydrous magnesium sulfate. The solvent was removed and the residual oil was fractionated under reduced pressure. The fraction distilling between 305-315° at 0.85 mm., (Lit. [45] b.p. 297-320°, 3 mm.) was collected as a viscous red, green fluorescent oil which, on standing, hardened to a red glassy material; yield 28.0 g. (72%). During the distillation there was evidence of decomposition occurring. This red solid could not be purified by chromatography, sublimation or recrystallization. An infrared spectrum of the red solid possessed a sharp peak at 1664 cm.$^{-1}$, indicative of a carbonyl peak.

An analytical sample was prepared by redistillation of the red material boiling between 267-268° at 0.05 mm.

Anal. Calcd. for $C_{25}H_{19}Cl$: C, 80.96; H, 5.16; Cl, 9.56
Found: C, 87.95; H, 5.59; Cl, 2.24

The analysis indicated that this was not the desired ketone.

o-Bromotoluene (XII) (39).

A solution of 162 g. (1.5 mole) of commercial o-toluidine in 880 ml. (6 mole) of 40% commercial hydrobromic acid in a 3 liter flask was cooled to 10° and diazotized with 116 g. (1.7 mole) of sodium nitrite, added about 10 g. at a time. After each addition the flask was stoppered and shaken until all the red fumes were absorbed. The temperature must be kept below 10°. When

diazotization was completed, 5 g. of copper powder was added, the flask was attached to a reflux condenser and heated very cautiously. As soon as the first sign of reaction was observed, the flask was cooled with ice. Nitrogen was evolved vigorously. When the reaction subsided, the mixture was heated half an hour on the steam bath. Then 1 liter of water was added and the mixture was distilled with steam until about 1.5 liters had passed over. The distillate was made alkaline with about 10 g. of powdered sodium hydroxide and the red bottom layer of crude o-bromotoluene separated. This weighs about 140 g. The crude product was washed with concentrated sulfuric acid, which removed almost all the color, and then twice with water. It was dried over calcium chloride, filtered and distilled from a modified Claisen flask. The yield of product boiling between 170-180° at 705 mm. was 90 g. (35%). (Lit.[39]b.p. 178-181°; 110-120 g., 42-47%).

o-Bromobenzylbromide (XIII) (40).

A solution of 188.5 g. (1.1 mole of o-bromotoluene and 4.4 g. benzoyl peroxide in 320 ml. of dry benzene was brought to vigorous reflux in a 2 liter three-necked flask fitted with a stirrer and an efficient reflux condenser. A mixture of 196 g. (1.1 mole) of N-bromosuccinimide and 4.4 g. of benzoyl peroxide was added portion wise through a wide-mouthed adapter. The dry powder was added as rapidly

as the violent foaming would permit and was worked down through the stem of the adapter with a stirring rod. Refluxing benzene washed the lower part of the adapter continuously. As soon as the foaming from the last addition of N-bromosuccinimide had subsided, the flask was cooled, first with a water bath and then an ice bath. The succinimide was filtered off and washed once with dry benzene. The benzene was removed at reduced pressure. The residue was distilled at 16 mm. Some unreacted o-bromotoluene was collected and recycled. The combined crude o-bromobenzyl bromide was distilled under reduced pressure, and the fraction boiling between 128-140° at 16 mm. was collected. This procedure yielded 200 g. (74%) of colorless o-bromobenzyl bromide.

o-Bromobenzaldehyde (XIV) (41).

18.4 g. (0.80 g.-atom) of sodium was dissolved in 800 ml. of absolute ethanol in a 2 liter round-bottomed flask fitted with a reflux condenser connected to a drying tube. The solution was allowed to cool to room temperature. 9.2 g. (0.103 mole) of 2-nitropropane, and 25 g. (0.101 mole) of o-bromobenzyl bromide were added in that order. The mixture was shaken at intervals for four hours. The reaction mixture became warm spontaneously, and a white precipitate of sodium bromide formed. After the reaction subsided the sodium bromide was separated by filtration and the ethanol was removed by distillation on a steam bath. The residue of

product and sodium bromide was dissolved in 320 ml. of ether and 480 ml. of water. The ether layer was separated and washed with two 75 ml. portions of 10% sodium hydroxide solution to remove any acetoxime and excess 2-nitropropane and was then washed with 75 ml. of water. The ether layer was dried with anhydrous magnesium sulfate. The ether was removed by distillation and the residual oil was distilled under reduced pressure. When the reaction was carried out under the same conditions for four hours and fifteen hours, the yields of o-bromobenzaldehyde boiling between 115-117° at 12 mm., 87.7 g. (59.3%) and between 115-118° at 12 mm., 97.2 g. (66.4%) respectively, were obtained. (Lit. [42] 118-119°, 12 mm.)

2-(2-Naphthylmethyl)bromobenzene (XV) (22).

A Grignard reagent was prepared from 5.1 g. (0.21 g.-atom) of magnesium turnings and 41.4 g. (0.20 mole) of 2-bromonaphthalene in 125 ml. of anhydrous ether. When the reaction was completed, a solution of 37.1 g. (0.20 mole) of 2-bromobenzaldehyde in 50 ml. of anhydrous ether was added dropwise with stirring. A yellow precipitate appeared. Heating under reflux was continued for two hours and then the mixture was allowed to stand overnight at room temperature. Then the mixture was decomposed with a 20% ammonium chloride solution. The ethereal layer was separated from the hard residue and the solution washed with water and then concentrated. The residual oil was dissolved in 293 ml. of 90% acetic acid, 7.0 g. (0.06 mole) of red phosphorus and

7.3 g. (0.03 mole) of iodine were added. This mixture was heated under reflux with stirring for 25 hours. The hot solution was filtered by suction to remove the unreacted phosphorus, allowed to cool and mixed with a large quantity of crushed ice. To this mixture, an iced 40% aqueous sodium hydroxide solution was slowly added with constant stirring until the mixture was just alkaline to litmus. The red oily layer was then separated and dissolved in ether and the aqueous layer was extracted with fresh ether. The combined ether layers were washed with a 20% aqueous sodium hydroxide solution to remove the free iodine and then washed again with water and dried over calcium chloride. The dry organic layer was concentrated and distilled twice under reduced pressure. The fraction distilling between 172-182° at 0.1 mm., (Lit.[22]b.p. 230-240°, 2 mm.) was collected as a nearly colorless oil; yield 28.0 g. (47%).

o-Fluorobenzoic Acid (33).

A mixture of 30 g. of o-fluorotoluene, 80 g. of potassium permanganate, 5 ml. of 10% aqueous sodium hydroxide and 1500 ml. of water was heated under reflux with stirring for 10 hours. The solution was filtered while hot to remove the manganese dioxide precipitate, cooled to room temperature and acidified with dilute sulfuric acid. The product which separated was filtered from the solution, washed with water and air dried; m.p. 121-123° (Lit.[5]120-122°).

Concentration of the aqueous solution gave 4.0 g. more of the same product. The total yield was 25 g. (64%).

o-Fluorobenzoyl Chloride (14).

A mixture of 35.5 g. (0.254 mole) of o-fluorobenzoic acid and 53 g. (0.254 mole) of phosphorus pentachloride were heated cautiously (hood!) in an one liter round-bottom flask equipped with a reflux condenser connected to a water trap. After the rather violent initial reaction had subsided the reaction mixture was heated at a bath temperature of about 100° until no more visual sign of reaction was noted. The volatile material was removed by distillation using a water aspirator to reduce the pressure. The residue was distilled at 11 mm. The fraction boiling between 85-86° (Lit. [5] 85-88°, 11 mm.) weighed 32.85 g. (82%).

2-Chloro-5-Methylbenzoic Acid (32).

A mixture of 50.0 g. (0.395 mole) of p-chlorotoluene with 150 ml. of carbon disulfide, was stirred well in a 500 ml. three-necked flask equipped with a solid addition adapter and a reflux condenser connected to a water trap. The solution was cooled to ice temperature and 50.0 g. (0.395 mole) of oxalyl chloride was added. The cold mixture was stirred well and while stirring 60.0 g. (0.43 mole) of aluminum chloride was added in two 30 g. portions. The first portion when added caused a vigorous reaction. After the reaction ceased another portion was added. Thereafter the ice was allowed to melt and the mixture was allowed to

stand at room temperature for 24 hours. The reaction mixture was cooled in an ice bath and poured with stirring into a mixture of 150 g. of ice, 100 g. of water and 20 ml. of concentrated hydrochloric acid. This mixture was stirred thoroughly in order to dissolve completely the aluminum compounds. Then the organic layer was separated and 50 ml. of 10% sodium hydroxide was added. The mixture was shaken and the aqueous portion was separated. The ether layer was further extracted with 25 ml. of 10% sodium hydroxide solution and separated. Finally 10 ml. of water was used to wash the ether layer. All of the aqueous material was combined and acidified to pH 1-2 with concentrated hydrochloric acid. The acid separated out as white crystals which were washed four times with water and dried in a dessicator; m.p. 163-164°; yield 32 g. (47.5%). This material was used without further purification in the following reaction.

2-Chloro-5-Methylbenzoyl Chloride (32).

A mixture of 19.0 g. (0.112 mole) of 2-chloro-5-methylbenzoic acid and 20.9 g. (0.112 mole) of phosphorus pentachloride were heated cautiously (Hood!) in a 100 ml. round-bottom flask equipped with a reflux condenser connected to a water trap. After the rather violent initial reaction had subsided the reaction mixture was heated at a

bath temperature of about 100° until no more visual sign of reaction was noted. The volatile material was removed by distillation using a water aspirator to reduce the pressure. The residue was distilled at 20 mm. The fraction boiling between 135-139° weighed 17.88 g. (94.7%).

Attempted Preparation of 8-Methyltriptycene (43).

A 250 ml. three-necked flask, equipped with a ball-and-socket sealed mechanical stirrer, a pressure compensated dropping funnel, and a reflux condenser connected to a mercury bubbler, was charged with 0.8 g. (0.033 g.-atom) of magnesium turnings and the apparatus was flamed. Then 7.5 g. (0.042 mole) of anthracene, and 35 ml. of anhydrous tetrahydrofuran (freshly distilled over lithium aluminum hydride) were added. In the dropping funnel there was placed a solution of 6.2 g. (0.03 mole) of 3-bromo-4-chlorotoluene in 15 ml. of anhydrous tetrahydrofuran. The system was flushed with dry nitrogen for 30 minutes to remove air. The gas flow was then stopped in order to prevent extensive loss of tetrahydrofuran. The mixture was heated to and maintained at 60° (bath temperature), and one-quarter of the 3-bromo-4-chlorotoluene solution was added with stirring. After addition another quarter of the solution was added dropwise, over a period of about 45 minutes, a yellow color was noticed which evidenced the start of reaction. When the reaction commenced, the remaining solution was added dropwise over a period of 1 hour, after which the mixture

was refluxed gently for 90 minutes. The homogeneous dark-brown mixture was poured into 100 ml. of methanol, which precipitates much of the unreacted anthracene. Without filtering, the solvents were removed under reduced pressure and the yellow residue was treated with two 50 ml. portions of 5% hydrochloric acid, filtered, and vacuum-dried. The dry yellow residue (10.7 g.) was dissolved in 45 ml. of hot p-xylene, then 5.0 g. (0.051 mole) of maleic anhydride was added. The mixture was refluxed for 20 minutes and set aside at room temperature for 2 hours. The maleic anhydride-anthracene adduct (9.2 g.) was removed by filtration, and the brown filtrate was refluxed for 2 hours with 80 ml. of 2 N sodium hydroxide solution. When cool, the organic layer was separated, washed three times with 50 ml. portions of water, and dried over calcium chloride. The solvent was removed at reduced pressure. The brown residue was dissolved in 70 ml. of carbon tetrachloride and chromatographed on 280 g. of acid-washed alumina, using 1 liter of the same solvent to elute. After evaporation of the solvent, there remained 1.82 g. of a yellow residue, which resisted all attempts to crystalize. The yellow residue was distilled under reduced pressure. The twice distilled fraction boiling between 117-118° at 0.015 mm. was collected as very viscous, colorless oil; yield 0.99 g.

Anal. Calcd. for $C_{21}H_{16}$: C, 93.99; H, 6.01
Found: C, 88.67; H, 6.95

The analysis indicated that this was not the desired hydrocarbon.

Attempted Preparation of 2-(2-Naphthylmethyl)-2'-chloro-5'-methylbenzophenone via the Cadmium Complex (3).

A Grignard reagent was prepared from 1.5 g. (0.06 g.-atom) of magnesium turnings and 18.0 g. (0.06 mole) of 2-(2-naphthylmethyl)bromobenzene in 250 ml. of anhydrous ether using a few drops of bromobenzene to initiate the reaction. After all the halide solution had been added the mixture was heated under reflux for 6 hours and cooled to room temperature. To this mixture was added 11.0 g. (0.06 mole) of anhydrous cadmium chloride in one portion. Heating under reflux was continued for another hour after which the ether was allowed to distill from the mixture as 150 ml. of anhydrous benzene was added to replace the ether. After cooling to room temperature 5.67 g. (0.03 mole) of 2-chloro-5-methylbenzoylchloride in 150 ml. of anhydrous benzene was added in one portion. Heating under reflux was continued for 6 hours after which the reaction mixture was poured on a mixture of ice and dilute hydrochloric acid. The organic layer was removed and the aqueous layer extracted three times with ether. The combined extract was washed with 10% sodium hydroxide, twice with water and dried over anhydrous magnesium sulfate. Concentration of the ether

solution yielded 4.45 g. of the 2-chloro-5-methylbenzoic acid, m.p. 163-164°. No other material could be isolated.

Attempted Preparation of 2-(2-Naphthylmethyl)2'-fluorobenzophenone via the Cadmium Complex (3).

A Grignard reagent was prepared from 1.5 g. (0.06 g.-atom) of magnesium turnings and 18.0 g. (0.06 mole) of 2-(2-naphthylmethyl)bromobenzene in 250 ml. of anhydrous ether using a few drops of bromobenzene to initiate the reaction. After all the halide solution had been added the mixture was heated under reflux for 90 minutes and cooled to room temperature. To this mixture was added 11.0 g. (0.06 mole) of anhydrous cadmium chloride in one portion. Heating under reflux was continued for another hour after which the ether was allowed to distill from the mixture as 150 ml. of anhydrous benzene was added to replace the ether. After cooling to room temperature 11.34 g. (0.06 mole) of 2-fluorobenzoyl chloride in 150 ml. of anhydrous benzene was added in one portion. Heating under reflux was continued overnight after which the reaction mixture was poured on a mixture of ice and dilute hydrochloric acid. The organic layer was removed and the aqueous layer extracted three times with ether. The combined extract was washed with 10% sodium hydroxide, twice with water and dried over anhydrous magnesium sulfate. The ether was then removed and the residual oil was distilled under reduced pressure. The fraction distilling between 61-62° at 0.3 mm. yielded 7.6 g.

of the starting 2-fluorobenzoyl chloride, another fraction distilling between 155-156° at 0.3 mm. yielded 8.7 g. of a colorless oil which crystallized on standing; m.p. 51-51.5°. An infrared spectrum of this crystalline material did not possess a peak at 1664 cm.$^{-1}$ which shows the absence of a carbonyl group. No further identification of this material was attempted.

2-(2-Naphthylmethyl)-2'-fluorobenzophenone (Xa) (35).

A Grignard reagent prepared in 150 ml. of anhydrous ether from 1.22 g. (0.05 g.-atom) of magnesium turnings and 11.8 g. (0.04 mole) of 2-(2-naphthylmethyl)bromobenzene was transferred slowly under nitrogen pressure to a stirred boiling solution containing 6.36 g. (0.04 mole) of o-fluorobenzoylchloride in 200 ml. of anhydrous benzene. The ether was allowed to distill off and an additional 150 ml. of dry benzene was added slowly. The mixture was stirred and refluxed for three hours at 75° and then allowed to cool to room temperature. The complex was decomposed with 250 g. of ice, 150 ml. of water and 40 ml. of concentrated sulfuric acid. After standing overnight, the organic layer was removed and the aqueous layer extracted once with benzene. The combined extract was washed twice with 10% sodium carbonate solution, twice with water, dried over anhydrous magnesium sulfate, concentrated and the residue distilled under reduced pressure. The fraction that redistilled between

195-199° at 0.1 mm. was collected as viscous yellow oil; yield 5.07 g. (37.2%).

An analytical sample was prepared by repeated recrystallization of the crude ketone from 95% ethanol. Large, white hexagonal crystals were obtained, m.p. 73-74°.

Anal. Calcd. for $C_{24}H_{17}OF$: C, 84.69; H, 5.03; F, 5.58
Found: C, 84.54; H, 5.18; F, 5.72

2-(2-Naphthylmethyl)-2'-chlorobenzophenone (Xb) (35).

A Grignard reagent prepared in 150 ml. of anhydrous ether from 1.22 g. (0.05 g.-atom) of magnesium turnings and 11.8 g. (0.04 mole) of 2-(2-naphthylmethyl)bromobenzene was transferred slowly under nitrogen pressure to a stirred boiling solution containing 6.61 g. (0.04 mole) of o-chlorobenzoyl chloride in 200 ml. of anhydrous benzene. The ether was allowed to distill off and an additional 150 ml. of dry benzene was added slowly. The mixture was stirred and refluxed for three hours at 75° and then allowed to cool to room temperature. The complex was decomposed with 250 g. of ice, 150 ml. of water and 40 ml. of concentrated sulfuric acid. After standing overnight, the organic layer was removed and the aqueous layer extracted once with benzene. The combined extract was washed twice with 10% sodium carbonate solution, twice with water, dried over anhydrous magnesium sulfate. The crude ketone which separated on concentration as yellow crystals was washed with cold 95%

ethanol, m.p. 104-107°; yield 5.4 g. (37.8%).

An analytical sample was prepared by repeated recrystallization of the crude ketone from 95% ethanol. White crystals were obtained, m.p. 110°.

Anal. Calcd. $C_{24}H_{17}OCl$: C, 80.78; H, 4.80; Cl, 9.94.
Found: C, 80.41; H, 4.91; Cl, 10.16.

2-(2-Naphthylmethyl)-2'-chloro-5'-methylbenzophenone (Xe) (35).

A Grignard reagent prepared in 150 ml. of anhydrous ether from 1.22 g. (0.05 g.-atom) of magnesium turnings and 8.95 g. (0.03 mole) of 2-(2-naphthylmethyl)bromobenzene was transferred slowly under nitrogen pressure to a stirred boiling solution containing 5.82 g. (0.03 mole) of 2-chloro-5-methylbenzoylchloride in 200 ml. of anhydrous benzene. The ether was allowed to distill off and an additional 150 ml. of dry benzene was added slowly. The mixture was stirred and refluxed for four hours at 75° and then decomposed with 250 g. of ice, 150 ml. of water and 40 ml. of concentrated sulfuric acid. After standing overnight, the organic layer was removed and the aqueous layer extracted once with benzene. The combined extract was washed twice with 10% sodium carbonate solution, twice with water, dried over anhydrous magnesium sulfate, concentrated and the residue distilled under reduced pressure. The fraction redistilled between 224-226.5° at 0.1 mm. was collected

as viscous yellow oil; yield 4.18 g. (60.4%).

An analytical sample was prepared by repeated recrystallization of the crude ketone from 95% ethanol. White needles were obtained, m.p. 97-98°.

Anal. Calcd. for $C_{25}H_{19}OCl$: C, 80.96; H, 5.16; Cl, 9.56.
Found: C, 81.55; H, 5.31; Cl, 9.52.

12-(2-Fluorophenyl)benz[a]anthracene (XIa (44).

A mixture of 0.5 g. (0.00147 mole) of 2-(2-naphthylmethyl)-2'-fluorobenzophenone, 30 ml. of glacial acetic acid and 15 ml. of 48% hydrobromic acid was sealed in a Carius tube and heated for seven hours at 180° in a Carius furnace. The tube was allowed to cool to room temperature and the content was made basic with a 10% solution of sodium hydroxide. This aqueous solution was extracted with 300 ml. of benzene. The benzene solution was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed until only a dark yellow oil remained. The residual oil was dissolved in 95% ethanol. This was clarified with charcoal and then allowed to cool. The hydrocarbon crystallized as light yellow needles, m.p. 122-125°; yield 0.37 g. (78.7%). To remove the traces of coloring materials, the yellow needles were dissolved in petroleum ether[5] and passed

[5] The petroleum ether used throughout this investigation had a boiling point of 30-60°.

through a column packed with alumina. A colorless viscous oil resulted after evaporation which was crystallized from 95% ethanol. Colorless crystals, m.p. 127-128°, were obtained.

Anal. Calcd. for $C_{24}H_{15}F$: C, 89.42; H, 4.69; F, 5.89.
Found: C, 88.93; H, 4.75; F, 5.90.

12-(2-Chlorophenyl)benz [a] anthracene (XIb) (44).

A mixture of 0.5 g. (0.00147 mole) of 2-(2-naphthylmethyl)-2'-chlorobenzophenone, 30 ml. of glacial acetic acid and 15 ml. of 48% hydrobromic acid was sealed in a Carius tube and heated for seven hours at 180° in a Carius furnace. The tube was allowed to cool to room temperature and the content was made basic with a 10% solution of sodium hydroxide. This aqueous solution was extracted with 300 ml. of benzene. The benzene solution was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed until only a dark yellow oil remained. The residual oil was dissolved in 5 ml. of ether, mixed with a little alumina. The ether was evaporated and the dry mixture of alumina and organic material was chromatographed on an alumina column wet packed with petroleum ether. Petroleum ether was used as the eluent to remove the blue fluorescent fraction. Concentration of the petroleum ether solution yielded a small amount of a colorless oil which, on standing, crystallized as white crystals. The hydro-

carbon was recrystallized from 95% ethanol, as white crystals, m.p. 144-145°; yield 0.43 g. (90.5%).

Anal. Calcd. for $C_{24}H_{15}Cl$: C, 85.07; H, 4.47; Cl, 10.46.
Found: C, 84.74; H, 4.29; Cl, 10.62.

12-(2-Chloro-5-methylphenyl)-7,12-dihydrobenz[a]anthracene (XVI) (44).

A mixture of 0.5 g. of (0.00135 mole) 2-(2-naphthylmethyl)-2-chloro-5-methylbenzophenone, 30 ml. of glacial acetic acid and 15 ml. of 48% hydriodic acid was sealed in a Carius tube and heated for fifteen hours at 180° in a Carius furnace. The tube was allowed to cool to room temperature. Fine white needles appeared which were collected and recrystallized from 95% ethanol. The yield of the hydrocarbon was 0.29 g. (61%); m.p. 149-150°.

Anal. Calcd. for $C_{25}H_{19}Cl$: C, 84.61; H, 5.40; Cl, 9.99
Found: C, 84.16; H, 5.45; Cl, 10.29.

SUMMARY

SUMMARY

1. An improved synthetic route to prepare 2-bromonaphthalene is secured.

2. Three methods utilizing Grignard reagents were approached in order to prepare 2-(2-naphthylmethyl)-2'-halobenzophenones necessary for the study to obtain 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone. The only successful preparative method for the above ketones was found to be the reaction between a Grignard reagent and an acid halide. This procedure was applied to the preparation of the following ketones: 2-(2-naphthylmethyl)-2'-fluorobenzophenone (Xa), 2-(2-naphthylmethyl)-2'-chlorobenzophenone (Xb), and 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone (Xc).

3. Investigation of the sealed tube method revealed that the above ketones could be cyclized at 180° with a mixture of hydrobromic and acetic acids in seven hours. Under these conditions 12-(2-fluorophenyl)benz [a] anthracene (XIa), 12-(2-chlorophenyl)benz [a] anthracene (XIb), and 12-(2-chloro-5-methylphenyl)-7,12-dihydro-benz [a] anthracene (XVI) were obtained. Further study showed that 12-(2-chloro-5-methylphenyl)-7,12-dihydro-benz [a] anthracene (XVI) could be

obtained in a much better yield when the above procedure was altered by using a mixture of hydriodic and acetic acids.

4. In order to obtain 2-methyldibenzo[a,l]pyrene (II) 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz[a] anthracene (XVI) was reacted with potassium hydroxide and quinoline. Although the results were not definite the qualitative tests and the ultraviolet and infrared spectra suggest an intermediate dihydro compound XVII.

5. The ultraviolet and infrared spectra of six new compounds were recorded.

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ABSTRACT.

In a recent study of cyclodehydrogenation reactions of potential carcinogenic or carcinolytic hydrocarbons Zajac pointed out that ring closure of 12-(3-methylphenyl)-benz[a]anthracene might take place at either of the two ortho positions of the phenyl ring. These positions are not equivalent with respect to the methyl group and ring closure might yield either 2-methyldibenzo[a,l]pyrene or 4-methyldibenzo[a,l]pyrene or both.

The objectives of the present investigation are to study possibilities and methods to prepare 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone in a sufficient yield so that a study of the cyclization reaction under a variety of conditions can be made in order to prepare 2-methyldibenzo[a,l]pyrene.

During the course of the investigation an improved synthetic route to prepare 2-bromonaphthalene was secured.

Three methods utilizing Grignard reagents were approached in order to prepare 2-(2-naphthylmethyl)-2'-halobenzophenones necessary for the study to obtain 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone. The only successful preparative method for the above

ketones was found to be the reaction between a Grignard reagent and an acid halide. This procedure was applied to the preparation of the following new ketones: 2-(2-naphthylmethyl)-2'-fluorobenzophenone, 2-(2-naphthylmethyl)-2'-chlorobenzophenone, and 2-(2-naphthylmethyl)-2'-chloro-5'-methylbenzophenone.

Investigation of the sealed tube method revealed that the above ketones could be cyclized at 180° with a mixture of hydrobromic and acetic acids in seven hours. Under these conditions the new compounds 12-(2-fluorophenyl)benz[a]anthracene, 12-(2-chlorophenyl)benz[a]anthracene, and 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz[a]anthracene were obtained. Further study showed that 12-(2-chloro-5-methylphenyl)-7,12-dihydro-benz[a]anthracene could be obtained in a much better yield when the above procedure was altered by using a mixture of hydriodic and acetic acids.

In order to obtain 2-methyldibenzo[a,l]pyrene 12-(2-chloro-5-methylphenyl)-7,12-dihydrobenz[a]anthracene was reacted with potassium hydroxide and quinoline. Although the results were not definite the qualitative tests and the ultraviolet and infrared spectra suggest an intermediate dihydro compound.

The ultraviolet and infrared spectra of six new compounds were recorded.