I. REACTIONS OF NON-ACTIVATED ARYL HALIDES WITH STRONG BASIC AND NUCLEOPHILIC AGENTS

II. EVIDENCE FOR CYCLOHEXYNE AS AN INTERMEDIATE IN THE COUPLING REACTION OF PHENYLLITHIUM WITH 1-CHLOROCYCLOHEXENE

III. REACTIONS OF NON-ACTIVATED ARYL HALIDES WITH STRONG BASES AT HIGH TEMPERATURES

IV. THE SYNTHESIS OF SOME FOUR-MEMBERED RING COMPOUNDS

Thesis by

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In Partial Fulfillment of the Requirements

For the Degree of

Doctor of Philosophy

California Institute of Technology

Pasadena, California

1958

To my wife

ACKNOWLEDGEMENTS

The author wishes to express sincere appreciation to Professor John D. Roberts for his invaluable help and encouragement during the course of this work and in the preparation of this thesis.

Acknowledgement is due also to the Institute for scholarships, to the National Science Foundation for a fellowship and to the Du Pont Company for a summer grant.

The author is indebted to Dr. Robert Krall for many helpful discussions and collaboration in part of the work reported in Part IV.

ABSTRACT

Part I. Previous studies have shown that non-activated aryl halides are aminated by alkali amides in liquid ammonia by the way of a benzyne intermediate. Nucleophilic substitution products are formed with some strong bases and aryl halides in liquid ammonia, provided alkali amides are present. A study of the mechanism and the scope of such reactions has been made. It has been shown that the first step is the formation of benzyne through reaction of alkali amide and aryl halide. The intermediate is then attacked competitively by the various nucleophilic species (including amide ion) present in solution. Thus, when o- and p-bromotoluene were treated with sodium phenylacetylide in liquid ammonia, the product contained, in addition to aromatic amines, approximately equimolar amounts of 2- and 3-methyldiphenylacetylene and 3- and 4-methyldiphenylacetylene respectively. Benzyne has been found to be attacked by good nucleophiles. The ease of attack of nucleophilic species cannot be directly correlated either with base strength or nucleophilicity as measured in simple S_N2 reactions.

Part II. Cyclohexanone-2-^{14}C has been converted to 1-phenylcyclohexene by way of 1,1-dichlorocyclohexane and 1-chlorocyclohexene. Oxidation of a benzenesulfenyl chloride derivative of 1-phenylcyclohexene gave benzoic acid which contained 23% of the radiocarbon present in 1-phenylcyclohexene. This is consistent with an elimination-addition mechanism, in which 1-chlorocyclohexene loses a molecule of

hydrogen chloride to give cyclohexyne as a reaction intermediate.

Part III. The reaction of p-chloro, p-bromo and p-iodotoluene with potassium anilide in refluxing aniline gave approximately equimolar mixtures of m- and p-tolylphenylamine. These product compositions are consistent with a benzyne (elimination-addition) mechanism.

Part IV. 1,1-Difluoro-2-piperidino-3-phenyl-2-cyclobutene (I) has been obtained by treating 1,1,2-trifluoro-2-chloro-3-phenylcyclobutane with piperidine. Treatment of I with concentrated sulfuric acid gave 2-piperidino-3-phenyl-2-cyclobutenone.

TABLE OF CONTENTS

PART PAGE

PART PAGE

PART I.

REACTIONS OF NON-ACTIVATED ARYL HALIDES WITH STRONG BASIC AND NUCLEOPHILIC AGENTS

CHAPTER I

INTRODUCTION

In contrast with aliphatic halides, aryl halides that do not contain strongly electron-attracting substituents show little tendency to undergo nucleophilic substitution. However, they may be made to undergo nucleophilic substitution either by employing very strongly basic nucleophilic agents, such as metallic amides and organolithium compounds, or by carrying out the reactions at high temperatures.

It has been found that such substitutions are often accompanied by rearrangement.*

Some of the most striking features of this type of rearrangement reaction are:

1) With substituted aryl halides, the orientation effects are independent of those influences which are usually associated with nucleophilic or electrophilic substitutions in aromatic nuclei.

2) Neither the starting materials nor the products are isomerized under the reaction conditions.

3) The entering groups have never been found farther than a carbon atom away from the position occupied by the leaving halogen.

4) In contrast with aliphatic nucleophilic substitution,

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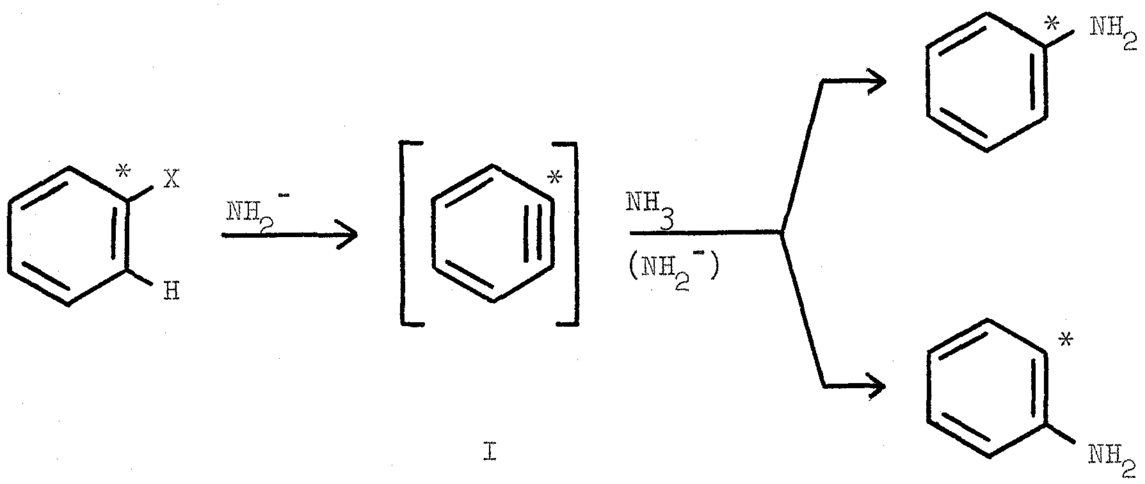
*For a complete survey of the literature up to 1956, see Ref. 1, 2 and 3.

in which the order of ease of displacement is I>Br>Cl>F,[4] and with the nucleophilic displacement of activated aryl halides, in which the order of ease of displacement generally is F > Cl > Br,[5] the relative reactivities of unsubstituted halobenzenes with potassium amide in liquid ammonia are Br > I > Cl >> F.[6]

5) There must be at least one hydrogen atom *ortho* to the halogen.

6) The reactions are very rapid with metallic amides in liquid ammonia.

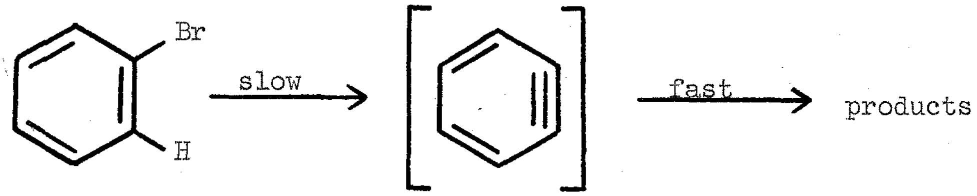
In order to elucidate the mechanism of such a reaction, Roberts and co-workers[2,7] treated chloro- and iodobenzene-1-^{14}C with potassium amide in liquid ammonia and obtained aniline in which the $-NH_2$ group was attached to the 2-position to the extent of 51.8% and 53.0% respectively. On the basis of these results, they proposed an elimination-addition mechanism, in which the aryl halide lost the elements of hydrogen halide to give the neutral benzyne intermediate (I). In this intermediate, the 1- and 2-positions have become equivalent and a molecule of ammonia (or amine) can add at either end of the triple bond. The fact that aniline-2-^{14}C forms in slightly larger proportions than expected for a completely symmetrical intermediate was explained by assuming an isotope effect.



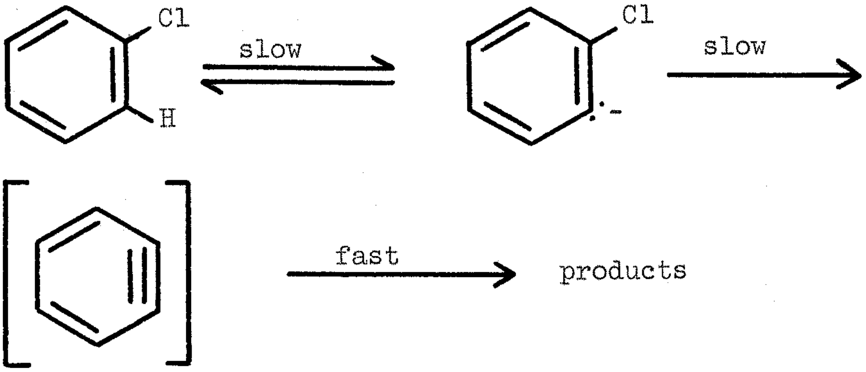
I

By a careful study of the rates of reaction and deuterium exchange of chloro- and bromobenzene-2-^{2}H with potassium amide in liquid ammonia, Roberts and co-workers[2] showed that the initial step in the reaction is the removal of a proton by an amide ion. In the case of bromobenzene the removal of a proton and of an halide ion is a concerted process (Mechanism 1), whereas with chlorobenzene, it is a stepwise process (Mechanism 2).

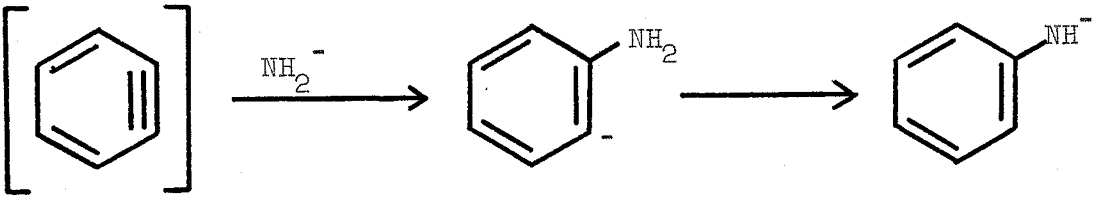
Mechanism 1



Mechanism 2



The amination of the benzyne intermediate appears to occur in two steps, the first being the addition of amide ion and the second being a fast abstraction of a proton from solvent or an intramolecular proton shift.



The direction of addition in substituted benzynes in general takes place in such a way as to provide the most favorable location of the negative charge with respect to the inductive effect of the substituents.

CHAPTER II

REACTION OF ARYL HALIDES WITH STRONG NUCLEOPHILIC AGENTS IN THE PRESENCE OF METALLIC AMIDES IN LIQUID AMMONIA

In 1936 Bergstrom and co-workers[6,8] reported that chlorobenzene, bromobenzene and iodobenzene react with sodium or potassium amide in liquid ammonia solution at -33° to give aniline in approximately 50% yield, along with smaller amounts of diphenylamine, triphenylamine, and p-aminobiphenyl. They also observed that potassium anilide and potassium diphenylamide under the same conditions failed to react with chlorobenzene and bromobenzene, unless a small amount of potassium amide was added. Similarly, potassium diphenylmethide and potassium triphenylmethide reacted very slowly with chlorobenzene in liquid ammonia solution at -33°; however, the slow addition of potassium amide caused a very marked increase in the rate of reaction. The reaction products were triphenylmethane and tetraphenylmethane, respectively. Potassium diphenylmethide was found to catalyze the reaction of potassium diphenylamide with chlorobenzene. The authors concluded that this was possibly due to the formation of amide ion through the following equilibrium:

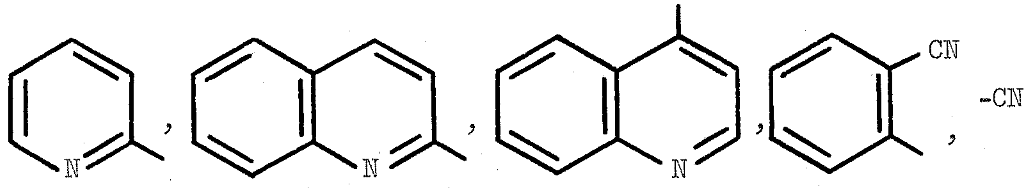
$$(C_6H_5)_2CHK + NH_3 \rightleftharpoons (C_6H_5)_2CH_2 + KNH_2$$

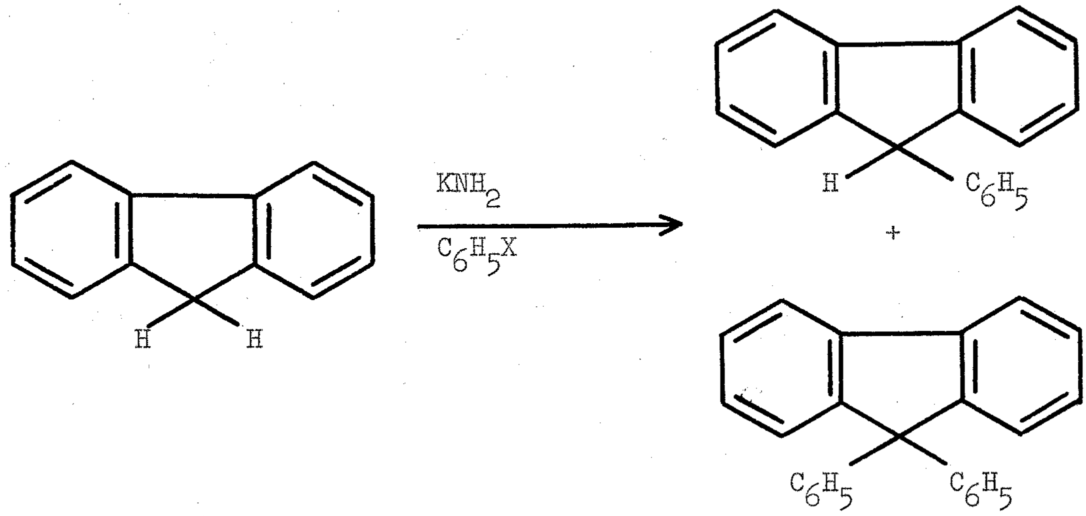
Since potassium diphenylmethide ($pK_a = 34$)[9] is a weaker base than potassium amide ($pK_a = 36$)[9], the equilibrium would be expected to lie far on the left.

Bergstrom and co-workers[10,11,12] have reported that quinaldine, lepidine, *alpha*-picoline, *o*-tolunitrile and fluorene react with chlorobenzene and bromobenzene in the presence of potassium amide in liquid ammonia in the following way:

$$RCH_3 \xrightarrow[C_6H_5X]{KNH_2} RCH_2(C_6H_5) + RCH(C_6H_5)_2 + (RC(C_6H_5)_3)$$

R =





Recently Levine and co-workers[13] have shown that ketones can be phenylated in liquid ammonia in the presence of potassium amide.

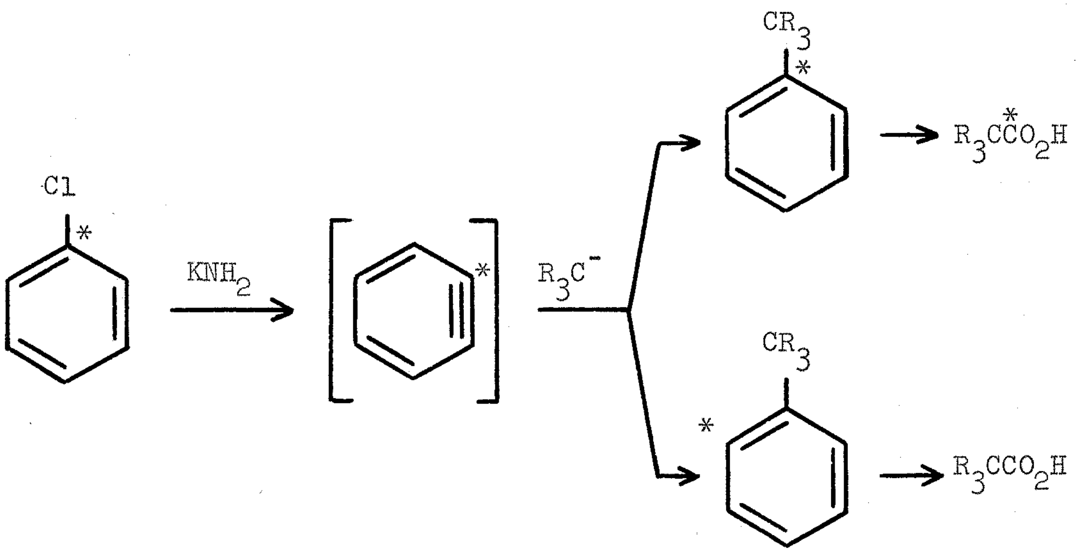
In all the above reactions aniline, diphenylamine and triphenylamine are always formed as side products. This might indicate that the metallic amides dehydrohalogenate the aryl halide molecules with the formation of benzyne, which is then attacked in a competitive manner by amide ions and other nucleophilic agents present in solution.

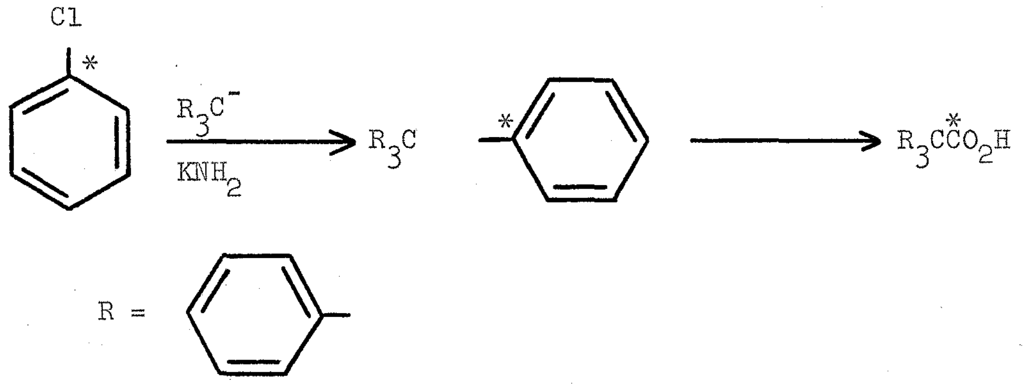
It was the purpose of this research to establish whether these reactions proceed via a benzyne intermediate and to determine whether nucleophilicity or base strength determines the ease of attack of a molecule or ion on benzyne.

CHAPTER III

MECHANISM OF THE REACTION BETWEEN STRONG NUCLEOPHILES AND ARYL HALIDES IN THE PRESENCE OF ALKALI AMIDES IN LIQUID AMMONIA

In order to determine whether the reaction between aryl halides with strong nucleophilic agents in the presence of potassium amide in liquid ammonia proceeds through a benzyne intermediate, the reaction between potassium triphenylmethide and chlorobenzene was first investigated. It was hoped that a way could be found to degrade the resulting tetraphenylmethane to triphenylacetic acid; by employing chlorobenzene-1-^{14}C, it could have been possible to determine whether the reaction proceeded through a benzyne intermediate or by direct substitution. In the first case the radioactivity of triphenylacetic acid would have been 87.5% of the radioactivity of tetraphenylmethane, in the second case it would have been the same as that of tetraphenylmethane.



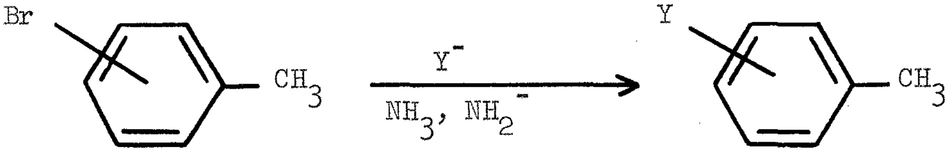


However, no successful degradation scheme could be worked out for conversion of tetraphenylmethane to triphenylacetic acid. In attempts to labilize one of the phenyl rings by substitution it was found that the only derivative of tetraphenylmethane that could be prepared in moderate yield was trinitrotetraphenylmethane, obtained by treating tetraphenylmethane with fuming nitric acid. All attempts to brominate, mercurate and mononitrate tetraphenylmethane led only to the recovery of unchanged starting material.

The reaction between sodium phenylacetylide and aryl halides was investigated next. Diphenylacetylene was obtained in 26% yield from the reaction of sodium phenylacetylide with bromobenzene. When p-bromotoluene was substituted for bromobenzene, the reaction product contained, besides small amounts of 3- and 4-methyldiphenylacetylene, large amounts of diaryl- and triarylamines. Attempts to determine the ratio of the two acetylenes by oxidative degradation did not lead to satisfactory results, for it was shown that the oxidation did not proceed quantitatively. In addition, no satisfactory method could be found to identify the resulting acids. Finally, the two acetylenes were separated quantitatively from the reaction product by elution with hexane through an alumina column and analyzed by means of infrared spectroscopy. The reaction between sodium phenylacetylide and o-bromotoluene was investigated in a similar way. In both cases the reaction appeared to proceed through a benzyne intermediate, the isomer ratios of the two acetylenes agreeing very closely with the isomer ratios obtained in the amination of the corresponding bromotoluenes.[3] The results are summarized in Table I.

TABLE I

Orientation in the Reaction of Bromotoluenes with Strong Nucleophilic Agents.



Isomer	Y	Ortho,%	Meta,%	Para,%
p-	$C_6H_5C{\equiv}C^-$	0	57	43
	NH_2^- [3,a]	0	62	38
o-	$C_6H_5C{\equiv}C^-$	49.3	50.7	0
	NH_2^- [3]	48.5	51.5	0

[a] p-Chlorotoluene was used instead of p-bromotoluene.

In order to determine whether nucleophilicity or base strength is the determining factor in the attack of an anion on benzyne, bromobenzene was treated with a variety of strong bases and nucleophilic agents in the presence of potassium amide in liquid ammonia. The results are summarized in Table II.

It is evident from the data of Table II that base strength is not the determining factor in the attack of a nucleophilic species on benzyne, for triphenylmethane, aniline, fluorene, acetophenone and thiophenol, whose pK_a values range from 33 to 8.4, give comparable yields of products.

Similarly, it is not possible directly to correlate nucleophilicity with ease of attack on benzyne, for while nucleophilicity decreases in the following order[4]: $C_6H_5S^- > I^- > CN^- > (CH_3)_3CO^- > C_6H_5O^-$, the ease of attack on benzyne appears to decrease in the following order: $C_6H_5S^- > C_6H_5O^- > I^-$, CN^- , $(CH_3)_3CO^-$.

Some of the most important factors which determine nucleophilicity are: the solvation energy of the base, the strength of its bond with the carbon atom that is being attacked, its steric effect, and if a change in charge state is involved, the electronegativity and polarizability of the reacting atoms.

The nucleophilic ability of the above-mentioned anions has been determined by using aliphatic halides as substrates, and since the transition state during the attack of an anion on benzyne is of a rather different nature from the transition

TABLE II

Reaction of Strong Bases and Nucleophilic Agents with Bromobenzene.

$$C_6H_5Br \quad + \quad R^- \quad \xrightarrow[NH_3]{NH_2^-} \quad C_6H_5R \quad + \quad Br^-$$

R-H	pK_a	Reaction time, hr.	RH/C_6H_5Br mole ratio	Yield %
Ammonia [6]	36	--	0.7 to 1.5	56
Triphenylmethane	33	4.25	0.33	39
Aniline[8]	27	--	--	57
Fluorene	25	5.0	0.5	58 [a]
Phenylacetylene	21	0.75	4.0	26
Acetophenone[13]	19	--	--	28
_t_-Butyl alcohol	18	0.75	2.0	0
Pyrrole	16.5	3.0	1.6	1
Phenol	10.0	2.5	1.0	4
Thiophenol	8.4	3.5	1.0	42
Hydrogen iodide		8.0	6.2	0
Hydrogen cyanide	9.1	4.0	1.8	0

[a] Combined yield of 9-phenyl- and 9,9-diphenylfluorene.

state in S_N2 reactions, it is perhaps not surprising that the order of reactivity of the attacking anions is different.

Solvation of a nucleophilic agent usually has a very important effect on both the energy and the entropy of activation. Since the solvent used in benzyne-type reactions was different from those employed in determining the nucleophilicity of bases toward alkyl halides, no direct comparison is possible.

The relative differences between the resonance energies of the transition states and the reactants may also be expected to play some part in determining the ease of attack of anions on benzyne.

Steric effects are probably of secondary importance, for the bulky triphenylmethide ion competes very well with amide ion; this, however, may be due to the fact that the smaller amide ion is very heavily solvated whereas the triphenylmethide ion is not.

CHAPTER IV

EXPERIMENTAL

Reaction of Strong Bases and Nucleophilic Agents with Aromatic Halides in the Presence of Alkali Amides in Liquid Ammonia.--The apparatus used for the reaction of strong bases and nucleophilic agents with aromatic halides in the presence of alkali amides in liquid ammonia consisted in part of a 1-l. three-necked flask fitted with a ball-and-socket sealed mechanical stirrer, a Dry Ice condenser and a tube extending to the bottom of the flask. A second, 2-l., three-necked flask was fitted with a ball-and-socket sealed mechanical stirrer, a short inlet tube and a Dry Ice condenser connected to a drying tower. The Dry Ice condenser attached to the 1-l. flask was connected by means of rubber tubing to a T-tube, through which flowed a very gentle stream of dry nitrogen.

After the apparatus had been thoroughly dried by flashing with a Bunsen burner and flushing with dry nitrogen, the two condensers were filled with acetone-Dry Ice, and the required amounts of liquid ammonia were condensed in the two flasks. All traces of water in the liquid ammonia were removed by adding small amounts of sodium or potassium metal until the blue color in the solution persisted for at least one minute. Sodium or potassium amide was prepared in both flasks by dissolving the required amounts of alkali metals in liquid ammonia and carefully adding a small amount of anhydrous ferric chloride. A very exothermic reaction took place and, after a few minutes, the blue color disappeared, indicating complete conversion of the metal to the corresponding amide. The appropriate compound containing an active hydrogen was carefully added to the 2-l. flask and 15-30 min. were allowed for the establishment of the following equilibrium, which in most cases was far to the right:

$$RH + MNH_2 \rightleftharpoons RM + NH_3$$

The aryl halide was then added dropwise to the 2-l. flask and the tubes attached to the two flasks were connected by means of rubber tubing. The alkali amide solution (or slurry, in the case of sodium amide) was forced slowly in small amounts from the 1-l. flask into the 2-l. flask by momentarily closing the outlet tube of the nitrogen stream. In a few cases, a Fisher Electric Hosecock, operated by a solenoid timer, was advantageously employed. After all the amide had been added, the reaction mixture was allowed to stand for varying amounts of time, then the unreacted bases were decomposed by careful addition of an excess of ammonium chloride or water.

The reaction flask was then opened to the atmosphere and the liquid ammonia was allowed to evaporate overnight. The residue was dissolved in an organic solvent and water and the products isolated as described in other sections of the Experimental Part.

Tetraphenylmethane.--Tetraphenylmethane was prepared by treating potassium triphenylmethide with a halobenzene in liquid ammonia in the presence of potassium amide.

The amounts of reagents employed and the reaction conditions are summarized in Table III.

After all the potassium amide had been added, the reaction mixture was allowed to stand for at least 30 min., then an excess of ammonium chloride was added. The solid residue was taken up in hot benzene and water. The organic layer was washed several times with dilute mineral acid and water and then filtered. The benzene was evaporated; the residue was washed several times with small amounts of ether and recrystallized from benzene-acetic acid.

4,4',4"-Trinitrotetraphenylmethane.--4,4',4"-Trinitrotetraphenylmethane was prepared by the method of Gomberg and Berger in 57% yield; m.p. 327-329°, lit.,[14] 330°.

Attempted Preparation of 4-Nitrotetraphenylmethane.--Four attempts were made to prepare 4-nitrotetraphenylmethane from tetraphenylmethane and nitric acid. The reaction conditions and the amounts of reagents employed are summarized in Table IV.

Recrystallization of the reaction products from various solvents, such as acetic acid, acetic anhydride, benzene, benzene-ligroin, acetic acid-acetic anhydride led only to the isolation of starting material.

TABLE III

Preparation of Tetraphenylmethane.

Trial	Materials used, mole				Reaction time, hr.	% yield
	$(C_6H_5)_3CK$	KNH_2	C_6H_5X	X		
1[a]	0.025	0.026	0.088	Cl	0.5	10
2	0.025	0.165	0.135	Cl	1.0	15-20
3	0.025	0.165	0.135	Cl	1.5	21
4	0.10	0.500	0.60	Cl	1.0	10
5[b]	0.10	0.500	0.60	Cl	2.0	40
6[c]	0.10	0.46	0.30	Br	2.75	25[d]
7[c]	0.10	0.46	0.30	Br	4.25	39[e]

[a] Potassium amide was added all at once to the reaction mixture.

[b] Potassium amide (0.10 mole) was added to the potassium triphenylmethide solution; chlorobenzene and potassium amide were slowly added alternatively in 0.2 mole portions to the reaction mixture.

[c] The addition of potassium amide was regulated by using a Fisher Electric Hosecock operated by a solenoid timer.

[d] m.p. 277-282°

[e] m.p. 275-281°; the yield of pure tetraphenylmethane, m.p. 282.5-283.5° was 31%.

TABLE IV

Attempted Preparation of 4-Nitrotetraphenylmethane.

Trial	Materials used, mmole.		Solv.	Temp., °C	% Recovery	Reaction time, hr.
	$(C_6H_5)_4C$	HNO_3				
1	0.78	50 ml. (67%)	--	85-90°	56	3
2	0.81	50 ml. (88%)	--	85-90°	62	0.17
3	1.00	1.1	Ac_2O	85-90°	69	0.5
4	4.30	17.2[a] (88%)	Ac_2O	130-140°	91	4.5

[a] Nitrous acid-free nitric acid, prepared by the method of Roberts et al.[15] was employed.

Attempted Preparation of 4-Bromotetraphenylmethane.--Two attempts were made to prepare 4-bromotetraphenylmethane from tetraphenylmethane and bromine in refluxing acetic acid-acetic anhydride solution. Ferric bromide and iron filings were used as catalysts. In both cases large amounts of unreacted tetraphenylmethane were recovered from the reaction mixture (80% and 87% respectively).

Attempted Mercuration of Tetraphenylmethane.--Tetraphenylmethane (1.0 g., 3.1 mmole) and mercuric acetate (15 g., 4.6 mmole) were dissolved in 250 ml. of refluxing acetic anhydride. The reaction mixture was refluxed for

24 hours, it was cooled and the solid which crystallized was collected and washed with several small portions of warm 20% acetic acid. Tetraphenylmethane, m.p. 280-284°, was recovered in 90% yield.

In a second trial, a tenfold excess of mercuric acetate was used. The reaction conditions were the same as the ones employed above. The only product that could be isolated from the reaction mixture was tetraphenylmethane, m.p. 283-285°, which gave no m.p. depression on admixture with an authentic sample.

Diphenylacetylene.--Diphenylacetylene was prepared by treating sodium phenylacetylide with a halobenzene in liquid ammonia in the presence of sodium amide. The amounts of reagents employed and the reaction conditions are summarized in Table V.

After the liquid ammonia had evaporated, the residue was dissolved in ether and water; the organic layer was washed several times with dilute hydrochloric acid and water. The ether was evaporated, and the unreacted phenylacetylene and halobenzene were distilled under reduced pressure.

In Trial #5, the product, after the phenylacetylene and bromobenzene had been removed, was dissolved in low-boiling petroleum ether (30-60°); a small amount of an insoluble blue compound was removed by filtration, and the solution was eluted through a column packed with 250 g. of

TABLE V

Preparation of Diphenylacetylene.

Trial	Materials used, mole					Reaction time, hr.	% Yield
	$C_6H_5C{\equiv}CH$	MNH_2, at start	$NaNH_2$ added	C_6H_5X	X		
1	0.30	0.25[a]	--	0.28	Cl	1	500 mg. of oil
2	0.18	0.15	--	0.18	Cl	1.5	100 mg. of oil
3	0.144	0.218	--	0.144	Cl	0.5	1.3 g. of oil
4	0.182	0.182	0.364	0.185	Br	0.75	--
5	0.93	0.935	0.615	0.236	Br	0.75	26%

[a] In this trial potassium amide was used. Since potassium phenylacetylide is insoluble in liquid ammonia, sodium amide was employed in all the other trials.

acid-washed alumina which had been activated by heating for 30 min. to a dull red color in a nitrogen atmosphere. Diphenylacetylene (11.0 g., 26%), m.p. 51-60°, was obtained. This compound was identified by comparison of its infrared and ultraviolet spectra with those of an authentic sample.

Attempted Reaction of *o*-Bromoanisole with Sodium Phenylacetylide in the Presence of Alkali Amides in Liquid Ammonia.-- An attempt was made to prepare anisylphenylacetylenes through the reaction of *o*-bromoanisole with sodium phenylacetylide in the presence of alkali amides in liquid ammonia. The amounts of reagents employed and the reaction conditions are summarized in Table VI.

TABLE VI

o-Bromoanisole with Sodium Phenylacetylide and Alkali Amides in Liquid Ammonia.

Trial	Materials used, mole			Reaction time, hr.
	$C_6H_5C{\equiv}CNa$	MNH_2	$C_6H_4Br(OCH_3)$	
1	0.437	0.152[a]	0.00875	1.5
2	0.437	0.091[b]	0.0875	0.5
3	0.437	0.182[b]	0.0875	0.5

[a] Sodium amide was used.

[b] Potassium amide was used.

In Trial 1, the product, after the starting materials had been removed by distillation, was eluted with carbon tetrachloride through an alumina column. A total of 19 fractions were collected. No definite compounds could be identified.

In Trials 2 and 3, only small amounts of tarry materials (0.5 g. and 0.7 g. respectively) were obtained.

Reaction of p-Bromotoluene with Sodium Phenylacetylide in the Presence of Potassium Amide in Liquid Ammonia.--Potassium amide (0.38 mole) in 300 ml. of liquid ammonia was slowly added during 1.5 hours to 1 l. of liquid ammonia containing 0.72 mole of sodium phenylacetylide and 0.26 mole of distilled p-bromotoluene. After all the potassium amide had been added, the mixture was allowed to stand 0.5 hr., then treated with an excess of ammonium chloride and the solvent allowed to evaporate overnight. The solid residue was dissolved in dilute hydrochloric acid and pentane. The organic layer was washed several times with dilute hydrochloric acid and water, then it was dried over anhydrous magnesium sulfate and the solvent was evaporated on a steam bath. The residue was distilled through a semimicro column[16] to 40° (2 mm.) to remove phenylacetylene and p-bromotoluene.

Since preliminary experiments had shown that the diarylamines present in the product could not be removed either by distillation through a 100-cm. spinning band column or by extraction with concentrated mineral acid, the residue after the distillation was eluted with hexane through a 3.4 x 30-cm. column packed with acid-washed alumina which had been activated by heating at 125° for 12 hours in vacuo. 3- and 4-Methyldiphenylacetylene were eluted completely with 3-l. of solvent. A succeeding 1-l. fraction contained no high-boiling residue. The solvent was evaporated; an infrared spectrum of the residue showed the presence of only 3- and 4-methyldiphenylacetylene contaminated with a small amount of p-bromotoluene. The product was again eluted with 1 l. of carbon tetrachloride through a 2 x 20-cm. column packed with alumina which had been activated by the above method to remove some silicon grease which contaminated the product. The column was then washed with ether, but only a small amount of silicon grease (less than 10 mg.) was obtained.

After the carbon tetrachloride was evaporated, 7.8 g. (15.8%) of a mixture of 3- and 4-methyldiphenylacetylene was obtained.

Ultraviolet Spectra of Benzoic, m- and p-Toluic Acid and their Sodium Salts.--All the spectra were taken in 95% ethanol with 1.00-mm. cells in a Cary Recording Spectrophotometer (Model 11 M).

Acid	λmax., mμ	log ϵ
Benzoic	228 255 (min.) 272.5 280	4.09 2.77 2.97 2.88
_m_-Toluic	231.5 258.5 279 286.5	4.05 2.75 2.09 2.04
_p_-Toluic	237	2.76
Salt (0.3 N. NaOH)		
Sodium benzoate	222.5 262 269 276	3.97 2.79 2.77 2.61
Sodium _m_-toluate	226.5 274 282	3.83 2.90 2.73
Sodium _p_-toluate	230.5 265.5 272.5	4.08 2.81 2.66

Oxidation of Diphenylacetylene to Benzoic Acid.--Various attempts were made to oxidize diphenylacetylene to benzoic acid. All the reactions were carried out at room temperature in pyridine solution. It was found that alkaline hydrogen peroxide was ineffective and that sodium permanganate solutions gave a 33% yield of benzoic acid, most of the starting material being converted to benzil. The benzil was further oxidized to benzoic acid with alkaline hydrogen peroxide but in most cases a large amount of benzilic acid was formed.

A satisfactory conversion of diphenylacetylene to benzoic acid was achieved by the following procedure: a solution of 1.5 g. of diphenylacetylene and 6 g. of sodium permanganate trihydrate in 150 ml. of pyridine was allowed to stand at room temperature for one hour, then 17 g. of 30% hydrogen peroxide was added slowly, followed by 1 g. of sodium hydroxide in 20 ml. of water. The solution was allowed to stand for one hour at room temperature, then 50 ml. of water and an excess of sodium bisulfite was added. The mixture was filtered and the precipitate was washed with methanol; the combined filtrates were made strongly alkaline and evaporated to dryness. The residue was dissolved in water, filtered, extracted with methylene chloride and acidified. Benzoic acid (1.45 g., m.p. 122-123.5°) was obtained. By extraction of the mother liquors with ether, 0.30 g. of benzoic acid, m.p. 122-123°, was obtained. Both fractions gave a negative test for benzilic acid.[17] The total yield of benzoic acid was 85%.

Oxidation of *m*- and *p*-Toluic Acid.--One g. of acid was dissolved in 50 ml. of water containing 2 g. of sodium hydroxide; the solution was heated on the steam bath and a solution of 4 g. of sodium permanganate trihydrate in 75 ml. of water was added. The whole was allowed to stand for one-half hour on the steam bath, then the permanganate was reduced with sodium bisulfite, the solution was made strongly alkaline, the manganese dioxide removed by filtration and the filtrate poured into an excess of hydrochloric acid. The acid was collected by filtration, washed with water, dissolved in base and again precipitated by addition of mineral acid. Isophthalic acid (0.95 g.) was obtained in 76% yield; terephthalic acid (1.1 g.) was obtained in 90% yield.

Separation of Isophthalic and Terephthalic Acid.-- Terephthalic acid (308 mg.) and isophthalic acid (163 mg.) were dissolved in 20 ml. of ammonium hydroxide. The excess ammonia was removed by heating; to the hot solution a solution of 1.2 g. of barium chloride in 5 ml. of water was added. The solution was allowed to stand on the steam bath for one-half hour, then it was cooled and allowed to stand for 12 hours. The precipitate was centrifuged and washed with 3 ml. of water. Both the solution and the residue were digested one hour with hydrochloric acid on the steam bath; the two acids were filtered and dried for one hour at 110°. Crude isophthalic acid (240 mg.) and terephthalic acid (211 mg.) were recovered.

2-, 3- and 4-Methylstilbene.--4-Methylstilbene was prepared by the method of Meerwein, Buchner and van Emster.[18] Thus from 70 g. (0.65 mole) of p-toluidine and 90 g. (0.61 mole) of cinnamic acid, there was obtained, after one recrystallization from ethanol, 33.0 g. (24%) of 4-methylstilbene; m.p. 118-120.5°, lit.,[19] 119.5°.

3-Methylstilbene was prepared by the same method in 17% yield; m.p. after two recrystallizations from methanol

40-45°, lit.,[19] 48°.

2-Methylstilbene was prepared by the same method in 5% yield; b.p. 125-140° (1 mm.), lit.,[19] 125° (2 mm.).

2-, 3- and 4-Methyldibromostilbene.--4-Methyldibromostilbene was prepared by the method of 'Organic Syntheses'.[20] From 33 g. (0.17 mole) of 4-methylstilbene was obtained 35 g. of crude product, m.p. 184-187°. Upon evaporation of the mother liquors, 1.0 additional g. of product m.p. 194-196.5°, was obtained. The yield of pure 4-methyldibromostilbene was 31.0 g. (51.5%); m.p. 199-200°, lit.,[19] 188°.

Anal. Calcd. for $C_{15}H_{14}Br_2$: C, 50.88; H, 3.98; Br, 45.14. Found: C, 50.78; H, 4.05; Br, 45.16.

3-Methyldibromostilbene was prepared by the same method in 70% yield; m.p. 182-183°.

Anal. Calcd. for $C_{15}H_{14}Br_2$: C, 50.88; H, 3.98; Br, 45.14. Found: C, 51.00; H, 4.04; Br, 45.12.

2-Methyldibromostilbene was prepared by the same method in 55% yield; m.p. 159-161°, lit.,[19] 159°.

2-, 3- and 4-Methyldiphenylacetylene.--4-Methyldiphenylacetylene was prepared by the method of 'Organic Syntheses'.[20] From 31 g. (0.0865 mole) of 4-methyldibromostilbene was obtained 16 g. (96%) of 4-methyldiphenylacetylene, m.p. 71.5-72.5°. After one sublimation in vacuo, the m.p. of the product was raised to 72.5-73.5°.

Anal. Calcd. for $C_{15}H_{14}$: C, 93.71; H, 6.29. Found: C, 93.74; H, 6.23.

3-Methyldiphenylacetylene was prepared by the same method in 76.5% yield from 3-methyldibromosilbene; b.p. 126-128° (2 mm.), m.p. 30-31°.

Anal. Calcd. for $C_{15}H_{12}$: C, 93.71; H, 6.29. Found: C, 93.78; H, 6.25.

2-Methyldiphenylacetylene was prepared by the same method in 92% yield from 2-methyldibromostilbene; b.p. 120-122° (2 mm.). The product was further purified by elution with hexane through a column packed with acid-washed alumina and very slow distillation at 70° in a short-path distillation apparatus.

Anal. Calcd. for $C_{15}H_{12}$: C, 93.71; H, 6.29. Found: C, 93.58; H, 6.43.

Ultraviolet spectra of Diphenylacetylene, 2-, 3- and 4-Methyldiphenylacetylene.--All the spectra were taken in 95% ethanol with 1.00-mm. cells in a Cary Recording Spectrophotometer (Model 11 M).

Compound	λ max., mμ	log ϵ
Diphenylacetylene	221.5	4.26
	264.5	4.35
	270.0	4.39
	279.5	4.51
	288.0	4.35
	296.5	4.45

Compound	$\lambda_{max.}$, mμ	log ϵ
2-Methyldiphenylacetylene	267.0	4.34
	282.5	4.49
	292.0	4.34
	301.5	4.40
3-Methyldiphenylacetylene	265.0	4.34
	273.5	4.39
	280.5	4.50
	290.0	4.34
	298.7	4.42
4-Methyldiphenylacetylene	267.0	4.37
	273.5	4.41
	280.5	4.53
	291.0	4.39
	300.0	4.48

Analysis of the Mixture of Acetylenes obtained by treating Sodium Phenylacetylide with *p*-Bromotoluene in the Presence of Potassium Amide in Liquid Ammonia.--An infrared spectrum of the mixture of acetylenes obtained by treating sodium phenylacetylide with *p*-bromotoluene in the presence of potassium amide in liquid ammonia showed the presence of *p*-bromotoluene, 3- and 4-methyldiphenylacetylene. The mixture was analyzed using a Perkin-Elmer (Model 21) Infrared Spectrophotometer at 12.28μ, 12.48 μ and 12.85μ. Calibration graphs were constructed from the absorptions of the pure constituents at each wavelength. Cells 0.1-mm. thick were used; the solvent used was carbon disulfide. The experimental data are summarized in Tables VII, VIII, and IX.

TABLE VII

Infrared Analyses of p-Bromotoluene, 3- and 4-Methyldiphenylacetylene.

Compound	Conc.[a]	-log I/I$_o$		
		12.28µ	12.48µ	12.85µ
p-Bromotoluene	119.0	0.050	1.0	0.039
	22.4	0.025	0.545	0.016
	10.3	0.011	0.271	0.005
3-Methyldiphenylacetylene	81.59	0.0443	0.0405	0.1739
	20.9	0.0119	0.0097	0.4237
	18.3	0.0097	0.0079	0.3840
	14.7	0.0079	0.0061	0.3072
	11.4	0.0057	0.0061	0.2418
	9.80	0.0057	0.0039	0.2125
4-Methyldiphenylacetylene	99.4	1.585	0.0829	0.0429
	22.5	0.5513	0.0218	0.0097
	14.2	0.3726	0.0137	0.0017
	12.8	0.2899	0.0057	0
	8.03	0.2132	0.0017	0

[a] mg. of compound per g. of solution.

TABLE VIII

Calibration Graphs for the Infrared Analyses of Mixtures of *p*-Bromotoluene, 3- and 4-Methyldiphenylacetylene.

Compound	Wavelength, μ	Intercepts[a]	Method of plotting
p-Bromotoluene	12.28	x=0, y=0 x=28, y=0.031	visual
	12.48	x=0, y=0 x=28, y=0.700	visual
	12.85	x=0, y=0.018	visual
3-Methyldiphenylacetylene	12.28	x=1.0, y=0 x=28, y=0.015	least squares
	12.48	x=0, y=0 x=28, y=0.0125	visual
	12.85	x=0, y=0.005 x=28, y=0.675	least squares
4-Methyldiphenylacetylene	12.28	x=0, y=0 x=28, y=0.735	visual[b]
	12.48	x=0.8, y=0 x=28, y=0.027	least squares[c]
	12.85	x=0, y=0 x=28, y=0.012	visual

[a] Conc. in mg. of sample/g. of solution was plotted along the x-axis, $-\log I/I_0$ along the y-axis.

[b] The point at x=22.5 was rejected because the % transmission of the solution was very low, 28.1%. The other points fell exactly on a line passing through the origin.

[c] The point at x=10.8 was rejected, for its average deviation was greater than three times the average deviation of the other points.

TABLE IX

Data for Analysis of Mixtures of p-Bromotoluene, 3- and 4-Methyldiphenylacetylene.

Sample	-log I/I_o			3- to 4-Methyldiphenylacetylene ratio
	12.28 μ	12.48 μ	12.85 μ	
Mixture 1[a]	0.4935	-	0.3778	49.4 : 50.6
Mixture 2[b]	0.4750	-	0.5751	61.2 : 38.8
Mixture 2[c]	0.3170	-	0.3893	61.2 : 38.8
Mixture 3[d]	0.343	0.125	0.354	57.1 : 42.9

[a] The actual 3- to 4-methyldiphenylacetylene ratio was 47.7 : 52.3.

[b] The actual 3- to 4-methyldiphenylacetylene ratio was 61.2 : 38.8.

[c] Analyzed after chromatography through an alumina column.

[d] Obtained by treating p-bromotoluene with sodium phenylacetylide. The mixture contained 15.0% by weight of p-bromotoluene.

Reaction of o-Bromotoluene with Sodium Phenylacetylide in the presence of Potassium Amide in Liquid Ammonia.--The reaction of o-bromotoluene with sodium phenylacetylide in the presence of potassium amide in liquid ammonia was carried out as with the p-isomer.

The crude product, after the starting materials had been removed by distillation, was eluted with hexane through a column containing 300 g. of activated alumina. Both 2- and 3-methyldiphenylacetylene were completely eluted with 2 l. of solvent. An infrared analysis showed that a small amount of o-bromotoluene and high-boiling aliphatic hydrocarbons (probably from the hexane) were present with the two acetylenes.

An elemental analysis showed that the bromine content of the mixture was 1.65%, which corresponds to 3.5% of o-bromotoluene.

A carbon disulfide solution of the mixture, containing 42.9 mg. of the mixture per g. of solution, was analyzed by infrared spectroscopy and by using the calibration curve for 3-methyldiphenylacetylene (see Table VIII) was found to contain 19.8 mg. of 3-methyldiphenylacetylene (46% of the mixture). Since none of the other components absorbed in the region of the spectrum used to determine the concentration of this compound, the error in the analysis was probably less than 2%. No direct determination of 2-methyldiphenylacetylene could be made, since the compound was not available in very pure form and no suitable peak in the infrared spectrum could be found.

An analysis of the infrared spectra of the three methyldiphenylacetylenes showed that their absorption in the 3.0-3.7 region of the infrared spectrum was practically identical. In order to determine the amounts of aliphatic hydrocarbons present in the mixture, solutions of 3-methyldiphenylacetylene and hexane in carbon disulfide in different proportions and at different concentrations were analyzed spectroscopically. It was found that when the 3-methyldiphenylacetylene to hexane ratio was 94.7 : 5.3, the spectra of the above mixture and the mixture obtained from the reaction of o-bromotoluene and phenylacetylene matched very closely. The amount of 2-methyldiphenylacetylene present in the mixture was determined by difference.

The results of the analysis are summarized below.

Compound	% Composition (by weight)
o-Bromotoluene	3.5
Aliphatic hydrocarbons	5.3
3-Methyldiphenylacetylene	46.2
2-Methyldiphenylacetylene	45.0

The 3- to 2-Methyldiphenylacetylene ratio determined from the above data was 50.7 : 49.3.

N-Phenylpyrrole.--N-Phenylpyrrole was prepared by the method of Allen, Gilbert and Young.[21]

Reaction of Potassium Pyrrolate with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--Potassium amide (0.45 mole) in 500 ml. of liquid ammonia was added during a period of three hours to a solution containing 0.5 mole of potassium pyrrolate and 0.311 mole of bromobenzene in 600 ml. of liquid ammonia. The solvent was allowed to evaporate slowly, so that the total volume of solution was kept approximately constant.

The reaction mixture, after all the potassium amide had been added, was allowed to stand 45 min., then an excess of ammonium chloride was added, followed by 500 ml. of ether. After the solvents had evaporated, the residue was dissolved in ether and water; the organic layer was washed five times with dilute hydrochloric acid and two times with distilled water. The ether was evaporated and the residue distilled through a semimicro column.[16] The results of the distillation are summarized below.

Frac.	Press., mm.	Temp., °C.	Wt., g.
1	6.6	28	
2	1	64-70	1.0
3	1	88-100	0.3

Fraction 2 solidified upon standing; its m.p. was 53-58°; after a sublimation and three recrystallizations from 70% ethanol the m.p. was raised to 59-60°. Its infrared and ultraviolet spectra were identical with those of N-phenylpyrrole; its m.p. showed no depression when mixed with an authentic sample of N-phenylpyrrole. The yield of crude N-phenylpyrrole was 1.0 g. (1.35%).

9-Phenyl-9-hydroxyfluorene.--9-Phenyl-9-hydroxyfluorene was prepared by the method of Ullmann and von Wusteinberger.[22]

9-Phenylfluorene.--9-Phenylfluorene was prepared by the method of Ullmann and von Wusteinberger.[22]

9-Phenyl-9-chlorofluorene.--9-Phenyl-9-chlorofluorene was prepared by the method of Kliegl.[23]

9,9-Diphenylfluorene.--9,9-Diphenylfluorene was prepared by the method of Bachmann.[24] Contrary to the reports of this author, the main product from the reaction of 9-phenyl-9-chlorofluorene with phenylmagnesium bromide was 9,9'-diphenyl-9,9'-bifluorenyl, m.p. 203-205°. Only 250 mg. of pure 9,9-diphenylfluorene, m.p. 219-222°, was obtained from treatment of 26 g. (0.094 mole) of 9-phenyl-9-chlorofluorene with 0.2 mole of phenylmagnesium bromide.

Reaction of 9-Fluorenyl Potassium with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--Potassium amide (0.53 mole) in liquid ammonia was added during five hours to a solution of 9-fluorenylpotassium (0.229 mole) and bromobenzene (0.45 mole) in 200 ml. of ether and 500 ml. of liquid ammonia. The reaction mixture was allowed to stand for 15 min., an excess of ammonium chloride was added, and the solvents were allowed to evaporate. The residue was dissolved in benzene and water; the organic layer was washed several times with dilute hydrochloric acid and water, then the solvent was evaporated.

Since the solubility of 9-phenylfluorene in 95% ethanol is much less than 50 mg./100 ml., while 9,9-diphenylfluorene is practically insoluble in the same solvent, the residue was digested with 100 ml. of 95% ethanol, cooled and washed with 100 ml. of 95% ethanol.

The residue was treated in the same way with two 500-ml. portions of 95% ethanol. The resulting product weighed 39.3 g.

An infrared spectrum of the product showed that the strong band at 2.95 μ of diphenylamine, was absent; the ultraviolet spectrum of the mixture showed a minimum at 297 mμ, where triphenylamine has a strong maximum.

The mixture was analyzed by means of ultraviolet spectroscopy. All the spectra were taken in benzene solution with 1.00-mm. cells in a Cary Recording Spectrophotometer

(Model 11M). The results of this analysis are summarized in Table X.

The yield of 9-phenylfluorene was 20.8-23.9 g. (37.6-42.0%), the yield of 9,9-diphenylfluorene was 13.0-15.6 g. (17.8-21.4%).

A sample weighing 2.9 g. was fractionally sublimed. The results are summarized below.

Frac.	Temp., °C.	Wt., g.	M.p., °C.
1	below 80	0.20	110-111
2	80-130	1.40	139-144
3	130-135	0.35	180-215
4	135-170	0.95	220-222
Residue (black tar)		less than 0.1	

Fraction 2 was recrystallized twice from ethanol; its m.p. was 148.5-149.0°. The ultraviolet spectrum of this compound was identical with that of 9-phenylfluorene; its m.p. showed no depression when mixed with an authentic sample of the above compound.

Fraction 4, after two recrystallizations from benzene, had a m.p. of 222-224°; its m.p. was not depressed when mixed with an authentic sample of 9,9-diphenylfluorene, and its ultraviolet spectrum was identical with the one of 9,9-diphenylfluorene.

Reaction of Potassium Thiophenolate with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--Potassium amide (0.44 mole) in 250 ml. of liquid ammonia

TABLE X

Analysis of a Mixture of Fluorene, 9-Phenylfluorene and 9,9-Diphenylfluorene.

Compound	Conc., mg./l.	Absorption, O.D. Units			Amount present in the mixture, mg.
		301.5mμ	305.0mμ	310.0mμ	
Fluorene	231	1.35	0.45	0.03	3.0
9-Phenylfluorene	378	0.62	1.37	0.14	21.8
9,9-Diphenylfluorene	464	0.53	0.45	1.13	12.7
Mixture	375	0.68	0.97	0.40	

was added during 3.5 hours to a solution of potassium thiophenolate (0.34 mole) and bromobenzene (0.346 mole) in 700 ml. of liquid ammonia. An excess of ammonium chloride was then added and the solvent was allowed to evaporate. The residue was dissolved in water and ether; the organic layer was washed first with dilute hydrochloric acid, then with a sodium hydroxide solution and finally with water. It was dried over anhydrous magnesium sulfate; the ether was evaporated and the residue distilled from a distilling flask. The results of this distillation are summarized below.

Frac.	Press., mm.	Temp., °C.	Wt., g.
1	3	120-128	7.9
2	3	128-136	10.4
3	3	136-144	11.5
4	3	144-164	11.6

The ultraviolet spectra of the first three fractions showed them to consist mostly of diphenyl sulfide; the infrared spectra showed the presence of diphenylamine. The infrared and ultraviolet spectra of fraction 4 were almost identical with the spectra of pure diphenyl disulfide.

The first three fractions were combined and analyzed for sulfur and nitrogen content.

Anal. Calcd. for $C_{12}H_{10}S$: S, 17.22. Found: S, 16.79; N, 0.55.

From the above data it was possible to calculate the composition of the combined first three fractions: diphenyl sulfide, 88.7%; diphenyl disulfide, 4.7%; diphenylamine, 6.6%. The amount of diphenyl sulfide present was 26.4 g. (0.141 mole, 41.5%).

A small amount of the combined first three fractions was oxidized at room temperature with 30% hydrogen peroxide in acetic acid. The resulting product melted at 125°, and showed no m.p. depression when mixed with an authentic sample of diphenyl sulfone. Its infrared and ultraviolet spectra were also identical with those of diphenyl sulfone.

The amount of sulfur present in fraction 4 was determined.

Anal. Calcd. for $C_{12}H_{10}S_2$: S, 29.38. Found: S, 21.14.

After standing for a few days in the refrigerator, fraction 4 solidified partially. The supernatant liquid was removed by filtration; 8 g. of a slightly yellow solid, m.p. 50-56°, was obtained. After two recrystallizations from ethanol, the m.p. of the solid was raised to 60°; no m.p. depression was obtained when the solid was mixed with an authentic sample of diphenyl disulfide. Its infrared and ultraviolet spectra were also identical with those of diphenyl disulfide.

Reaction of Potassium Phenolate with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--Potassium amide (0.64 mole) in 500 ml. of liquid ammonia was added to a mixture of 0.5 mole of potassium phenolate and

0.51 mole of bromobenzene in 500 ml. of liquid ammonia during 2.5 hours. The solution was allowed to stand for one hour, then the unreacted amides were carefully hydrolyzed with 20 ml. of water. Water (750 ml.) was added, and the mixture was extracted with two 300-ml. portions of benzene. The combined extracts were washed in order with 500 ml. of 2% sodium hydroxide, two 500-ml. portions of 2% hydrochloric acid and water. The organic layer was dried over anhydrous magnesium sulfate and distilled through a semimicro column.[16] The amount of bromobenzene recovered was 15 g. (0.095 mole).

The fraction boiling in the range of 76-108° (2 mm.; 3.8 g.) was shown to contain diphenylamine and diphenyl ether by ultraviolet and infrared spectroscopy. A ferric chloride test was positive, indicating the presence of phenol. The mixture was analyzed by means of ultraviolet spectroscopy in 95% ethanol. The results are summarized in Table XI.

The yield of diphenyl ether was 2.98 g. (3.5%, or 4.2% based on unrecovered bromobenzene).

Part of the product (1.2 g.) was dissolved in anhydrous ether and treated with anhydrous hydrogen chloride. Diphenylamine hydrochloride was removed by filtration; the filtrate was washed with a dilute sodium hydroxide solution to remove the phenol present and dried over anhydrous magnesium sulfate. The solvent was removed on the steam bath;

TABLE XI.

Analysis of a Mixture of Phenol, Diphenylamine and Diphenyl Ether.

Compound	Conc., mg./l.	Optical Density[a]		% in Mixture
		240 mμ	310 mμ	
Phenol	463	0.05	0.000	7.4[b]
Diphenyl-amine	437	1.07	1.45	14.2
Diphenyl ether	375	1.17	0.00	78.4
Mixture	254	0.73	0.120	

[a] Cells 1.00-mm. thick were employed. In those cases in which the values of the optical density were very low, cells 10.0-mm. thick were employed and the resulting value was divided by ten.

[b] By difference.

the residue was nitrated by the method of Matsumara.[25] The product, after four recrystallizations from acetic acid, melted at 194-196°; lit.,[25] 195-197°.

Attempted Reaction of Potassium *t*-Butoxide with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--A suspension of sodium amide (0.6 mole) in 250 ml. of liquid ammonia was added during 45 min. to a solution of potassium *t*-butoxide (1.2 mole) and bromobenzene (0.6 mole) in 750 ml. of liquid ammonia. The solution was allowed to stand one hour, the unreacted bases were decomposed by the dropwise addition of water and the solvent was allowed to evaporate. The residue was dissolved in ice-cold water and ether; the organic layer was washed three times with an ice-cold solution of 0.5% hydrochloric acid and then with a solution of potassium carbonate. The basic water extract was treated with bromine water, but no precipitate formed.

The ether layer was washed with cold water, dried over anhydrous magnesium sulfate and distilled. Seventeen g. of bromobenzene was recovered. The product that distilled next was diphenylamine. No trace of t-butyl phenyl ether could be detected.

Attempted Reaction of Sodium Cyanide with Bromobenzene in the Presence of Sodium Amide in Liquid Ammonia.--Anhydrous sodium cyanide (0.81 mole) and 0.45 mole of bromobenzene were added to 700 ml. of liquid ammonia. A suspension of 0.652 mole of sodium amide in liquid ammonia was added in small portions during four hours. The unreacted sodium amide was neutralized with an excess of ammonium chloride. The solvent was evaporated with a stream of nitrogen and the residue extracted with ether and water. The organic layer was dried over anhydrous magnesium sulfate, the solvent was evaporated and the residue distilled through a semimicro column. The results are summarized below.

Frac.	Press., mm.	Temp., °C.	Wt., g.	Material[a]
1	9	39-46	14.8	Bromobenzene
2	9	58-68	0.2	
3	9	69-70	5.0	Aniline
4	1	88-105	0.6	
5	1	105-107	8.0	Diphenylamine
6	1	108-131	1.5	
7	1	131-139	2.5[b]	Triphenylamine
Residue (brown viscous oil)			7.0	

[a] Determined by infrared analysis.

[b] The distillation had to be interrupted because the distillate solidified in the condenser.

The residue was refluxed with 100 ml. of ethanol containing 10.0 g. of potassium hydroxide for 60 hours. The solution was evaporated to dryness under reduced pressure. The residue was dissolved in water, extracted with ether, acidified and again extracted with ether. Evaporation of the ethereal solution gave less than 10 mg. of a yellow oil.

Attempted Reaction of Potassium Iodide with Bromobenzene in the Presence of Potassium Amide in Liquid Ammonia.--A solution of 0.436 moles of potassium amide in 500 ml. of liquid ammonia was added during eight hours to a solution of 450 g. (2.71 mole) of anhydrous potassium iodide and 79 g. (0.5 mole) of bromobenzene. The total volume of solution in the reaction flask was maintained constant by allowing the solvent to evaporate slowly. The unreacted base was neutralized with an excess of ammonium chloride, the solvent was evaporated and the residue was extracted with water and ether. The organic layer was washed several times with dilute mineral acid and water, dried over anhydrous magnesium sulfate and distilled through a semimicro column. The results are summarized below.

Frac.	Press., mm.	Temp., °C.	Wt., g.	n_D^{20}
1	753	34		
2	18-19	51	33.5	1.5592
3	10	above 100		

An infrared spectrum of fraction 2 showed the total absence of all the bands characteristic of iodobenzene.

PART II

EVIDENCE FOR CYCLOHEXYNE AS AN INTERMEDIATE IN THE COUPLING REACTION OF PHENYLLITHIUM WITH 1-CHLOROCYCLOHEXENE

INTRODUCTION

About fifty years ago, Markownikow[26,27,28] treated 1,2-dibromocycloheptene with alcoholic potassium hydroxide and obtained a hydrocarbon that analyzed for C_7H_{10}. This compound was very easily oxidized by air, reacted with sodium giving a dark powder, reacted with bromine with evolution of hydrogen bromide, and when treated with hydrogen iodide gave an oil. The author proposed that the compound he had obtained was cycloheptyne.

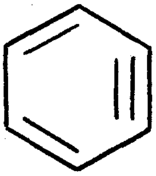
A few years later Favorsky and Boshowsky[29] attempted to prepared cyclohexyne from 1,2-dibromocyclohexene. This dihalide was unreactive toward zinc, copper, silver, and calcium; when treated with sodium, however, it gave dodecahydrotriphenylene and an unidentified substance $(C_6H_8)_4$. Similarly, when 1,2-dibromocyclopentene was treated with sodium, it gave <u>tris</u>-trimethylenebenzene. However, when 1,2-dibromocycloheptene was treated with sodium, 1,2-cycloheptadiene was obtained.[30,31] The structure of this compound was derived from the fact that it gave pimelic acid upon treatment with potassium permanganate and adipic acid upon treatment with ozone. Treatment of 1-chloro-2-bromocycloöctene with sodium gave cyclooöctyne.[32] It was later shown, however, that the compound obtained this way was contaminated with olefins.[33]

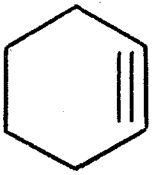
Cycloheptadecyne[34] and cyclopentadecyne-10-one[35] have been obtained by bromination of the corresponding olefins, followed by treatment of the dibromides with alcoholic potassium hydroxide. Blomquist and co-workers[36,37,38] obtained pure cycloöctyne, cyclononyne and cyclodecyne by treating the cyclic 1,2-diketones with hydrazine and oxidizing the resulting dihydrazones with mercuric oxide.

DISCUSSION

In acetylenic compounds of structure RC≡CR', the two carbon atoms and the two groups attached to them are co-linear. In a 6-membered carbocyclic ring containing a triple bond, the two triply bonded carbon atoms and the two directly attached carbon atoms can hardly exist in a linear configuration. In any case such a molecule would possess a very large amount of strain and for this reason the existence of such molecules was considered to be impossible until recently.

Roberts and co-workers have recently shown that benzyne (I),[2,3,7] a compound having a formal triple bond in a 6-membered ring, is an intermediate during the reaction of aryl halides with very strong bases.

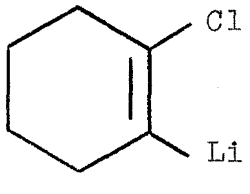

I


II

Presumably the angle strain at the triple bond in benzyne cannot be much relieved by distortion of the other ring bond angles without some loss of resonance energy of the benzene ring. The cyclohexyne (II) ring system should not suffer from this disadvantage and therefore might be less strained. Thus, by analogy, cyclohexyne might at least be capable of existence as an unstable reaction intermediate.

On this basis it appears possible that 1-halocyclohexenes, when treated with very strong bases, might lose a molecule of hydrogen halide and yield cyclohexyne (II). This compound could then react further with any nucleophilic agent present or it might polymerize, as sometimes it appears to be the case with benzyne.[39]

For this reason, the reactions of 1-chlorocyclohexene with strong bases were investigated. In 1944, Wittig and Harborth[40] reported that this halide, when treated with phenyllithium at 100°, produced 1-phenylcyclohexene and biphenyl. These authors assumed that the first step in this reaction was a metal-hydrogen interchange to give the intermediate III.



III

III, which was supposed to possess activated chlorine, was postulated to react immediately with phenyllithium to give 1-phenylcyclohexene.

The formation of biphenyl was assumed to proceed by metal exchange between 1-phenylcyclohexene and phenyllithium, followed by removal of the elements of lithium hydride. The resulting 1-phenyl-1,3-cyclohexadiene was then thought to undergo a further metal exchange reaction with phenyllithium, followed again by elimination of lithium hydride with formation of biphenyl.

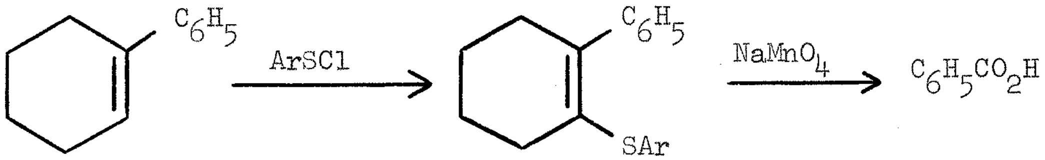
Recently, Jenny and Roberts[41] have shown that the formation of biphenyl through the coupling of fluorobenzene with phenyllithium probably proceeds by way of a benzyne intermediate and because of the similarity of this reaction to the coupling of 1-chlorocyclohexene it seemed reasonable that cyclohexyne might be the reaction intermediate.

When an attempt was made to repeat Wittig's coupling reaction between phenyllithium and 1-chlorocyclohexene at 100°, only very small amounts of 1-phenylcyclohexene were obtained. However, when the reaction temperature was increased from 100° to 150°, 1-phenylcyclohexene was obtained in yields ranging from 13% to 28%. Other nucleophilic displacement reactions were less successful. For example, when 1-chlorocyclohexene was treated with sodium or potassium amide in liquid ammonia, a very fast reaction took place and a very high-boiling product was obtained from which, however, no definite compounds could be isolated. 1-Chlorocyclohexene did not react with sodium phenylacetylide in liquid ammonia solution. Concentrated sulfuric acid reacted smoothly with 1-chlorocyclohexene with formation of cyclohexanone; on the other hand, sodium ethoxide proved to be quite unreactive. In fact, after heating this compound with a two-fold excess of sodium ethoxide in ethanol for 21 hours at 220°, 61% of starting material was recovered. At 340° the reaction went nearly to completion in one hour, but no definite compounds could be isolated, for the reaction product was heavily contaminated with condensation products of ethanol which arose from a Guerbet-type reaction of ethanol.

From the above results, it can be seen clearly that the behavior of 1-chlorocyclohexene towards strong bases somewhat parallels the behavior of non-activated aryl halides. Since aryl halides react with the above reagents via a benzyne intermediate, it is possible that the former compound also reacts via an acetylenic intermediate.

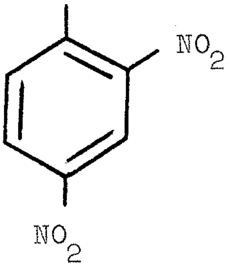
In an attempt to determine whether cyclohexyne was an intermediate in the phenyllithium coupling reaction, 1-chlorocyclohexene which had been prepared from cyclohexanone-2-^{14}C was treated with phenyllithium. Assuming kinetic isotope effects to be negligible, the 1-chlorocyclohexene so obtained should be an exactly equimolar mixture of 1-chlorocyclohexene-1-^{14}C (IVa) and 1-chlorocyclohexene-6-^{14}C (IVb) since there are two equally probable ways for hydrogen chloride to split out of the intermediary 1,1-dichlorocyclohexane-2-^{14}C in the reaction of the ketone with phosphorus pentachloride. If the coupling reaction proceeded via the acetylenic intermediate, the amount of 1-phenylcyclohexene-1-^{14}C formed should have been 25% of the total amount of 1-phenylcyclohexene-x-^{14}C, assuming no isotope effects (Mechanism I). On the other hand, if the reaction proceeded by direction substitution (Mechanism II), or through the steps suggested by Wittig and Harborth (Mechanism III), no 1-phenylcyclohexene-1-^{14}C should have formed.

The 1-phenylcyclohexene-x-^{14}C obtained in the reaction was degraded by the following scheme:



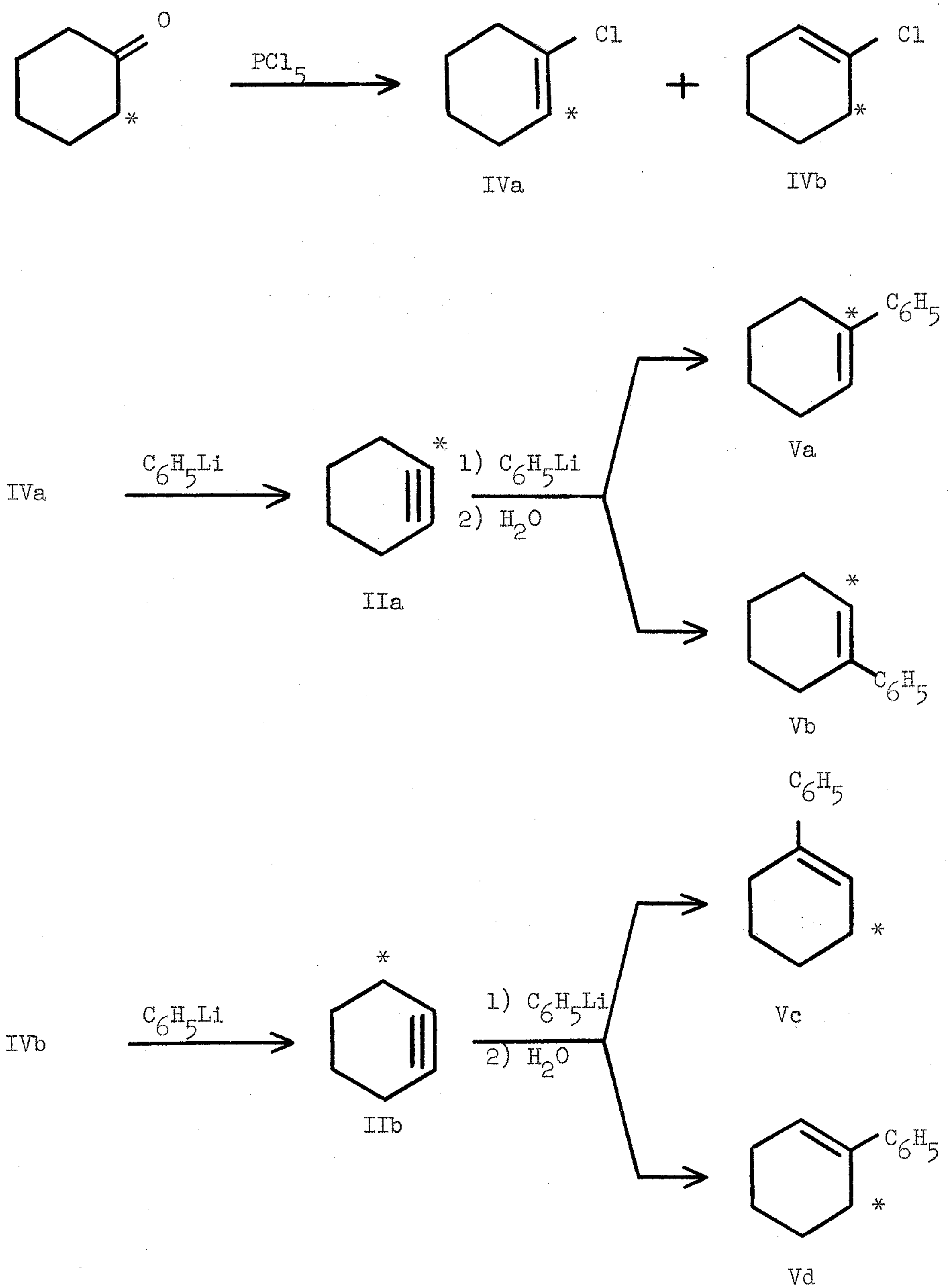
VI VII

Ar =



The results of the ^{14}C analyses are summarized in Table XII.

Mechanism I

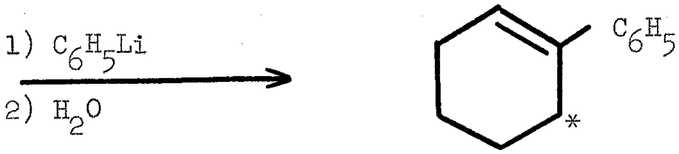

O
PCl5
Cl
*
IVa
IVb
IVa
C6H5Li
IIa
1) C6H5Li
2) H2O
C6H5
Va
Vb
IVb
C6H5Li
IIb
1) C6H5Li
2) H2O
Vc
Vd

Mechanism II

IVa

Vb

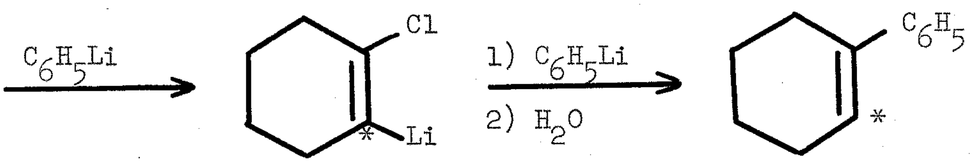
IVb



Vd

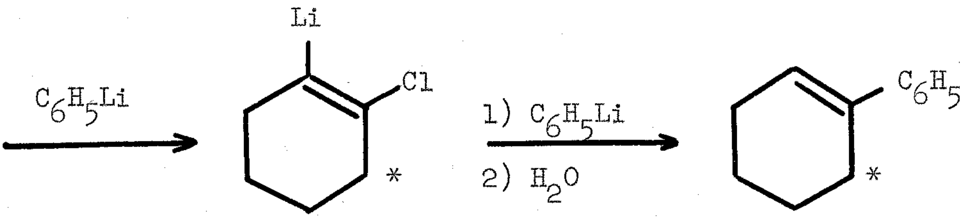
Mechanism III

IVa



Vb

IVb



Vd

TABLE XII

Radioactivity Analyses of Degradation Products of 1-Phenylcyclohexene-x-^{14}C.

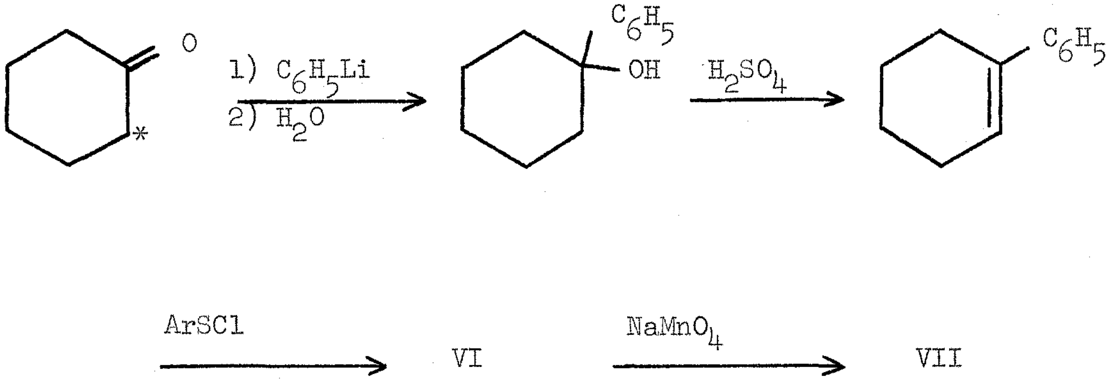
Compound	Meas. Act. (μc./mmole)	% Tot. Act.
VI	0.1217 ± 0.006 [a]	(100)
VII	0.02797 ± 0.0026 [a]	23.0 ± 0.4

[a] Average of four determinations.

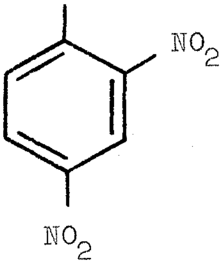
Reaction rates at ^{14}C-labeled positions have been noted to be as much as 10% less than those at ^{12}C-positions.[42] In the addition of amide ion to benzyne an apparent 4-6% isotope effect has been observed. This value is an overall effect which may be a combination of isotope effects on the addition and/or degradation steps for location of the ^{14}C.

In the formation of IV and V intramolecular isotope effects are expected to operate, while the formation of II and VII, obtained in low yields, will probably be accompanied by an intermolecular isotope effect. The compounds IVa, IIa, Va and the benzoic acid (VII) obtained from the 2,4-dinitrobenzenesulfenyl chloride derivative of Va (and possibly Vb) will probably be formed in lower yields than the corresponding compounds IVb, IIb, Vb, Vc, Vd and the benzoic acid obtained from the 2,4-dinitrobenzenesulfenyl chloride derivative of Vc and Vd. With all of these reactions (possibly excepting the oxidation of the 2,4-dinitrobenzenesulfenyl chloride derivative of Vb) inter- or intramolecular isotope effects will lower the activity of VII. The measured activity of VII (0.02729 μc./mmole) is lower than the activity of VII expected on the basis of Mechanism I with the assumption of no isotope effect (0.1217/4 = 0.03042 μc./mmole) by the factor 100(0.03042 - 0.02797) / 0.03042 = 8%. For lack of experimental data it is not possible to calculate exactly the overall isotope effect in the formation of 1-phenylcyclohexene and its degradation. In view of the fact that there are possibly four steps in which an isotope effect may be present, the difference between the expected activity of VII (Mechanism I) and the observed value is probably entirely due to isotope effects. It cannot be excluded, however, that a small part of the reaction between 1-chlorocyclohexene and phenyllithium proceeds by Mechanism II.

In order to show that the reaction of 1-phenylcyclohexene with 2,4-dinitrobenzenesulfenyl chloride was not accompanied by phenyl migration, 1-phenylcyclohexene was prepared from cyclohexanone-2-^{14}C and degraded according to the following scheme:



Ar =



The results of the ^{14}C analyses are summarized in Table XIII.

TABLE XIII

Radioactivity Analyses of Degradation Products of 1-Phenylcyclohexene-x-^{14}C

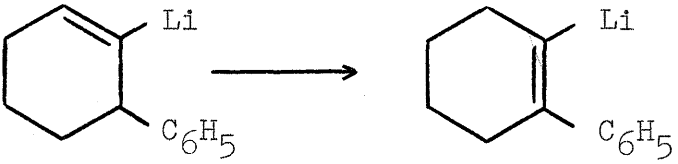
Compound	Meas. Act. (μc./mmole)	% Tot. Act.
VI	0.1968 ± 0.0018 [a]	(100)
VII	0.0002 ± 0.0002 [b]	0.1 ± 0.1

[a] Average of three determinations.

[b] Average of two determinations.

The formation of 1,2-cyclohexadiene (VIII) (Mechanism IV) cannot be excluded categorically on the basis of the above results.

The intermediate VIII could add phenyllithium either by Path A or Path B. In the first case, no 1-pehnylcyclohexene-1-^{14}C would be formed; in the second case, only 3-phenylcyclohexene-3-^{14}C and 3-phenylcyclohexene-1-^{14}C would be formed. In the latter case, in order to have 1-phenylcyclohexene formed, the following isomerization would have to take place:

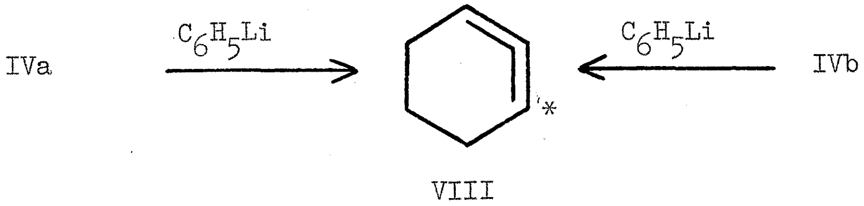


IX

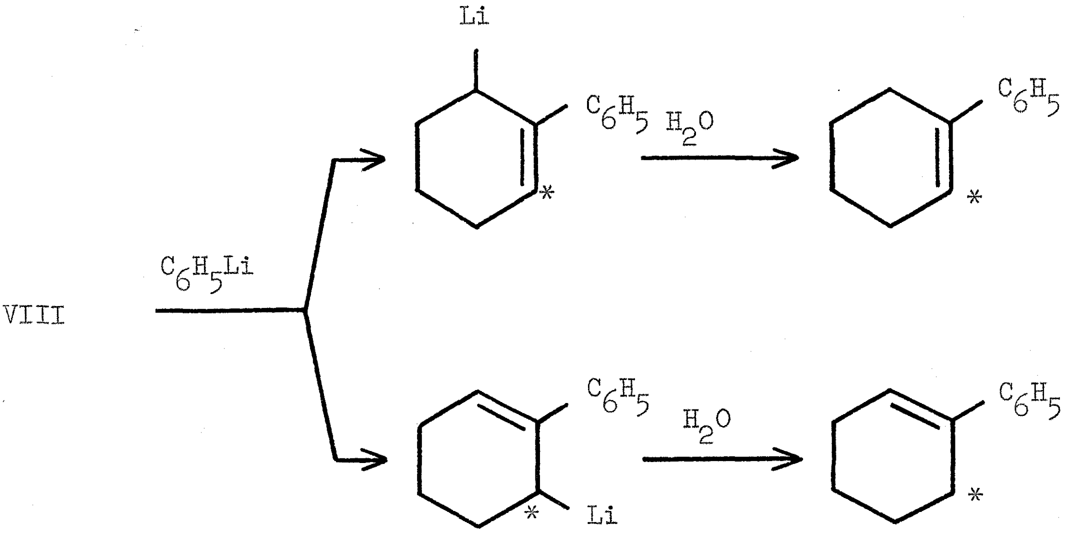
Since the carbon-lithium bond in IX is partially polarized, with the carbon atom having a partial negative charge, a base-catalyzed rearrangement in which the first step would be a proteon abstraction, would be made more difficult. Fort[43] has found that the base-catalyzed rearrangement of allylbenzene to propenylbenzene proceeds only with difficulty. In addition, isopropenyllithium does not appear to isomerize to allyllithium.[44]

Favorsky[45] has found that the nucleophilic attack of ethoxide ions on allene proceeds exclusively by Path A, with formation of ethyl isopropyl ether.

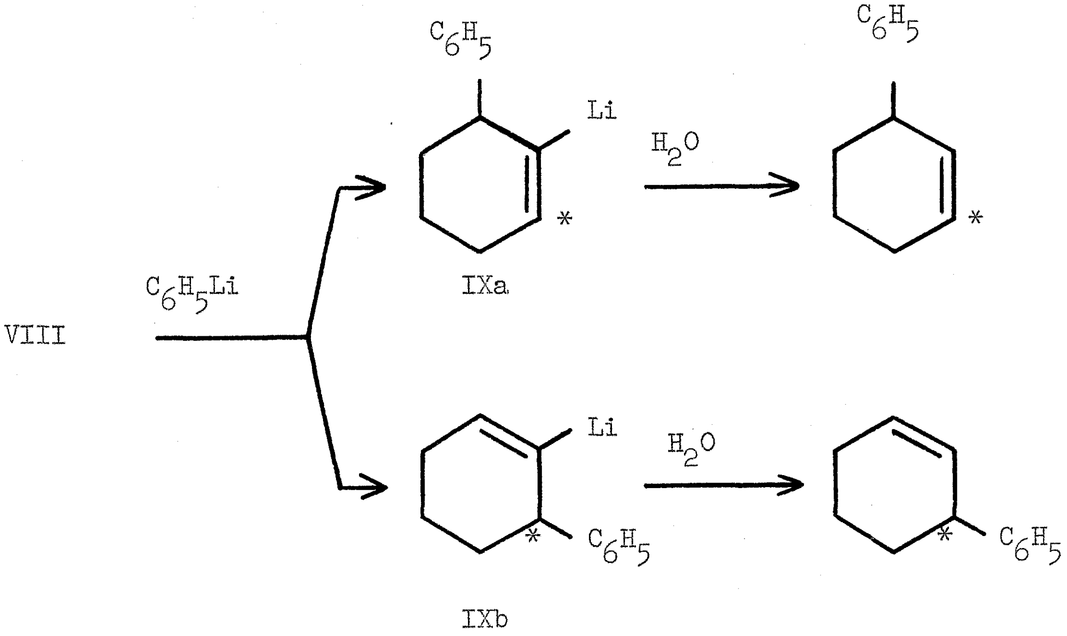
If 1,2-cyclohexadiene were the only intermediate in the reaction of 1-chlorocyclohexene with phenyllithium, Mechanism IV



Path A



Path B



the radiochemical results could be explained only by assuming that the reaction proceeds by Path A and Path B at almost exactly the same rate; in addition, IXa and IXb would have to isomerize at a very fast rate, for no evidence has been found for 3-phenylcyclohexene as a reaction product.

In view of the above considerations, it appears unlikely that VIII is an intermediate during the reaction of 1-chlorocyclohexene with phenyllithium.

The formation of biphenyl as a side product during the reaction of 1-chlorocyclohexene with phenyllithium is probably due to the reaction of bromobenzene which is usually present in solution with phenyllithium. In an experiment in which 1-chlorocyclohexene was omitted, biphenyl was obtained in 5.5% yield. It cannot be excluded, however, that a small amount of biphenyl may be formed by the metal interchange-elimination mechanism proposed by Wittig and Harborth.[40]

EXPERIMENTAL

1-Chlorocyclohexene.--1-Chlorocyclohexene was prepared from cyclohexanone and phosphorus pentachloride by the method of Mousseron and Jacquier[46] in yields varying from 40% to 60%.

1-Phenylcyclohexanol.--Cyclohexanone (0.1 mole) was slowly added to 0.15 mole of phenyllithium in 250 ml. of ether. The solution was allowed to reflux 30 min., then it was cooled and carefully treated with water. The organic layer was washed three times with water and the ether was evaporated on the steam bath. The residue was dissolved in ligroin and allowed to stand overnight in the refrigerator. Pure 1-phenylcyclohexanol (12.1 g., m.p. 61.5-63°) was obtained. The solvent was evaporated from the mother liquors and the residue was recrystallized from ligroin. Three additional grams of 1-phenylcyclohexanol, m.p. 61-62.5 was obtained. The total yield was 84%.

1-Phenylcyclohexene.--1-Phenylcyclohexanol (5.5 g.) was refluxed for 5 hr. with 24 ml. of 12% sulfuric acid. The product was treated with hexane and water, the organic layer was washed several times with water and distilled through a semimicro column.[16] 1-Phenylcyclohexene (4.5 g., 91%), with an infrared spectrum identical with that of an authentic sample, was obtained.

Reaction of 1-Chlorocyclohexene with Sodium Ethoxide.--1-Chlorocyclohexene was treated with sodium ethoxide in ethanol. The reaction conditions and amounts of reagents are summarized below.

Trial	C_6H_5Cl, mole	NaOEt, mole	Reaction time, hr.	Temp., °C.	% C_6H_9Cl recovered
1	0.10	0.17	48	reflux	--
2	0.10	0.25	15	220	61
3	0.138	0.25	21	320	0
4	0.138	0.175	1	340	--

In trial 1, no reaction took place, for the acidified product gave only a cloudiness when treated with alcoholic silver nitrate.

In trial 3, a very complex mixture was obtained which boiled continuously from 58° C. atmospheric pressure to 127° C. at 45.5 mm. Thirteen fractions were collected in this range; an infrared spectroscopic analysis showed that they all contained compounds having hydroxyl and carbonyl functional groups.

Reaction of 1-Chlorocyclohexene with Alkali Amides in Liquid Ammonia.--1-Chlorocyclohexene was treated with sodium and potassium amide in liquid ammonia for periods of time ranging from 0.5 to 2.0 hr. The reaction conditions and amounts of reagents used are summarized below.

Trial	C_6H_9Cl, mole	MNH_2, mole	Reaction time, hr.	% C_6H_9Cl recovered
1	0.10	0.34 [a]	2.0	0
2	0.10	0.10 [b]	0.5	10
3	0.25	0.28 [a]	0.25	5

[a] Sodamide was employed.
[b] Potassium amide was employed.

The unreacted bases were neutralized, the solvent was evaporated and the residues were dissolved in ether and water. The organic layers were dried over anhydrous magnesium sulfate and distilled through a semimicro column.[16] In all cases, the products boiled above 100° at 1 mm. and consisted of very complex mixtures from which no definite compounds could be isolated.

Attempted Reaction of 1-Chlorocyclohexene with Sodium Phenylacetylide in Liquid Ammonia.--1-Chlorocyclohexene (43 mmole) was treated with 109 mmole of sodium phenylacetylide in 250 ml. of liquid ammonia for 2.0 hr. The unreacted base was neutralized, the solvent was evaporated and the residue was dissolved in ether and water. The organic layer was distilled through a semimicro column.[16] After all the starting materials had been distilled, only a few mg. of brown tar remained.

Reaction of 1-Chlorocyclohexene with Phenyllithium.--1-Chlorocyclohexene was treated with phenyllithium in ether solution. The reaction conditions and the amounts of reagents used are summarized below.

Trial	C_6H_9Cl, mole	C_6H_5Li, mole	Reaction time, min.	Temp., °C.	Solvent vol., ml.
1	0.05	0.10	45	100	100
2	.05	.05	22	100	100
3	.05	.14	22	100	100
4	.05	.13	16	100	100
5		.14	16	100	100
6	.05	.13	15	100	0
7	.086	.15	30	140	200
8	.086	.25	30	145	250
9	.178	.30	30	150	250
10	.100	.25	40	150	250

The reaction products were carefully treated with water; the organic layers were washed several times with water, dried over anhydrous magnesium sulfate and distilled through a semimicro column.[24]

In trials 1, 2, 3, 4 and 6 1-phenylcyclohexene was obtained in less than 10% yield; in all cases the product contained large amounts of biphenyl.

In trial 5, biphenyl, m.p. 63-66° was obtained in 5.5% yield. The identity of this material was proved by infrared spectroscopy.

In trials 7, 8 and 9, 1-phenylcyclohexene was obtained in yields ranging from 13% to 15%.

In trial 10, in which 1-chlorocyclohexene which had been prepared from cyclohexanone-2-^{14}C was used, 1-phenylcyclohexene was obtained in 28.5% yield. An infrared analysis of the product showed that biphenyl was present in very small amounts.

1-Phenylcyclohexene Nitrosochloride.--1-Phenylcyclohexene nitrosochloride was prepared by the method of Schaeffer and Collins.[47] Thus, from 910 mg. of 1-phenylcyclohexene, 148 mg. (11.5%) of 1-phenylcyclohexene nitrosochloride, m.p. 131-132° d., lit. 134-135° d., was obtained.

Attempted Preparation of 2-Phenylcyclohexanone.--Crude 1-phenylcyclohexene (2.0 g., 12.8 mmole) was added to 18.6 mmole of perbenzoic acid in chloroform solution. After 18 hr., 2 ml. of boron trifluoride etherate was added to the solution. The solution was allowed to stand 30 min., then it was washed twice with a dilute sodium hydroxide solution and once with water. The solvent was evaporated and the residue eluted through 110 g. of acid-washed alumina. Hexane, hexane-benzene (3:1 and 1:1), benzene and chloroform were successively used as eluents. With the exception of 0.4 g. of biphenyl, which was originally present in the 1-phenylcyclohexene, only small amounts of oily products were obtained.

Reaction of 1-Phenylcyclohexene with 2,4-dinitrobenzenesulfenyl chloride. A. At Room Temperature.--1-Phenylcyclohexene (0.95 g.) and 1.40 g. of 2,4-dinitrobenzenesulfenyl chloride were dissolved in 25 ml. of dry acetic acid. After three days, 0.81 g. of yellow crystalline product was separated by filtration. The product melted at 119-123°

with evolution of gas and resolidification. The new product melted near 140°. The solid product and the mother liquors were recrystallized three times from acetic acid and once from ethanol-chloroform. Yellow needles, m.p. 140-141.5 (1.18 g.), were obtained.

B. On the Steam Bath.--1-Phenylcyclohexene (3.5 g.) and 3.8 g. of 2,4-dinitrobenzenesulfenyl chloride were dissolved in 75 ml. of glacial acetic acid. The solution was allowed to stand on the steam bath for 45 min., then an excess of water was added and the oil which formed was allowed to solidify. The supernatant liquid was decanted and the product was recrystallized from acetic acid and from ethanol-chloroform. Pure 1-phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene (5.0 g., 86%), m.p. 139.5-140.5°, was obtained. This compound is sensitive to air oxidation and to light and slowly decomposes upon standing.

Anal. Calcd. for $C_{18}H_{16}N_2O_4S$: C, 60.66; H, 4.53; N, 7.86; S, 9.00. Found: C, 60.87; H, 4.48; N, 8.00; S, 8.91.

Oxidation of 1-Phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene to Benzoic Acid. A. With Chromic Anhydride.--1-Phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene (690 mg., 1.95 mmoles) was added to 2.4 g. of chromic anhydride, 50 ml. of acetic acid, 5 ml. of water and 10 ml. of concentrated sulfuric acid. The mixture was refluxed for 30 min., cooled, poured into 400 ml. of water and the whole extracted with

250 ml. of ether. The ether solution was washed with water and extracted with 10% sodium hydroxide solution. The basic extract was acidified with dilute sulfuric acid and extracted with ether. On evaporation of the solvent there was obtained 115 mg. of crude benzoic acid. One recrystallization from water, followed by vacuum sublimation at 100° and 10 mm. gave 58 mg. (25%) of pure benzoic acid, m.p. 121.5-123°.

In two similar attempts, the above results could not be reproduced and the benzoic acid was heavily contaminated with a yellow compound that could not be separated either by recrystallization or sublimation.

B. With Sodium Permanganate.--To 920 mg. of 1-phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene was added 1.0 g. of sodium hydroxide and 17.0 g. of sodium permanganate trihydrate in 125 ml. of pyridine and 10 ml. of water. The mixture was refluxed for 1 hour, the excess permanganate was reduced with a saturated solution of sodium sulfite, the manganese dioxide removed by filtration. The filter cake was washed with dilute sodium hydroxide and the combined filtrates were evaporated almost to dryness. The residual basic solution was extracted with ether, acidified with dilute sulfuric acid and extracted with ether. The solvent from the second ether extract was removed through a semimicro column, and the residue was heated for several hours on the steam bath with 2 g. of tin and 10 ml. of concentrated hydrochloric acid. The mixture was poured into water and extracted with ether. The ether extract was washed with water, dried over anhydrous magnesium sulfate and the solvent was evaporated through a semimicro column. The residue was dissolved in 10 ml. of hot water, centrifuged, and allowed to crystallize in an ice bath. After one sublimation at 100° (10 mm.), 78 mg. (25%) of benzoic acid, m.p. 122-123°, was obtained.

<u>Determination of the Radioactivity of 1-Phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene and Benzoic Acid</u>.--The radioactive analyses of 1-phenyl-2-(2,4-dinitrophenylmercapto)-cyclohexene (VI) and benzoic acid (VII) were made using the vibrating-reed electrometer method of Neville.[48] The results are summarized below.

<u>Reaction of 1-Chlorocyclohexene with Sulfuric Acid</u>.--1-Chlorocyclohexene (10.0 g., 0.086 mole) was treated with 100 ml. of 90% sulfuric acid at 50°. After 45 min. the reaction mixture was added to crushed ice and extracted with ether. The organic layer was dried over anhydrous magnesium sulfate and the solvent evaporated through a semimicro column.[16] The residue (6.4 g., 75%) was proved to be cyclohexanone by its infrared spectrum and by formation of its 2,4-dinitrophenylhydrazone, m.p. 161-162°, lit.,[49] 162° and semicarbazone, m.p. 164-165°, lit.,[49] 166°.

Compound	mg.	^{14}C-Activities[a]	μc/mmole	Δ[b]
VI	11.40	18.66 ± 0.22[c]	0.1228	0.0011
	12.67	20.54 ± 0.25[c]	0.1217	0.0000
	12.28	27.46 ± 0.37[c]	0.1213	0.0004
	20.50	33.00 ± 0.30[c]	0.1208	0.0009
		Average	0.1217	0.0006
	18.22	48.76 ± 0.45[d]	0.2008	0.0040
	24.28	63.36 ± 0.38[d]	0.1958	0.0010
	13.59	35.11 ± 0.30[d]	0.1939	0.0029
		Average	0.1968	0.0026
VII	9.64	10.51 ± 0.18[c]	0.02802	0.00005
	12.03	13.17 ± 0.31[c]	0.02815	0.00018
	14.20	15.52 ± 0.20[c]	0.02810	0.00013
	11.04	11.86 ± 0.22[c]	0.02761	0.00036
		Average	0.02797	0.00018
	8.98	0.07 ± 0.07[d]	0.0002	0.0002
	10.73	0.07 ± 0.07[d]	0.0002	0.0002
		Average	0.0002	0.0002

[a] Sample activities in mvolts. The activities have been corrected for background.

[b] Deviation from the average value.

[c] From the reaction of 1-chlorocyclohexene with phenyllithium.

[d] From the dehydration of 1-phenylcyclohexanol-2-^{14}C.

PART III

REACTIONS OF NON-ACTIVATED ARYL HALIDES WITH STRONG BASES AT HIGH TEMPERATURES

DISCUSSION

In recent years it has been shown that alkali amides in liquid ammonia[2,3,7] and refluxing piperidine[50,51] and organolithium compounds[41,52] react with non-activated aryl halides by the way of a benzyne intermediate.* Strong bases and nucleophiles in liquid ammonia react with aryl halides in liquid ammonia only in the presence of alkali amides.[6,8,10,11,12] Sodium and potassium hydroxide react with aryl halides only at very elevated temperatures.[53,54,55,56] By changing the reaction temperature and the base concentration, the mechanism of this reaction may change from elimination-addition to direct substitution.[53]

In order to determine whether alkoxides react with non-activated aryl halides by the way of a benzyne intermediate, the reaction between sodium cyclohexoxide and bromobenzene in refluxing cyclohexanol was investigated. It was found, however, that after three days the reaction had proceeded to an extent of less than 10%.

Sodium and potassium anilides do not react with halobenzenes in liquid ammonia, but potassium anilide[57] and potassium diphenylamide[57] react with bromobenzene at elevated temperatures to give diphenylamine and triphenylamine respectively. In order to study the mechanism of

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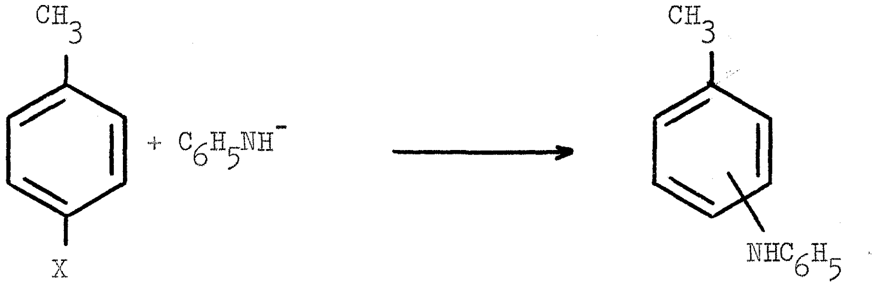
* For a discussion of this mechanism, see Part I of this Thesis.

such a reaction, p-chloro-, p-bromo- and p-iodotoluene were treated with potassium anilide in refluxing aniline. The resulting mixtures of p- and m-tolylphenylamine were analyzed by means of infrared spectroscopy. The results are summarized in Table XIV.

TABLE XIV

Results of the Reaction of p-Halotoluenes with Potassium Anilide.



X = Cl, Br, I

p-Halotoluene	Total yield, %	Meta, %	Para, %
Cl	53	53 ± 3	47 ± 3
Br	50	53 ± 3	47 ± 3
I	43	52 ± 3	48 ± 3

If a direct substitution reaction were competing with the elimination-addition reaction, the ratios of the two isomers should have been different for the three p-halotoluenes. The fact that all three p-halotoluenes give essentially the same product mixtures is good evidence that the reaction proceeds exclusively by the way of a benzyne intermediate. It cannot be excluded, however, that in the case of p-iodotoluene a small amount (about 2%) of direct displacement takes place; the analytical procedure, however, was not precise enough to verify this fact.

EXPERIMENTAL

Reaction of Potassium Anilide with Bromobenzene.--Potassium anilide was prepared by adding 4.2 g. (0.107 mole) of potassium metal to 250 ml. of refluxing aniline. Bromobenzene (20 g., 0.128 mole) was added and the solution refluxed for two hours. At the end of this time, the reaction mixture was allowed to cool and ethanol was cautiously added. Hexane and ether were added; the mixture was washed with water and the solvents evaporated. The residue was distilled through a semimicro column.[16] Diphenylamine (11.0 g., 60%) m.p. 49-52°, whose infrared spectrum was identical with the spectrum of an authentic sample of diphenylamine, was obtained.

Reaction of Potassium *m*- and *p*-Toluidide with Bromobenzene.--The reaction conditions were the same as the ones used in the preparation of diphenylamine. Five g. (0.128 mole) of potassium and 30 g. (0.198 mole) of bromobenzene were used. The yield of crude diarylamine was 14.5 g. (61.5%). The products were purified by precipitation with anhydrous hydrogen chloride in ether, followed by treatment with water, extraction with ether and recrystallization from pentane.

Reaction of Potassium Diphenylanilide with Bromobenzene.--To 25 g. (0.148 mole) of diphenylamine in 250 ml. of refluxing xylene was added 4.0 g. (0.10 mole) of potassium. The reaction was very slow, and even after four hours of refluxing about 20% of the potassium was still unreacted. Bromobenzene (30 g., 0.198 mole) was added, and the reaction mixture was allowed to reflux for 18 hours. Ethanol and a small amount of water were added; the organic layer was washed with water, dried over anhydrous magnesium sulfate, saturated with anhydrous hydrogen chloride and filtered. The filtrate was evaporated and the residue recrystallized from ethyl acetate. Crude triphenylamine (1.0 g., 2.7%) was obtained. After several recrystallizations from ethyl acetate-ethanol, 500 mg. of pure product, m.p. 126-127°, whose m.p. was not depressed by admixture with an authentic sample of triphenylamine, was obtained.

Reaction of p-Chloro, p-Bromo- and p-Iodotoluene with Potassium Anilide.--Potassium (5.6 g., 0.144 mole) was added to 250 ml. of refluxing aniline. The appropriate p-halotoluene (0.10 mole) was added, and the reaction mixture was allowed to reflux 15 minutes. Water was cautiously added to decompose the unreacted bases. Ether was added, the organic layer was washed several times with dilute hydrochloric acid, dried over anhydrous magnesium sulfate and saturated with anhydrous hydrogen chloride. The precipitate was washed with ether, treated with water, extracted with ether, and flash distilled to remove all of the tarry material present. The composition of the distillate was determined by taking its infrared spectrum in carbon disulfide in the 11.75-14.00 μ region and comparing it with the spectra of synthetic mixtures of m- and p-tolylphenylamines.

PART IV

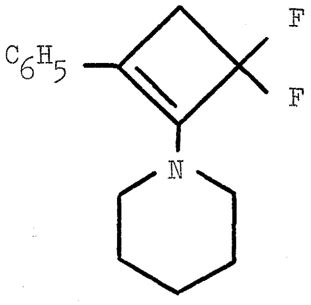
THE SYNTHESIS OF SOME FOUR-MEMBERED RING COMPOUNDS

DISCUSSION

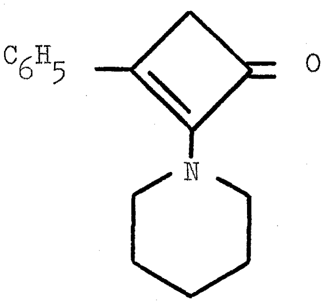
In an attempt to determine the behavior of halocyclobutanes toward strong bases, 1,1-difluoro-2,2-dichloro-3-phenylcyclobutane was treated with a 2.3-fold excess of potassium amide in liquid ammonia. The reaction product consisted largely of tarry material, from which 1,1-difluoro-2-chloro-3-phenyl-2-cyclobutene could be isolated in small yield. When the same compound was allowed to stand overnight with piperidine, 1,1-difluoro-2-chloro-3-phenyl-2-cyclobutene was obtained in 79% yield.

Treatment of 1,1,2-trifluoro-2-chloro-3-phenylcyclobutane with piperidine led to completely unexpected results. The expected 1,1,2-trifluoro-3-phenyl-2-cyclobutene could be isolated in small yields only by quenching the reaction after a short time. If the reaction was allowed to proceed overnight, a very high boiling compound which contained nitrogen (I) was obtained. The ultraviolet spectrum of I had strong absorption maxima at 230 mμ and 311 mμ and a very low intensity maximum in the 380-390 mμ region. Its infrared spectrum showed the characteristic methylene band at 3.42μ and a very strong band at 6.02μ, which was indicative of unsaturation. Its n.m.r. spectrum showed the absence of vinyl hydrogen.

I reacted with sodium permanganate and bromine and quickly polymerized in light and air. When I was treated with concentrated sulfuric acid, hydrogen fluoride was evolved and a new crystalline nitrogen-containing compound (II) was obtained. The ultraviolet spectrum of II had maxima at 231 mμ, 239 mμ and a very broad peak in the 360-370 mμ region; its infrared spectrum showed the methylene band at 3.42μ and two very strong peaks at 5.75 and 6.20μ. Its n.m.r. spectrum again showed the absence of a vinyl hydrogen. Treatment of II with an alcoholic solution of 2,4-dinitrophenylhydrazine gave a copious orange precipitate. Reduction of II with zinc amalgam and hydrochloric acid gave phenylcyclobutane. On the basis of the above evidence and of elemental analyses, the following structures were proposed for I and II:



I



II

EXPERIMENTAL

1,1-Difluoro-2,2-dichloro-2-phenylcyclobutane.--1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane was prepared by the method of Silversmith and Roberts[58] in 65% yield.

1,1-Difluoro-2-chloro-3-phenyl-2-cyclobutene.--1,1-Difluoro-2,2-dichloro-3-phenyl-2-cyclobutene was prepared by the method of Silversmith and Roberts[58] in 83% yield.

1,1,2-Trifluoro-2-chloro-3-phenylcyclobutane.--1,1,2-Trifluoro-2-chloro-3-phenylcyclobutane was prepared by the method of Silversmith and Roberts[58] in 67% yield.

Reaction of 1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane with Potassium amide in Liquid Ammonia.--1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane (23 g., 0.10 mole) was added to 300 ml. of liquid ammonia containing 0.23 mole of potassium amide. The solution became brown, and the liquid ammonia started to boil vigorously. After two hours an excess of ammonium chloride was added to the reaction mixture to neutralize any unreacted potassium amide. After all the liquid ammonia had evaporated, the residue was taken up in water and ether. The organic layer was washed with water, dried over anhydrous magnesium sulfate and distilled. 1,1-Difluoro-2-chloro-3-phenyl-2-cyclobutene

(5.6 g., 28%) was obtained. A large amount of undistillable tarry material was left.

Reaction of 1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane with Piperidine.--1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane (10.0 g., 0.043 mole) was added to 35 ml. of piperidine. An exothermic reaction took place and a precipitate appeared. The mixture was allowed to stand overnight; it was then taken up in ether and water and the organic layer was washed with water. 1,1-Difluoro-2-chloro-3-phenyl-2-cyclobutene (6.75 g., 79%), whose infrared spectrum was identical with the spectrum of an authentic sample of 1,1-difluoro-2-chloro-3-phenyl-2-cyclobutene was obtained.

Reaction of 1,1,2-Trifluoro-2-chloro-3-phenylcyclobutane with Piperidine.--1,1,2-Trifluoro-2-chloro-3-phenylcyclobutane (10.0 g., 0.045 mole) was added to 35 ml. of piperidine. An exothermic reaction took place and a precipitate appeared. The reaction mixture was allowed to stand overnight; it was then taken up in water and ether, the organic layer was washed with water, dried over anhydrous magnesium sulfate and distilled. 1,1-Difluoro-2-piperidino-3-phenyl-2-cyclobutene (I) (10.6 g., 95%), b.p. 110-111° (1 mm.) was obtained. In subsequent trials, the yield of product dropped to about 65%, but the b.p. increased to 113-114° (0.5 mm.).

Anal. Calcd. for $C_{15}H_{17}NF_2$: C, 72.26; H, 6.87; N, 5.62. Found: C, 72.30; H, 7.00; N, 5.67.

When the reaction between 1,1,2-trifluoro-2-chloro-3-phenylcyclobutane and piperidine was quenched after two hours, 1,1,2-trifluoro-3-phenyl-2-cyclobutene, b.p. 40-41° (1 mm.), whose identity was proved by infrared spectroscopy, was obtained in 12% yield.

1,1-Difluoro-2-piperidino-3-phenyl-2-cyclobutene reacted readily with sodium permanganate in pyridine and bromine in carbon tetrachloride.

2-Piperidino-3-phenyl-2-cyclobutenone (II).--1,1-Difluoro-2-piperidino-3-phenyl-2-cyclobutene (27.5 g., 0.11 mole) was treated with 50 ml. of 96% sulfuric acid at 50°. The reaction mixture became hot and a large amount of hydrogen fluoride was evolved. After 12 minutes, the reaction mixture was added to an excess of crushed ice. A white solid separated and was collected by filtration. Upon washing with a large excess of water the white solid (probably a sulfate salt) became yellow. The product was air dried. 2-Piperidino-3-phenyl-2-cyclobutenone (24.0 g., 97%) was obtained, which after several recrystallizations from pentane, melted at 47.5-48.5°.

Anal. Calcd. for $C_{15}H_{17}ON$: C, 79.26; H, 7.54. Found: C, 79.00; H, 7.62.

Clemmensen Reduction of 2-Piperidino-3-phenyl-2-cyclobutenone.--Zinc powder (250 g.) was treated with a solution of 25 g. of mercuric chloride in 250 ml. of water and 12.5 ml. of concentrated hydrochloric acid. The supernatant liquid was decanted and the solid washed with distilled water. Water (250 ml.), 250 ml. of concentrated hydrochloric acid, 25 ml. of ethanol and 20 g. of 2-piperidino-3-phenyl-2-cyclobutenone (0.090 mole) were added to the amalgamated zinc. The reaction mixture was allowed to reflux for 75 minutes and then steam distilled. The distillate was extracted with ether; the organic layer was dried over anhydrous magnesium sulfate and carefully distilled. Phenylcyclobutane (2.6 g., 22%) whose infrared spectrum was identical with the spectrum of an authentic sample of phenylcyclobutane, was obtained.

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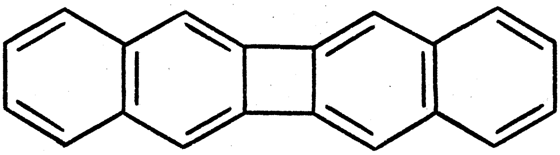
PROPOSITIONS

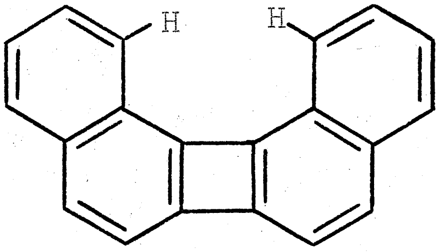
1. It is proposed that the first step in the formation of phenyl azide from α-nitrosophenylhydrazine[1] is the rearrangement of the latter compound to β-nitrosophenylhydrazine. In order to determine the mechanism of this reaction, kinetic studies and studies with α-nitrosophenylhydrazine-β-^{15}N are proposed.

2. It is proposed that 1-chlorocyclopentene-1-^{14}C will condense with phenyllithium at high temperatures with formation of approximately equimolar quantities of 1-phenylcyclopentene-1-^{14}C and 1-phenylcyclopentene-2^{14}C.

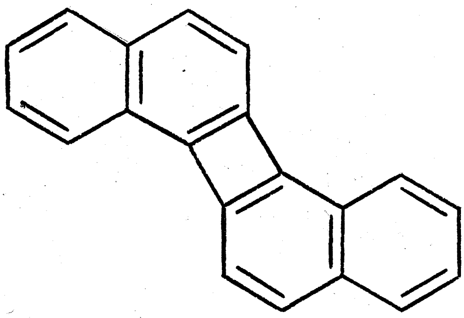
3. 2,3-Binaphthylene (I)[2] and 1,2-binaphthylene (II)[3] have been synthesized. II is considerably less stable than I. This may be because of the electronic configurations or because of interaction of the 8,8' hydrogens in II. A synthesis of 1,2'-1',2-binaphthylene (III) is proposed. This compound, according to simple M.O. calculations should possess the same delocalization energy of II, but is free of any steric hindrance.



I



II



III

4. It is proposed that the compound C_7H_{10} prepared by Markownikow[4] is 1,2-cycloheptadiene and not cycloheptene, as the author suggested. It is further proposed that cycloheptyne may rearrange immediately to 1,2-cycloheptadiene. In order to test this hypothesis, the oxidation of 1,2-cycloheptadione dihydrazone with mercuric oxide should be investigated.

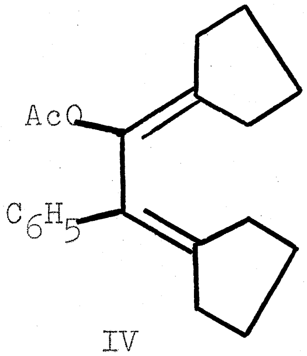
5. A method to determine whether biphenyl, which is formed as a side product in the coupling of 1-chlorocyclohexene with phenyllithium, arises as a result of a series of dehydrogenations of 1-phenylcyclohexene[5] or from a Fittig-type reaction, is proposed.

6. It is proposed that sodium phenoxide and diphenyl ether exist in equilibrium at high temperatures. In order to test this hypothesis, sodium phenoxide-x-^{14}C should be used.

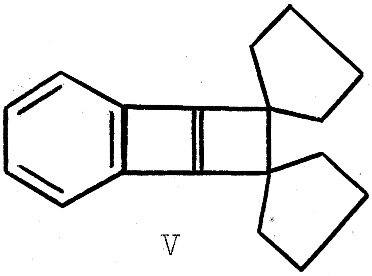
7. It is proposed that in order to determine the approximate values of the isotope effects during the formation of 1-phenylcyclohexene from 1-chlorocyclohexene, 1-chlorocyclohexene-1-^{14}C and 1-chlorocyclohexene-2-^{14}C should be employed.

8. A study of the reaction between substituted allenes and nucleophilic agents is proposed.

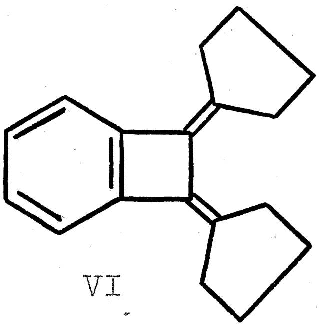
9. It is proposed that the reaction between IV and aluminum chloride[6] should be reinvestigated, for it appears very likely that V, which is the structure assigned to the product, should be very unstable.[7] Structure VI fits all the experimental data and is probably more stable.



IV



V



VI

10. It is proposed that the decomposition of chlorine azide in pentane solution proceeds by the way of a free radical mechanism and follows first order kinetics.

11. A study of the reaction mechanism between quartz and calcite to give wollastonite is suggested.

12. It is proposed that nitrogen, rather than ammonia, played a very important part in the formation of organic compounds on earth during early geological times. Some experiments designed to test this hypothesis are suggested.

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