October 4, 1957

To the Graduate Council:

I am submitting herewith a dissertation written by Donald Richard Larkin entitled "An Investigation of the Reduction of Carbon-Carbon Unsaturation by Alkali Metals in Liquid Ammonia." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

Jerome F. Eastham
Major Professor

We have read this dissertation and recommend its acceptance:

David T. Kung

Hilton A. Smith

William H. Fletcher

David A. Shirley

Accepted for the Council:

Dale Hawthorne
Dean of the Graduate School

AN INVESTIGATION OF THE REDUCTION OF CARBON-CARBON UNSATURATION BY ALKALI METALS IN LIQUID AMMONIA

A DISSERTATION

Submitted to
The Graduate Council
of
The University of Tennessee
in
Partial Fulfillment of the Requirements
for the Degree of
Doctor of Philosophy

---

by

Donald Richard Larkin

December, 1957

ACKNOWLEDGMENT

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CHAPTER I

HISTORICAL AND THEORETICAL BACKGROUND

A. The Properties of Liquid Ammonia

The properties of liquid ammonia are similar in many ways to those of water. Liquid ammonia has the very high specific heat of 1.10 calories per gram.[1] Hydrogen bonding occurs to a considerable degree although not as extensively as in water. Evidence of hydrogen bonding as reflected in boiling points is shown in Table I. The dielectric constant is 22 at -33° which is also very high for a solvent which is comparatively inert to reactive metals. (Hexane has a dielectric constant of 1.87.) Liquid ammonia is a much better solvent for organic compounds than is water. Even such large molecules as steroids can be put into solution in ammonia by using a co-solvent such as diethyl ether. Liquid ammonia's major disadvantage as a solvent is its low boiling point, -33.4°. However, for many purposes it can be used at room temperature without special equipment (other than a good hood) since it evaporates slowly due to its high heat of vaporization, 327 calories per gram.[1]

An acid-base system for ammonia[2] can be envisioned analogous to the acid-base system for water, i. e.:

$$2NH_3 \rightleftharpoons \underset{\text{Acid}}{NH_4^+} + \underset{\text{Base}}{NH_2^-}$$

TABLE I

EVIDENCE FOR HYDROGEN BONDING OF AMMONIA

Compound	Molecular Weight	Boiling Point
CH_4	16	-150°
NH_3	17	- 33°
H_2O	18	100°

$$2H_2O \rightleftharpoons H_3^+O + OH^-$$

Acid Base

This autoionization of ammonia into ammonium ions and amide ions must occur to a very limited degree, however, since the pKa of ammonia is 34.[2] Ammonium salts and all compounds having pKa values smaller than 34 will behave as acids in ammonia. Alcohols such as tert-amyl alcohol (pKa 19) and ethyl alcohol (pKa 18) are useful acids in the ammonia system. The metal amides, such as sodium amide and potassium amide, are strong bases.

The most unique and useful property of liquid ammonia as a reaction medium is its ability to dissolve the alkali and alkaline earth metals. Reactions between organic compounds and these metals may be carried out in a homogeneous medium. Solutions of sodium and lithium in ammonia are quite stable in the absence of a catalyst and have been kept for months, after which evaporation of the ammonia left these metals unchanged. The more active metals, cesium and rubidium, react more rapidly. Transition element metals such as iron and nickel will catalyze the following reaction between alkali metal and ammonia.[3]

$$Na + NH_3 \xrightarrow{Fe} NaNH_2 + 1/2\ H_2$$

All dilute solutions of alkali metals in liquid ammonia have the same characteristic deep blue color. It is believed that these solutions consist of solvated metal cations and electron anions in equilibrium with the metal.

$$M + x\ (NH_3) \rightleftharpoons M^+(NH_3)_a + e^-\ (NH_3)_b$$

$$(a + b = x)$$

Since the spectra of all alkali metal-in-ammonia solutions are practically identical, the blue color is attributed to the solvated electrons.[4]

Although the simple solvated electron concept does not explain all features of the metal-in-ammonia system, there is a large amount of experimental evidence in support of it. When an electrical current is passed through a metal-in-ammonia solution, the blue color migrates toward the anode.[4] Also transference measurements show that in dilute solutions the negative particle in the solution carries seven times as much current as the positive particle (metallic ion). Finally, solutions of metals have lower densities than solutions of salts or liquid ammonia itself. This increase in volume of the solution is attributed to the considerable volume of the envelope of ammonia molecules associated with the electron.[5]

Whatever its exact nature, a "solution of electrons" is chemically unique. Much remains to be learned of the chemical reactions effected by such solutions.

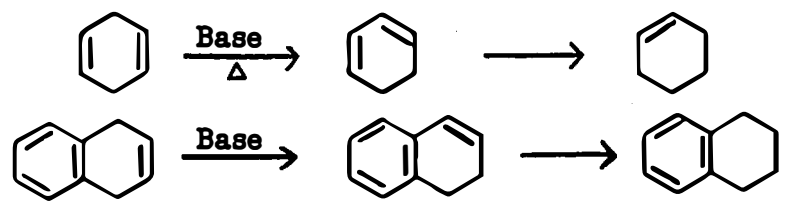
B. The Reduction of Carbon-Carbon Unsaturation by the Alkali Metal-Alcohol-Ammonia System

The literature to 1950 on the reactions of organic compounds with the alkali metals in liquid ammonia is covered in an excellent review by Watt.[6] Here we will be concerned only with the reduction of carbon-carbon unsaturation by alkali metal-alcohol-ammonia systems. In effect these systems yield hydrogen which causes the reduction of a variety of organic compounds. In general:

$$x\,M + x\,ROH + Z \longrightarrow x\,ROM + ZH_x$$
(Z = organic compound)

Specific reductions effected are illustrated by the examples in Table II. The examples given are predominately from the recent literature but no attempt has been made at an exhaustive survey.

It can be seen that this method is sufficiently powerful to reduce an aromatic ring and specific enough to add only two hydrogen atoms. In many cases the initial product is a 1,4-dihydro-derivative which is not further hydrogenated because unconjugated unsaturation is not reduced by the metal-alcohol-ammonia system. However, if an initial 1,4-dihydro-derivative is isomerized to the 1,2-dihydro-derivative, as in equations 1 and 2, then further reduction can take place.[35] Such a reaction sequence, reduction-isomerization-reduction, has proved useful in organic synthesis.



(1)

(2)

C. The Theory of Reductions by Dissolving Metals and by the Metal-Alcohol-Ammonia System

The chemical reduction of carbon-carbon unsaturation by dissolving metals* has been studied by a large number of investigators.[36] For reductions by these reagents to take place it is usually necessary for

*Examples of dissolving metal reactions are the reduction of a nitro-group by tin and hydrochloric acid and the Bouveault-Blanc ester reduction.

TABLE II

REDUCTIONS BY THE ALKALI METAL-ALCOHOL-AMMONIA SYSTEM

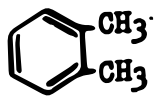
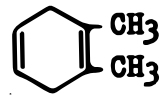
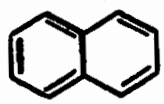
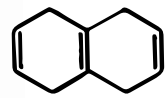
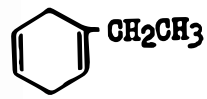
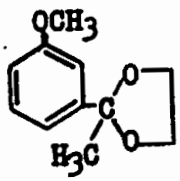
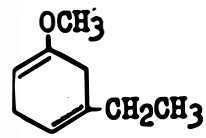
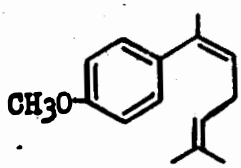
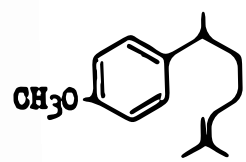
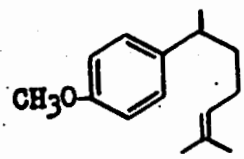
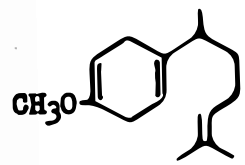
Starting Material	Product	Yield	Alkali Metal	Reference
		83% 60-70% 80%	Na Na Na	7 8 9
		69%	Na	9
		65%	Na	10
		85%	Na	11
		91%	Na	11
		78%	Na	12
		85%	Na	12

TABLE II

REDUCTIONS BY THE ALKALI METAL-ALCOHOL-AMMONIA SYSTEM (Continued)

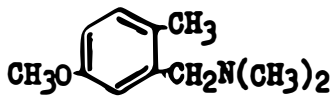
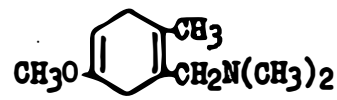
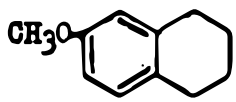
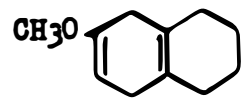
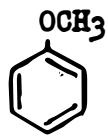
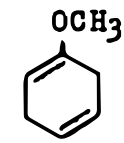
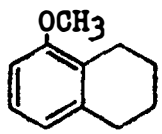
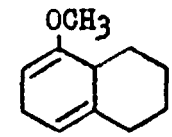
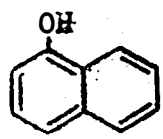
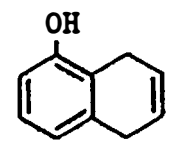
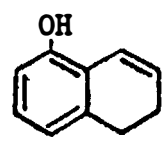
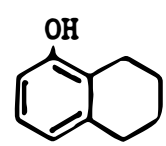
Starting Material	Product	Yield	Alkali Metal	Reference
		90%	Na	13
		35% 88%	Na Li	15 15
		90% 90%	Na Li	15 15
		89%	Li	15
		83-93%	Li	15
		65-85%	Na	29
		79%	K	30

TABLE II

REDUCTIONS BY THE ALKALI METAL-ALCOHOL-AMMONIA SYSTEM (Continued)

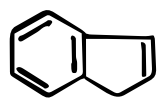
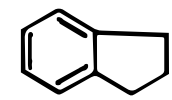
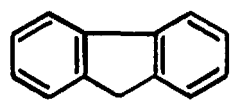
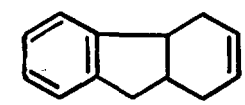
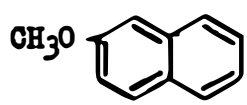
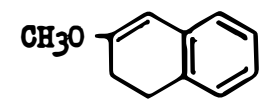
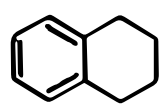
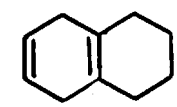
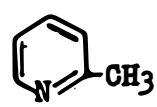
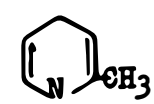
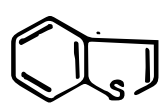
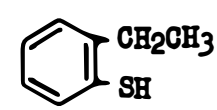
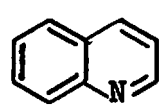
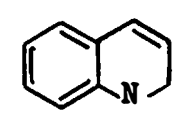
Starting Material	Product	Yield	Alkali Metal	Reference
		36%	Na	23
		85%	Na	23
		---	Na	24
		57%	Na	25
		80% 91%	Na Na	26 29
		---	Na	55
		66%	Na	27
		91%	Na	28

TABLE II

REDUCTIONS BY THE ALKALI METAL-ALCOHOL-AMMONIA SYSTEM (Continued)

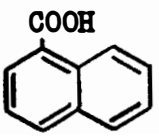
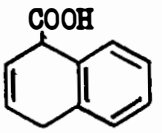
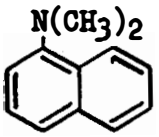
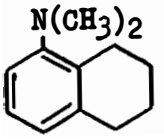
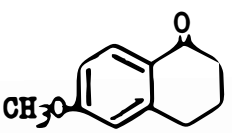
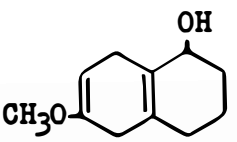
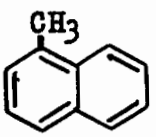
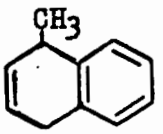
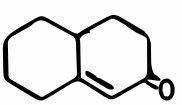
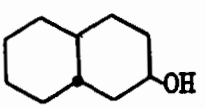
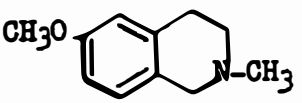
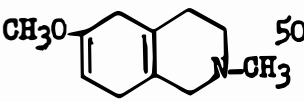
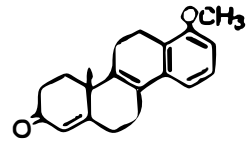
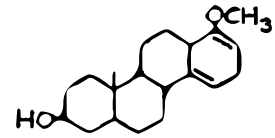
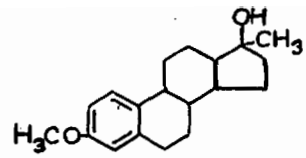
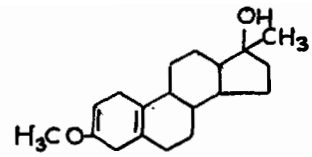
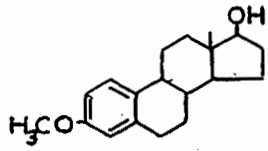
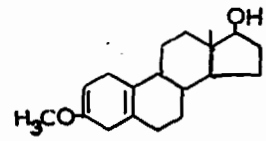
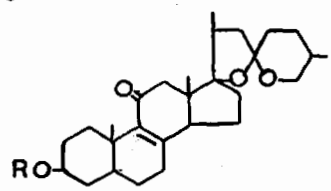
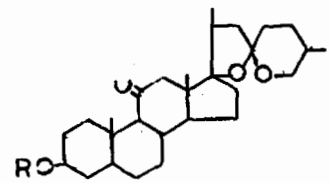
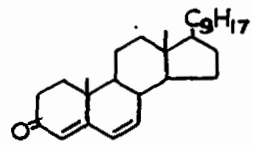
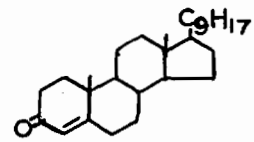
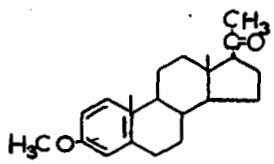
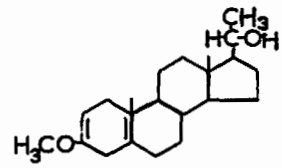
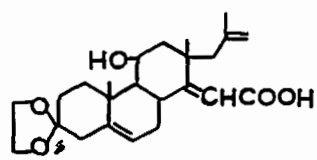
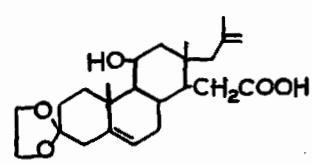
Starting Material	Product	Yield	Alkali Metal	Reference
		66%	Na	29
		---	Na	31
		80%	K	32
		---	Na	33
		---	Na	25
		70%	Na	22
		50%	Na	18

TABLE II

REDUCTIONS BY THE ALKALI METAL-ALCOHOL-AMMONIA SYSTEM (Continued)

Starting Material	Product	Yield	Alkali Metal	Reference
		35%	Li	76
		62%	Li	16
		90%	Li	14
		- - -	Li	17
		80%	Li	20
		- - -	Li	21
		78%	K	19

the unsaturation to be conjugated.[37]* In most of these reductions the position of hydrogen addition is that which would be expected for an attack by a nucleophilic reagent.**

The oldest theory of reduction is that of Baeyer[40] who believed that the dissolving metal reacted with the solvent to produce atomic hydrogen and that this "nascent" hydrogen then reduced the organic compound more rapidly than it could combine with itself to form molecular hydrogen. Modern proponents of this theory define nascent hydrogen merely as hydrogen which does not have the properties which molecular hydrogen has under the same experimental conditions.[6] According to this theory the nascent hydrogen interacts in some unknown manner with the solvent which then has a direct role in the reduction.***

The nascent hydrogen theory is no longer widely accepted although some modern authors still use it.[43] It was first rejected by Willstätter, Seitz and Bumm[41] who found that the heterogeneous reduction of stilbene by sodium amalgam was 90 per cent efficient based on the amount of sodium amalgam used, i. e., only 10 per cent of molecular hydrogen was formed. They considered this yield to be impossibly high if hydrogen atoms were the actual reducing agents. They also demonstrated that the ability of

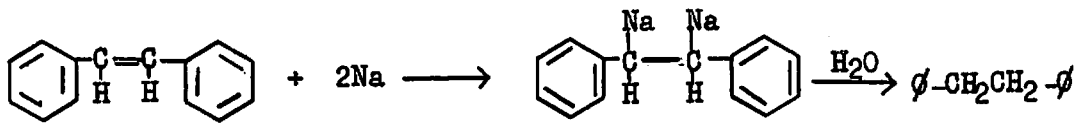
---

*Recently it has been shown that 1-hexene, but not 2-hexene, can be reduced to hexane by sodium and alcohol in liquid ammonia.[38]

**One exception is the reduction of 2-naphthol (reaction with molten sodium amide gives 2-hydroxy-5-aminonaphthalene) to give 2-tetralone.[39]

***One principal objection to nascent hydrogen mechanisms is the lack of definition given to the chemical moieties used in such mechanisms.

sodium amalgams of varying strengths to reduce double bonds and to liberate hydrogen from water were not always parallel. This led Willstatter to propose a mechanism in which metallic sodium was added to the double bond and subsequently replaced through solvent hydrolysis. Supporting



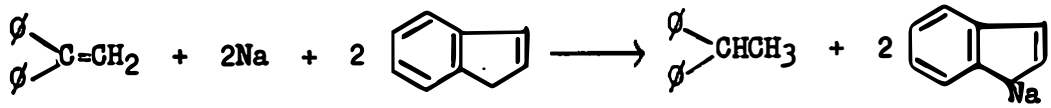
this theory at the time was the fact that only those compounds which form organo-sodium compounds in inert solvents had been reduced by dissolving metals.[42]

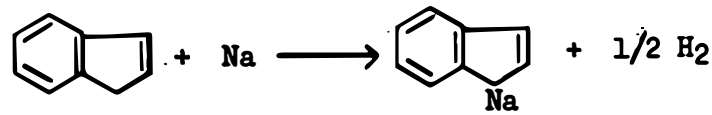
There are some objections to Willstatter's theory, as originally proposed. One objection, first expressed by Hückel, was to the necessity of the establishment of a carbon metal bond. Hückel has pointed out that in the reduction of naphthalene to 1,4-dihydronaphthalene by calcium, the calcium ion is not large enough to be attached to both the 1 and the 4 carbon atoms at the same time.[44] Thus Hückel believed that a salt or ionic type bond was formed between the metal and the organic compound as an intermediate in the reduction.*

Prins[45] and Ziegler[46] have presented similar experimental evidence against the nascent hydrogen theory. Unfortunately both men worked, as did all early workers, with heterogeneous reaction media. Prins found that aqueous hydrochloric acid reacted more rapidly with strips of iron and magnesium in the presence of nitrobenzene than it did in its ab-

*Hückel found that stable organo-sodium compounds of naphthalene can be formed in liquid ammonia by working at low temperatures. Such intermediates reacted irreversibly with hydrogen ions furnished by any compound present which was a stronger acid than the product.[44]

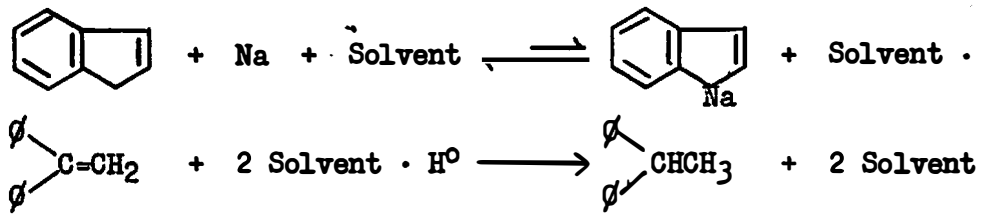
sence. Ziegler measured the rate of the following two reactions. Each was run in an inert solvent with the sodium being present in the form of a fine sand. The first reaction is much faster than the second.





This second reaction then is not a likely step in the first.

However, the nascent hydrogen theory cannot be discarded completely since many alternate mechanisms can be proposed, i. e.:



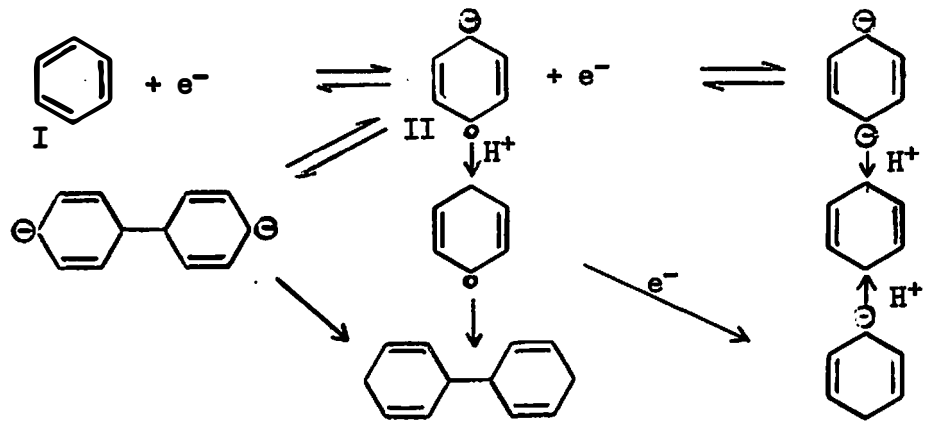
It can be argued that the first reaction consists of a rapidly established equilibrium which lies far to the left. In the absence of any compound accepting nascent hydrogen, a fast reaction, the nascent hydrogen slowly combines to form molecular hydrogen. Although this mechanism does not appear likely and does not explain the predominately nucleophilic position of attack by the hydrogen, there is as yet no way to completely exclude it.

Michaelis and Schubert[47] have proposed that reduction by dissolving metals consists of the consecutive addition of two electrons, followed by two protons. This view has been most fully developed by Birch to explain reduction by the alkali metal-alcohol-ammonia system. Birch has postulated that such reactions proceed by the addition of two electrons to form a dicarbanion intermediate which is stabililized through

solvolysis by the ammonia. Birch believes and emphasizes that ammonia owes its superiority over hydrocarbon solvents in reductions to its solvolytic properties and high dielectric strength, both of which stabilize ionic intermediates.[48]

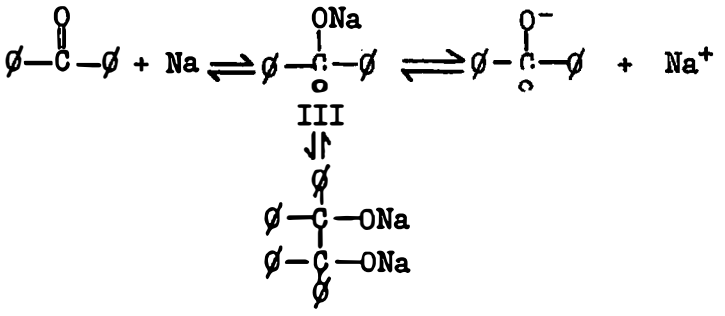
The reaction scheme, Chart One, proposed by Birch[49] shows the possible intermediates in the reduction of benzene. The reduction will be represented here in terms of carbanions rather than of non-ionized salts which may be in equilibrium with them.

CHART ONE

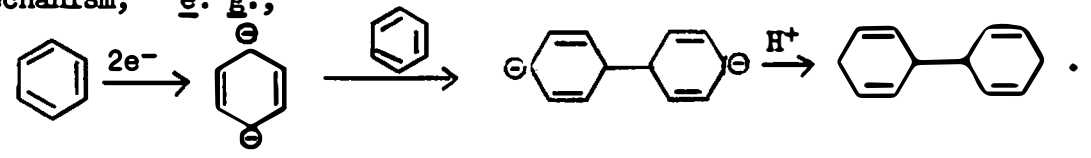


The principal products are determined by irreversible proton addition to the positions of highest charge density in the ionic intermediates. (For reversible additions the products would be determined by considerations of equilibrium, i. e., the relative free energies of the products.) Further, products can be determined by the rates of secondary reactions such as dimerization.

The existence of the carbanion-radical, II, is based on analogy to such compounds as ketyls[50] and semiquinones.[51] For example, the following reactions seem well established for a ketyl (III).

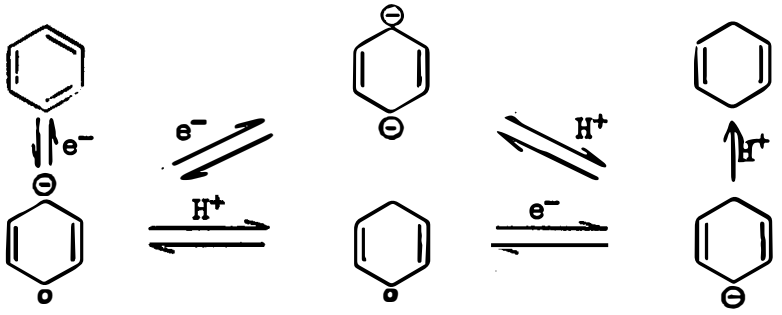


The existence of radicals or carbanion-radicals cannot be based on the fact that dimers are formed. Dimers could arise by a purely ionic mechanism,[46] e. g.,



Since extensive dimerization does not occur in the presence of alcohol, the previous mechanism for the reduction of benzene will be simplified to that shown in Chart Two.

CHART TWO



The essential step in the reaction[49] is the addition of one electron to give a carbanion-radical or of two electrons to give a dicarbanion. Polarographic data[49] indicates that the rate determining step is the reversible addition of the first electron.

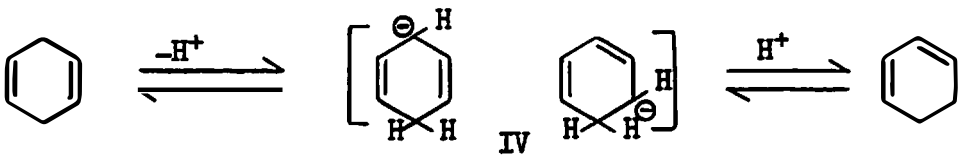
The equilibrium, the first phase of the above mechanism, is far to the left because of the high resonance energy of the benzene ring and the high charge interaction in the dicarbanion. The equilibrium lies

farther to the right where the resonance possibilities for the carbanion are greater, as in addition of electrons to naphthalene derivatives, or there are electronegative atoms to accept the electrons, as in addition of electrons to ethyl benzoate.[52] In such cases reduction occurs with greater facility.

The second phase of the mechanism is the irreversible addition of protons to carbanions forcing the reaction to completion.

In support of the ionic mechanism of reduction, Birch[52] states, without experimental evidence, that the reaction of sodium in ammonia with alcohol is slow while the reaction of carbanions with protons proceeds rapidly. This makes it unlikely that atomic hydrogen or metal hydrides could intervene in the reduction.

One of the intermediates in the benzene reduction, the carbanion of 1,4-dihydrobenzene,[12] is also an intermediate in the isomerization of 1,4-dihydrobenzene to 1,2-dihydrobenzene. Since the position of equi-



IV

librium in this isomerization lies almost completely to the right, the conjugated isomer, 1,2-dihydrobenzene, must be the more stable isomer, i. e., have the lower free energy. The simultaneous addition of both protons to the dicarbanion seems unlikely so we must now explain why the more stable isomer is not obtained as a primary reaction product.

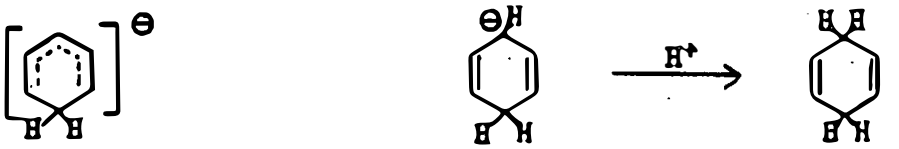
Quantum mechanics[53] show that in the carbanion,

$$\left[CH_2 \text{----} CH \text{----} CH \text{----} CH \text{----} CH_2\right]^{\ominus},$$

the charge density is highest on the middle carbon atom as in

$$CH_2{=}CH{-}\overset{\ominus}{C}H{-}CH{=}CH_2.$$

By analogy the carbanion, IV, has its charge concentrated as in resonance form V, and irreversible proton addition would logically produce

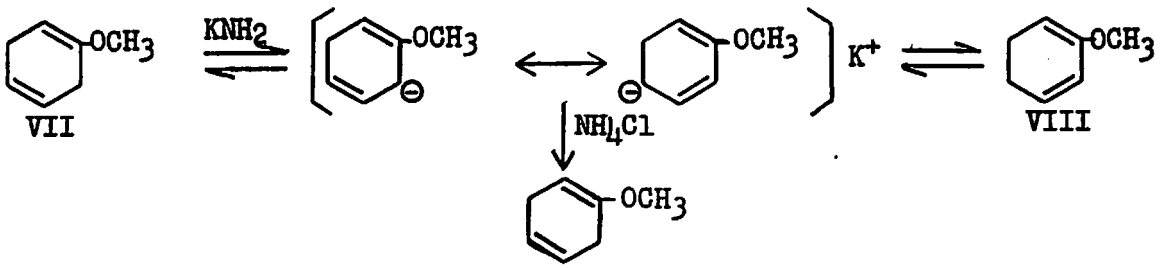


IV V VI

primarily the unconjugated derivative (VI).

Birch[54] has demonstrated the logic of this, another of the many reactions in which the products are kinetically controlled, by investigating the equilibrium in Chart Three. By using a catalytic amount of

CHART THREE



VII VIII

potassium amide in NH_3 the unconjugated isomer (VII) could be converted into the conjugated isomer (VIII). Here the proton addition is reversible because both ammonia and dihydroanisole have about the same acid strength. Since the conjugated isomer has the lower free energy it is the major product in this equilibrium.

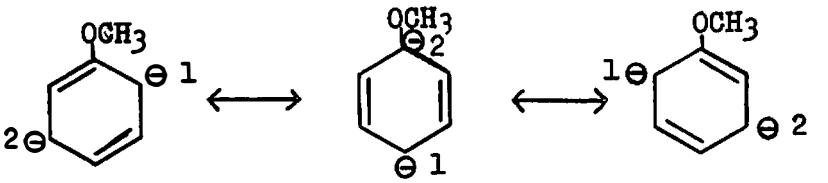
When either the conjugated or the unconjugated isomer was treated with a two or three mole excess of potassium amide it was converted almost entirely into the potassium salt. When a large amount of a strong acid (ammonium chloride or water) was added quickly to this salt irreversible proton addition occurred and the chief product was the unconjugated

or high energy isomer.*

A final consideration which Birch has given to these reductions in ammonia is a rule for predicting the positions of the entering hydrogen atoms. From correlation of experimental data, Birch states[49] that the rule of addition of hydrogen atoms to a benzene ring is as follows: the atoms are added in positions 1,4 to each other, avoiding carbon atoms carrying electron-repelling groups in the order $N(CH_3)_2 > OCH_3 >$ alkyl, and being attracted to carboxyl groups.

The rationale employed by Birch[49] to explain this rule may be illustrated with anisole.

There are three "low-energy" resonance forms for a dicarbanion intermediate from this benzene derivative where the electrons are distinguished by the numbers 1 and 2. Birch assumes that each charge is



"dispersed among alternate carbon atoms, one charge to each set of three carbons." The 1,3,5-charge, electron 2, raises the energy of the system

Electron 1

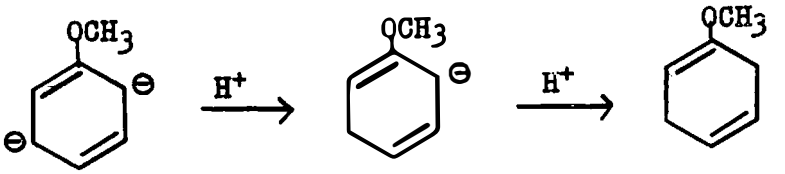
Electron 2

more than the 2,4,6-charge, electron 1, because of the electron repelling power of the methoxyl group. Therefore the 1,3,5-charge should

---

*This phenomenon is not unusual. Careful acidification of the sodium salt of acetoacetic ester at -70° affords the pure enol form.[56] Yet the keto form is more stable and this system is more labile than the one mentioned above.

react first and its point of greatest electron density will be at the 3 and 5 positions. The second hydrogen ion will then add para to the first to give the product.

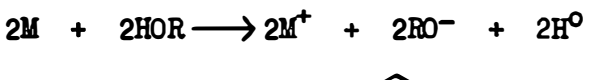


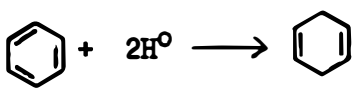
D. Statement of the Problem

Two general reaction mechanisms have been suggested for the reduction of carbon-carbon unsaturation by alkali metal-alcohol-ammonia systems; these will be designated as the "nascent hydrogen" mechanism and the "ionic" mechanism. The many detailed mechanisms are merely elaborations or variations of these two. Simplified representations of both mechanisms are given in Chart Four, where M represents an alkali metal, ROH an alcohol, and benzene a typical organic substrate undergoing reduction.

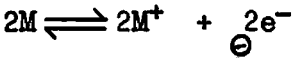
CHART FOUR

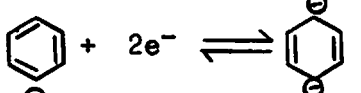
"Nascent hydrogen" mechanism

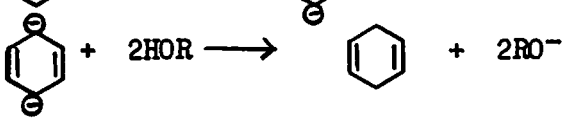




"Ionic" mechanism







The purpose of this work has been to find experimental evidence which will aid in choosing between the two modes of hydrogen addition. To accomplish this, the reactions of alkali metal in ammonia with alcohols, with organic substrates and alcohol, and with organic substrates alone have been carried out with careful control of reaction variables. Observations have been made on the effects of some of these variables on the course of the reactions and on the time required for the reactions.

While prosecuting this main problem, it has been necessary to solve several secondary problems connected with the synthesis and proof of structure of certain intermediates. In the discussion which follows the synthetic work is presented first.

CHAPTER II

PRESENTATION AND DISCUSSION OF RESULTS

A. Reduction of 1-Naphthol and Isomerization of the Product

The first types of compound considered for use as substrates in the reduction study were 1-substituted-naphthalenes. The reduction of 1-naphthol (I),* as the 1-naphthoxide ion, to 5,8-dihydro-1-naphthol (II) by sodium in alcohol[57] and by sodium and alcohol in liquid ammonia[29] has been reported. The metal-alcohol-ammonia system employed in this study was found to give an almost quantitative yield of the dihydroderivative from 1-naphthol. However, replacement of the hydroxyl group by other substituents lowers the yield of the 5,8-dihydronaphthalene derivative and gives rise to complicating side reactions.[32] In some instances the isolated double bond initially formed is labile under the reaction conditions and shifts into the conjugated position. When this occurs the conjugated double bond is reduced more rapidly than the naphthalene ring and the only easily isolable reduction product is a tetralin.**

Since the dihydronaphthalenes with a conjugated double bond appeared to be rapidly and completely reduced at this double bond by the metal-in-ammonia systems, emphasis was shifted to the dihydro-

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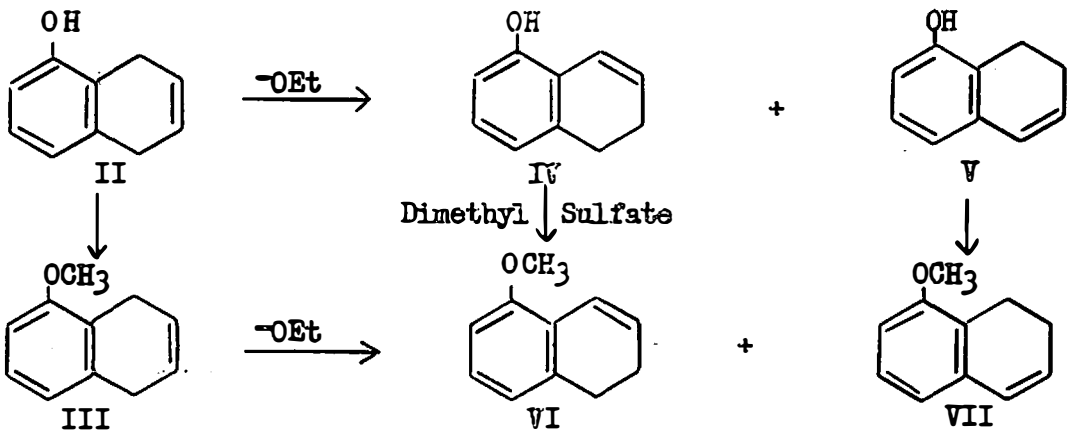
*The Roman numerals begin anew in this chapter.

**Throughout this thesis the terms 1,2,3,4-tetrahydronaphthalene and oxy-1,2,3,4-tetrahydronaphthalene will be replaced by the shorter terms tetralin and tetralone respectively.

naphthalenes in a search for suitable substrates. In 1921 Rowe and Levin[57] had isomerized 1-hydroxy-5,8-dihydronaphthalene (II) to a conjugated isomer, either 1-hydroxy-5,6-dihydronaphthalene (IV) or 1-hydroxy-7,8-dihydronaphthalene (V), Chart Four, but had not differentiated between the two possibilities. The isomerized compound, IV or V, and its

CHART FOUR



methyl ether, 1-methoxy-5,6-dihydronaphthalene (VI) or 1-methoxy-7,8-dihydronaphthalene (VII) were both reduced to the corresponding tetralins by alkali metal and alcohol in liquid ammonia.

In order to use these compounds, it was first necessary to elucidate their structures. It has now been demonstrated that the base catalyzed isomerization of 5,8-dihydro-1-naphthol (II) or its methyl ether (III) gives predominately the 5,6-dihydro isomer, IV or VI, contaminated with some 7,8-dihydro isomer, V or VII. Samples of the liquid, isomerized methyl ether, were obtained by methylating the crystalline product of the base-catalyzed isomerization of 5,8-dihydro-1-naphthol (II) and by methylating 5,8-dihydro-1-naphthol and then isomerizing with

base.* If either sample of methyl ether were emulsified in water and treated with bromine, a 56 per cent yield of a crystalline 1-hydroxy-2,5-dibromo-8-methoxytetralin** (VIII) resulted. That the structure assigned this compound is correct was shown in Chart Five.

Oxidation of the dibromohydrin (VIII) with chromium trioxide in acetic acid produced an 80 per cent yield of a dibromoketone (IX). Dehydrobromination of this dibromoketone in collidine with the rigorous exclusion of oxygen gave methoxyhydroxybromonaphthalene (X). This compound could be isolated only if the reaction were run in a narrow temperature range. The compound was so unstable to air oxidation that no concerted attempt was made to purify it. Instead it was converted into a stable dimethoxybromonaphthalene (XI) by treatment with dimethyl sulfate. The Grignard reagent of the dimethoxybromonaphthalene was formed by treatment with magnesium and decomposed by treatment with alcohol to give a good yield of product which was shown to be the known

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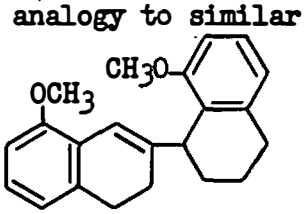
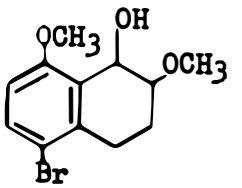
*Purification of the isomerized methyl ether by distillation always left a residue in the pot. Trituration of this residue with acetone gave a crystalline dimer, $C_{22}H_{24}O_2$, m.p. 148°. Although this dimer was not completely characterized, analogy to similar dimerizations[58] indicatesstructure i for it.



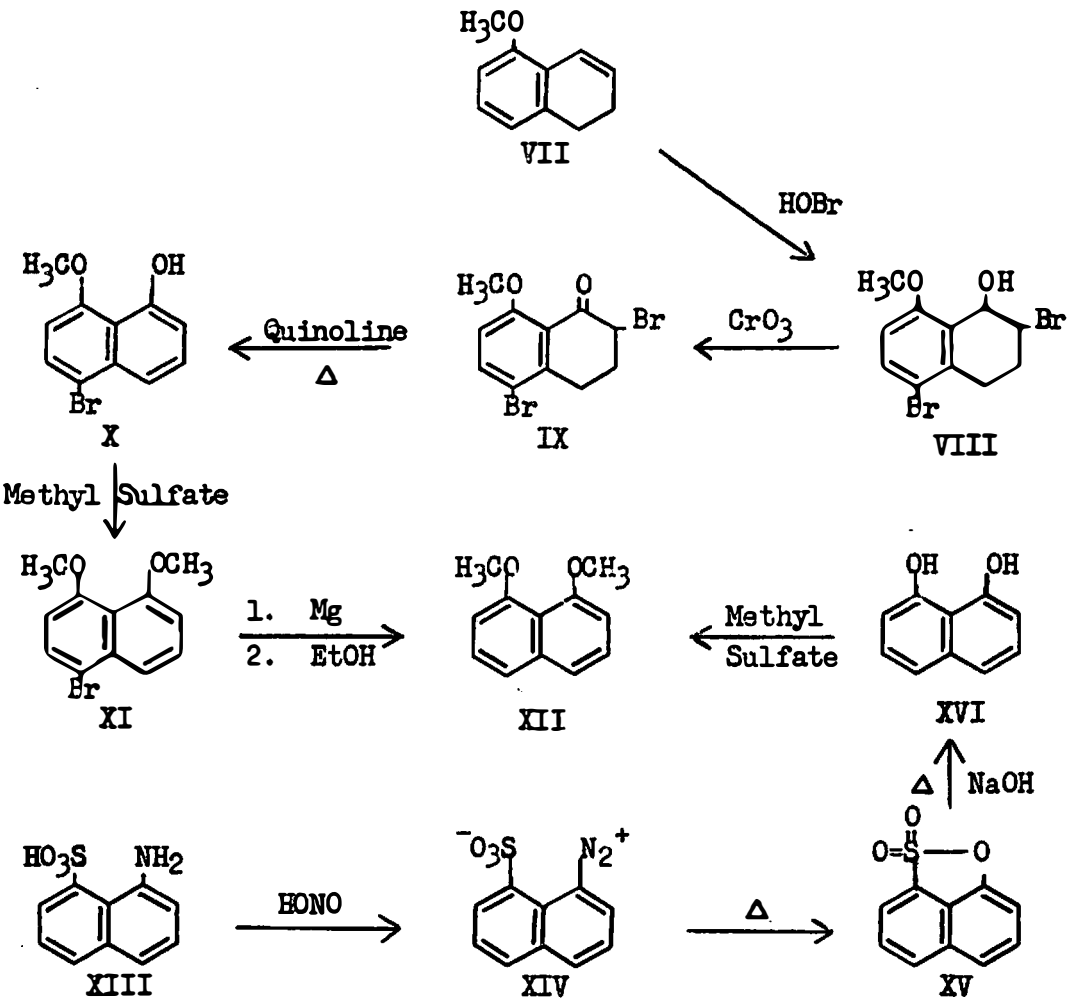
i

**Treatment of 1-hydroxy-2,5-dibromo-8-methoxytetralin with methanolic silver nitrate gave no rearrangement product. The only compound isolated, $C_{12}H_{15}O_3$, m.p. 141.5° was apparently formed by displacement of bromide by methoxide and is formulated as 1-hydroxy-2,8-dimethoxy-5-bromotetralin, ii.[90]



ii

CHART FIVE


H3CO
VII
HOBr
H3CO OH
Br
VIII
CrO3
H3CO O
Br
Br
IX
Quinoline
Δ
H3CO OH
Br
X
Methyl Sulfate
H3CO OCH3
Br
XI
1. Mg
2. EtOH
H3CO OCH3
XII
Methyl Sulfate
OH OH
XVI
Δ
NaOH
HO3S NH2
XIII
HONO
−O3S N2+
XIV
Δ
O
O=S—O
XV

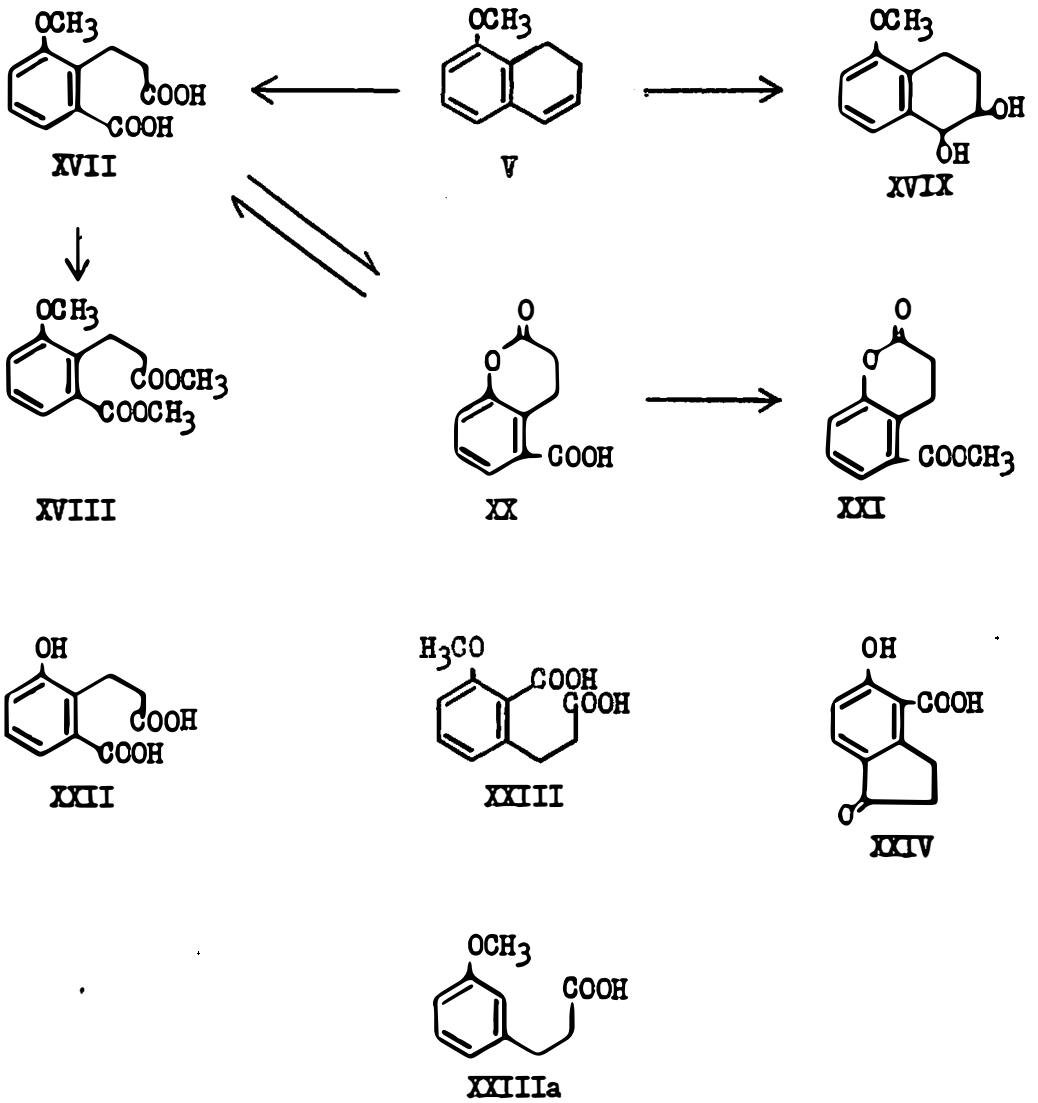
1,8-dimethoxynaphthalene (XII) by its melting point, ultraviolet spectrum, and mixed melting point with an authentic sample.

Isolation of the 1,8-dimethoxynaphthalene by this procedure showed the original methoxynaphthalene derivative to be the 5,6-dihydro isomer. Had it been the 7,8-dihydro isomer, 1,5-dimethoxynaphthalene would have been obtained by the route shown in Chart Five.

The authentic sample of 1,8-dimethoxynaphthalene (XII) was prepared using procedures from the literature, Chart Five. 8-Aminonaphthalene-1-sulfonic acid (XIII) was diazotized and the crystalline 1-diazonaphthalene-8-sulfonic acid (XIV) obtained was transformed into 1,8-naphthosultone (XV) by boiling water.[93] A sodium hydroxide fusion of this sultone gave 1,8-naphthalenediol (XVI) which, on treatment with dimethyl sulfate, yielded 1,8-dimethoxynaphthalene.[91,92]

Although the degradation of Chart Five showed the methyl ether produced in Chart Four to be primarily the 5,6-dihydro isomer (VI), an oxidative degradation, Chart Six, of this isomerization product showed that a small amount of 7,8-dihydro-1-methoxynaphthalene was present. First attempts at oxidation, with chromium trioxide in acetic acid, osmium tetroxide in ether, and potassium permanganate in acetone-piperidine demonstrated that the methyl ether was very sensitive to oxidation. No pure organic materials could be isolated from these reactions. Finally a very mild oxidation with permanganate at 0° was found to yield a small amount of 3-(2-methoxy-6-carboxyphenyl)-propanoic acid (XVII) and an even smaller amount of <u>cis</u>-1,2-dihydroxy-5-

CHART SIX


OCH3
COOH
COOH
XVII
OCH3
V
OCH3
OH
OH
XVIX
OCH3
COOCH3
COOCH3
XVIII
O
O
COOH
XX
O
O
COOCH3
XXI
OH
COOH
COOH
XXII
H3CO
COOH
COOH
XXIII
OH
COOH
O
XXIV
OCH3
COOH
XXIIIa

methoxytetralin (XVIX). The dibasic acid (XVII) gave a dimethyl ester (XVIII) on treatment with diazomethane. Cleavage of the ether linkage of XVII with hot pyridinium chloride gave a lactone-acid (XX), the ultra-violet spectrum of which was almost identical with that of the dibasic acid (XVII) itself. The lactone acid, 5-carboxy-3,4-dihydrocoumarin (XX) gave a methyl ester (XXI) with diazomethane which has maxima in its infrared spectrum consistent with a lactone carbonyl (1788 $cm.^{-1}$) and a methyl ester carbonyl (1730 $cm.^{-1}$). The lactone-acid (XX) was cleaved by saponification with sodium hydroxide and carefully acidified at 0^{o} in an attempt to obtain 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid (XXII). This attempt was unsuccessful, as might be expected, because of the rapid lactonization of a compound with the structure (XXII) of the expected product. The lactone ring of XX could be kept open, however, by cleavage with hot base in the presence of an excess of dimethyl sulfate. Since ether formation is not reversible under basic conditions the starting dibasic acid (XVII) was reobtained.

The physical and chemical evidence presented above can only fit structure XVII* for the dibasic acid. If the acid, 3-(2-carboxy-3-methoxyphenyl)-propanoic acid (XXIII), obtainable from 5,6-dihydro-1-methoxynaphthalene (VI) were treated with hot pyridinium chloride, a

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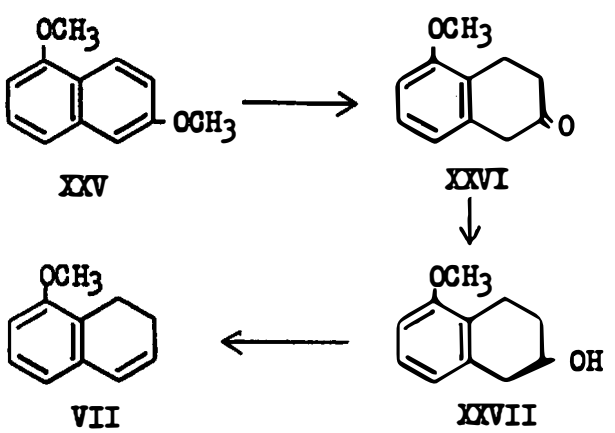
*Aromatic carboxyl groups ortho to methoxyl groups decarboxylate more readily than meta or aliphatic carboxyl groups. If the dibasic acid initially produced possessed structure XXIII instead of structure XVII, then XXIIIa would be obtained under mild decarboxylation conditions. Conditions severe enough to give any decarboxylation always gave complete decarboxylation indicating structure XVII for the dibasic acid.

compound, 4-carboxy-5-hydroxyindanone (XXIV), with the same empirical formula as XX might conceivably have been produced. However, XXIV and its methyl ester would have given positive tests for ketonic carbonyl and phenolic hydroxyl groups. The actual compound (XX) and its methyl ester did not respond to tests for either of these functional groups.

Since 5,6-dihydro-1-naphthol (IV) could be obtained by recrystallization of the mixture from the isomerization of 5,8-dihydro-1-naphthol, it was decided that 7,8-dihydro-1-naphthol (V) and 1-methoxy-7,8-dihydronaphthalene (VII) should be synthesized for comparison purposes and for possible use as substrates in the studies on reduction by alkali metals.

The known 5-methoxy-2-tetralone (XXVI) was prepared from 1,6-dimethoxynaphthalene (XXV) by the method of Cornforth, Cornforth and Robinson,[60] Chart Seven. Reduction of the tetralone (XXVI) with lithium

CHART SEVEN



aluminum hydride gave 2-hydroxy-5-methoxytetralin* (XXVII), which on heating with a mixture of molten potassium and sodium hydroxide dehydrated to give a good yield of 1-methoxy-7,8-dihydronaphthalene (VII).

An attempt to prepare 1-methoxy-7,8-dihydronaphthalene (VII) by pyrolysis of the benzoate of 2-hydroxy-5-methoxytetralin (XXVII) failed. The ester (XXVII) distilled unchanged from a pot temperature of 360°.

A 40 per cent yield of 3-(2-methoxy-6-carboxyphenyl)-propanoic acid (XVII) could be obtained by oxidation of the pure 1-methoxy-8-dihydronaphthalene (VII) with potassium permanganate. However, no crystalline bromohydrin was isolated upon treatment of VII with bromine water under conditions which give a 58 per cent of bromohydrin with the 5,8-isomer (VI).

Only resins were produced when 1-methoxy-7,8-dihydronaphthalene (VII) was heated with either pyridinium chloride or methyl magnesium iodide to cleave the ether linkage. Since no method could be devised for cleaving the ether linkage without causing dimerization and/or polymerization of this styrene-type molecule, an alternate synthesis (Chart Eight) was used to prepare 1-hydroxy-7,8-dihydronaphthalene.

Treatment of the sodium salt of 1,6-dihydronaphthalene with chloromethyl methyl ether gave 1,6-bismethoxymethoxynaphthalene (XXVIII, Chart Eight). This compound can be considered to be an

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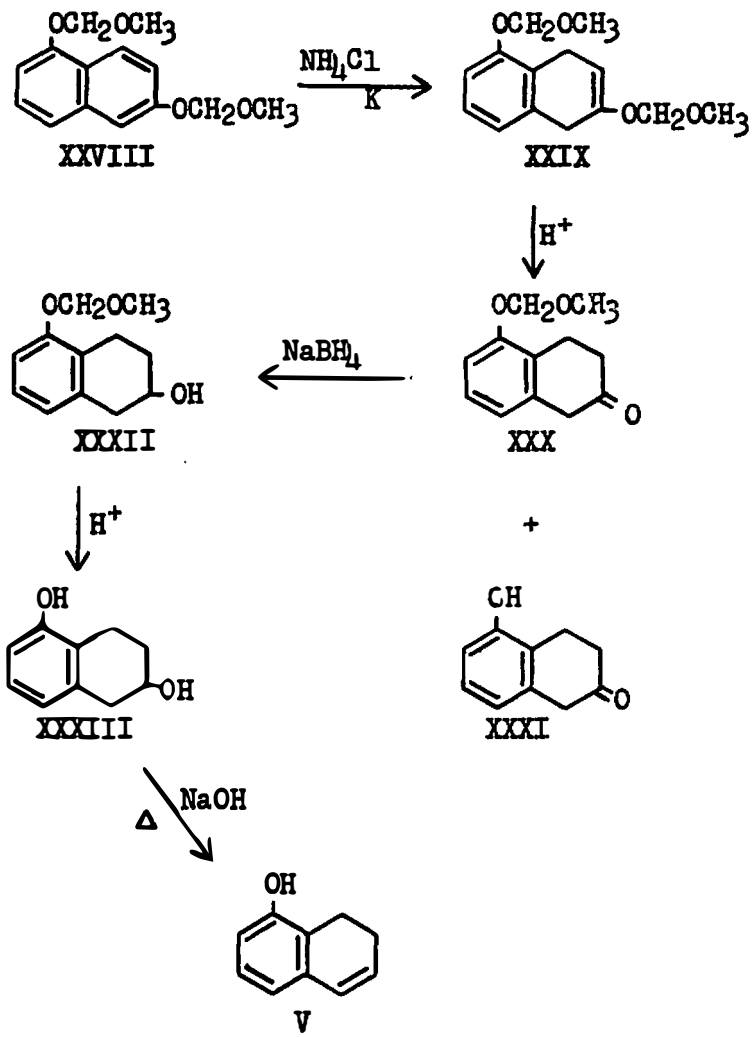
*Attempts to reduce 2,5-dihydroxynaphthalene directly to either 5-hydroxy-2-tetralone or 2,5-dihydroxytetralin with potassium and alcohol in ammonia failed.

CHART EIGHT


OCH2OCH3
OCH2OCH3
XXVIII
NH4Cl
K
OCH2OCH3
OCH2OCH3
XXIX
H+
OCH2OCH3
O
XXX
NaBH4
OCH2OCH3
OH
XXXII
H+
+
OH
OH
XXXIII
CH
O
XXXI
Δ
NaOH
OH
V

acetal formed from formaldehyde, 1,6-dihydroxynaphthalene and methanol and as such should be stable to base yet easily decomposable with acid. Potassium and ammonium chloride in liquid ammonia reduced the diacetal (XXVIII) to 1,4-dihydro-2,5-bismethoxymethoxynaphthalene (XXIX). Although this compound was not purified because of an expected instability to distillation temperatures, its ultraviolet spectra showed that the reduction was almost quantitative. Treatment of the dihydro compound (XXIX) with strong acid gave only high melting organic products but treatment with dilute mineral acid for a short period of time gave both 5-methoxymethoxy-2-tetralone (XXX) and 5-hydroxy-2-tetralone (XXXI), albeit in poor yield. A viscous oil which could not be induced to crystallize was obtained by treating the sodium salt of 5-hydroxy-2-tetralone (XXXI) with sodium borohydride in methanol. A lithium aluminum hydride reduction of 5-methoxymethoxy-2-tetralone (XXX) proceeded satisfactorily to give liquid 2-hydroxy-5-methoxymethoxynaphthalene (XXXII) which was hydrolyzed to crystalline 2,5-dihydroxytetralin (XXXIII) with dilute mineral acid. Dehydration of the dihydroxytetralin* (XXXIII) with molten alkali produced 1-hydroxy-7,8-dihydronaphthalene (V).

The ultraviolet spectra of these dihydronaphthalenes are quite interesting. Structures with isolated double bonds such as II and III have spectra which are almost indistinguishable from those of phenol and anisole respectively. On the other hand structures with conjugated

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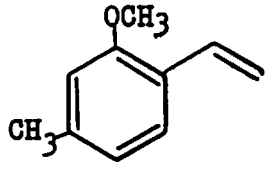
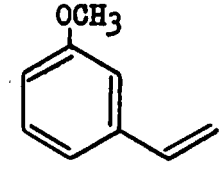
*Treatment of 2-hydroxy-5-methoxymethoxytetralin (XXXII) directly with molten alkali gave a product melting above 250°.

double bonds are distinguished by having about five-fold more intense absorption in the 250-270 mμ region of the spectrum.* Thus compounds with structures such as IV, VII, XXXIV and XXXV are easily distinguishable from unconjugated isomers of similar structure through their ultraviolet spectra although other physical properties may be almost identical. However, it is not so easy to distinguish the conjugated isomers themselves from one another.

It is intructive to compare the spectra of some such isomeric pairs, as IV-V, VI-VII and XXXIV-XXXV. In these, the first structure

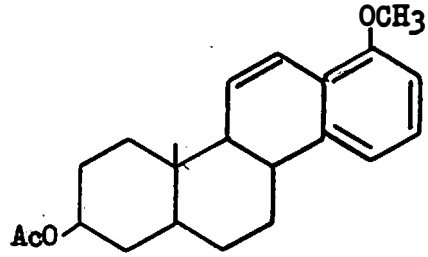


XXXIV

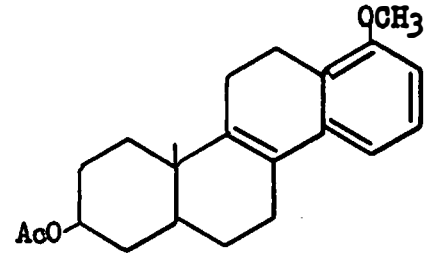


XXXV

has the double bond in the ortho position to a methoxyl group and the second structure has the double bond in the meta position. When this work was begun the only such pair in the literature for which ultraviolet spectra were known was the 1-methoxyoctahydrochrysenes,[62] XXXVI-XXXVII. The spectra of the chrysenes were misleading in that



XXXVI



XXXVII

*Daub and Vandenbelt[61] call this the first primary band.

XXXVI, the ortho isomer, had considerable fine structure in the 280-320 mμ region whereas XXVII, the meta isomer, had no such fine structure. This fine structure was originally mistakenly taken to be indicative of an ortho double bond.

The data for the simpler o-methoxystyrene (XXXIV) was also available.[63] m-Methoxystyrene (XXV), a known compound was synthesized by methods in the literature and its spectrum determined. Both of these styrenes* have the 280-320 mμ fine structure. Afterwards, when 7,8-dihydronaphthol and its methyl ether were synthesized they were both also found to have absorption in the 280-320 mμ region. It follows then that any generalization about a correspondence between double bond position and fine structure is invalid.

On the other hand there does seem to be a correlation between the intensities of the maxima and the position of the double bond. The spectra of these pairs of isomers (IV-V, VI-VII and XXXIV-XXXV) are qualitatively similar but in each case the maximum of the ortho isomer is more intense than that of the meta isomer. This generalization appears to hold quite well for a wide variety of benzene derivatives** and affords a method of distinguishing between ortho and meta isomers

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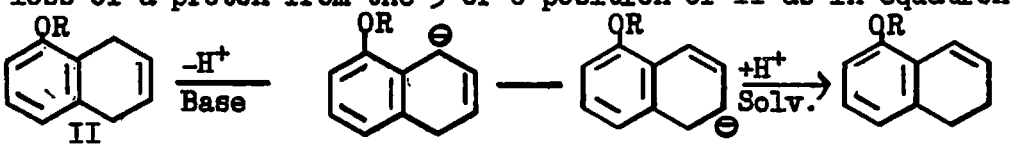
*These compounds are not actually isomers. In the original literature survey, structure XXIV was thought to be the simple ortho-methoxystyrene and the mistake was not discovered until XXXV had been synthesized and its spectrum had been taken. Fortunately the presence of a side chain alkyl group has little effect on the ultraviolet spectrum of these compounds.

**An inspection of the thirty spectra of ortho and meta benzene derivatives listed in articles by Daub and Vandenbelt[61] and by Buraway and Chamberlain[64] discloses that in all but two cases the absorption of the "first primary band" is more intense for the ortho isomer. The two exceptions are chlorbenzoic acid and the salt of that acid.

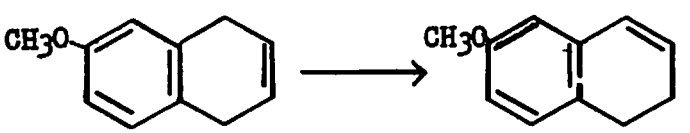
when the spectra of both isomers are known. The maxima and the intensities of absorption are listed for the styrene type pairs mentioned above and for the analogous hydroxy and methoxybenzaldehydes[64] in Table III.

From chemical and spectral evidence the ratio of 5,6-dihydro to 7,8-dihydro-1-naphthol is estimated to be 4:1 in the isomerization of 5,8-dihydro-1-naphthol. Isomerization of this naphthol's methyl ester (II) also favors production of the 5,6-dihydro isomers. This base-catalyzed isomerization almost certainly involves the initial loss of a proton from the 5 or 8 position of II as in equation 1.



(1)

It would seem that a correlation might exist between the position of isomerization and the acidity of the hydrogen atoms on the carbon atoms adjacent to the benzene rings. The reported isomerization of 5,8-dihydro-2-methoxynaphthalene (XXXVIII) to 5,6-dihydro-2-methoxynaphthalene (XXXIX) was interpreted by Birch[65] in such a manner, i. e., in this case (equation 2) as indicating that a methylene group meta



XXXVIII XXIX

(2)

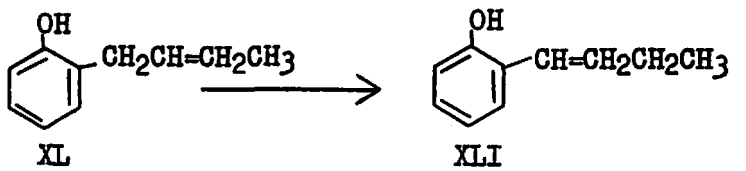
to a methoxyl is more acidic than is a para-methylene group. Such an interpretation seems particularly appealing since it is known that a hydroxyl group meta to methoxyl is more acidic than is a para-hydroxyl group, Chart Nine. In a similar vein, Bader[66] has reported that o-

TABLE III

COMPARISON OF SPECTRA OF ORTHO AND META ISOMERS

Compound	First Primary Band λ_{max}	logϵ	Secondary Band λ_{max}	logϵ
IV	265	3.90	300	3.45
V	267	3.65	299	3.24
VI	265	3.94	296	3.38
VII	265	3.89	298	3.33
XXXIV	250	4.06		
XXXV	250	3.89	- -	- -
o-Hydroxybenzaldehyde	254	4.10	324	3.64
m-Hydroxybenzaldehyde	254	3.98	315	3.48
o-Methoxybenzaldehyde	253	4.02	321	3.66
m-Methoxybenzaldehyde	253	3.98	309	3.48

crotylphenol (XL) is isomerized (equation 3) more rapidly than is p-

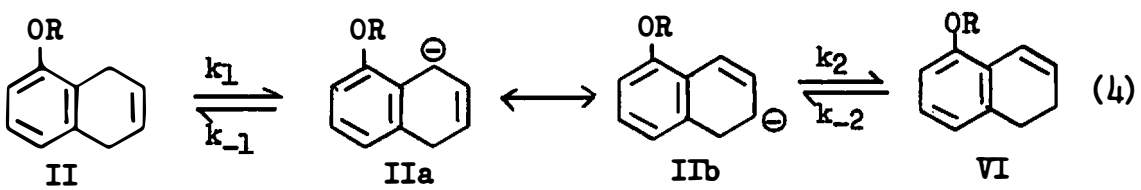


XL XLI (3)

crotylphenol. Here the relative rates of isomerization are in accord with the relative acidities of hydroxyl ortho and para to a hydroxyl group, Chart Nine.

From the treatment shown in Chart Nine, it would seem rather unusual to find that the isomerization of the 5,8-dihydronaphthol (or its methyl ether) proceeds in the direction which it does. This direction of isomerization would indicate that a methylene group ortho to hydroxyl or methoxyl is more reactive than the same group in the meta position. This is in direct opposition to the acidities of hydroxyl groups ortho and meta to hydroxyl or methoxyl group.

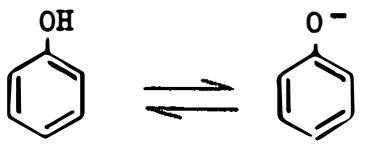
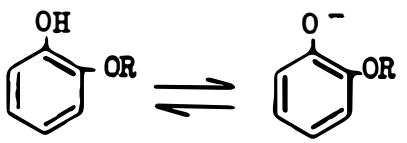
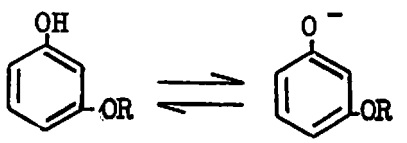
That Birch's treatment of the isomerization is incomplete can be seen by a more thorough look at the probable mechanism. The isomerization of 1-methoxy-5,8-dihydronaphthalene (II) almost certainly proceeds through an intermediate carbanion represented by the low energy resonance forms IIa and IIb. The rate constants controlling the transformation may then be represented as in equation 4.



II IIa IIb VI (4)

The reverse reaction, k_{-2}, must be negligibly small since conjugated isomers, such as VI are stable in molten alkali. Further, the concen-

CHART NINE[67,102]

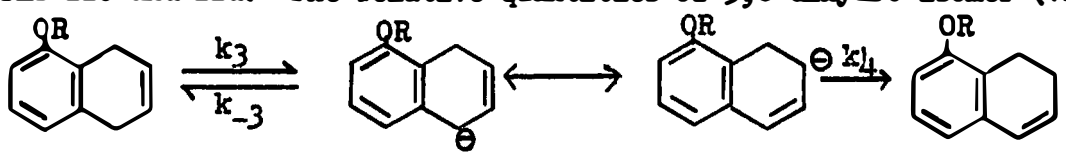
COMPOUND	K x 10^{10}	
	2.82	
	R=H	R=CH_3
	3.31	1.18
	3.63	2.24
	1.10	0.63

tration of IIa-b can never be large; that is, the methylene group in II is only weakly acidic. This means that $(k_{-1} + k_2) >> k_1$. Finally, one can assume that the rates of proton association, k_{-1} and k_2, are controlled by the electron densities at the position of association.[49] From analogous reactions* one can deduce that the charge density represented by IIa is much greater than that represented by IIb and therefore that $k_{-1} >> k_2$.

With the above assumptions and the stationary-state approximation[77] the following rate expression can be derived from the formation of 1-methoxy-5,6-dihydronaphthalene (VI) from II.

$$\text{Rate VI} = \frac{k_1 k_2}{k_{-1} + k_2} [\text{II}] \simeq \frac{k_1 k_2}{k_{-1}} [\text{II}] = K_1 k_2 [\text{II}] \qquad (5)$$

A similar rate expression can be derived for the formation of 1-methoxy-7,8-dihydronaphthalene (VII) from II through the low energy resonance forms IIc and IId. The relative quantities of 5,6-dihydro-isomer (VI)



(6)

II IIc IId VII

$$\text{Rate VII} = \frac{k_3 k_4}{k_{-3} + k_4} [\text{II}] \simeq \frac{k_3 k_4}{k_{-3}} [\text{II}] = K_3 k_4 [\text{II}] \qquad (7)$$

and 7,8-dihydro-isomer (VII) will be controlled by the relative values of both the equilibrium constants, K_1 and K_3, and the rate constants, k_2 and k_4, equation 8.

---

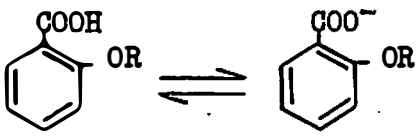
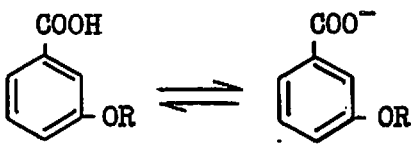
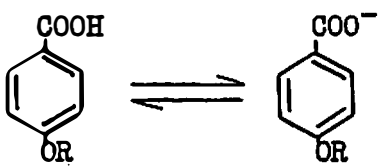
*For example, Ingold, deSalas and Wilson[69] found that when a $\beta\gamma$-unsaturated nitrile (1-cyclohexenylacetonitrile) was placed in a 0.1 N sodium ethoxide solution in deuterated ethanol, the exchange of two hydrogen atoms for two deuterium atoms was immeasureably fast. Under these conditions the isomerization to the $\alpha\beta$-unsaturated nitrile had a half-life of seven hours.

$$\frac{\text{Rate VI}}{\text{Rate VII}} = \frac{K_1 k_2}{K_3 k_4} = \frac{\text{Amount 5,6-Isomer}}{\text{Amount 7,8-Isomer}} \qquad (8)$$

The above treatment emphasizes the concept of the distribution in charge on the intermediate carbanions (IIa, IIb, etc.). This suggests that the use of substituted phenols as models for establishing the relative acidities (K ratios, equation 8) of the involved methylene groups is not realistic. Ionization of a phenol produces an anion with its charge highly localized on one atom. Ionization of one of the involved methylene groups produces an anion with its charge distributed over three atoms. Better models for the latter ionizations might be substituted benzoic acids, which also produce an anion with the charge distributed over three atoms. In this connection it can be noted that the effect of variously positioned hydroxy and methoxy substituents upon the acidity of phenol does not parallel the effects of such substituents upon the acidity of benzoic acid (Charts Nine and Ten).

The experimental findings reported herein, coupled with those of Birch and Bader, show that the rate of isomerization of the three atom allyl groups placed ortho, meta or para to hydroxyl or methoxy decreases in that order. Parallel to these rates are the acidities of the three atom carboxyl group ortho, meta or para to hydroxyl and meta or para to methoxyl. In most of the isomerizations the relative rates are apparently largely controlled by the relative acidities (K ratios, equation 8) of the allyl groups involved, which in turn are predictable from similarly situated carboxyl groups. Only in the case of competitive isomerization of an allyl group ortho and meta to methoxyl do relative carboxyl acidities not run parallel, i. e., ortho and meta methoxybenzoic acids

CHART TEN[102]

COMPOUND	$K \times 10^5$	
	6.30	
	R=H	$R=CH_3$
	105	8.14
	8.32	8.14
	2.65	3.39

have the same ionization constant.

For this latter case the relative rates of isomerization are apparently controlled by the relative association rates (k ratios, equation 8) of the carbanions produced, e. g., $k_2 > k_4$. These association rates in turn are controlled by the relative electron densities at the positions of association, e. g., the contribution of IIb to IIa-b is greater than that of IId to IIc-d. This last statement can be logically rationalized as an ortho effect. The ortho substituent, by decreasing solvation in its vicinity will decrease the contribution of IIa in IIa-b. This type of ortho effect can be recognized in a comparison of the acidities of substituted phenols and benzoic acids.

The ortho and meta substituted (methoxy or hydroxy) phenols or benzoic acids are all more acidic than the unsubstituted parent compounds. This is in accord with the expected inductive effect of the substituents. The ortho substituted phenols, in which this inductive effect should be greatest, are however weaker acids than the meta derivatives. The explanation for this is that with the ortho substituted phenols, the charge on the conjugate base requires solvation in the vicinity of the substituent. The larger this substituent (methoxyl or hydroxyl) the greater the decrease in acidity in going from the meta to the ortho isomer (Chart Nine). On the other hand, the ortho substituted benzoic acids where the charge in the conjugate base is distributed and solvation in close proximity to the substituent is not required are either equally acidic as the meta isomer (methoxyl case) or considerably more acidic

than the meta isomer (hydroxyl case)*.

In summary, by use of equation 8 a correlation of the isomerization rates or isomer ratios of certain allylic rearrangements has been made. This has been done by assuming a parallelism between the acidity of the allyl groups involved and similarly substituted carboxyl groups to predict ionization constant ratios (e. g., K_1/K_3) and by assuming an ortho effect to predict association rate ratios (e. g., k_2/k_4). Whether these assumptions with equation 8 will correlate or predict relative rates for other similar allylic rearrangements remains to be seen. To this end the rates and position of isomerization of other 1- and 2-substituted-5,8-dihydronaphthalenes are now under investigation.[103] To date the only data gathered in this extended study concerns the relative rates of isomerization of 5,8-dihydro-1-naphthol and its methyl ether.

The kinetics of the isomerization of both 1-methoxy-5,8-dihydronaphthalene and 5,8-dihydro-1-naphthol were measured in tert-amyl alcohol at 100° using spectrophotometric methods of analysis. In the presence of excess potassium amylate the kinetics were first order during the first 30 per cent of the reaction. The first order rate constant of the methyl ether (III), 3.49×10^{-3} min.$^{-1}$ was not much larger than that of the free naphthol (II) 2.93×10^{-3} min.$^{-1}$. While these

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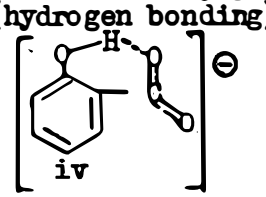
*In actual fact the ortho-hydroxybenzoic acid is sufficiently more acid than other hydroxy and methoxybenzoic acids to require the proposal of some extra stabilizing effect for the conjugate base of the ortho-hydroxy acid. Internal solvation (hydrogen bonding) has been suggested[102] for this effect, i. e., iv.



iv

figures do not mean much in the absence of data on the unsubstituted parent naphthalene (1,4-dihydronaphthalene), it is somewhat surprising that the two rates are so close. It was expected that the rate of formation of the intermediary carbanion from the free naphthol would be reduced (and thereby the rate of isomerization of the free naphthol would be less than that of its methyl ether) by effective removal of this free naphthol as its conjugate base (IIe) in the basic isomerization medium. Possibly this effect is offset by this conjugate base (IIe) acting as an internal base to facilitate production of the carbanion (IIa), equation 9.

IIe IIa (9)

B. Preparation of 1-Substituted-dihydronaphthalenes

A series of compounds with styrene-type double bonds were desired for use as the organic substrates in the alkali metal-alcohol-ammonia reductions. Experience had shown that reduction of the double bond is an easily effected reaction. Substituted styrenes, themselves, were not used for two reasons. They are easily polymerized and they are, for the most part, fairly volatile liquids. Substituted dihydronaphthalenes which have the styrene-type double bond have neither of these disadvantages in so great a degree.

For these reasons a search was carried out for a simple method of preparing 1-substituted 5,6- or 7,8-dihydronaphthalenes other than

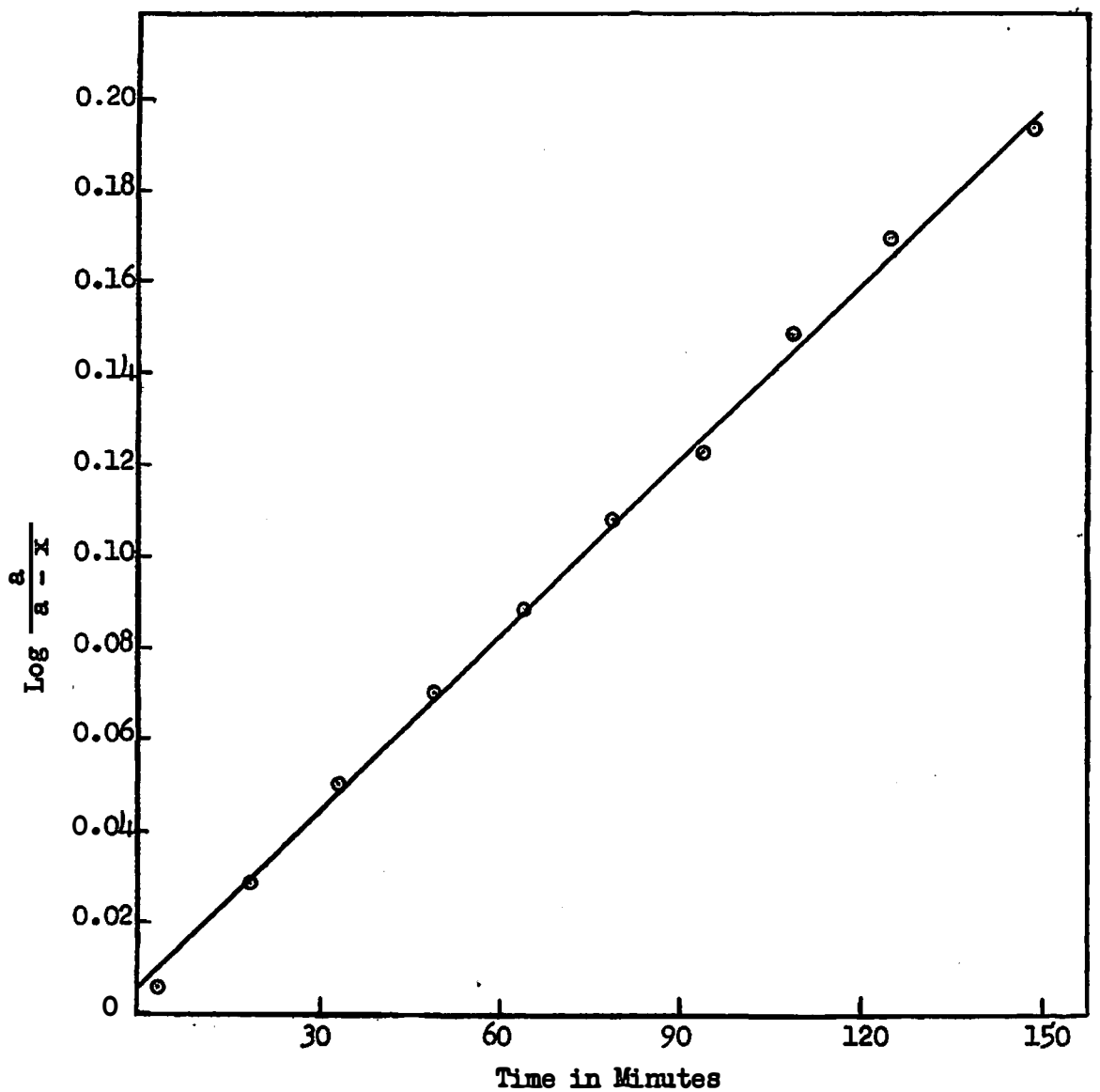


Figure 1

First order plot for the isomerization of 5,8-dihydro-1-naphthol (II) at 100° in a tert-amyl alcohol solution 0.133 M in the potassium salt of this alcohol. The slope of this line shows k to be 2.97×10^{-3} min.$^{-1}$.

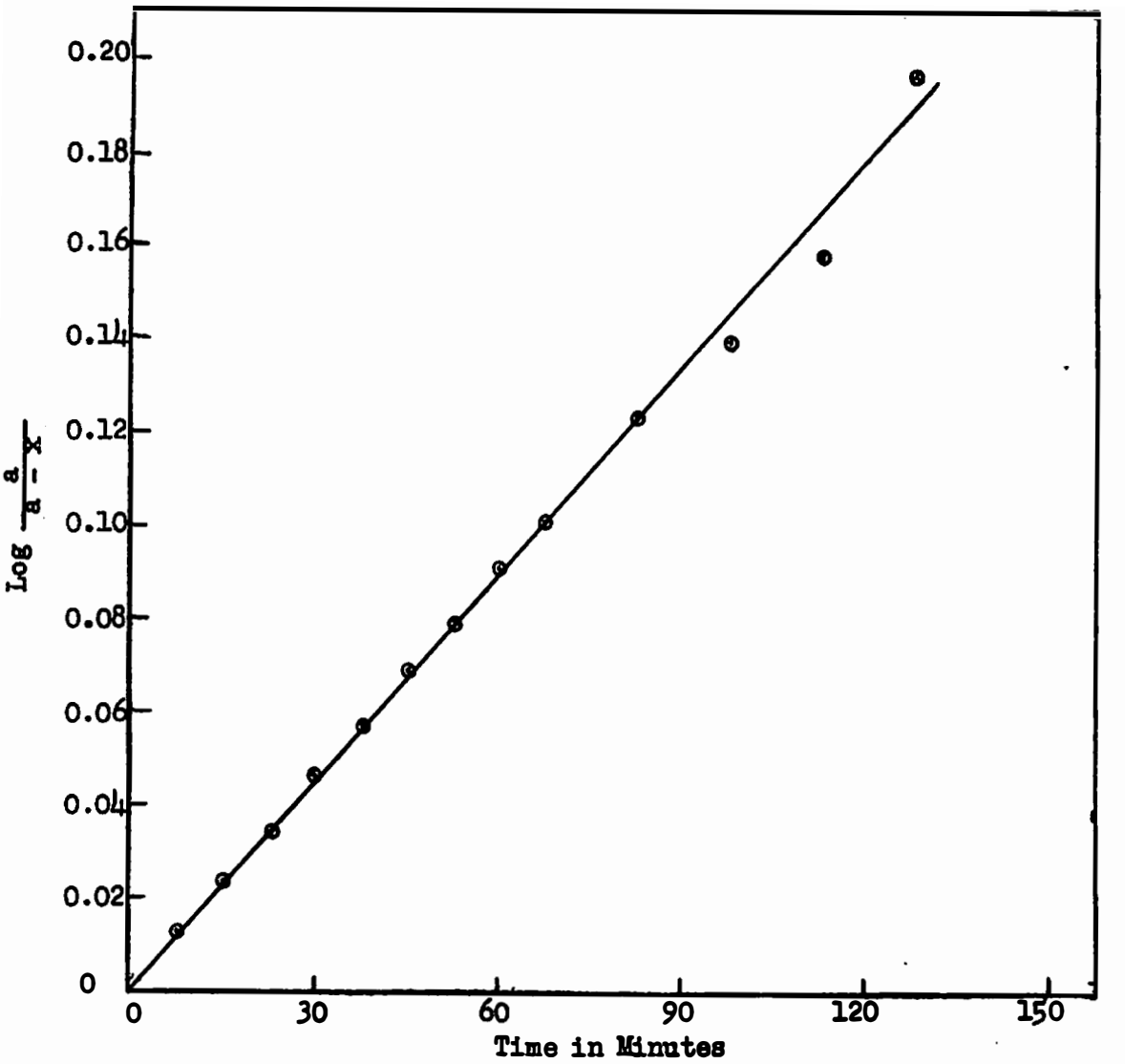


Figure 2

First order plot for the isomerization of 1-methoxy-5,8-dihydronaphthalene (III) at 100° in a tert.-amyl alcohol solution 0.135 M in the potassium salt of this alcohol. The slope of this line shows k to be 3.44×10^{-3} min.$^{-1}$.

the 1-hydroxy and 1-methoxy compounds. An amino group in the 1-position would be desirable since it can be replaced by a number of useful substituents via diazotization reactions. Reduction of 1-naphthylamine with potassium and ammonium chloride in liquid ammonia and subsequent isomerization with base gives 1-amino-5,6- or 7,8-dihydronaphthalene. Unfortunately, diazotization of this compound produced in most instances only unmanageable resins.[32]

An alternate synthetic route to 1-substituted 7,8-dihydronaphthalenes would be through 2-hydroxy-5-aminotetralin (XLIX). An attempt was made to prepare XLIX as shown in Chart Ten. The 2-hydroxy-5-aminotetralin (XLIX) was to be diazotized to introduce a variety of substituent groups and then dehydrated by base to give the corresponding olefin.*

5-Amino-2-methoxynaphthalene (XLV) was prepared by the method of Butenandt and Schramm[70] through methylation of 5-acetamido-2-hydroxynaphthalene followed by deacetylation. Reduction of XLV with potassium and ethanol in liquid ammonia gave an almost quantitative yield (as determined from ultraviolet spectra) of 1,4-dihydro-2-methoxy-5-aminonaphthalene (XLVI) as a viscous oil. This oil was not purified because of an expected instability to heat. Instead, it was dissolved in dry ether and hydrogen chloride was bubbled in to give a precipitate of amine hydrochloride, XLVII, which could be purified by dissolving in alcohol and precipitating with ether. This amine hydrochloride (XLVII)

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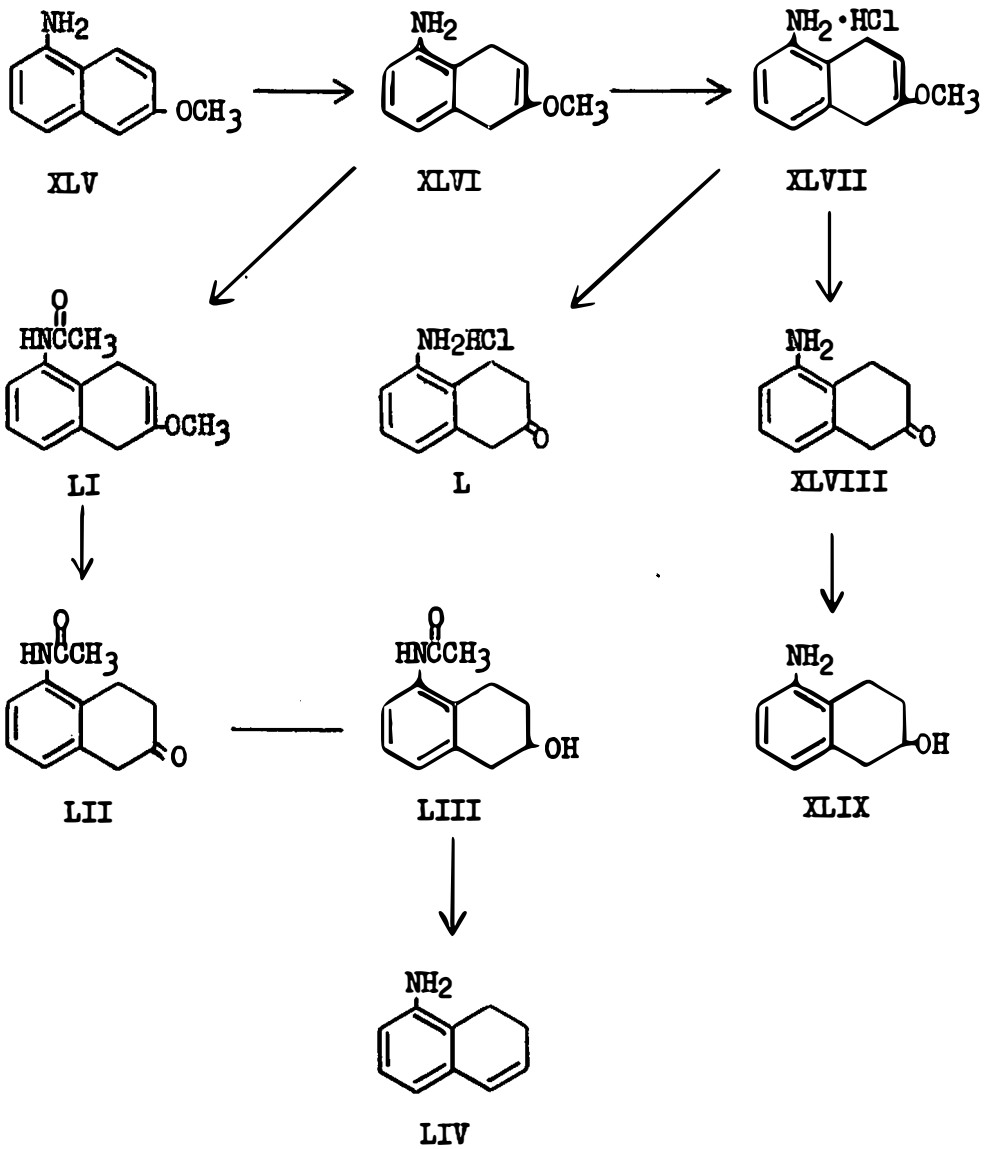
*Acid-catalyzed dehydration would have led to extensive dimerization of the styrene-type double bond first produced.

CHART ELEVEN



was treated with aqueous hydrochloric acid to cleave the enol-ether linkage and 5-aminotetralone (XLVII) was isolated as a white powder which rapidly polymerized on standing.*

To avoid polymerization of the aminotetralone (XLVII), a process was devised wherein XLVII was kept in aqueous solution as the amine hydrochloride (L) after cleavage of the enol-ether linkage and then added dropwise to a basic solution of sodium borohydride. An amine was isolated from this treatment which yielded a crystalline acetate but neither compound gave an interpretable elemental analysis.

Treatment of the free amine (XLVI) with acetic anhydride before a hydrolysis of the enol ether gave crystalline 1,4-dihydro-2-methoxy-5-acetamidonaphthalene (LI). This was refluxed with dilute mineral acid for a few minutes to cleave the enol-ether without hydrolyzing the acetamido group. The yield of 2,5-acetamido-2-tetralone (LII) was poor. Reduction of the ketone (LII) with sodium borohydride in methanol produced 2-hydroxy-5-acetamidotetralin (LIII). This compound was extremely soluble in water and was only isolated through a lengthy continuous extraction with ethyl acetate. 7,8-Dihydro-1-aminonaphthalene (LIV), a colorless liquid, was prepared by the simultaneous dehydration and saponification of 2-hydroxy-5-acetamidonaphthalene with molten alkali. 1-Acetamido-7,8-dihydronaphthalene (LIVa) was prepared as a crystalline derivative of LIV.

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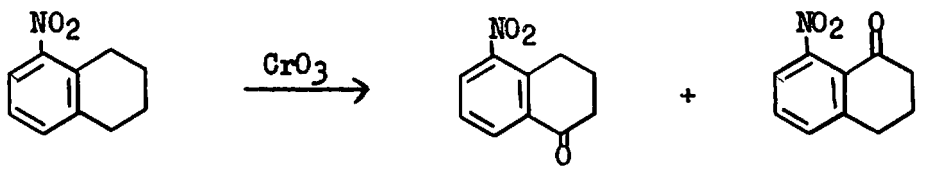
*Cyclohexanone and aniline polymerize rapidly at room temperature in the absence of any catalyst.[89]

This synthesis was successful in that a desired product, 1-amino-7,8-dihydronaphthalene, was obtained but the overall yield was too low for it to be used as a general preparative method for other 1-substituted 7,8-dihydronaphthalenes.

A second general approach to 1-substituted dihydronaphthalenes pursued was through 1-substituted 5 and 8-nitrotetralin derivatives, e. g., LVI, LVII, LVIII, LIX, LX, etc. The plan was to introduce various functional groups through reduction and diazotization of the nitro group and then to introduce the desired styrene-type double bond by an elimination reaction of the 1-substituent on the tetralin nucleus.

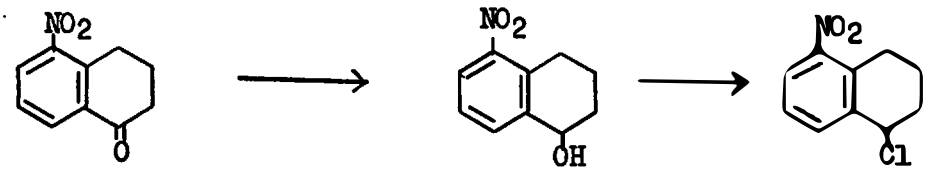
The Japanese chemist, Nakamura,[71] has separated 8-nitro-1-tetralone (LVI) and 5-nitro-1-tetralone (LVII) from the chromic acid oxidation products of 5-nitrotetralin (LV). In repeating this work, tetralin was



LV LVII LVI (1)

nitrated by the method of Schroeter to give equal amounts of 5-nitrotetralin and 6-nitrotetralin. The two isomers were obtained in crystalline form by a fractional distillation followed by fractional freezing out of the isomers. Oxidation of the 5-nitrotetralin produced a good yield of mixed nitrotetralones. From this mixture 5-nitro-1-tetralone could be obtained in a fair degree of purity by a tedious series of fractional recrystallizations. Only a very small amount of 8-nitro-1-tetralone was ever isolated in a purified state.

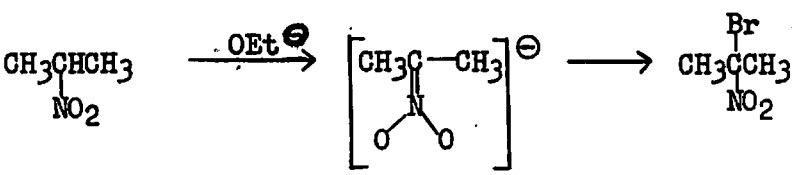
5-Nitro-1-tetralone (LVII) was not reduced by sodium borohydride in methanol. A new reduction method developed by Brown[72] which uses aluminum chloride and lithium aluminum hydride in bis-(2,2'-dimethoxy)-ethyl ether reduced LVII to yield 1-hydroxy-5-nitrotetralin (LVIII).

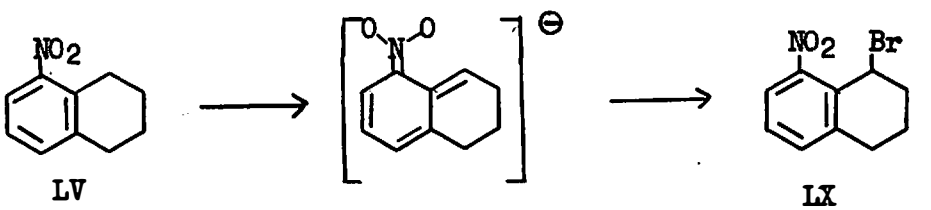


LVII LVIII LIX (2)

Since 1-hydroxytetralins are sometimes difficult to dehydrate[99] LVIII was transformed into 1-chloro-5-nitrotetralin (LIX) by treatment with thionyl chloride. At this stage the overall yield of the chloronitrotetralin (LIX) from the starting tetralin was so low and so tedious to obtain that the approach through LIX was abandoned.

Several reactions involving an active methylene group were investigated with the object of selectively introducing a group into the 2-position of 5-nitrotetralin. Bromination of 2-nitropropane in sodium ethoxide[73] produces 2-bromo-2-nitropropane, equation 3. Repetition of

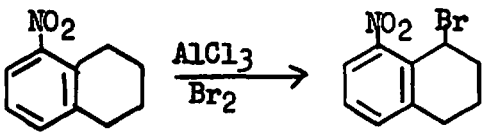
 (3)



LV LX (4)

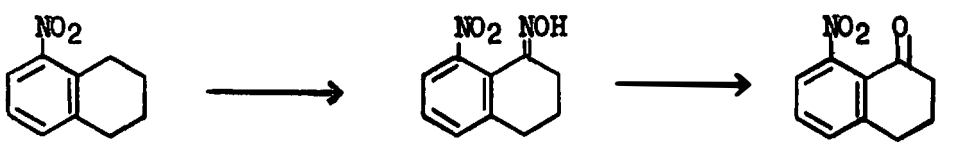
these conditions with the nitrotetralin, equation 4, gave not a trace of 1-bromo-8-nitrotetralin (LX). The reaction of 5-nitrotetralin in the

dark at 0° with bromine and aluminum chloride, equation 5, gave an extremely lacramatory crystalline product which, by elemental analysis, could contain only a few per cent of the desired 1-bromo-8-nitrotetralin (LX).



LX (5)

After some experimentation it was found possible to form in low yield an oxime, 1-oximino-8-nitrotetralin (LXI) by treating 5-nitrotetralin with amyl nitrite and sodium ethoxide, equation 6. One con-

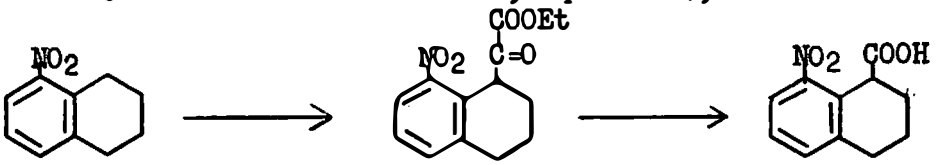


LXI LVI (6)

dition found necessary for this reaction was the addition of dry ethyl ether as a diluent; otherwise the reaction would, after sitting quietly at room temperature for days, become violently exothermic. The use of a stronger secondary base such as potassium isopropoxide in place of the sodium ethoxide resulted in reduction of the nitro- group with concurrent oxidation of the alcohol to acetone. The oxime (LXI) could be hydrolyzed with mineral acid to yield 8-nitro-1-tetralone (LVI). The overall yield of purified nitrotetralone was only about 10 per cent. This route was then abandoned.

Ortho and para nitrotoluenes differ from meta-nitrotoluene in having active methyl groups which can undergo condensation with diethyl oxalate.[74] Hydrolysis of the condensation product and oxidation with

30 per cent hydrogen peroxide produces nitrophenylacetic acids in good overall yield. The same reaction, equation 7, was tried with 5-nitro-

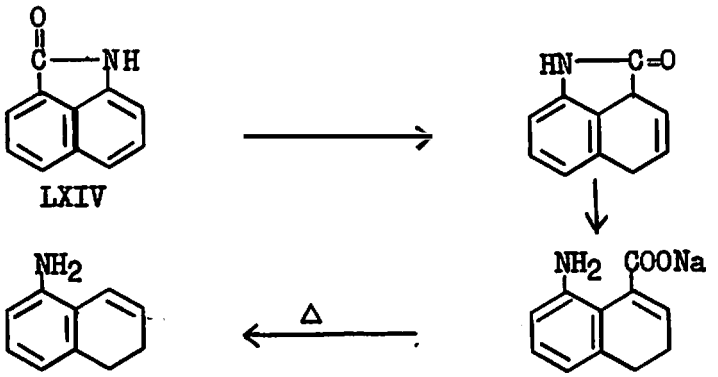


LXII LXIII (7)

tetralin but the yield of black acidic solid which was obtained was amorphous, was not amenable to purification and did not exceed 15 per cent, presumably because of steric hindrance which would not be present in as great a degree in ortho-nitrotoluene.

A final method which was considered for obtaining the 1-amino-dihydronaphthalene, Chart Twelve, involved the reduction, isomerization and decarboxylation of the known 1,8-naphtholactam (LXIV). Each of these reactions occurs readily in similar compounds. A thorough test

CHART TWELVE



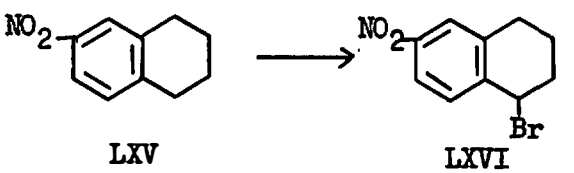
LXIV

of this scheme was not made because of the difficulty of preparing large amounts of the starting naphtholactam (LXIV). The lactam (LXIV) was reduced with potassium and alcohol in liquid ammonia but the product was not completely characterized. More details of this work are given in Chapter III.

C. Preparation of 2-Substituted-dihydronaphthalenes

In the reduction of dihydronaphthalens to tetralins the reduction of the benzene ring is a possible side reaction. 2-Substituted-naphthalenes are more likely to have the aromatic ring which contains the substituent reduced than are 1-substituted-naphthalenes.[29] For this reason 1-substituted-dihydronaphthalenes were considered more desirable than 2-substituted-dihydronaphthalenes in this work. However, because of the difficulty of preparing the 1-substituted compounds, the 2-substituted dihydronaphthalenes (e. g., LXXVII, XCII, etc.) were finally prepared. It was then shown that they could be reduced cleanly to the 6-substituted-tetralins by potassium and alcohol in liquid ammonia.

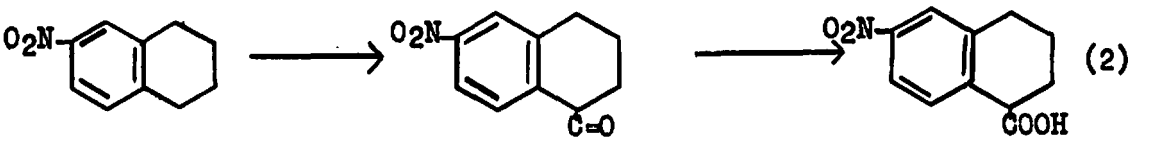
Several attempted syntheses of the 2-substituted compounds were from 6-nitrotetralin produced along with the 5-isomer by nitrating tetralin. Concurrent with the work on this 5-isomer some of the same reactions, such as bromination in the presence of aluminum chloride, equation 1, were carried out with 6-nitrotetralin. The bromination reaction was no more successful with 6-nitrotetralin than with 5-nitro-



LXV LXVI (1)

tetralin. On the other hand the condensation of diethyl oxalate with 6-nitrotetralin, equation 2, after modification over the preparation of Reissert[74] by using a large excess of base, followed by oxidation

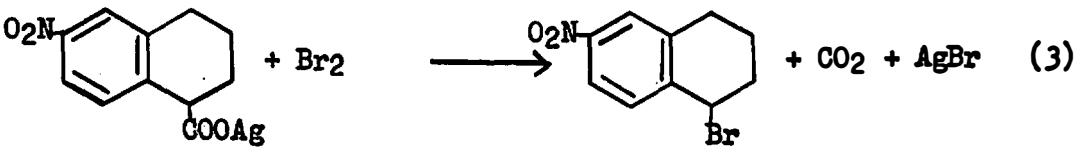
of the initial product produced a large yield of acidic material.*



LXV LXVII LXVIII (2)

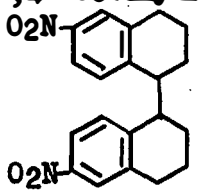
Unfortunately the product 1-carboxy-6-nitrotetralin (LXVIII) was obtained as an impure black powder from which an analytically pure sample was not obtained. Purification methods included elution from an ion exchange resin and an attempted vacuum distillation of the methyl ester (which decomposed) in addition to recrystallizations from many organic solvents. Dissolving in aqueous sodium bicarbonate and reprecipitating with acid gave the best appearing material, a yellow powder.

Replacement of the carboxyl group of impure LXVIII with bromine via the Hunsdiecker reaction (equation 3) did not occur. For this re-



LXIV LXVI (3)

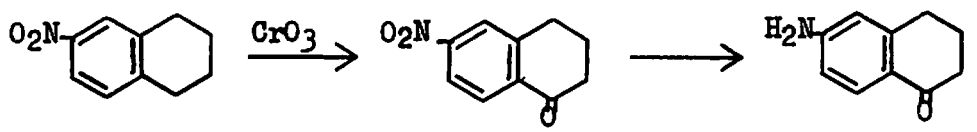
*A yellow crystalline compound $C_{20}H_{20}N_2O_4$, m.p. 202°, was obtained as a biproduct of the preparation of 1-carboxy-6-nitrotetralin. 1,2-bis-(p-nitrophenyl) ethane can be isolated from the condensation of p-nitro toluene and diethyl oxalate[74] so this compound is by analogy assigned the structure 1,2,3,4,1',2',3',4'-octahydro-6,6'-dinitro-1,1'-binaphthyl, iii.



iii

action to occur, the silver salt must be scrupulously dry. The impure starting material apparently did not meet this requirement, perhaps because of water of crystallization. The Schmidt reaction also failed with the impure 1-carboxy-6-nitrotetralin (LXVIII).

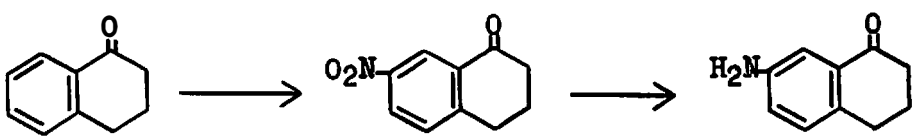
Oxidation of 6-nitrotetralin with chromium trioxide in acetic acid gave 6-nitro-1-tetralone (LXX), a compound previously reported only in the patent literature. Reduction of LXX with stannous chloride and hydrochloric acid produced 6-amino-1-tetralone (LXXI).



(4)

LXV LXX LXXI

6-Amino-1-tetralone (LXXI) could, almost certainly, have been used to synthesize a number of 2-substituted dihydronaphthalenes. However, 7-amino-1-tetralone (LXXIII) was finally employed because it can be readily produced more easily in large quantities. This was done by nitrating commercially available 1-tetralone with fuming nitric acid and reducing the 7-nitro-1-tetralone (LXXII) obtained, equation 5. Both



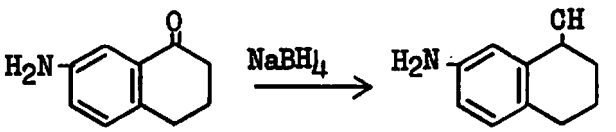
(5)

LXXII LXXIII

aminotetralones, LXXI and LXXIII, are stable in contrast to 5-amino-2-tetralone (XLVIII), which polymerized rapidly when isolated. In the final synthetic routes to the desired dihydronaphthalenes from LXXIII,

crystalline compounds were isolated and purified at every step.

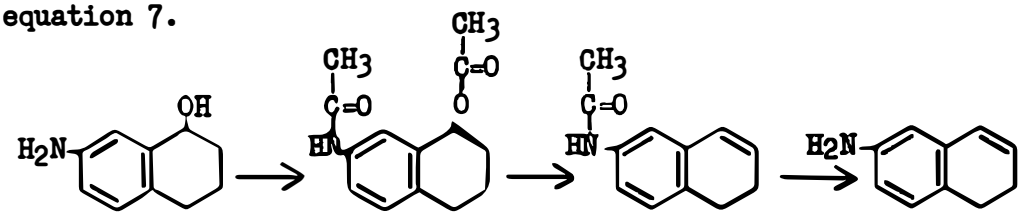
Reduction of crystalline 7-amino-1-tetralone (equation 6) with



(6)

LXXIII LXXIV

sodium borohydride in methanol yielded 1-hydroxy-7-aminotetralin (LXXIV). Several methods of dehydrating the aminoalcohol (LXXIV) were tried. Thionyl chloride in pyridine gave crude resinous material. Diacetylation of the aminoalcohol (LXXIV) produced 1-acetoxy-7-acetamidotetralin (LXXV) which was pyrolyzed to form the olefin, LXXVI. Saponification of 2-acetamido-5,6-dihydronaphthalene with potassium hydroxide in refluxing ethylene glycol yielded 2-amino-5,6-dihydronaphthalene, LXXVII, equation 7.



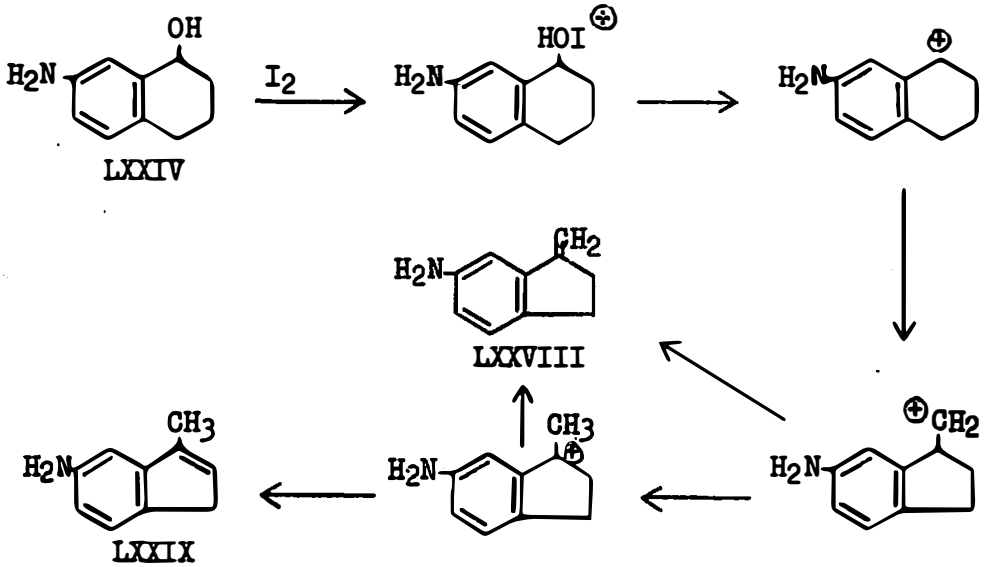
(7)

LXXIV LXXV LXXVI LXXVII

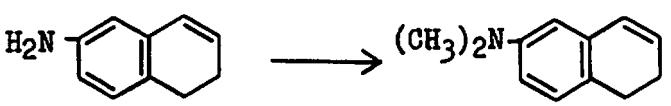
In a search for a shorter dehydration procedure 1-hydroxy-7-aminotetralin was vacuum distilled in the presence of a crystal of iodine. The product formed has the same empirical formula as LXXVII but a different melting point and ultraviolet spectrum. Since pyrolysis of an ester to form an olefin rarely causes rearrangement of the carbon skeleton[100] LXXVII is assumed to be properly assigned as 2-amino-5,6-dihydronaphthalene. On the other hand, iodine could cause carbonium ion formation during dehydration and rearrangement to give either 1-

methylene-6-aminoindane (LXXVIII) or 3-methyl-5-aminoindene (LXXIX), Chart Thirteen. It is believed that the product from the iodine-catalyzed reaction has one of these two structures.

CHART THIRTEEN



2-Amino-5,6-dihydronaphthalene, LXXVII, was converted into 2-N, N-dimethylamino-5,6-dihydronaphthalene (LXXX) by methylation with dimethyl sulfate in aqueous sodium bicarbonate, equation 8. Treatment of



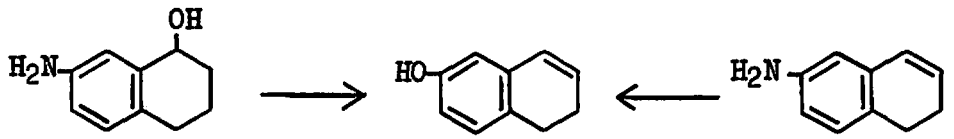
(8)

LXXVII LXXX

the crude product with acetic anhydride was done to convert any incompletely methylated amine to easily removable neutral material.

1-Hydroxy-5,6-dihydronaphthalene (LXXXI) was prepared through diazotizing either 1-hydroxy-7-aminotetralin (LXXIV) or 2-amino-5,6-dihydronaphthalene (LXXVII) and decomposing the diazonium salt solution

in hot sulfuric acid, equation 9. The yields were never good probably

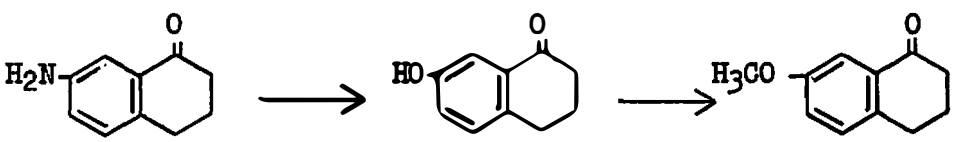


(9)

LXXIV LXXXI LXXVII

because the hydroxyolefin (LXXXI) is very susceptable to acid catalyzed dimerization and polymerization. No 1,7-dihydroxytetralin was isolated in the formation of the hydroxyolefin LXXXI from the aminoalcohol LXXIV.

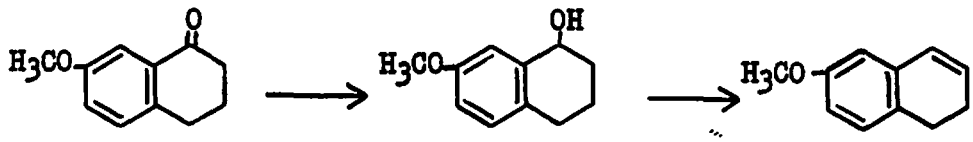
Because of the poor yield noted above, 2-methoxy-5,6-dihydronaphthalene (LXXXV) was not prepared by methylating 1-hydroxy-5,6-dihydronaphthalene (LXXXI). Instead, the known 7-hydroxy-1-tetralone was formed in good yield through diazotization of 7-aminotetralone LXXIII and converted with dimethyl sulfate into the 7-methoxy-1-tetralone (LXXXIII), equation 10.



(10)

LXXIII LXXXII LXXXIII

Lithium aluminum hydride reduction of 7-methoxy-1-tetralone (LXXXIII) yielded 1-hydroxy-7-methoxytetralin (LXXXIV) as a crystalline solid which melted just above room temperature. When LXXXIV was vacuum distilled, it partially dehydrated to give impure 2-methoxy-5,6-dihydronaphthalene (LXXV), equation 11. An analytically pure sample of this compound was never obtained, apparently because of its tendency to polymerize on heating. This was the only dihydronaphthalene prepared which polymerized so easily.

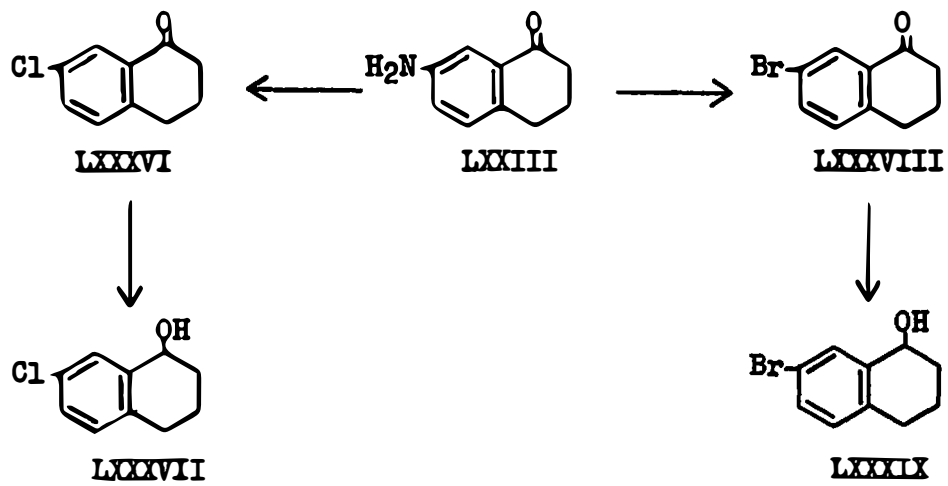


(11)

LXXXIII LXXXIV LXXV

7-Chloro-1-tetralone (LXXXVI) and 7-bromo-1-tetralone (LXXXVIII) are both known compounds which were easily prepared in a pure form via diazotization of 7-amino-1-tetralone in the presence of the appropriate cuprous halide. The chloroketone and bromoketone were transformed into 1-chloro-1-hydroxytetralin (LXXXVII) and 7-bromo-1-hydroxytetralin (LXXXIX) respectively by reduction with excess lithium aluminum hydride.

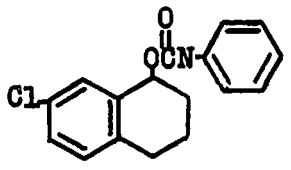
CHART FOURTEEN



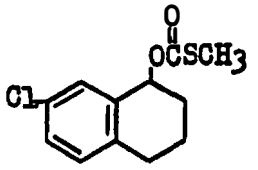
LXXXVI LXXXIII LXXXVIII

LXXXVII LXXXIX

The phenylurethan (XC) of 1-hydroxy-7-chlorotetralin was prepared by heating this alcohol with phenyl isocyanate in the absence of moisture. The phenylurethan (XC) is simpler to prepare than the methyl xanthate (XCI) which it resembles in structure and which is used in the Chugaev

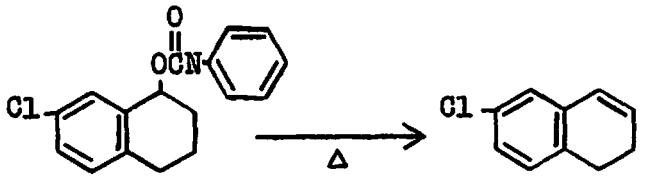


XC



XCI

olefin preparation. Pyrolysis of the phenylurethan (XC) gave the olefin, 2-chloro-5,6-dihydronaphthalene (XCII), equation 12. The ole-

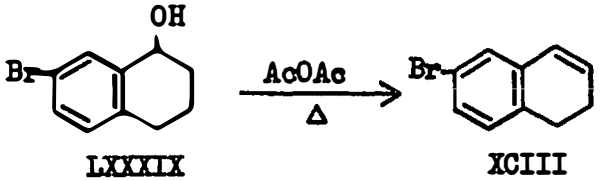


(12)

XC XCII

fin (XCII) could not be separated from diphenylurea, a product of the pyrolysis, by a simple distillation. Therefore, polar reaction products, such as the diphenylurea, were first removed from the chlorohydrocarbon (XCII) by filtration through a column of activated alumina.

Since diphenylurea produced in the pyrolysis of urethan is a nuisance to remove, the bromoalcohol (LXXXIX) was dehydrated by pyrolysis of its acetate, rather than its urethan, to yield 7-bromo-5,6-dihydronaphthalene (XCIII), equation 13. It was not necessary to purify

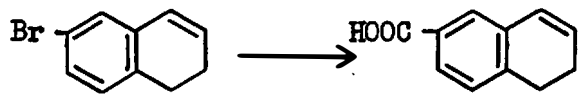


(13)

LXXXIX XCIII

the intermediate acetate.

A Grignard reagent was formed from 2-bromo-5,6-dihydronaphthalene (XCIII) by the entrainment method. Carbonation of this Grignard reagent formed 5,6-dihydro-2-naphthoic acid (XCIV), equation 14.



XCIII XCIV

D. Time Duration Experiments

An actual rate has never been determined for any reaction of an alkali metal in ammonia. At the outset of this work, some preliminary experiments showed that the reductions to be studied were too rapid to be easily amenable to studies by the usual kinetic methods. However, a sequence of experiments has been carried out to show the total time required for certain reactions of an alkali metal in ammonia. Such "total time" measurements are related to rates of reaction and can be used to throw some light upon the mechanism of reduction.

An overall reduction reaction is represented by equation 1 where S represents an organic substrate with a substituent R, M is any alkali metal and HX is an acid or proton source such as ammonium chloride or alcohol. The "ionic" (equations 4, 5, and 6) and "nascent hydrogen" (equations 2 and 3) mechanistic schemes are the oversimplified ones discussed in the introduction (page 19).

$$RS + 2M + 2HX \longrightarrow RSH_2 + 2MX \quad (1)$$

"Nascent Hydrogen"

$$2M + 2HX \longrightarrow 2MX + 2H^{o} \quad (2)$$

$$2H^{o} + RS \longrightarrow RSH_2 \quad (3)$$

"Ionic"

$$2M \rightleftharpoons 2M^{+} + 2e^{-} \quad (4)$$

$$RS + 2e^{-} \rightleftharpoons RS^{=} \quad (5)$$

$$RS^{=} + 2HX \longrightarrow RSH_2 + 2X^{-} \quad (6)$$

The question to be considered now is whether the "nascent hydrogen" route in which electrons from the metal, M, react first with the acid, HX, or the "ionic" route in which the electrons first attack the substrate, RS, is the more probable representation of the actual mechanism.

If the "nascent hydrogen" mechanism or a modification of it is correct, it seems highly unlikely that the substrate can be reduced more rapidly than the acid, HX. That is, the rate of reaction of alkali metal with acid should not be affected by the presence or absence of an organic substrate. If the first step, equation 2, can occur at all it can occur in the absence of a reducible substrate in which case hydrogen gas will be evolved.

A comparison has been made of the lengths of time required for an alkali metal in ammonia to react completely with acid alone, with acid and organic substrate both present, and with substrate alone. In this study, potassium metal, an alcohol, and 1-naphthoxide ion were used as alkali metal, acid, and substrate, respectively. In each experiment one of two alcohols was employed, ethyl and tert-amyl. Most of the ex-

periments were carried out with only the named reactants in an anhydrous atmosphere of nitrogen, while some were carried out in the presence of added oxygen, moisture, ether and alkoxide ion. The experimental results are summarized in Table IV. Briefly stated, Table IV shows the reaction between potassium metal and tert-amyl alcohol in ammonia is considerably slower than the reduction of the 1-naphthoxide ion by the combined action of metal and alcohol in ammonia. This is considered to be good evidence for the "ionic" route, that is, for some mechanism in which the organic substrate takes up electrons more rapidly than does the tert-amyl alcohol or proton from it.

For gathering the data in Table IV, the first technique utilized was as follows. This technique produced the reduced product, 5,8-dihydro-1-naphthol, in good yield. One solution was prepared by allowing one mole of potassium to react with three moles of tert-amyl alcohol in liquid ammonia and than adding to this one mole of 1-naphthol. To this liquid ammonia solution which then contained one mole of potassium-1-naphthoxide and three moles of tert-amyl alcohol was added a second liquid ammonia solution containing slightly less than two moles of potassium. (In the following discussion, the reaction which occurs when all three reactants, potassium, alcohol, and substrate, are mixed in ammonia will be referred to as the reduction reaction.) The length of time required for the potassium to react after mixing of the solutions was easily observable by the disappearance of its characteristic intense blue color. Initially these reactions were carried out in open Dewar flasks with no provisions for the exclusion of moisture or air. Mixing

was accomplished by simply pouring the contents of one flask into the other. If mixing were too rapid the cold (-33°) liquid ammonia solutions boiled over and the experiment was ruined. Under these original conditions, runs 1 and 2, Table IV, the time required for reaction of approximately 0.3 M potassium with alcohol and 1-naphthoxide ion was extremely brief, being always less than five seconds. Since rapid and complete mixing of the liquid ammonia solutions was not attained in these experiments, the rate controlling process was probably this rate of mixing.

The times required for the reaction of potassium in ammonia with alcohol alone and with organic substrate alone was measured in the same general manner. As shown in Table IV (runs 5 and 6), the reaction between 0.26 molar potassium and 0.46 molar tert-amyl alcohol requires about one hundred fifty seconds to go to completion. (In the following discussion the reaction which occurs when only potassium and an alcohol are mixed in ammonia will be referred to as the hydrogen liberation reaction.) The reaction of potassium with 1-naphthoxide ion in the absence of alcohol (runs 8 and 9) is considerably slower, six hundred seconds being required for the reaction between 0.26 molar potassium and 0.28 molar potassium 1-naphthoxide to occur.*

To obtain more precise data, an apparatus was constructed, Figure 3, which would allow more rapid mixing of the reaction solutions and

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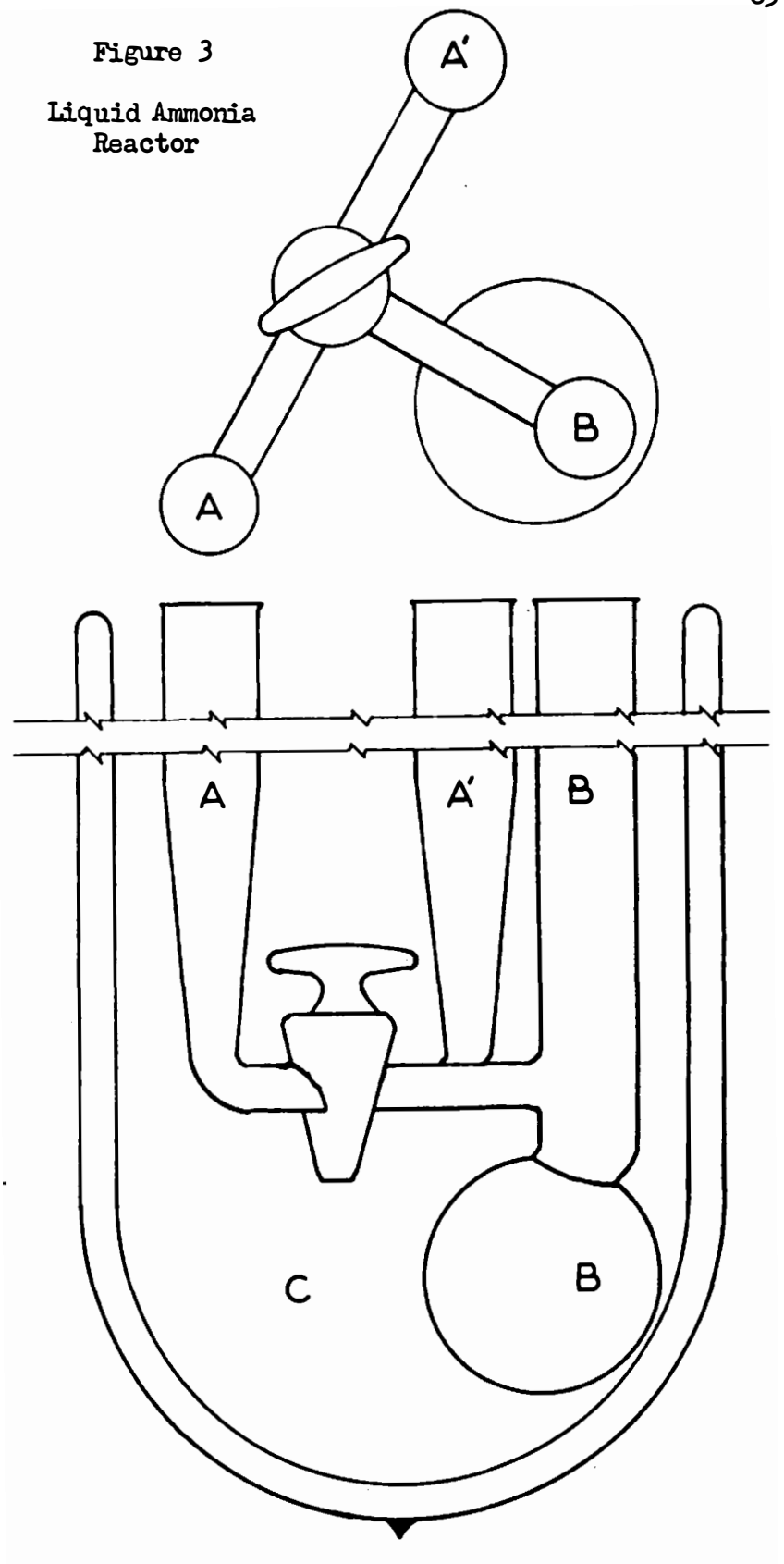
*The nature of the products of the reaction of potassium and 1-naphthoxide ion in ammonia in the absence of an added proton source has not been investigated.

Figure 3

Liquid Ammonia Reactor



would not be open to the atmosphere. For each run the apparatus was carefully dried and the two previously described ammonia solutions were prepared in two arms of the apparatus - substrate and alcohol in one, alkali metal in the other. These two solutions were then forced under a head of nitrogen into an atmosphere of nitrogen in the third arm. In this apparatus with the potassium still a few tenths molar all reaction times were longer, Table IV, but the reaction of potassium and alcohol with substrate (runs 11 and 12, twenty to thirty seconds) is still much faster than the reaction of potassium with amyl alcohol (run 13, about sixteen hundred seconds).

More runs were made than are represented in Table IV. The reproducibility of the data shown was quite good. Runs 15 and 16 were made three years after runs 11 and 12, with which they are comparable; the total times in these four runs are in good agreement relative to all possible experimental errors.

After observation of the considerable difference in total reaction times observed in an air atmosphere and in a nitrogen atmosphere the cause for this difference was sought. Apparently something present in air accelerates the rates of both the reductions (compare run 2 with run 11) and the hydrogen liberations (compare run 5 with run 13). The first possibility considered was moisture. However, addition of water (runs 17 and 18)* had little or no effect on the reduction time

*When a measured amount of water was added to the compartment containing the potassium alkoxide (previous to adding 1-naphthol) a white precipitate, which was probably potassium hydroxide, formed and would not redissolve.

required.

The second possibility investigated was oxygen. The compartment into which the ammonia solutions were forced for reaction was filled with oxygen instead of the usual nitrogen. When the solutions were then forced into this compartment, reaction occurred; that is, the blue coloration disappeared virtually as rapidly as the solutions mixed (run 19).* Work up of this reaction carried out in the presence of oxygen showed that the reduction had occurred in 96 per cent yield. This shows that there is no gross consumption of the potassium by oxygen. The oxygen or something derived from it is therefore acting as a catalyst for reduction by potassium!

A satisfactory explanation for how this catalysis is effected by oxygen has not been evolved. One idea tested was that the oxygen acted as an electron transfer agent. The reaction of potassium with oxygen, as shown in equation 7 has been postulated previously.[75] In fact, po-

$$K + O_2 \longrightarrow K^+ + O_2^- \qquad (7)$$

tassium superoxide, KO_2, is a known chemical species.** However, if the oxygen catalyzed the reduction by transferring an electron from the potassium to the organic substrate through the superoxide ion, then potassium superoxide should also be a reducing agent. This has not proved

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*Actually the coloration disappeared as rapidly as the solutions were mixed for the mixing of the first 60 per cent of the solutions. Toward the end of the mixing, apparently most of the oxygen had been displaced or consumed and the blue coloration persisted very briefly (ca. three seconds) in the reaction compartment.

**The reaction of potassium in ammonia with a stream of oxygen to form potassium superoxide is not a fast reaction. It requires some minutes even with a rapid stream of oxygen. Further, the yellow superoxide is rather insoluble in ammonia.

to be so. Potassium superoxide was prepared in ammonia to which was then added some potassium 1-naphthoxide. After a period of several hours of stirring the reactants together, work up yielded only recovered 1-naphthol in the organic fraction.

Other factors which might affect the two reactions being compared, liberation of hydrogen by potassium and an alcohol versus reduction of a substrate by the same pair, and which have been investigated include use of a diluent inert solvent (ether), variation of the alcohol and addition of alkoxide ion. None of these factors significantly affect the rate of the reduction reaction. In runs 20 and 25, all three of the above factors were changed from run 15, yet the reaction times for these three reductions are not significantly different. On the other hand, either variation of the alcohol or addition of alkoxide ion causes a profound change in the rate of hydrogen liberation from the alcohol. For example, runs 21 and 13 are roughly comparable (the alcohol to potassium ratio in each is about 1.5) with the exception that ethyl alcohol was employed in runs 21 and tert-amyl alcohol in run 13. This change in alcohol increased the time required for hydrogen liberation by a factor of over two and a half.

Even more striking is the effect of added alkoxide ion. The only difference between runs 21 and 24 is the initial presence in the latter of an amount of potassium ethoxide equivalent to the initial quantity of alcohol. This difference increased the time required for hydrogen liberation by a factor of seventeen. Comparison of run 23 with run 24 suggests that a further increase in the relative amount of additive

sodium ethoxide beyond that equivalent to the alcohol would further slow the hydrogen liberation reaction.

In summary, the data in Table IV show that substrate reduction caused by potassium and an alcohol in ammonia can proceed six hundred times faster* than hydrogen liberation by potassium and the alcohol in ammonia. Certain additives (ether, moisture) have no great effect on the rates of either of these reactions while another (oxygen) significantly accelerates the rate of each. Other factors change the rate of one of these reactions without affecting the other. Thus the time required for the reaction liberating hydrogen may be extended virtually indefinitely by the addition to the ammonia of alkoxide ion. Such addition has no effect on the reduction reaction rate however. Finally, variation of the alcohol also has a profound effect on the time required for hydrogen liberation, but none on the time required for the reduction. These data are consistent with the concept of reduction of the substrate by the metal or its electrons and are not consistent with the concept of reduction by hydrogen liberated from the alcohol.

Among other factors which affect the rate of reduction of a substrate is, of course, the nature of the substrate itself. The factors which were examined by the runs reported in Table IV were related to the reduction of one substrate, the 1-naphthoxide ion. Certain other substrates are reduced much more rapidly. Runs with one such substrate, the 5,6-dihydro-1-naphthoxide ion are reported in Table V. The work-

*The ratio of total times for runs 24 and 25 is 620.

TABLE IV

TIME DURATION REACTIONS WITH POTASSIUM-1-NAPHTHOXIDE IN LIQUID AMMONIA

Run No.	Initial Molarity 1-Naphthoxide	Initial Molarity Alcohol	Potassium	Additives and Atmospheres[a]	Reaction Time in Seconds
1[b]	0.13	0.46 (amyl)	0.26	Air atm.	1
2[b]	0.13	0.46 (amyl)	0.26	Air atm.	2
5[b]	- - -	0.46 (amyl)	0.26	Air atm.	135
6[b]	- - -	0.46 (amyl)	0.26	Air atm.	200
8[b]	0.22	- - - - - -	0.26	Air atm.	600
9[b]	0.28	- - - - - -	0.26	Air atm.	600
11[c]	0.12	0.46 (amyl)	0.24	- - - -	30
12[c]	0.14	0.46 (amyl)	0.28	- - - -	27
13[c]	- - -	0.46 (amyl)	0.28	- - - -	1650
14[c]	- - -	0.46 (amyl)	0.11	- - - -	870
15[d]	0.12	0.37 (amyl)	0.24	- - - -	22
16[d]	0.12	0.37 (amyl)	0.24	- - - -	26
17[d]	0.12	0.37 (amyl)	0.24	0.04 M water	24
18[d]	0.12	0.37 (amyl)	0.24	0.04 M water	19
19[d]	0.12	0.34 (ethyl)	0.24	Oxygen atm.	5[e]
20[d]	- - -	0.34 (ethyl)	0.24	Oxygen atm.	20
21[d]	- - -	0.34 (ethyl)	0.24	25% Ether	622
23[d]	- - -	0.34 (ethyl)	0.12	25% Ether and 0.34 M KOEt	2340
24[d]	- - -	0.34 (ethyl)	0.24	25% Ether and 0.34 M KOEt	10600

TABLE IV

TIME DURATION REACTIONS WITH POTASSIUM-1-NAPHTHOXIDE IN LIQUID AMMONIA (Continued)

Run No.	Initial Molarity 1-Naphthoxide	Alcohol	Potassium	Additives and Atmospheres[a]	Reaction Time in Seconds
25[d]	0.12	0.34 (ethyl)	0.24	25% Ether and 0.34 M KOEt	17

[a]The reactions were run in a nitrogen atmosphere unless otherwise noted.

[b]Runs 1 through 9 were the experiments performed in open Dewar flasks at -33°.

[c]Runs 11 through 14 were run in a small reactor at -38° in a Dry Ice acetone bath.

[d]Runs 15 through 25 were run in a large reactor at -33° in a liquid ammonia bath.

[e]See footnote, page 67.

TABLE V

TIME DURATION REACTIONS WITH POTASSIUM-5,6-DIHYDRO-1-NAPHTHOXIDE IN LIQUID AMMONIA

Run No.	Initial Molarity 5,8-Dihydro-1-naphthoxide	Ethanol	Potassium	Reaction Time in Seconds
26	- - -	0.43	0.050	11
27	- - -	0.43	0.050	30
28	0.12	- - -	0.24	147
29	0.12	- - -	0.24	128
30	0.12	0.34	0.24	0.003[b]

[a]The solvent for these runs was 25% ether - 75% ammonia by volume.

[b]See footnote, page 73.

up after reduction of this substrate by potassium and ethanol in ammonia gives in good yield 5,6,7,8-tetrahydro-1-naphthol. Accomplishment of this reduction with the previously described reaction (see page 64) showed that this reaction is extremely fast. Under the proper conditions, the blue coloration was discharged faster than the mixed solutions could flow through the "T" of glass tubing connecting the three arms of the reactor. It was possible to measure the distance of flow in the "T" through which the blue coloration of the mixed solutions persisted. From this and a knowledge of the parameters controlling the flow rate, it was possible to calculate a total time for the electrons from one quarter molar potassium to be consumed: 3×10^{-3} seconds.*

The pertinent data for one of these very fast reduction reactions is recorded (run 29). As before, the reaction of potassium with substrate in the absence of an alcohol is still relatively slow (runs 26 and 28). The hydrogen liberation reaction between potassium and alcohol at comparable concentrations is also still very slow (run 21). The time required for the hydrogen liberation reaction differs from the time required for the reduction in this case by a factor of 2×10^{5}!

Not only does this arresting ratio point up a very large rate of acceptance of electrons, equation 5, by an organic ion (a negatively charged ion!); it also points up the fact that the carbanions produced by this electron acceptance can accept protons (equation 6) much more

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*This time should be called an upper limit since mixing, even by the flow technique was probably the rate controlling effect. Other reduction reactions (see section E, chapter II) have been demonstrated to occur even more rapidly.

rapidly than the electrons themselves can attack these protons (equation 2). This latter conclusion is drawn from the fact that a proton source (alcohol) is needed to get the very fast rate of discharge of blue coloration in the reaction between the substrate and the potassium. In fact, in general a proton source is needed to allow reduction of a substrate by alkali metal in ammonia. A satisfactory explanation for the necessity of the proton source is that electron acceptance by the substrate (equation 5) is a rapid and reversible reaction with a real position of equilibria (i. e., a finite concentration of all species) which is followed by an irreversible proton acceptance reaction (equation 6).

Carbanions are relatively large and bulky by nature and are probably even more bulky through solvation by the ammonia solvent. Electrons, on the other hand, are among the smallest and most mobile chemical species known. For these reasons it is difficult to comprehend why carbanions should react more rapidly with protons than do electrons. Related to this phenomenon and equally difficult to comprehend is the fact that although added alkoxide ion profoundly retards the rate of attack by electrons on the proton source, this additive has no significant effect on the rate of attack by carbanions on this proton source (c.f. the discussion of runs 21 and 24 from Table IV).

E. Competitive Reactions

Competitive reactions can be a powerful tool in elucidating the paths of reaction mechanisms. The general technique and use of competitive reactions has recently been reviewed.[78] It was the intention of this

work to study the relative rates of reaction of potassium 5,6-dihydro-1-naphthoxide, 1,2-dihydronaphthalene, 2-methoxy-5,6-dihydronaphthalene, 2-amino-5,6-dihydronaphthalene, 2-bromo-5,6-dihydronaphthalene, 2-chloro-5,6-dihydronaphthalene and 2-carboxy-5,6-dihydronaphthalene under the same reaction conditions. Since it had previously been shown that potassium 5,6-dihydro-1-naphthoxide is reduced in excellent yield to the corresponding tetralin and because this compound and its reduction product are isolable through their acidity, the naphthoxide was used as a standard for comparison in all of these competitive reactions.

First it was necessary to examine the reduction of the 2-substituted-5,6-dihydrotetralins, equation 1, under the conditions to be employed for the competitive reactions. Several disappointing discoveries were made in this preliminary examination.

(1)

X = H, OCH_3, NH_2, COOH, Br, Cl

The first disappointment was the discovery that the 2-carboxy-5,6-dihydronaphthalene formed an ammonium salt which was insoluble in the ammonium-ether solvent used in this work. This salt is reducible by potassium and alcohol in liquid ammonia but it would be meaningless to have a heterogeneous reaction competing with a homogeneous reaction.

Equally disappointing and also somewhat surprising was the discovery that halogen in the halo-dihydronaphthalenes was reduced as fast or faster than the double bond. When chloro or dihydronaphthalene was re-

duced with excess potassium, the product was tetralin as shown by elemental analysis and ultraviolet spectra. The reduction of 2-bromo-5,6-dihydronaphthalene with two equivalents of potassium gave 72 per cent reduction of the nuclear bromine as determined by elemental analysis. The bromine is reduced approximately two and one-half times faster than the double bond, the reduction of which probably has a half-life of less than 0.001 seconds. Similar work with 2-chloro-5,6-dihydronaphthalene showed that the aromatic chlorine and the styrene double bond are reduced at about equal rates.

The three remaining compounds, 1,2-dihydronaphthalene, 2-methoxy-5,6-dihydronaphthalene and 2-amino-5,6-dihydronaphthalene, were all quantitatively reduced to the corresponding tetralins under the conditions to be employed for the competitive reactions. These conditions involved mixing ammonia solutions of the substrates and alcohol and of the potassium in the reactor (Figure 3) as in the total time studies.

The reductions can be represented by the following generalized equations where B represents the potassium-1-naphthoxide and A is one of the 2-substituted-dihydronaphthalenes.

$$A + 2K + 2EtOH \xrightarrow{k_1} AH_2 + 2KOEt \qquad (2)$$

$$B + 2K + 2EtOH \xrightarrow{k_2} BH_2 + 2KOEt \qquad (3)$$

A mixture of A and B in liquid ammonia was allowed to react with less than a stoichiometric amount of K, potassium metal, in the presence of excess EtOH, ethanol. When the reaction was complete B and BH_2, which are acidic, were separated from the non-acidic A and AH_2 by extraction into aqueous base. The fractions of A and of B which remain

unreduced were determined by ultraviolet spectrophotometry.

Provided that the reductions are first order in organic substrate, that the same mechanism applies for both reactions and that the reaction of A with the reagents, potassium and ethanol, does not affect the reaction of B with these reagents, and vice versa, then the ratio of rate constants can be calculated with equation 4.[78]

$$\frac{k_1}{k_2} = \frac{\text{logarithm of fraction A remaining}}{\text{logarithm of fraction B remaining}} \qquad (4)$$

Results from the competitive reductions have been calculated using equation 4 and are tabulated in Table VI.

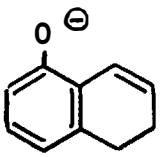
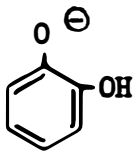
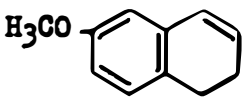
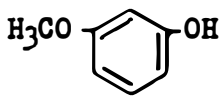
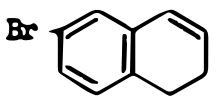
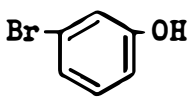
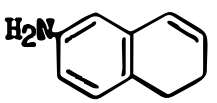
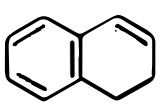
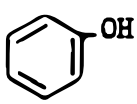
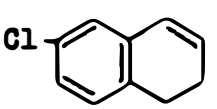
The assumption that the reaction is first order in substrate can be tested by varying the relative initial concentrations of A and B. Equation 4 shows that the ratio k_1/k_2 is independent of substrate concentration. When A was dihydronaphthalene, the ratio of A to B was varied from 2:1 through 1:1 to 1:2 without changing the ratio of rate constants.

From these values the most significant feature of Table VI is the slight difference in the relative rates of reaction of the compounds reported. The selectivity which organic compounds exhibit in reactions depends to a great extent upon the nature of the reagents with which they react. There is a large difference in the reaction rates of even very similar compounds when they react with unreactive species.* On the other hand, more reactive species show little differ-

*Toluene is brominated six hundred times as rapidly as benzene. However, toluene undergoes a Friedel-Crafts isopropylation (with the highly "active" isopropyl cation) only twice as fast as benzene.[108]

TABLE VI[102,103]

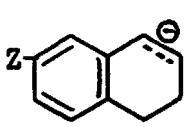
COMPARISON OF RELATIVE RATE VALUES WITH IONIZATION CONSTANTS

Compound	Relative Rate		Compound	Ionization Constants
	Runs	Average		
		1		8.37×10^{-13}
	1.80 2.03 1.91	1.9		2.24×10^{-10}
		2.0*		7.77×10^{-10}
	3.27 2.80	3.0		1.35×10^{-10}
	3.44 4.39 3.73	3.8		1.15×10^{-10}
		4.5*		9.55×10^{-10}

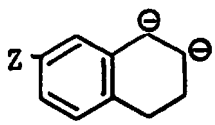
*Estimated from the amount of potassium consumed and an assumption as to the relative rates of reduction of the halogen and the double bond.

entiation in their rates of reaction with various types of compounds.* The little differentiation shown in Table VI suggests that the reagent causing the reduction is extremely reactive. The concept of an electron in solution as the reducing agent well fits this description.

Most of the differentiation which appears in Table VI is too slight and too close to possible experimental error to allow much interpretation. It does appear significant, however, that all of the 2-substituted-dihydronaphthalenes react more rapidly than the standard, the 5,6-dihydro-1-naphthoxide ion. This is logical if one assumes that the rate controlling process in the reduction of a dihydronaphthalene is the reversible addition of either one or two electrons to form a carbanion of the types VCa-b and VCd respectively.

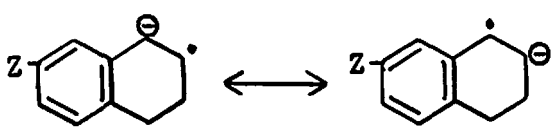


VCa-b

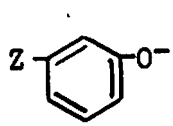


VCd

Carbanion Ca-b is represented by two low energy resonance forms, Ca and Cb. In either case (VCa-b or VCd) a substituent in the aromatic



VCa VCb

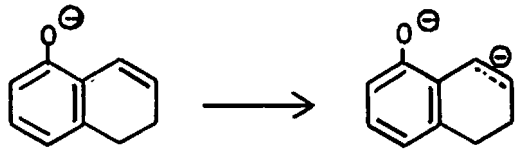


VCl

*Most reagents reacting with the carbon-hydrogen bond distinguish sharply between the primary, secondary and tertiary types as well as between the allyl and vinyl types of C-H bond. Recently, however, one reagent, the methylene radical, has been found to be sufficiently reactive to show almost no preference between any of these types in its reactions with the C-H bond.[109]

ring (Z) might be expected to have the same general effect on the stability of the carbanion as it does on the stability of corresponding phenoxide ion (VCl). Those dihydronaphthalenes which form a carbanion most easily should be reduced most rapidly.

Along with the relative rate constants of the substituted dihydronaphthalenes, the ionization constants (a measure of the stability of the phenoxide ion) of the correspondingly substituted phenols are listed in Table VI. It appears that the differences in the energies of formation of carbanions from the various 2-substituted dihydronaphthalenes will be negligibly small. However, it will take more energy to form a carbanion from the naphthoxide ion IVa, equation 5,



IVa IVb-c

(the ionization constant of the corresponding phenoxide ion is 1000 times smaller than any of the other ionization constants in Table V) because the molecule already possesses a net negative charge. One would therefore expect potassium 5,6-dihydro-1-naphthoxide to be reduced more slowly than the other dihydronaphthalenes if the carbanion IVa is an intermediate in the rate determining step. On the other hand, there is no apparent reason for a neutral species (such as nascent hydrogen) to attack IVa less rapidly than the other dihydronaphthalenes.

The one general difference in rates of reaction noted in Table V is thus logically interpreted on the basis of an ionic or electron addition mechanism but not on the basis of a nascent hydrogen mechanism.

CHAPTER III

EXPERIMENTAL*

A. Reduction of 1-Naphthol and Isomerization of the Product

1. 5,8-Dihydro-1-naphthol (II)**

Six hundred milliliters of liquid ammonia was condensed into a three-necked, 1-l. flask equipped with a Dry Ice condenser and mechanical stirrer. After 110 ml. (1.85 mole) of absolute ethanol had been added to the flask, 23 g. (0.61 mole) of potassium metal was added in small portions and allowed to react. Powdered 1-naphthol (85 g., 0.61 mole) was added to the flask slowly to give a solution of potassium 1-naphthoxide. There was added to the flask in small portions sufficient potassium metal to impart a blue color to the solution for one minute. About 50 g. of metal was required. The mouths of the flask were loosely covered with glassine paper and the liquid ammonia was allowed to evaporate at room temperature.

Ice was added to the reaction products and the resulting solution diluted to 3 l. with water and acidified with concentrated hydrochloric acid. The cream-colored precipitate was collected on a Büchner

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*Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee and Weiler and Strauss Microanalytical Laboratory, Oxford, England. The melting points and boiling points are uncorrected, unless otherwise stated. The melting points were determined on a Fisher-Johns melting point block. All ultraviolet spectra were taken on a Beckman Model DU spectrophotometer using 95 per cent ethanol as a solvent.

**The Roman numerals in the experimental section correspond to those in Chapter II.

funnel, washed with water and allowed to dry. The product was vacuum distilled, b.p. 120°/1 mm., and recrystallized from hexane. The yield of colorless prisms was 67 g. or 80 per cent of the theoretical yield. The product melted at 72-73.5° corr.; melting points of 75° and 74° are recorded in the literature.[29,57] The ultraviolet spectrum of the product is similar to that of phenol. There are maxima at 273 mμ and 279 mμ with molar extinction coefficients of 1700 and 1600 respectively.

2. Reduction of 1-Naphthol and Isomerization of the Product

A three-necked 1-l. flask was equipped with a Dry Ice condenser and mechanical stirrer. One hundred ten milliliters (1.85 mole) of absolute ethanol was added to the flask, 600 ml. of liquid ammonia was condensed into the flask and 23 g. (0.61 mole) of potassium was added in small pieces. After complete reaction of the initial potassium, 85 g. (0.61 mole) of powdered 1-naphthol was added slowly to give a solution of potassium 1-naphthoxide. Sufficient potassium was added in small pieces to impart a blue color to the solution for one minute, about 50 g. being required. Two hundred fifty milliliters of xylene was added to the cold reaction mixture and the liquid ammonia was allowed to evaporate over-night. One hundred fifty milliliters of ethanol was added and the solution was refluxed for eight hours. This solution was worked up by the two alternate methods, a and b, described in the following two sections.

a. Isolation of 5,6-dihydro-1-naphthol (IV). The 5,6-dihydro-1-naphthol was isolated by extracting the above reaction mixture with 2 l. of water. The water extract was cooled by the addition of ice and

acidified with concentrated hydrochloric acid. The cream colored precipitate was collected on a Büchner funnel, washed with water and dried to give a 90 per cent yield of crude 5,6-dihydro-1-naphthol. The product was subjected to both a steam distillation and a vacuum distillation in an attempt to purify it. Colorless needles with a melting point of 64-67° were obtained. After a series of recrystallizations from benzene, benzene-hexane and hexane, the product had a melting point of 69.2-70.7° corr. A mixed melting point of the product with 5,8-dihydro-1-naphthol was depressed only slightly. However, the two compounds have very different ultraviolet spectra. 5,6-Dihydro-1-naphthol has maxima at 265 mμ, 300 mμ and 308 mμ with molar extinction coefficients of 8000, 2800 and 2200 respectively.

b. Preparation of 1-methoxy-5,6-dihydronaphthalene. One hundred ten milliliters of concentrated hydrochloric acid was slowly added to the ethanol-xylene solution of isomerized dihydronaphthol. One hundred fifty milliliters of methyl sulfate was added to the mixture dropwise and potassium hydroxide solution was added as needed to keep the reaction mixture basic. After addition of the methyl sulfate was complete, the mixture was poured into a 2-l. flask and refluxed for two hours. Sufficient concentrated ammonium hydroxide was added to decompose the excess methyl sulfate and the reaction mixture was diluted with 1 l. of water. The xylene layer was separated and the water layer was extracted with benzene, which then was combined with the xylene layer. The combined extracts were washed with dilute hydrochloric acid and with aqueous sodium bicarbonate and dried over magnesium sulfate.

The solvent was removed under reduced pressure on the steam bath and the product vacuum distilled, b.p. 130-131°/15 mm. The yield was 94-100 g. (85-90 per cent) of a colorless oil. It had a density at 25° of 1.16 g./ml. and N_D^{25} of 1.5882. The ultraviolet spectrum of 1-methoxy-5,6-dihydronaphthalene has maxima at 265 mμ, 296 mμ and 307 mμ with molar extinction coefficients of 8550, 2400, and 200 respectively.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55.
Found: C, 82.54; H, 7.70.

3. 1-Methoxy-5,8-dihydronaphthalene (III)

5,8-Dihydro-1-naphthol (60 g., 0.41 mole) and potassium hydroxide (23 g., 0.41 mole) were dissolved in 200 ml. of water in a 500 ml. flask equipped with a reflux condenser, mechanical stirrer and dropping funnel. Thirty-eight milliliters of methyl sulfate (51.6 g., 0.41 mole) were added to the flask dropwise and the reaction mixture was stirred until it became acidic. The solution was made alkaline again with 5.75 g. (0.10 mole) of potassium hydroxide and an additional 9.5 ml. of methyl sulfate was added. When the solution again became acidic, the consecutive addition of 5.75 g. potassium hydroxide and 9.5 ml. methyl sulfate was repeated. Finally, sufficient ammonium hydroxide was added to decompose the excess methyl sulfate. The reaction mixture was poured into 500 ml. of water and extracted with ether three times. The ether extract was dried over magnesium sulfate and the ether removed under reduced pressure. The product was purified by a vacuum distillation to give a colorless oil, b.p. 123-124°/11 mm., N_D^{25} 1.5735. The yield was 55 g., which is 84 per cent of the theoretical yield. The ultraviolet

spectrum of 1-methoxy-5,8-dihydronaphthalene has maxima at 269 mμ and 277 mμ with molar extinction coefficients of 2100 and 1810 respectively.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55.

Found: C, 82.40; H, 7.65.

4. Isomerization of 1-Methoxy-5,8-dihydronaphthalene

Fifty grams of potassium metal was added in small pieces to 250 ml. of absolute ethanol which had previously been heated to reflux in a 1-l. round-bottom flask equipped with reflux condenser. When the potassium and alcohol had reacted completely, 250 ml. of xylene and 100 g. of 1-methoxy-5,8-dihydronaphthalene were added and the resulting solution was refluxed for eight hours. The reaction mixture was poured into ice-water and the xylene layer separated. The water layer was extracted with benzene which was then combined with the xylene layer. The combined extracts were washed with dilute hydrochloric acid and with aqueous sodium bicarbonate and dried over magnesium sulfate. The solvent was removed under reduced pressure on the steam bath and the product vacuum distilled to give 90 to 93 g. of a colorless oil. This compound has the same properties as the compound produced by methylation of 5,6-dihydro-1-naphthol.

5. Dimer of 1-Methoxydihydronaphthalene (i)

The tar left in the pot after the vacuum distillation of 1-methoxy-5,6-dihydronaphthalene was triturated with acetone to leave a white crystalline material. After two recrystallizations from methanol this product melted at 147.5-148.5°. A Rast molecular weight determination gave

a value of 304; 320 is the calculated value for the molecular weight of a simple dimer. The ultraviolet spectrum of the product has maxima at 280 mμ, ca. 300 mμ and 325 mμ with molar extinction coefficients of 3700, 850 and 570 respectively.

Anal. Calcd. for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55.
Found: C, 82.48, 82.38; H, 7.56, 7.44.

6. 1-Acetoxy-5,8-dihydronaphthalene

A small amount of p-toluenesulfonic acid was added to 5 g. of 5,8-dihydro-1-naphthol dissolved in 10 ml. of isopropenyl acetate and the resulting solution was heated for one hour on the steam bath. The excess isopropenyl acetate and the acetone resulting from the reaction were removed in vacuo and the residue was vacuum distilled, b.p. 170-171°/23 mm., to give 4.1 g. of 1-acetoxy-5,8-dihydronaphthalene as a colorless liquid, N_{Hg}^{25} 1.5367.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43.
Found: C, 76.75; H, 6.57.

7. 1-Acetoxy-5,6-dihydronaphthalene

Approximately 0.1 g. of p-toluenesulfonic acid was added to 5 g. of 5,6-dihydro-1-naphthol dissolved in 10 ml. of isopropenyl acetate and the resulting solution was heated for one hour on the steam bath. The excess isopropenyl acetate and the acetone resulting from the reaction were removed in vacuo. The residue was distilled, b.p. 280°/745 mm., gave 1-acetoxy-5,6-dihydronaphthalene as a white, wax-like semisolid, m.p. 72-75°. The ultraviolet spectrum shows maxima at 265 mμ and 300 mμ with molar extinction coefficients of 7000 and 1800 re-

spectively.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43.
Found: C, 76.28; H, 6.63.

8. 5-Hydroxytetralin

To 275 ml. of liquid ammonia in a three-necked, 500-ml. flask equipped with a Dry Ice condenser and mechanical stirrer were added 52 ml. (0.87 mole) of absolute ethanol and 11 g. (0.28 mole) of potassium metal in small portions. After these reagents had completely reacted, 40 g. (0.28 mole) of 5,6-dihydro-1-naphthol was added. Next, sufficient potassium was added in small pieces to impart a blue color to the solution for one minute, 22.8 g. being required. The mouths of the flask were covered with glassine paper and the liquid ammonia was allowed to evaporate overnight at room temperature. One liter of water and ice was added to the reaction products and the mixture was acidified with hydrochloric acid. The product was collected on a Büchner funnel, washed with water and vacuum distilled, b.p. 115°/1.05 mm., to give 31.5 g. (79 per cent yield) of purified material. After one recrystallization from hexane, the melting point of the product was 69-70.5°, literature melting point 70-71°. The ultraviolet spectrum of 5-hydroxytetralin has maxima at 273.5 mμ and 280 mμ with molar extinction coefficients of 1400 and 1350 respectively. The absence of any absorption above 295 mu showed that the reduction was essentially complete.

9. 5-Methoxytetralin

To 300 ml. of liquid ammonia in a three-necked, 500-ml. flask equipped with a Dry Ice condenser and mechanical stirrer were added 15 ml. (0.257 mole) of absolute ethanol and 11 g. (0.069 mole) of 1-methoxy-5,6-dihydronaphthalene. To the reaction mixture was added 5.35 g. (0.138 mole) of potassium metal in small pieces. The mouths of the flask were covered loosely with glassine paper and the liquid ammonia was allowed to evaporate at room temperature. The residue was dissolved in water and extracted with benzene. The benzene was removed in vacuo and the product vacuum distilled, b.p. 140-141°/19 mm. to give an 80 per cent yield of a colorless liquid, N_{Hg}^{25} 1.5458. The ultraviolet spectrum of 5-methoxytetralin has maxima at 270.5 mμ and 278.5 mμ with molar extinction coefficients of 1490 and 1475 respectively. The molar extinction coefficient of 125 at 295 mμ indicates that there is less than 2.5 per cent of unreduced starting material in the product.

10. 1-Hydroxy-2,5-dibromo-8-methoxytetralin (VIII)

In a 2-l. flask equipped with mechanical stirrer, condenser and dropping funnel were placed 10 g. (0.0625 mole) of 1-methoxy-5,6-dihydronaphthalene and 250 ml. of water. A water emulsion of the starting material was formed by adding 2 g. of "Tide" and stirring vigorously.[68] The reaction mixture was heated to 70° and 1300 ml. of aqueous 5 per cent sodium bromide solution containing 15 g. (0.094 mole) of bromine was added dropwise with vigorous stirring. When the addition was

completed, unreacted hypobromous acid was present as shown by the yellow color of the reaction mixture and by a test with potassium iodide.* A stream of air was bubbled through the reaction mixture to remove the excess bromine. The organic material was allowed to settle and the supernatant aqueous solution was decanted. A 55-56 per cent yield (11.5-11.6 g.) of white solid could be obtained by washing the reaction products with methanol. It was recrystallized twice from methanol to give white crystals, m.p. 157.5-159°. The ultraviolet spectrum of 1-hydroxy-2,5-dibromo-8-methoxytetralin is similar to that of phenol with maxima at 282 mμ and 290 mμ with molar extinction coefficients of 2000 and 1850 respectively.

Anal. Calcd. for $C_{11}H_{12}O_2Br_2$: C, 39.31; H, 3.60; Br, 47.56.
Found: C, 39.19; H, 3.72; Br, 47.52.

11. 2,8-Dimethoxy-1-hydroxy-5-bromotetralin (ii)

Six grams (0.015 mole) of 1-hydroxy-2,5-dibromo-8-methoxytetralin and 2.6 g. (0.026 mole) of sodium carbonate were dissolved in 60 ml. of methanol in a 500-ml. flask equipped with a magnetic stirrer. To this was added dropwise 5 g. (0.0295 mole) of silver nitrate dissolved in 120 ml. of methanol and 10 ml. of water. The reaction mixture was allowed to stir for one hour at room temperature and then refluxed for one hour on the steam bath. The reaction mixture was concentrated to half its volume, poured into water and the water solution extracted with benzene.

*Hypobromous acid liberates iodine from potassium iodide which can then be detected by extraction into chloroform.

The benzene was evaporated to leave 2.3 g. of a semi-crystalline mass, m.p. 93-97°. Recrystallization from methanol and then from benzene-petroleum ether gave colorless crystals, m.p. 140.5-141.5°. The compound had a spectrum which was similar to that of anisole with a maximum at 283 mμ with a molar extinction coefficient of 1750. It is assumed to be 2,8-dimethoxy-1-hydroxy-5-bromotetralin.[90]

Anal. Calcd. for $C_{12}H_{15}O_3Br$: C, 50.19; H, 5.27; Br, 27.83.
Found: C, 50.19, 50.33; H, 5.33, 5.27; Br, 26.92, 26.77.

12. 2,5-Dibromo-8-methoxy-1-tetralone (IX)

Seven and one half grams (0.075 mole) of chromium trioxide was dissolved in 10 ml. of water which was then added to 430 ml. of glacial acetic acid. The chromium trioxide solution was added to 25 g. (0.077 mole) of 1-hydroxy-2,5-dibromo-8-methoxytetralin in 430 ml. of glacial acetic acid in a 2-l. flask. The resulting reaction mixture was stirred mechanically for three hours to dissolve all of the starting material. The reaction mixture was allowed to stand overnight at room temperature and then diluted with 3.5 l. of water and allowed to stand for an additional three days in the cold room (5°). The yellow powder which precipitated was collected on a Büchner funnel, washed with water and allowed to dry. The yield was 20.2 g. (81 per cent of the theoretical yield) m.p. 110-113°. Three recrystallizations from methanol gave yellow cubes, m.p. 118.5-120° C. The spectrum of the product has maxima at 263 mμ and 335 mμ with molar extinction coefficients of 7350 and 3700 respectively.

Anal. Calcd. for $C_{11}H_{10}O_2Br$: C, 39.55; H, 3.02; Br, 47.85.
Found: C, 39.83, 39.92; H, 3.22, 3.15; Br, 47.49, 47.33.

13. 1-Methoxy-4-bromo-5-hydroxynaphthalene (X)

To find the optimum temperature for dehydrobromination preliminary tests were run using 0.5 g. of 2,5-dibromo-8-methoxy-1-tetralin in 20 ml. of collidine. The ultraviolet spectra of the products were examined to see if dehydrobromination had occurred. No reaction took place at 100° or 125°. At 170° dehydrobromination occurred but no product could be isolated from the viscous tars produced in the reaction. A temperature of 150° was chosen as the best reaction temperature.

In a 500-ml. flask equipped with a mechanical stirrer were placed 18.5 g. of 2,5-dibromo-8-methoxy-1-tetralone and 250 ml. of collidine which had been freshly distilled under nitrogen. The reaction mixture was placed under a nitrogen atmosphere and heated to 150-155° for forty-five minutes. The reaction mixture was cooled, filtered to remove carbonaceous material and poured into a cracked ice-hydrochloric acid mixture. The acid mixture was extracted three times with chloroform. Evaporation of the chloroform gave 6 g. of a viscous black tar. It could not be sublimed or vacuum distilled under ordinary conditions. The crude product was distilled in a molecular still at a pot temperature of 240-250° and a pressure of 0.2 mm. The yield was approximately 3.5 g. (25 per cent) of a white sticky semi-solid. This product was oxidized so rapidly in air that no further attempt at purification was made. It was used as described in the following experiment.

14. 1,8-Dimethoxy-4-bromonaphthalene (XI)

Five grams (0.021 mole) of crude 1-methoxy-4-bromo-5-hydroxy-naphthalene was dissolved in 30 ml. of methanol and made basic with 1.2 g. (0.021 mole) of potassium hydroxide. While the reaction mixture was stirred and heated on the steam bath 1.95 ml. (2.65 g., 0.021 mole) of methyl sulfate was added dropwise through a dropping funnel. The alternate addition of 1.2 g. of potassium hydroxide and 1.95 ml. of methyl sulfate was repeated three times. The excess methyl sulfate was destroyed with ammonium hydroxide and the reaction mixture was extracted with chloroform. The chloroform extract was filtered and evaporated. The residue from the evaporation was sublimed at a pot temperature of 160-170° at 0.2 mm. The yield of white material m.p. 90; was 1.4 g. or 25 per cent of the theoretical yield. The melting point after three recrystallizations was 93-94.5°. The ultraviolet spectrum of this compound has maxima at 308.5 mμ, 323 mμ and 336.5 mμ with molar extinction coefficients of 9350, 8200 and 6700 respectively.

Anal. Calcd. for $C_{12}H_{11}O_2Br$: C, 53.95; H, 4.15; Br, 29.92.
Found: C, 53.78, H, 4.34; Br, 30.05.

15. 1,8-Dimethoxynaphthalene (XII)

The Grignard reagent of 1,8-dimethoxy-4-bromonaphthalene was made by the entrainment method with methyl iodide and then converted into 1,8-dimethoxynaphthalene by reaction with ethanol. Magnesium turnings (0.60 g., 0.025 mole) were placed in a three-necked, 50 ml. flask equipped

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*1,8-Naphthalenediol was observed to have a similar spectrum with maxima at 305 mμ, 320 mμ and 334 mμ whose molar extinction coefficients are 6600, 6800 and 8100 respectively.

with a condenser, dropping funnel and magnetic stirrer. The apparatus was placed under a head of nitrogen and flamed to remove moisture. The reaction was started by adding a drop of methyl iodide in 2 ml. of dry ethyl ether. Then 1.1 g. (0.0041 mole) of 1,8-dimethoxy-4-bromonaphthalene and 0.60 g. (0.0041 mole) of methyl iodide were dissolved in 20 ml. of ethyl ether and added dropwise just fast enough to keep the reaction mixture refluxing. After complete addition the reaction mixture was heated on the steam bath for forty minutes. On cooling a black liquid separated from the ether and settled to the bottom of the reaction flask. An ethereal solution of alcohol was added slowly to the stirred reaction mixture. When the vigorous reaction had subsided, a dilute aqueous solution of hydrochloric acid was added. The reaction mixture was then filtered to remove unreacted magnesium and extracted with benzene. Evaporation of the benzene extract gave 0.5 g. or 65 per cent yield of crude material. After sublimation at a bath temperature of 100-110° at 0.3 mm., it had a melting point of 110-130°. Three recrystallizations from methanol gave colorless plates, m.p. 159-159.5° corr. A mixed melting point with an authentic sample of 1,8-dimethoxynaphthalene, m.p. 160.5° corr.,* showed no depression. The ultraviolet spectrum of 1,8-dimethoxynaphthalene shows maxima at 298.5 mμ, 315.5 mμ, and 330 mμ having molar extinction coefficients of 7700, 6650 and 6900 respectively.

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*The literature reports melting points of 161° and 162° for 1,8-dimethoxynaphthalene.[91,92]

16. Preparation of Authentic 1,8-Dimethoxynaphthalene (XII)

A sample of 1,8-dimethoxynaphthalene was prepared for comparison with the 1,8-dimethoxynaphthalene ultimately obtained from 1-methoxy-5,6-dihydronaphthalene. First, 1,8-dihydroxynaphthalene was synthesized from 1-amino-8-naphthalenesulfonic acid by the method of Boeseken.[93] Two hundred grams of 1-amino-8-naphthalenesulfonic acid were dissolved in 91 g. of potassium carbonate in 3 l. of water. The solution was heated with 30 g. of decolorizing carbon and filtered. On cooling, the potassium salt precipitated.

A 4-l. flask containing 100 ml. of concentrated hydrochloric acid, 200 ml. of water and 55 g. of the potassium salt of 1-amino-8-naphthalenesulfonic acid was cooled to 0° in an ice bath. Forty grams of potassium nitrite dissolved in 2200 ml. of water was added to the flask slowly with stirring to keep the temperature below 5°. The 1-diazonaphthalene-8-sulfonic acid which crystallized was collected on Büchner funnel and air dried. The crude diazonium salt was dropped in small portions into 1 l. of boiling water contained in a 2-l. Erlenmeyer flask. The 1,8-naphthosultone produced formed a crystalline, blue powder which was collected on a Büchner funnel and then recrystallized from benzene. The yield of naphthosultone, m.p. 155°, was 26 g., 59 per cent of the theoretical yield.

Seven grams of 1,8-naphthosultone were mixed with 50 g. of potassium hydroxide and 10 ml. of water and heated to 200-230° for twenty minutes in an evaporating dish covered with asbestos paper. The cooled reaction mixture was decomposed by breaking it into small pieces and dropping the pieces into 600 g. of cracked ice containing 100 ml. of

hydrochloric acid. The resulting solution was boiled with norite, cooled and filtered to give 2.5 g. of light brown leaflets of 1,8-dihydroxynaphthalene, m.p. 142-145°. The crude material could be sublimed at a pot temperature of 180° and a pressure of 15 mm.

1,8-Dimethoxynaphthalene was prepared by the method of Schmid, Ebnöther and Burger.[91] Two grams (0.0125 mole) of 1,8-dihydroxynaphthalene was dissolved in a solution of 2.92 g. (0.052 mole) of potassium hydroxide in 37 ml. of water. To this solution 4.9 ml. (0.052 mole) of methyl sulfate was added dropwise with vigorous stirring. After a half-hour, the reaction mixture was heated to 60°. At thirty minute intervals 37 ml. of the potassium hydroxide solution and 4.9 ml. of methyl sulfate were added. After this process had been repeated three times a final 37 ml. portion of potassium hydroxide solution was added and the reaction was heated for one hour under reflux.

The reaction mixture was extracted with ether, the ether evaporated and the residue sublimed at a bath temperature of 150° and a pressure of 0.15 mm. After two recrystallizations 1,8-dimethoxynaphthalene was obtained as colorless crystals, m.p. 159-159.5° corr.

17. Attempted Chromium Trioxide Oxidation of the Isomerization Product

A chromium trioxide oxidation was carried out by the method of Ingold and Piggott.[94] Thirty grams (0.30 mole) of chromium trioxide, 25 ml. of acetic acid and 25 ml. of concentrated sulfuric acid were dissolved in 950 ml. of water. To 400 ml. of this solution was added 5.2 g. (0.033 mole) of 1-methoxy-5,6-dihydronaphthalene and the mixture was shaken frequently for four hours. After standing for four days

with occasional shaking the reaction mixture was heated for one hour on the steam bath and then filtered. No pure material could be isolated from the brown semi-solid mass of organic material which was left on the filter paper.

18. Attempted Osmium Tetroxide Oxidation of the Isomerization Product.

To a solution of 1.0 g. of 1-methoxy-5,6-dihydronaphthalene in 125 ml. of dry ethyl ether was added a solution of 0.125 g. of osmium tetroxide in 10 ml. of ether and 3.75 ml. of 30 per cent hydrogen peroxide. The solution was allowed to stand at room temperature for twenty-four hours, after which the ether was removed under reduced pressure. The remaining material was stirred with 2 g. of sodium sulfite in 30 ml. of water for twenty-four hours to remove osmium metal. This solution was extracted with chloroform and the chloroform was dried and evaporated to give 0.120 g. of white needles, m.p. 75-95°, which were not examined further.

19. Permanganate Oxidation of the Isomerization Product

A slurry of 10 g. (0.0625 mole) of 1-methoxy-5,6-dihydronaphthalene* in 100 ml. of acetone and 100 ml. of water was prepared in a three-necked, 1-l. flask. The flask and its contents were cooled to 0° in an ice-salt bath. The reaction mixture was stirred while chipped ice was added regularly to the flask throughout the reaction to keep the

*The 1-methoxy-5,6-dihydronaphthalene employed in this experiment was that prepared by methylation of the crude isomerization product of 5,8-dihydro-1-naphthol.

temperature below 5°. Sixteen grams (0.100 mole) of potassium permanganate was dissolved in 400 ml. of water and added dropwise to the flask through a dropping funnel. After three hours the manganese dioxide formed in the reaction was removed by filtration and washed with aqueous sodium bicarbonate which was then added to the filtrate. The clear yellow filtrate obtained in this way was extracted twice with chloroform. The manganese dioxide was washed with chloroform and this washing added to the chloroform extract. Decomposition of the manganese dioxide with hydrochloric acid and sodium bisulfite left no organic material.

a. cis-1,2-Dihydroxy-5-methoxytetralin (XVIX). Evaporation of the chloroform extract obtained above gave a small amount (0.5 g., 4 per cent) of cis-1,2-dihydroxy-5-methoxytetralin* as well as some unreacted starting material. The crude glycol was purified first by sublimation at 130° (bath temperature) and 15 mm. It was then recrystallized five times from methanol. The final product had a melting point of 150-151°.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27.

Found: C, 68.08; H, 7.41.

b. 3-(2-Methoxy-6-carboxyphenyl)-propanoic acid (XVII). The filtrate from the permanganate oxidation described above, after being extracted with chloroform, was acidified and cooled overnight in a cold room. The precipitate of cream colored needles was collected on

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*Dr. R. Pappo kindly furnished a sample of the isomeric glycol, cis-1,2-dihydroxy-8-methoxytetraline, m.p. 125°, which could have been obtained from 1-methoxy-5,6-dihydronaphthalene.

a Büchner funnel, washed with water and dried. The yields of the acid ranged from 1.3 to 2.5 g. (8 to 16 per cent). After three recrystallizations from methanol the melting point of the acid was 221°-222°. The product, 3-(2-methoxy-6-carboxyphenyl)-propanoic acid, has a maximum in its ultraviolet spectrum at 293 mμ with a molar extinction coefficient of 2500. m-Hydroxybenzoic acid has a maximum at 296 mμ with a molar extinction coefficient of 2500.[61]

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.92; H, 5.40.

Found: C, 58.81; H, 5.42.

20. Attempted Glycol Preparation From the Isomerization Product

Ten grams (0.0625 mole) of 1-methoxy-5,6-dihydronaphthalene was dissolved in 800 ml. of acetone in a three-necked, 3-l. flask equipped with mechanical stirrer and dropping funnel.[96] The flask was placed in an ice-salt bath and when cooled to -5°, 30 ml. of piperidine and 24 g. (0.152 mole) of powdered potassium permanganate were added with stirring. After thirty minutes 50 ml. of acetic acid in 60 ml. of acetone was added slowly over a twenty minute period. The reaction mixture was stirred for an additional four hours at 0° to -2° after which 500 ml. of chloroform were added. Next, 77.5 ml. of concentrated hydrochloric acid in 375 ml. of water and 35 g. of sodium bisulfite in 250 ml. of water were added to decompose the manganese dioxide formed in the reaction. The reaction mixture was allowed to come to room temperature and stirred for one hour. It was then extracted twice with chloroform and the chloroform removed in vacuo on the steam bath. From the residue 0.80 g. of 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid

crystallized leaving 7.10 g. of crude viscous oil which was not further resolved.

21. Attempted Decarboxylation of 3-(2-Methoxy-6-carboxyphenyl)-propanoic Acid

a. Copper chromite. 3-(2-Methoxy-6-carboxyphenyl)-propanoic acid (0.5 g.) and 0.5 g. of copper chromite catalyst in 10 ml. of quinoline were heated to 165° for twenty-five minutes. A stream of nitrogen was bubbled continuously through the reaction mixture. No reaction could be detected. Essentially all of the starting material was recovered from the quinoline.

b. Copper chromite at 230°. 3-(2-Methoxy-6-carboxyphenyl)-propanoic acid (0.25 g.) and 0.25 g. of copper chromite catalyst in 5 ml. of quinaldine were heated to 230° for twenty minutes. A stream of nitrogen was bubbled constantly through the solution.

22. Methyl 3-(2-Methoxy-6-carbomethoxyphenyl)-propanoate (XVIII)

Five grams (0.022 mole) of 3-(2-methoxy-6-carboxyphenyl)-propanoic acid was dissolved in 150 ml. of tetrahydrofuran. To this was added 120 ml. of ethyl ether containing approximately 3.3 g. (0.079 mole) of diazomethane. After a few minutes the excess diazomethane in the reaction mixture was destroyed with acetic acid. The ether-tetrahydrofuran reaction mixture was extracted with aqueous sodium bicarbonate and with water, dried over magnesium sulfate and distilled under reduced pressure to leave 5.60 g. (100 per cent yield) of crude ester, m.p. 65°. After three recrystallizations from methanol, the methyl 3-(2-methoxy-6-carbomethoxyphenyl)-propionate melted at 75-76°.

Anal. Calcd. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39.
Found: C, 61.96; H, 6.57.

23. Lactone of 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid (XX)

Fifteen grams of pyridine hydrochloride and 4.8 g. of 3-(2-methoxy-6-carboxyphenyl)-propanoic acid were mixed together and heated to 210° for three and one half hours. Hydrogen chloride gas was bubbled through the solution during this time. The reaction mixture was poured into 100 ml. of dilute hydrochloric acid and allowed to cool. The precipitated product was collected on a Büchner funnel. It was purified by dissolving it in aqueous sodium bicarbonate, filtering to remove insoluble impurities, and reprecipitating it with hydrochloric acid. The yield of crude material, m.p. 160-170°, was 3.1 g. or 76 per cent of the theoretical yield. Recrystallization from tetrahydrofuran-benzene gave colorless cubes, m.p. 173-175°. The ultraviolet spectrum of the lactone of 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid has a maximum at 295 mμ with a molar extinction coefficient of 2650.

Anal. Calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.20.
Found: C, 62.08, 62.10; H, 4.04, 4.14.

24. Lactone of 3-(2-Hydroxy-6-carbomethoxyphenyl)-propanoic Acid (XXI)

An ethereal solution of diazomethane was prepared by adding 0.4 g. of nitrosomethyl urea to 2 ml. of chilled 40 per cent aqueous potassium hydroxide covered by a layer of 4 ml. of ethyl ether. The diazomethane (evolved on decomposition of the nitrosomethyl urea) in the ether layer was decanted into a solution of 0.1 g. (0.00052 mole) of the lactone of 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid in 2 ml. of di-

methyl formamide. After a few minutes the excess diazomethane was destroyed with acetic acid. The ether solution was extracted with aqueous sodium bicarbonate, dried over magnesium sulfate and distilled under reduced pressure to leave 0.1 g. (93 per cent yield) of crude ester. After a vacuum distillation, the product melted at 93-98°. It was then recrystallized three times from methanol to give the pure lactone of 3-(2-hydroxy-6-carbomethoxyphenyl)-propanoic acid, m.p. 101-102°. The infrared spectrum has maxima at 1788 $cm.^{-1}$ (lactone carbonyl) and 1730 $cm.^{-1}$ (methyl ester carbonyl).

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89.
Found: C, 64.03; H, 4.74.

25. Attempted Saponification of the Lactone of 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid (XX) to 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid (XXII)

To 1.0 g. of sodium hydroxide in 20 ml. of ethanol and 5 ml. of water was added 0.5 g. of the lactone of 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid. After refluxing for one and one-half hours the reaction mixture was poured into cold dilute hydrochloric acid. Extraction with chloroform and evaporation of the chloroform gave 0.45 g. of starting material.

26. Conversion of the Lactone of 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid (XX) Into 3-(2-Methoxy-6-carboxyphenyl)-propanoic Acid

The lactone of 3-(2-hydroxy-6-carboxyphenyl)-propanoic acid (0.70 g., 0.0031 mole) was added to potassium hydroxide (0.90 g., 0.016 mole) in 15 ml. of water and the resulting mixture was heated on the steam

bath for one hour. Then 3 ml. (0.033 mole) of methyl sulfate in 10 ml. of ethanol were added dropwise to the hot reaction mixture. Additional potassium hydroxide was added as needed to keep the reaction mixture basic. Finally the basic reaction mixture became clear* and was extracted with chloroform. Evaporation of the chloroform extract left only a small residue of colored material.

The reaction mixture was acidified whereupon small needles crystallized. (This is in contrast to the starting material which always crystallized in cubes.) The yield of product was 0.8 g. (95 per cent), m.p. 221-222°. A mixed melting point with 3-(2-methoxy-6-carboxyphenyl)-propanoic acid showed no depression.

27. Partial Characterization of the Lactone of 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid[97]

a. Ferric chloride test. The compound did not give a positive ferric chloride test for a phenolic hydroxy group.

b. Attempted oxime formation. No derivative was observed to form with hydroxylamine hydrochloride. In this test 0.5 g. of the compound was mixed with 0.5 g. of hydroxylamine hydrochloride and dissolved in 25 ml. of pyridine which contained 2.5 ml. of absolute ethanol.[98] After refluxing for six hours the reaction mixture was poured into strong

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*Naphthols usually contain air oxidation products which are dark in basic solution and light or colorless in acid solution. When the basic reaction mixture became colorless it was concluded that the phenolic hydroxyl group was completely methylated and the reaction was stopped.

aqueous hydrochloric acid which then was placed in an ice bath. The only material obtained had a melting point of 171-173° and was probably starting material. A tetralone should have formed an oxime.

c. Attempted sodium borohydride reduction. No reaction could be observed between the compound and sodium borohydride. One half gram of the compound was dissolved in 20 ml. of aqueous sodium bicarbonate. To this was added 0.1 g. of sodium borohydride in 3 ml. of water. The reaction mixture was allowed to stand overnight and then was acidified. A quantitative yield of starting material, m.p. 171-173°, was recovered. If the compound had had a ketonic carbonyl group it should have been reduced to a hydroxyl group.

28. Attempted Reduction of 1,6-Dihydroxynaphthalene to 5-Hydroxy-2-tetralone (XXXI)

To 500 ml. of liquid ammonia in a three-necked, 1-l. flask equipped with a Dry Ice condenser and mechanical stirrer were added 21.8 g. (0.475 mole) of absolute ethanol and 18.5 g. (0.475 mole) of potassium metal in small portions. When the potassium and ethanol had completely reacted, 24.5 g. (0.157 mole) of 1,6-dihydroxynaphthalene were added to form the naphthoxide salt. Finally 12.5 g. (0.314 mole) of potassium metal were added in small pieces. The condenser was removed from the flask and the ammonia was allowed to evaporate overnight at room temperature. The residual reaction products were dissolved in ice water, acidified, and extracted with benzene. The benzene was removed in vacuo leaving a black semi-solid tar from which no pure product could be isolated.

29. 5-Methoxy-2-tetralone (XXVI)

5-Methoxy-2-tetralone was prepared by the method of Cornforth, Cornforth and Robinson.[60] To 53 g. (0.28 mole) of 1,6-dimethoxynaphthalene in 600 ml. of refluxing absolute ethanol was added 55 g. (2.4 mole) of sodium metal in small pieces. When the sodium had completely reacted, 600 ml. of water and 600 ml. of concentrated hydrochloric acid were added to the alcohol solution in one portion and the solution was then refluxed for fifteen minutes. The reaction mixture was cooled and extracted with ether. The ether was removed under reduced pressure and the oil remaining was shaken with 350 ml. of concentrated aqueous sodium bisulfite solution. The sodium bisulfite solution was cooled in an ice bath for thirty minutes after which the bisulfite addition product was collected on a Büchner funnel, washed with ether and dried. The bisulfite addition product was shaken with 200 ml. of dilute aqueous sodium carbonate solution and the tetralone extracted from this mixture into ether. The ether was removed under reduced pressure to leave 27.5 g. or 52 per cent yield of 5-methoxy-2-tetralone.

30. 5-Methoxy-2-hydroxytetralin (XXVII)

To 1.70 g. (0.045 mole) of a slurry of lithium aluminum hydride in 150 ml. of dry ethyl ether was slowly added 27.5 g. (0.155 mole) of 5-methoxy-2-tetralone dissolved in 100 ml. of dry ethyl ether. When the addition of 5-methoxy-2-tetralone was complete, the reaction mixture was refluxed on the steam bath for one hour. The excess lithium aluminum hydride then was decomposed with a dilute ethereal solution of alcohol. Next the reaction mixture was diluted with water, acidified

with dilute hydrochloric acid and extracted with ether. The ether was removed under reduced pressure and the product was vacuum distilled, b.p. 126-129°/0.3 mm. The yield of distilled product, m.p. 59-60°, was 21.2 g. or 77 per cent of the theoretical yield. Two recrystallizations from ligroin and one recrystallization from ligroin-benzene gave long white needles of 5-methoxy-2-hydroxytetralin, m.p. 73-74°.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92.
Found: C, 74.37; H, 7.79.

31. Benzoate of 5-Methoxy-2-hydroxytetralin

Five grams of 5-methoxy-2-hydroxytetralin were mixed with 15 g. of benzoyl chloride and heated for fifteen minutes on the steam bath. The reaction mixture was then poured into water and the acid produced neutralized with sodium bicarbonate. The product was collected on a Büchner funnel and air dried. After recrystallization of the ester from methanol, an essentially quantitative yield, 7.6 g., of the benzoate of 5-methoxy-2-hydroxytetralin, m.p. 111-112°, was obtained.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43.
Found: C, 76.41; H, 6.49.

32. 1-Methoxy-7,8-dihydronaphthalene (VII)

Attempts to prepare 1-methoxy-7,8-dihydronaphthalene by pyrolysis of the benzoate of 5-methoxy-2-hydroxytetralin failed. This compound distilled unchanged at 240°/760 mm. from a pot temperature of 360°.

The 5-methoxy-2-hydroxytetralin was dehydrated in a mixture of molten potassium hydroxide and sodium hydroxide. Seven and one half grams of 5-methoxy-2-hydroxytetralin was mixed in a 50-ml. distilling flask with 12.5 g. of potassium hydroxide and 12.5 g. of sodium hydroxide and heated to 260-300° in a Wood's metal bath. After thirty minutes* the reaction mixture was poured onto ice, diluted with water and extracted with ether. The ether was evaporated to leave 6.15 g., 90 per cent yield, of crude product. It was purified by a vacuum distillation, b.p. 145°/23 mm., N_D^{27} 1.5828. The ultraviolet spectrum of 1-methoxy-7,8-dihydronaphthalene has maxima at 265 mμ and 298 mμ with molar extinction coefficients of 7800 and 2130 respectively.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55.

Found: C, 82.37; H, 7.52.

33. Attempted Demethylation of 1-Methoxy-7,8-dihydronaphthalene

Magnesium metal (0.16 g., 0.0067 mole) was placed in a 50-ml. three-necked flask equipped with reflux condenser, dropping funnel and magnetic stirrer. The apparatus was flamed to remove moisture and a nitrogen atmosphere was maintained inside the flask. One gram (0.007 mole) of methyl iodide dissolved in 20 ml. of dry ethyl ether was added to the flask dropwise. When all of the magnesium had been consumed, 1.0 g. (0.0062 mole) of 1-methoxy-7,8-dihydronaphthalene was added and the ethyl ether was distilled. The mixture remaining was heated to 160-170° (pot temperature) for forty-five minutes, during

*At these temperatures the molten base ate through the glass of the distilling flask in about thirty minutes.

which time there was an evolution of gas.

The reaction mixture was triturated with dilute hydrochloric acid and extracted with ether. The ether solution was extracted with aqueous potassium hydroxide. The potassium hydroxide extract was poured onto chipped ice and acidified with hydrochloric acid. A colloidal precipitate formed which was extracted into chloroform. Evaporation of the chloroform left a viscous oil which quickly set to resin-like hardness. No pure compound could be obtained from this residue.

34. Reaction of 1-Methoxy-7,8-dihydronaphthalene With Hydrobromous Acid

An emulsion of 1 g. (0.00625 mole) of 1-methoxy-7,8-dihydronaphthalene in 25 ml. of water in a 200-ml. three-necked flask was formed by adding a small amount of "Tide" and stirring vigorously with a magnetic stirrer. A solution of 1.5 g. (0.0094 mole) of bromine in 130 ml. of 5 per cent sodium bromide solution was added dropwise. Less than 5 mg. of solid material could be isolated from the viscous oil which separated. This is in contrast to the 56 per cent yield of bromohydrin which was obtained from 1-methoxy-5,6-dihydronaphthalene.

35. Oxidation of 1-Methoxy-7,8-dihydronaphthalene (VII)

To a slurry of 1 g. (0.00625 mole) of 1-methoxy-7,8-dihydronaphthalene in 10 ml. of acetone and 10 ml. of water in a three-necked, 100 ml. flask equipped with magnetic stirrer and dropping funnel was added dropwise 2.7 g. (0.0172 mole) of potassium permanganate in 40 ml. of water. The flask was placed in an ice bath and cracked ice was kept inside the flask to keep the temperature below 5°. After two hours the

action mixture was diluted to 200 ml. with water, filtered to remove manganese dioxide, acidified with hydrochloric acid and placed in the cold room overnight. The precipitated acid was collected on a Büchner funnel, washed with water and air dried. The yields from three runs were 28.6, 25.0 and 32.0 per cent. A mixed melting point with the 3-(2-methoxy-6-carboxyphenyl)-propanoic acid previously obtained did not depress.

36. 1,6-bis-Methoxymethoxynaphthalene (XXVIII)

To 350 ml. of refluxing absolute methanol was added 7.2 g. (0.313 mole) of sodium metal in small pieces. The sodium methoxide solution produced in this manner was cooled and placed in a 1-l. flask equipped with a dropping funnel, reflux condenser and mechanical stirrer. Fifty grams (0.313 mole) of 1,6-dihydroxynaphthalene were dissolved in the sodium methoxide solution and 25 g. (0.313 mole) of chloromethyl methyl ether were added dropwise. When the reaction mixture had been stirred for two hours there was added to it an additional amount of sodium methoxide solution made by reacting 7.2 g. of sodium with 100 ml. of methanol. After this another 25 g. of chloromethyl methyl ether was added dropwise to the reaction solution. After two more hours, a final sodium methoxide solution made from 3.6 g. of sodium and 50 ml. of methanol was added and 12.5 g. of chloromethyl methyl ether was added dropwise. The reaction mixture was allowed to stand overnight at room temperature and then poured into 1 l. of water. The water solution was extracted three times with ether and the ether was removed from the extracts under reduced pressure. The residual crude product was purified

by distillation. The yield of purified 1,6-bis-methoxymethoxynaphthalene, b.p. 147-148°/0.3 mm., N_D^{29} 1.3812, was 47 g., 60 per cent of the theoretical yield. Its ultraviolet spectrum has maxima at 235 mu (broad), 283 mμ, 315 mμ and 300 mμ with molar extinction coefficients of 18200, 5300, 2250 and 2100 respectively.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50

Found: C, 67.83, 67.61; H, 6.40, 6.65.

37. 1,6-bis-Methoxymethoxy-5,8-dihydronaphthalene (XXIX)

To 1200 ml. of liquid ammonia in a three-necked, 2-l. flask equipped with a Dry Ice condenser and mechanical stirrer was added 60 g. (0.24 mole) of 1,6-bis-methoxymethoxynaphthalene in 100 ml. of dry ethyl ether. Thirteen grams (0.24 mole) of ammonium chloride and 9.7 g. (0.24 mole) of potassium metal in small pieces were added. The alternate addition of ammonium chloride and potassium metal was repeated four more times. In all 65 g. of ammonium chloride and 48.5 g. of potassium metal were added. The flask openings were covered loosely with glassine paper and the ammonia was allowed to evaporate overnight at room temperature. The residue was dissolved in water and extracted three times with ether. Evaporation of the dried ether gave 57 g. (94 per cent yield) of a dark oil. No attempt was made to purify this oil. However, an ultraviolet spectrum of the crude oil shows that reduction has taken place. The spectrum was similar to that of a simple anisole with a maximum at 267 mμ and a molar extinction coefficient of 1650. The very intense maximum at 235 mμ of 1,6-bis-methoxymethoxynaphthalene had disappeared completely.

38. Hydrolysis of 1,6-bis-Methoxymethoxy-5,8-dihydronaphthalene

Thirty-six grams of crude 1,6-bis-methoxymethoxy-5,8-dihydronaphthalene was dissolved in 150 ml. of water and 400 ml. of 95 per cent ethanol and heated to boiling. Five milliliters of concentrated hydrochloric acid was added and the solution was allowed to boil for five minutes. After this it was poured onto ice, diluted with water and extracted with chloroform.

a. 5-Hydroxy-2-tetralone (XXXI). The chloroform extract from the hydrolysis of 1,6-bis-methoxymethoxy-5,8-dihydronaphthalene was extracted twice with aqueous potassium hydroxide. This potassium hydroxide extract was poured onto ice and acidified with hydrochloric acid. A black tar which settled from solution was separated. Extraction of the acidic water solution with chloroform and subsequent evaporation of the chloroform gave more black phenolic-smelling tar. From a sublimation, bath temperature 180°/10.5 mm., of the combined tars 2 g., 8.5 per cent yield, of purified phenol were obtained. The melting point of 5-hydroxy-5-tetralone was 155-162° d.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22

Found: C, 74.06, 74.19; H, 6.17, 6.44.

b. 5-Methoxymethoxy-2-tetralone (XXX). The chloroform extract from the hydrolysis of 1,6-bis-methoxymethoxy-5,8-dihydronaphthalene, after being extracted with aqueous potassium hydroxide, was evaporated in a stream of air to leave a viscous brown liquid. This liquid was poured into a beaker of magnetically stirred sodium bisulfite solution

consisting of 100 g. of sodium bisulfite dissolved in 250 ml. of water and 65 ml. of ethanol. The sodium bisulfite addition product, which formed after about ten minutes, was collected on a Büchner funnel, washed with ether and decomposed by mixing with 200 ml. of aqueous sodium carbonate. The 5-methoxymethoxy-2-tetralone was extracted with ether; the ether was evaporated, and the compound was distilled, b.p. 125-160°/ 5 mm. The yield of the tetralone, a colorless liquid, was 7.2 g., 22.5 per cent of the theoretical yield. The product was not further purified.

39. Attempted Reduction of 5-Hydroxy-2-tetralone

The potassium salt of 5-hydroxy-2-tetralone was made by dissolving 5.3 g. (0.033 mole) of 5-hydroxy-2-tetralone in 75 ml. of methanol and adding 2.05 g. of potassium hydroxide in a small amount of water. This solution of the potassium salt then was added dropwise to a magnetically stirred slurry of 1.2 g. (0.032 mole) of sodium borohydride in methanol. After four hours the reaction mixture was dissolved in water, cooled, acidified and extracted with benzene. The benzene was evaporated in a stream of air leaving a black tar which was distilled, b.p. 160-170°/0.75 mm., to give a yellow viscous oil which could not be induced to crystallize.

40. 5-Methoxymethoxy-2-hydroxytetralin (XXXII)

To a slurry of 0.80 g. (0.021 mole) of lithium aluminum hydride in 10 ml. of dry ether in a 100-ml. flask equipped with a reflux condenser, dropping funnel and magnetic stirrer was added 5 g. (0.0225

mole) of crude 5-methoxymethoxy-2-tetralone dissolved in 50 ml. of dry ether. After being stirred for one hour at room temperature, the reaction mixture was refluxed for thirty minutes on the steam bath. The excess lithium aluminum hydride was decomposed with a methanol-ether solution after which the reaction mixture was diluted with water. The solid inorganic material was dissolved by the addition of sodium potassium tartrate and the reaction mixture was extracted with ether. The ether layer was dried over magnesium sulfate and evaporated. The residue was vacuum distilled, b.p. 158-160°/1.75 mm., to give 3.5 g. of 5-methoxymethoxy-2-hydroxytetralin as a viscous colorless liquid. N_D^{32} 1.5428.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74.
Found: C, 69.45, 69.26; H, 7.72, 7.71.

41. 2,5-Dihydroxytetralin (XXXIII)

One gram of 5-methoxymethoxy-2-hydroxytetralin was dissolved in 10 ml. of ethanol and 4 ml. of water and heated to reflux on the steam bath. To the hot solution was added 0.12 ml. of concentrated hydrochloric acid and the solution was refluxed for one hour. The solution was then poured over ice, diluted with water and extracted with ether. The ether was dried and evaporated in a stream of air to leave 0.57 g., 78 per cent yield, of crude product which was sublimed at a bath temperature of 180°/3 mm. Recrystallization from benzene gave 2,5-dihydroxytetralin as white discs, m.p. 127-128°.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 73.14; H, 7.37.
Found: C, 72.95, 73.25; H, 7.05, 7.05.

42. 7,8-Dihydro-1-naphthol (V)

A mixture of 0.5 g. of 2,5-dihydroxytetralin, 1 g. of potassium hydroxide and 1 g. of sodium hydroxide was placed in a copper tube (ca. 12 mm. diameter, sealed at one end) under a nitrogen atmosphere and heated to 290° for ten minutes. The mixture was allowed to cool and dissolved in cold water. It was acidified, extracted with ether and the ether evaporated in a stream of air. The semi-solid residue was sublimed to give 0.18 g. of white product, m.p. 65-70°. Colorless plates, m.p. 73.5-74.5°, were obtained after three recrystallizations from hexane. A mixed melting point with 5,6-dihydro-1-naphthol (produced by the isomerization of 5,8-dihydro-1-naphthol) showed no depression. The ultraviolet spectrum of 7,8-dihydro-1-naphthol has maxima at 267 mμ, 299 mμ and 309 mμ with molar extinction coefficients of 4500, 1750 and 1500 respectively.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.90.

Found: C, 81.83, 81.73; H, 6.77, 6.61.

43. Preparation and Spectrum of 3-Methoxystyrene

3-Methoxystyrene was prepared by the method of Sutzbacher[95] in order to compare its spectrum with that of the product of the isomerization of 5,8-dihydro-1-methoxynaphthalene.

First a Perkin-Doebner reaction was used to make 3-methoxycinnamic acid. In this reaction 8.45 g. (0.062 mole) of 3-methoxybenzaldehyde, 12.5 g. (0.12 mole) of malonic acid, 25 ml. of pyridine and 0.7 ml. of piperidine were heated together for two hours on the steam bath. The mixture was refluxed for fifteen minutes after which

it was poured onto cracked ice containing 33 ml. of concentrated hydrochloric acid. The yield of precipitated 3-methoxycinnamic acid as white needles, m.p. 116-117°, was 11.5 g., 95 per cent of the theoretical yield.

3-Methoxystyrene was formed by decarboxylation of 3-methoxycinnamic acid. This was effected by distilling 3-methoxystyrene from a mixture of 10 g. of 3-methoxycinnamic acid, 40 ml. of quinoline, 1 g. of anhydrous copper sulfate and 0.6 g. of hydroquinone at a pot temperature of 260°. The product was washed with dilute sulfuric acid, dried and vacuum distilled. The yield of 3-methoxystyrene as a colorless liquid, b.p. 93-95°/17 mm., N_D^{25} 1.5590, was 2.4 g. The literature values are: b.p. 90-93°/15 mm., N_D^{16} 1.555. The ultraviolet spectrum has maxima at 250 mμ and 293 mμ with molar extinction coefficients of 8600 and 2150 respectively.

44. Kinetics of the Base-Catalyzed Isomerization of 1-Methoxy-5,8-dihydronaphthalene and of Potassium 5,8-Dihydro-1-naphthoxide

In 500 ml. of dry, oxygen-free tert-amyl alcohol there was dissolved 5.35 g. of potassium metal. The solution was maintained at 100° under a nitrogen atmosphere and 6 g. of 5,8-dihydro-1-naphthol was added to the reaction flask at time zero. At fifteen minute intervals 5 ml. aliquots were removed from the reaction flask and added to 65 ml. of chilled 0.0274 N ethanolic hydrochloric acid in 100-ml. volumetric flasks. Each aliquot was diluted to 100 ml. with ethanol and the precipitated potassium chloride allowed to settle. A portion of each diluted aliquot was then further diluted 10:1 with ethanol. The concen-

tration of product in each aliquot was determined spectroscopically. The spectrum of the product has a maximum at 299 mμ while the starting material absorbs negligibly at this wavelength. The rate constant was determined graphically (Figure 1). After the final aliquot had been removed, the concentration of potassium tert-amoxide in the residual reaction mixture was determined by titration with standard ethanolic hydrochloric acid, using phenolphthalein as indicator.

The kinetics of the isomerization of 1-methoxy-5,8-dihydronaphthalene were determined in precisely the same manner except that aliquots were taken at seven and one-half minute intervals. Only 4.0 g. (0.103 mole) of potassium metal was used while 6.57 g. (0.0411 mole) of 1-methoxy-5,8-dihydronaphthalene was added.

The isomerizations of both compounds followed first order kinetics for the first 30 per cent of the reactions and then began to deviate slightly. The rate constant for potassium 5,8-dihydro-1-naphthoxide was 0.00297 $min.^{-1}$ at the base concentration of 0.133 N (see Figure 1). The rate constant for 1-methoxy-5,8-dihydronaphthalene was 0.00344 $min.^{-1}$ in 0.135 N base (see Figure 2).

B. Preparation of 1-Substituted Dihydronaphthalenes

1. 5-Amino-2-methoxynaphthalene (XLV)

5-Amino-2-methoxynaphthalene was prepared by the method of Butenandt and Schramm.[70] To a 2-l. three-necked flask equipped with dropping funnel and mechanical stirrer were added 800 ml. of water, 24 g. (0.60 mole) of sodium hydroxide and 100 g. (0.50 mole) of crude

5-acetamido-2-hydroxynaphthalene. The flask was cooled to 5° in an ice-salt bath and 65 ml. (87 g., 0.70 mole) of methyl sulfate was added dropwise. The reaction mixture was maintained for two hours at 0° and then for four hours at room temperature. After this time the mixture was again made basic and an additional 10 ml. of methyl sulfate was added. The stirring was continued for another hour at room temperature after which the precipitated product was collected on a Büchner funnel and washed with dilute ammonium hydroxide. The product was dried overnight in vacuum at 65°. The yield of crude 5-acetamido-2-methoxynaphthalene was 103 g.

The 103 g. of crude 5-acetamido-2-methoxynaphthalene was dissolved in 750 ml. of 95 per cent ethanol and 200 ml. of concentrated hydrochloric acid in a 2-l. flask and refluxed for two hours on the steam bath. The reaction mixture was cooled in an ice bath and the precipitate collected on a Büchner funnel. The product was dried overnight in vacuum at 65° to give 71.5 g. of crude material. The filtrate was evaporated to give an additional 11.5 g. of product, 2-methoxy-5-naphthylamine hydrochloride.

A solution of 83 g. of 2-methoxy-5-naphthylamine hydrochloride and 40 g. of potassium hydroxide in 500 ml. of 95 per cent ethanol was refluxed three hours and filtered through fluted filter paper into 2 l. of water. The precipitated free amine was collected on a Büchner funnel and air dried. Vacuum distillation, b.p. 168°/2 mm., gave 49 g. of 5-amino-2-methyoxynaphthalene, m.p. 75°. A melting point of 74° is recorded in the literature[70,79] The overall yield of 5-amino-2-

methoxynaphthalene from 5-acetamido-2-hydroxynaphthalene was 57 per cent.

2. 1,4-Dihydro-5-amino-2-methoxynaphthalene (XLVI).

To 1800 ml. of liquid ammonia in a 3-l three-necked flask equipped with a Dry-Ice condenser and mechanical stirrer were added 100 ml. (1.72 mole) of absolute ethanol and 62 g. (0.36 mole) of 5-amino-2-methoxynaphthalene. Small pieces of potassium metal were dropped into the reaction mixture. When about 35 g. (0.9 mole) of potassium had been added the reaction mixture became blue and remained blue for one minute. The condenser was removed and the mouths of the flask were covered loosely with glassine paper and the liquid ammonia was allowed to evaporate overnight at room temperature. The reaction products were dissolved in 1 l. of ice water which was then extracted three times with ethyl ether. The ether solution was dried over magnesium sulfate and evaporated to give 60 g., of a viscous brown liquid. No attempt was made to purify the crude product, 1,4-dihydro-5-amino-2-methoxynaphthalene.

3. 1,4-Dihydro-2-methoxy-5-naphthylamine Hydrochloride (XLVII).

Ten grams of crude 1,4-dihydro-5-amino-2-methoxynaphthalene was dissolved in 50 ml. of ethyl ether and dry hydrogen chloride gas was bubbled through the solution. The precipitated amine hydrochloride was collected on a Büchner funnel, washed with ether and air dried. The crude product was recrystallized from methanol to give 10.5 g. of 1,4-dihydro-2-methoxyl-5-naphthylamine as white needles, m.p. 185-195d. The ultraviolet spectrum of 1,4-dihydro-2-methoxy-5-naphthylamine hydrochloride has a maximum at 285 mμ with a molar extinction coefficient of 1950. The absence of a maximum at 254 mμ indicated the absence of

starting 5-amino-2-methoxynaphthalene.*

Anal. Calcd. for $C_{11}H_{14}ONCl$: C, 62.41; H, 6.67; N, 6.62; Cl, 16.75.
Found: C, 62.22; H, 6.74; N, 6.98; Cl, 17.67.

4. Attempted Preparation of 5-Amino-2-tetralone (XLVIII)

Three hundred milliliters of water, 100 ml. of ethanol, 100 ml. of concentrated hydrochloric acid and 28.5 g. of 1,4-dihydro-2-methoxy-5-naphthylamine hydrochloride were placed in a 1-l. one-necked flask and refluxed for one hour. The reaction mixture was cooled in an ice bath and neutralized with ammonium carbonate. The precipitated 5-amino-2-tetralone was collected by filtration and dried overnight over potassium hydroxide in a vacuum desiccator. The yield of crude material was 21 g. The crude material apparently polymerized on this standing overnight. The product was not soluble in ether, methanol tetrahydrofuran, water or aqueous hydrochloric acid although it changed color under the last-named solvent.

5. Attempted Preparation and Reduction of 5-Amino-2-tetralone Hydrochloride

A solution of 11 g. (0.052 mole) 1,4-dihydro-2-methoxy-5-naphthylamine hydrochloride in 60 ml. of water, 60 ml. of ethanol and 35 ml. of concentrated hydrochloric acid was refluxed for twenty minutes. The solution was cooled and 15 g. of sodium hydroxide, 50 ml. of water and 50 ml. of ethanol was added. It was then added dropwise to a stirred solution of 1.0 g. (0.027 mole) of sodium borohydride and 20 g. of sodium hydroxide in 60 ml. of 1:1 ethanol-water solution. The reaction

*The ultraviolet spectrum of 2-methoxy-5-naphthylamine hydrochloride has a maximum at 254 mμ with a molar extinction coefficient of 14800.

mixture was heated for one hour on the steam bath, cooled, diluted with 500 ml. of water and extracted with ether. The ether was removed *in vacuo* and the residue was distilled, b.p. 128°/0.4 mm. to give 6 g. of a colorless liquid. The ultraviolet spectrum of this material has maxima at 237 mμ and 287 mμ with extinction coefficients of approximately 8000 and 2500 respectively. A mixture of 1 g. of the amine and 1.5 g. of acetic anhydride was heated for a few minutes on the steam bath. On cooling the mixture set to a crystalline mass which was collected on a Büchner funnel and washed with aqueous sodium bicarbonate. An analytical sample was prepared by recrystallizing from methanol to give long white needles, m.p. 156-157°. The elemental analysis could not be satisfactorily interpreted.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40.
Found: C, 76.07, 76.18; H, 8.07, 8.17; N, 7.51.

6. *1,4-Dihydro-5-acetamido-2-methoxynaphthalene (L1).*

Fifty grams (0.285 mole) of crude 1,4-dihydro-5-amino-2-methoxynaphthalene were placed in a 200 ml. Erlenmeyer flask cooled in an ice bath. One hundred twenty-five milliliters (1.25 mole) of acetic anhydride was added in three portions. After a few minutes the reaction mixture solidified. The reaction mixture was triturated with water, collected on a Büchner funnel, and washed with aqueous sodium bicarbonate solution until neutral. The crude product was recrystallized twice from benzene to give 44 g. of yellowish needles. It was then dissolved in 500 ml. of benzene and refluxed for two hours with 50 g. of norite. The hot mixture was filtered through fluted filter paper to give a colorless

filtrate from which the product crystallized in white needles, m.p. 156-157°. Recrystallization from methanol gave 35 g. of 1,4-dihydro-5-acetamido-2-methoxynaphthalene, m.p. 157-158°.

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45.
Found: C, 71.99, 71.63; H, 7.03, 6.91; N, 6.25, 6.38.

7. 5-Acetamido-2-tetralone (L11).

Ten grams of 1,4-dihydro-5-acetamido-2-methoxynaphthalene were dissolved in 125 ml. of ethanol and 100 ml. of water in a 500-ml. flask equipped with a reflux condenser and heated to reflux on the steam bath. Ten milliliters of concentrated hydrochloric acid were added and the reaction mixture was refluxed for fifteen minutes after which it was poured onto 250 g. of ice. The crude product crystallized and was collected on a Büchner funnel. After three recrystallizations from benzene 2.5 g. of 5-acetamido-2-tetralone, m.p. 175-176°, were obtained as long white needles.

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89.
Found: C, 70.73; H, 6.40; N, 6.77, 6.90.

8. 5-Acetamido-2-hydroxytetralin (L111).

To a solution of 0.60 g. (0.016 mole) of sodium borohydride in 40 ml. of methanol in a 250 ml. flask equipped with dropping funnel and magnetic stirrer were slowly added 3.0 g. (0.014 mole) of 5-acetamido-2-tetralone in 100 ml. of methanol. The reaction mixture was stirred for two hours and then poured into 800 ml. of cold, dilute hydrochloric acid. Extraction of the aqueous solution with benzene evaporation of

the benzene gave 0.15 g. of crude material. Three recrystallizations from benzene gave an unidentified product as white needles, m.p. 153-154°.

No further material could be obtained by extraction of the aqueous solution with benzene or ethyl ether. An overnight continuous extraction with ethyl acetate followed by evaporation of the ethyl acetate yielded 2.0 g. of white needles, m.p. 194-196°. After one recrystallization from benzene this product, 5-acetamido-2-hydroxytetralin, melted at 196-198°.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82
Found: C, 70.45, 70.57; H, 7.38, 7.15; N, 6.35, 6.45.

9. 7,8-Dihydro-1-aminonaphthalene (LIV)

A mixture of 2.0 g. of 5-acetamido-2-hydroxytetralin, 4.0 g. of potassium hydroxide and 4.0 g. of sodium hydroxide was placed in a stoppered glass test tube with a side arm and heated to 275-285° for fifteen minutes. Material which steam distilled out through the side arm was collected and dissolved in ether. The residue was cooled, dissolved in water, and extracted with ether. The ether extracts were combined, dried over magnesium sulfate and evaporated. The residue was vacuum distilled to give 0.70 g. of 7,8-dihydro-1-aminonaphthalene, colorless liquid, N^{27} 1.6342, b.p. 182°/30 mm. The ultraviolet spectrum of 7,8-dihydro-1-aminonaphthalene has maxima at 267 mu and 317 mu with molar extinction coefficients of 7350 and 2600 respectively.

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.72; H, 7.65; N, 9.65
Found: C, 82.88; H, 7.44; N, 9.63.

10. 7,8-Dihydro-1-acetamidonaphthalene (LV)

To 320 mg. of 7,8-dihydro-1-aminonaphthalene dissolved in 1 ml. of pyridine in a 10 ml. Erlenmeyer flask was added dropwise 300 mg. of acetic anhydride. After a few minutes the reaction mixture solidified. It was triturated with water, collected on a Büchner funnel and washed thoroughly with aqueous sodium bicarbonate solution. The product was recrystallized from benzene to give 330 mg. of white needles, m.p. 154-155°. After two more recrystallizations from benzene the 7,8-dihydro-1-acetamidonaphthalene melted at 157-158°. Its ultraviolet spectrum shows a maximum at 260 mu with a molar extinction coefficient of 8950.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48.

Found: C, 76.99; H, 7.06; N, 7.53.

11. Preparation and Separation of 5-Nitrotetralin and 6-Nitrotetralin

This nitration of tetralin is based on the method of Schroeter.[80] A cooled solution of 300 ml. of nitric acid (d = 1.42) and 600 ml. of sulfuric acid (d = 1.84) was added dropwise with vigorous mechanical stirring to 575 g. of tetralin in a 3-l. three-necked flask cooled by an ice-salt bath. Powdered dry ice was added directly to the reaction mixture to prevent its temperature from going above 0°. This required approximately 25 lbs. of dry ice. When the addition of the mixed acid was complete, the reaction mixture was stirred for one hour and then poured over cracked ice. The resulting mixture was diluted to 8 l. with water and extracted with 2 l. of carbon tetrachloride. The carbon tetrachloride extract was washed with water and aqueous sodium bicarbonate solution and filtered to remove resinous material. The carbon tetra-

chloride was removed by distillation and the residue was vacuum distilled to give 570-600 g. of a mixture of 5-nitrotetralin and 6-nitrotetralin, b.p. 115-145°/1 mm.

The mixture of nitrotetralins was divided into three equal fractions by a vacuum distillation through a three-foot column packed with glass helices. The first fraction collected, b.p. 115-125°/1 mm., was predominately 5-nitrotetralin and was placed in the cold room to crystallize. The second fraction was put aside for redistillation. The third of the material remaining in the pot was subjected to a simple vacuum distillation, b.p. 125-145°/1 mm., and placed in the cold room for the 6-nitrotetralin it contained to crystallize. The crystalline nitrotetralins were collected on a jacketed Buchner funnel cooled by ice-water and stored in the cold room. The filtrates were kept for redistillation with the above second fraction.

One such processing as described above gave from 600 g. of mixed nitrotetralins, 125 g. of the 5-isomer, 125 g. of 6-isomer, and 325 g. of recovered mixture.

12. 5-Nitro-1-tetralone (LVII)

To 100 g. (0.56 mole) of 5-nitrotetralin dissolved in 1600 ml. of glacial acetic acid and 50 ml. of concentrated sulfuric acid in a 3-l., three-necked flask equipped with a mechanical stirrer was added 158 g. (1.58 mole) of chromium trioxide slowly so that the temperature did not rise above 35°. After six hours the reaction mixture was poured over cracked ice, diluted to 8 l. with water and placed in the refrigerator. After standing for twelve hours, the precipitate which formed

was collected on a Büchner funnel, washed with aqueous sodium bicarbonate and dried. The yield of the crude mixture of 5-nitro-1-tetralone and 8-nitro-1-tetralone was 68 g. Repeated recrystallizations of this from ethanol gave 20 g. of 5-nitro-1-tetralone, m.p. 102°. Melting points of 102.5° [81] and 104° [71] are recorded in the literature.

13. Attempted Reduction of 5-Nitro-1-tetralone

A solution of 10 g. (0.053 mole) of 5-nitro-1-tetralone in 200 ml. of methanol was added dropwise to a stirred solution of 1.2 g. (0.031 mole) of sodium borohydride in 50 ml. of methanol. The reaction mixture was stirred for two hours, poured into 700 ml. of water and extracted with benzene. Evaporation of the benzene left 8 g. of a crude brown solid. Recrystallization from acetone-hexane gave, as a first crop, 1 g. of crystalline material, m.p. 100-101°. A mixed melting point with the starting material, 5-nitro-1-tetralone, did not depress.

14. 1-Hydroxy-5-nitrotetralin (LVIII)

To 10 g. (0.052 mole) of 5-nitrotetralone dissolved in 100 ml. of a 1.0 M bis-(2,2'-dimethoxy)-ethyl ether solution of sodium borohydride in a 250-ml. flask equipped with a magnetic stirrer was added dropwise 17 ml. of a 2.0 M bis-(2,2'-dimethoxy)-ethyl ether solution of aluminum chloride. The reaction mixture was stirred for six hours and then poured over 200 g. of crushed ice containing 20 ml. of concentrated hydrochloric acid. An oil separated and was extracted into ether. The ether extract was dried over magnesium sulfate and evaporated to leave 8.5 g. of yellowish cubes, m.p. 68-70°. After two re-

crystallizations from methanol and one from benzene, this product, 1-hydroxy-5-nitrotetralin, still melted at 68-70°.

Anal. Calcd. for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.74; N, 7.25.

Found: C, 62.44, 62.12; H, 5.54, 5.49; N, 7.35.

15. Preparation of 1-Chloro-5-nitrotetralin (LIX)

To 13.5 g. (0.105 mole) of thionyl chloride and one drop of pyridine in 20 ml. of benzene was added dropwise a solution of 18 g. (0.094 mole) of 1-hydroxy-5-nitrotetralin in 80 ml. of benzene. The solution was refluxed for one hour and then evaporated to dryness. Vacuum sublimation of the residue followed by recrystallization from benzene gave 16.1 g. (81 per cent yield) of 1-chloro-5-nitrotetralin as yellow needles, m.p. 32-34.5°.

Anal. Calcd. for $C_{10}H_{10}NO_2Cl$: C, 56.74; H, 4.76; N, 6.62; Cl, 16.75.

Found: C, 56.86, 56.83; H, 4.64, 4.83; N, 6.51; Cl, 16.87.

16. Attempted Brominations of 5-Nitrotetralin

a. Base catalyzed. A mixture of 17.7 g. (0.10 mole) of 5-nitrotetralin and 5.9 g. of sodium methoxide in 30 ml. of methanol was stirred for fifteen minutes at -5°. This mixture was then added dropwise with stirring to 17.6 g. (0.11 mole) of bromine in 30 ml. of chloroform at -10 to -15°. Cooling was discontinued and the reaction mixture was stirred for thirty-five minutes. More chloroform was added to the reaction mixture which was then washed with aqueous sodium bisulfite, aqueous sodium bicarbonate and water. Evaporation of the chloroform left a crystalline solid which was not a lachrymator so evidently no

α-bromination took place. The product was not further characterized.

b. Acid catalyzed. To 50 g. (0.35 mole) of 5-nitrotetralin and 0.5 g. of anhydrous aluminum chloride in 50 ml. of dry ether in a 500-ml. three-necked flask equipped with a mechanical stirrer was added dropwise 56.5 g. (0.35 mole) of bromine. The reaction mixture was kept in the dark and at 0° throughout the reaction. After four hours the solvent was distilled under reduced pressure and the viscous lachrymatory liquid remaining was placed in the cold room overnight. The product was collected on a Büchner funnel to give 31.5 g. of a white crystalline solid, m.p. 30°. Although the material was a potent lachrymator an elemental analysis indicated that only a small amount of bromination occurred.

Anal. Calc. for $C_{10}H_{10}NO_2Br$: Br, 31.2

Found: Br, 2.59.

17. 8-Nitro-1-tetralone (LVI)

To 40 ml. of refluxing absolute ethanol in a 200-ml., three-necked flask equipped with mechanical stirrer, reflux condenser and dropping funnel was added 4.7 g. (0.20 mole) of sodium in small pieces. The contents of the flask were protected from moisture by calcium chloride drying tubes on the condenser and dropping funnel. When the reaction with sodium was complete, the excess ethanol was distilled. The reaction flask was cooled in an ice-bath and 30 ml. of dry ethyl ether was added. A solution of 16.4 g. (0.95 mole) of 5-nitrotetralin in 12.5 g. (0.107 mole) of amyl nitrite was added dropwise. The reaction mixture was stirred overnight and allowed to come to room temp-

erature slowly. After standing for two days at room temperature, the reaction mixture was dissolved in 300 ml. of water which was then extracted twice with ether. Bubbling carbon dioxide through the water solution precipitated 2.3 g. (12 per cent yield) of the crude oxime of 8-nitro-1-tetralone. To 15 ml. of methanol were added 2 g. of the crude oxime, 2 g. of 38 per cent formaldehyde and 2 drops of sulfuric acid. The reaction mixture was refluxed for thirty minutes. Four milliliters of concentrated hydrochloric acid was added and refluxing was continued for ten minutes. The reaction mixture was poured into water and the crude precipitate was collected on a Büchner funnel and washed with water. A vacuum sublimation followed by recrystallization from benzene-hexane gave 0.5 g. of 8-nitro-1-tetralone, m.p. 145-147°. A melting point of 155° is recorded in the literature.[71]

18. Attempted Preparation of 1-Carboxy-8-nitrotetralin (LXIII)

To 400 ml. of refluxing absolute ethanol in a 1-l., three-necked flask equipped with mechanical stirrer, reflux condenser and dropping funnel was added 34.5 g. (1.5 mole) of sodium. The condenser and dropping funnel were equipped with calcium chloride drying tubes. When the sodium had completely reacted the solution was cooled to 15° and 219 g. (1.5 mole) of dry, freshly redistilled diethyl oxalate was added. To this cooled diethyl oxalate-sodium ethoxide solution was added dropwise a solution of 88.5 g. (0.5 mole) of 5-nitrotetralin in 150 ml. of absolute ethanol. After standing for three days at room temperature, a 100-ml. aliquot was taken out and worked up. No acidic solid material was isolated. The remainder of the reaction mixture was refluxed for four

hours and then diluted with 130 ml. of concentrated hydrochloric acid and 500 ml. of water. Approximately one-third of the solvent was evaporated by heating the solution on the steam bath and passing a stream of air over it. The water layer was decanted and the tar remaining was treated with four successive 500-ml. portions of 1 N potassium hydroxide until it was dissolved. Each portion was diluted to 1 l. with 1 N potassium hydroxide solution, filtered, treated with 65 ml. of 30 per cent hydrogen peroxide, and allowed to stand three hours at room temperature. The solutions were poured onto ice and acidified with hydrochloric acid. The brown precipitate which formed was collected on a Büchner funnel, washed with water and air-dried. The yield of crude acid was 18.7 g. All attempts at purification (see 1-carboxy-6-nitrotetralin) were futile.

19. Nitration of 1-Naphthoic Acid

To a hot solution of 100 g. (0.58 mole) of 1-naphthoic acid in 500 ml. of glacial acetic acid in a 2-l. beaker on the steam bath was added dropwise 100 ml. of fuming nitric acid (d = 1.50). The reaction solution was heated for three hours and then diluted with 10 l. of ice-water. The yellow precipitate was collected on a Büchner funnel, washed with water and dried at 100° to give 123 g. of a crude mixture of 5- and 8-nitronaphthoic acid.

20. Preparation and Separation of 5-Amino-1-naphthoic Acid and 1,8-Naphtholactam (LXIV)

A solution of 9.7 g. (0.045 mole) of a mixture of 5-nitro-1-naphthoic acid and 8-nitro-1-naphthoic acid in 30 ml. of concentrated ammonium hydroxide and 30 ml. of water was added to a solution of 150 g. (0.71 mole) of ferrous sulfate septahydrate in 320 ml. of concentrated ammonium hydroxide and 370 ml. of water. The reaction mixture was stirred at 80° for two hours. The reaction mixture was diluted with 1 l. of water, heated to boiling on a hot-plate and filtered. The filtrate was cooled and the precipitate which formed was collected on a Büchner funnel. The precipitate was dissolved in 1 l. of hot water which was then cooled. The precipitate was collected and washed thoroughly with dilute sodium hydroxide. It was recrystallized once from ethanol to give 2 g. of 1,8-naphtholactam, m.p. 182-184°. Melting points of 178° and 181° are recorded in the literature.[104,105,106] Neutralization of the basic washings gave 2.5 g. of 5-amino-1-naphthoic acid, m.p. 200-204°. Melting points of 212° and 199° are recorded in the literature.[107]

21. Reduction of 1,8-Naphtholactam

To a solution of 3.0 g. (0.018 mole) of 1,8-naphtholactam in 75 ml. of ammonia and 3 ml. of absolute ethanol in a 200-ml. flask equipped with magnetic stirring bar and Dry Ice condenser was added 2.3 g, (0.057 mole) of potassium in small pieces. When this amount of potassium had been added, the blue color persisted for about one minute. The ammonia was allowed to evaporate and the residue was triturated

with ice-water, collected on a Büchner funnel, washed with more water and air-dried. Two recrystallizations of this material from ethanol-water gave a yellow powder, m.p. 255-260°. This material was not investigated further; it may be a salt.

22. Attempted Reduction of the Sodium Salt of 8-Amino-1-naphthoic Acid

A solution of 3 g. (0.018 mole) of 1,8-naphtholactam and 1.1 g. (0.018 mole) of sodium hydroxide was prepared by heating the two together in 100 ml. of water. The solution was then evaporated to dryness on the steam bath. The residue was powdered and dissolved in 100 ml. of liquid ammonia in a 200-ml. flask equipped with magnetic stirring bar and Dry Ice condenser. To this was added 4 ml. of absolute ethanol and 2.4 g. (0.043 mole) of potassium in small pieces (until the blue color persisted for one minute). The ammonia was allowed to evaporate and the residue was triturated with dilute hydrochloric acid, collected on a Büchner funnel and washed with water. The residue was air-dried to give 2.5 g. of yellow powder. Recrystallization of this material from benzene gave yellow crystals which sublimed at 160° and melted at 184-185°. The ultraviolet spectrum of the material has a broad maximum at 245 mμ with a molar extinction coefficient of 10700. The material is assumed to be starting material, 1,8-naphtholactam.

Anal. Calcd. for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18

Found: C, 77.94, 78.09; H, 4.55, 4.17; N, 8.15, 8.28.

C. Preparation of 2-Substituted Dihydronaphthalenes

1. Attempted Acid-catalyzed Bromination of 6-Nitrotetralin

To 50 g. (0.35 mole) of 6-nitrotetralin and 0.5 g. of anhydrous aluminum chloride in 50 ml. of dry ether in a 500-ml., three-necked flask equipped with a mechanical stirrer was added dropwise 56.5 g. (0.35 mole) of bromine. The reaction mixture was kept in the dark and at 0° throughout the reaction. After four hours the solvent was distilled under reduced pressure and the viscous lachrymatory liquid remaining was placed in the cold room overnight. The product was collected on a Büchner funnel to give 33 g. of a white crystalline solid, m.p. 28°. Although the material was a potent lachrymator, an elemental analysis indicated that only a small amount of bromination occurred.

2. Attempted Preparation of 1-Carboxy-6-nitrotetralin (LXIII)

To 400 ml. of refluxing absolute ethanol in a 1-l., three-necked flask equipped with mechanical stirrer, reflux condenser and dropping funnel was added 34.5 g. (1.5 mole) of sodium. The condenser and dropping funnel were equipped with calcium chloride drying tubes. When the sodium had completely reacted, the solution was cooled to 15° and 219 g. (1.5 mole) of dry, freshly redistilled diethyl oxalate was added. To this cooled diethyl oxalate-sodium ethoxide solution was added dropwise a solution of 88.5 g. (0.5 mole) of 6-nitrotetrailin 150 ml. of absolute ethanol. After standing for two days at room temperature, 100 ml. of concentrated hydrochloric acid in 500 ml. of water was added. Approximately one-third of the solvent was evaporated by heating the solution on the steam bath and passing a stream of air over it. The water layer

was decanted and the tar remaining was treated with four successive 500-ml. portions of 1 N potassium hydroxide until it was dissolved. Each portion was diluted to 1 l. with 1 N potassium hydroxide solution, filtered, treated with 65 ml. of 30 per cent hydrogen peroxide, and allowed to stand three hours at room temperature. The solutions were poured onto ice and acidified with hydrochloric acid. The thick brown precipitate which formed was collected on a Büchner funnel, washed with water and air-dried. The yield of crude material was 89 g. Purification by dissolving in sodium bicarbonate solution and reprecipitating with acid gave a yellow powder, m.p. 155-160°d. An analytically pure sample was not obtained. Other methods of purification which were tried and which failed included treatment with bone charcoal, recrystallizations from various acetic acid-water mixtures, dimethyformamide, nitrobenzene, water with a trace of detergent added, and all common organic solvents. A vacuum distillation of the methyl ester (which decomposed) and elution from an ion exchange column (IR 400) also failed.

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33.
Found: C, 68.08; H, 4.85; N, 6.60.

3. Attempted Preparation of 1-Bromo-6-nitrotetralin

To 500 ml. of water containing 11.2 g. (0.20 mole) of potassium hydroxide was added a filtered tetrahydrofuran solution of 44 g. (0.20 mole) of crude 1-carboxy-6-nitrotetralin, m.p. 155-162d. A solution of 37.4 g. (0.22 mole) of silver nitrate in 100 ml. of water was added slowly with stirring. The precipitated silver salt was collected on a

Büchner funnel, washed with water and air-dried. The silver salt was powdered and dried three days at 65° in a vacuum oven. In a 200-ml., three-necked flask, equipped with magnetic stirrer and dropping funnel were placed 10 g. (0.031 mole) of the silver salt and 70 ml. of carbon tetrachloride which had been dried over phosphorus pentoxide. To remove the last traces of water 20 ml. of the carbon tetrachloride was distilled. The reaction mixture was cooled in an ice-bath and 5 g. (0.031 mole) of bromine in 10 ml. of carbon tetrachloride was added over a ten minute period. The reaction mixture was refluxed for two hours and the gases liberated by the reaction were bubbled through aqueous calcium hydroxide. The Hundsdiecker reaction occurred to a very limited extent as estimated by the amount of calcium carbonate formed. The reaction mixture was filtered and the carbon tetrachloride solution was washed with water and aqueous sodium bicarbonate and evaporated to dryness. A minute residue of unidentified material remained. This experiment was repeated four times with slight variations in the procedure but with the same lack of success.

4. Attempted Schmidt Reaction With 1-Carboxy-6-nitrotetralin

This reaction was run in a good hood. To a mixture of 10 g. (0.045 mole) of crude 1-carboxy-6-nitrotetralin, 40 ml. of concentrated sulfuric acid and 60 ml. of chloroform was added with stirring at 50-55°, 3.2 g. (0.05 mole) of sodium azide in small portions. After all of the azide had been added the mixture was heated for another thirty minutes at 50°, diluted with ice and made alkaline with potassium hydroxide pellets. There was very little solid material in the basic

solution so evidently no large amount of amine was formed.

5. 6,6'-Dinitro-1,2,3,4,1',2',3',4'-octahydro-1,1'-binaphthyl (iii)

When in the attempted preparation of 1-carboxy-6-nitrotetralin the basic solution was filtered just prior to treatment with hydrogen peroxide, a yellow-brown precipitate was left on the paper. This precipitate was washed once with hot ethanol and recrystallized from acetone to give small, light yellow crystals, m.p. 201-202°. Because of analogous reactions in the literature[74] the compound is formulated as 6,6'-dinitro-1,2,3,4,1',2',3',4'-octahydro-1,1'-binaphthyl.

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95.
Found: C, 67.90; H, 5.66; N, 7.79.

6. 6-Nitro-1-tetralone (LXX)

To 100 g. (0.56 mole) of 6-nitrotetralin dissolved in 1600 ml. of glacial acetic acid and 50 ml. of concentrated sulfuric acid in a 3-l., three-necked flask equipped with a mechanical stirrer was added 158 g. (1.58 mole) of chromium trioxide slowly so that the temperature did not rise above 35°. After six hours the reaction mixture was poured over cracked ice, diluted to 8 l. with water and placed in the cold room. After standing for twelve hours, a semi-solid precipitate formed on the bottom of the container. The water layer was decanted and the precipitate was extracted repeatedly with hot hexane which on cooling gave 40 g. (37 per cent yield) of yellow crystals. One recrystallization from absolute ethanol gave colorless crystals, m.p. 118-119°. A melting point of 118° is recorded in the literature.[82]

7. 6-Amino-1-tetralone (LXXI)

A solution of 108 g. (0.48 mole) of reagent-grade stannous chloride in 150 ml. of ethanol was added in portions to 30 g. (0.156 mole) of crude 6-nitro-1-tetralone in 300 ml. of ethanol. When the initial vigorous reaction had subsided the reaction solution was heated on the steam bath and evaporated to one-third of its original volume by a stream of air. It was then poured over 1000 g. of crushed ice and the resulting mixture was diluted to 2 l. with water. Solid sodium hydroxide was added to the mixture untill all of the tin was in solution as the stannate ion. The yellow precipitate remaining was collected on a Büchner funnel, washed with water and air-dried to give 22 g. of crude 6-amino-1-tetralone. Recrystallizations from boiling water and from hexane gave red needles, m.p. 125-128°. These needles were vacuum sublimed and recrystallized from benzene to give colorless flakes, m.p. 130-131°.

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69.
Found: C, 74.82; H, 6.77; N, 8.42.

8. 7-Nitro-1-tetralone (LXXII)

A 1-l. three-necked flask equipped with mechanical stirrer, dropping funnel and thermometer and containing 220 ml. of concentrated sulfuric acid was placed in a Dry Ice-acetone bath. To this was added 100 g. (0.70 mole) of 1-tetralone without allowing the temperature to rise above 0°. A solution of 50 ml. of fuming nitric acid (d = 1.50) and 110 ml. of concentrated sulfuric acid was added dropwise keeping the temperature below -15°. The reaction mixture was then immediately

stirred into 2000 g. of crushed ice and diluted to 5 l. with water. The precipitated material was collected on a Büchner funnel and washed several times with water. The precipitate was placed in 1 l. of water in a 3-l. beaker and stirred mechanically. Sodium bicarbonate was added until the mixture became slightly basic and the precipitate was recollected on a Büchner funnel and washed with water. One recrystallization from 95 per cent ethanol gave 120 g. of crude product. Recrystallization of the crude product from ethyl ether-hexane gave 7-nitro-1-tetralone as white needles, m.p. 104-105°. Melting points of 105° and 106° are recorded in the literature.[81,83] Evaporation of the mother liquors yielded a mixture of 7-nitro-1-tetralone and 5-nitro-1-tetralone.

9. 7-Amino-1-tetralone (LXXIII)

A solution of 240 g. (1.07 mole) of technical stannous chloride in 300 ml. of ethanol saturated with hydrogen chloride was added in portions to 60 g. (0.31 mole) of crude 7-nitro-1-tetralone in 600 ml. of ethanol. When the initial vigorous reaction had subsided the reaction solution was heated on the steam bath and evaporated to one-third of its original volume by a stream of air. It was then poured over 2000 g. of crushed ice and diluted to 4 l. total volume with water. Solid sodium hydroxide was added to the mixture until all of the tin was in solution. The yellow precipitate remaining was collected on a Büchner funnel, washed with water and air-dried. The yield of crude 7-amino-1-tetralone was 47 g. (93 per cent of the theoretical yield) melting 138-140°. Melting points of 136° and 140° are recorded in the literature.[83,81]

10. 1-Hydroxy-7-aminotetralin (LXXIV)

To a slurry of 5.1 g. (0.135 mole) of sodium borohydride and one pellet of potassium hydroxide in 20 ml. of methanol in a 1-l., three-necked flask equipped with mechanical stirrer was added in small portions a solution of 22 g. (0.135 mole) of 7-amino-1-tetralone in 350 ml. of methanol. The reaction mixture was stirred for two hours and then heated on the steam bath and evaporated to one-half of its original volume under a current of air. The solution was diluted with 100 ml. of water and the evaporation was continued until most of the alcohol was gone. The organic material was extracted into benzene and the benzene evaporated. Two recrystallizations from benzene gave 18 g. (82 per cent yield) of 1-hydroxy-7-aminotetralin, m.p. 96-97°.

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58.
Found: C, 73.49; H, 8.12; N, 8.38.

11. Attempted Dehydration of 1-Hydroxy-7-aminotetralin With Thionyl Chloride and Pyridine

A solution of 4.4 g. (0.032 mole) of thionyl chloride in 15 ml. of dry ethyl ether was added dropwise to a solution of 5 g. (0.030 mole) of 1-hydroxy-7-aminotetralin in 15 ml. of dry pyridine in a 100-ml. flask equipped with magnetic stirrer, reflux condenser and dropping funnel. After all of the thionyl chloride had been added, the reaction mixture was refluxed for two hours, diluted with ice and extracted with ether. Evaporation of the ether gave an intractable yellow gum.

12. 1-Acetoxy-7-acetamidotetralin (LXXV)

To 5.0 g. (0.020 mole) of 1-hydroxy-7-aminotetralin in 50 ml. of dry pyridine was added 22 ml. of acetic anhydride. The solution was heated for five minutes on the steam bath and then poured onto cracked ice. This was diluted to 750 ml. with water and the precipitated diacetyl derivative was collected on a Büchner funnel and washed with water. Two recrystallizations from benzene gave 4.9 g. (65 per cent yield) of white crystalline 1-acetoxy-7-acetamide, m.p. 156-157°.

Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93; N, 5.66.
Found: C, 68.18; H, 7.06; N, 5.75.

13. 2-Amino-5,6-dihydronaphthalene (LXXVII)

A small distillation apparatus was set up containing 20 g. of solid 1-acetoxy-7-acetamidotetralin. At a pot temperature of 230-240°/25 mm., 4.6 g. of acetic acid was distilled and collected. On cooling and scratching, the glassy residue, 15 g. was converted into a white waxy solid, m.p. 60-62°. The residue, crude 2-acetamido-5,6-dihydronaphthalene, was mixed with 45 ml. of ethylene glycol and 8.3 g. of potassium hydroxide and refluxed for three hours. The reaction mixture was then poured into 300 ml. of ice water. The white solid which precipitated was collected on a Büchner funnel, washed with water and dried to give 11.7 g. of material, m.p. 52-54°. When this material was vacuum distilled, b.p. 114°/0.2 mm. and recrystallized from hexane cubes, m.p. 68-69°, were obtained. The ultraviolet spectrum of 2-amino-5,6-dihydronaphthalene has a maximum at 267 mμ with an extinction coefficient of 5430.

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65.
Found: C, 82.84, 82.98; H, 7.56, 7.62; N, 9.83.

14. 2-Acetamido-5,6-dihydronaphthalene (LXXVI)

A mixture of 1 g. of 2-amino-5,6-dihydronaphthalene and 1 g. of acetic anhydride in a small Erlenmeyer flask was heated for five minutes on the steam bath. The reaction mixture was taken up in ether and washed with aqueous sodium bicarbonate. Evaporation of the ether left a white crystalline solid which was recrystallized once from hexane-benzene to give white platelets, m.p. 69-70°, of 2-acetamido-5,6-dihydronaphthalene.

Anal. Calcd. for $C_{12}H_{13}ON$: C, 76.97; H, 7.00; N, 7.48.
Found: C, 76.65; H, 6.99; N, 7.44.

15. 1-Methylene-6-aminoindane (LXXVIII) or 3-Methyl-5-aminoindene (LXXIX)

A small vacuum distillation apparatus was set up containing 8 g. of crude solid, 1-hydroxy-7-aminotetralin and a few crystals of iodine. At a pot temperature of 250° some material, b.p. 120°/0.3 mm., distilled and was collected and cooled to give 3.7 g. (52 per cent yield) of white solid, m.p. 38-40°. One recrystallization from benzene-hexane gave fluffy white flakes, m.p. 45-46°. The ultraviolet spectrum has a maximum at 311 mμ and a shoulder at 262 mμ with extinction coefficients of 1950 and 5450 respectively. The compound is believed to be either 1-methylene-6-aminoindane or the isomeric 3-methyl-5-aminoindene.

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65.
Found: C, 82.78; H, 7.47; N, 9.57.

16. 1-Methylene-6-acetamidoindane or 3-Methyl-5-acetamidoindene

A mixture of 1 g. of 6-amino-1-methyleneindane or 5-amino-3-methyindene and 1 g. of acetic anhydride in a small Erlenmeyer flask was heated for five minutes on the steam bath. The reaction mixture was taken up in ether and washed with aqueous sodium bicarbonate. Evaporation of the ether left a white crystalline solid which was crystallized from hexane-benzene to give white needles, m.p. 74-75°. A mixed melting point with 2-acetamido-5,6-dihydronaphthalene depressed slightly.

Anal. Calcd. for $C_{12}H_{13}ON$: C, 76.97; H, 7.00; N, 7.48
Found: C, 76.51; H, 7.00; N, 7.59.

17. 2-N,N-Dimethyamino-5,6-dihydronaphthalene (LXXX)

To a mixture of 12.6 g. (0.15 mole) of sodium bicarbonate, 7.25 g. (0.05 mole) of crude 2-amino-5,6-dihydronaphthalene and 25 ml. of water in a 100-ml. flask equipped with magnetic stirrer and dropping funnel was added dropwise 15.8 g. (0.125 mole) of dimethyl sulfate. After stirring for two hours at room temperature the reaction mixture was extracted with chloroform. The chloroform was evaporated and the residue was heated for fifteen minutes on the steam bath with 5 g. of acetic anhydride. The resulting mixture was dissolved in chloroform which was in turn washed with aqueous sodium bicarbonate and dried over sodium carbonate. The chloroform was evaporated and the residue vacuum distilled to give 1.1 g. (13 per cent yield) of 2-N,N-dimethylamino-5,6-dihydronaphthalene as a yellow liquid, N_D^{33} 1.6095, b.p. 116-117°/0.6 mm.

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09.
Found: C, 82.92; H, 8.74; N, 8.24.

18. 2-Hydroxy-5,6-dihydronaphthalene (LXXXI)

a. Diazotization of 2-amino-5,6-dihydronaphthalene. A finely divided precipitate of amine-sulfate was formed by dissolving 7.25 g. (0.05 mole) of 2-amino-5,6-dihydronaphthalene in 30 ml. of 6 N sulfuric acid in a 200-ml. beaker and cooling the resulting solution to 0° with stirring. A solution of 3.55 g. (0.05 mole) of 95 per cent sodium nitrite in 15 ml. of water was added slowly down the side of the beaker. The reaction mixture was stirred vigorously by hand and the temperature was kept below 3° by adding ice directly to it. The diazonium salt solution formed was added dropwise with stirring to 400 ml. of hot 10 per cent sulfuric acid in a 1-l. beaker. When the aqueous layer had cooled, it was decanted and the tarry residue was dissolved in ether. The ether was removed in vacuo and the residue subjected to two vacuum sublimations. The 1.1 g. (15 per cent yield) of crude crystalline material obtained was recrystallized once from hexane-benzene to give 2-hydroxy-5,6-dihydronaphthalene as silken white needles, m.p. 89-90°.

b. Diazotization of 1-hydroxy-7-aminotetralin. A solution of 7.1 g. (0.10 mole) of 95 per cent sodium nitrite in 15 ml. of water was added slowly to a stirred solution of 16.3 g. (0.10 mole) of 1-hydroxy-7-aminotetralin in 60 ml. of 6 N sulfuric acid. The temperature of the reaction mixture was kept between 0° and 5° by use of an ice-salt bath. When the addition was complete the reaction mixture was further stirred

for one hour at 0°. The diazonium salt solution was then added dropwise to a boiling solution of 90 ml. of water and 10 ml. of concentrated sulfuric acid. After five minutes the resulting mixture was cooled and extracted with ether. The ether extract was extracted with aqueous potassium hydroxide which was in turn acidified. The precipitated naphthol was taken up in ether and the ether was distilled under reduced pressure. The viscous residue was vacuum sublimed to give 3 g. (20 per cent yield) of yellow crystals. Two recrystallizations from hexane-benzene gave 2-hydroxy-5,6-dihydronaphthalene as silken white needles, m.p. 89-90°. The ultraviolet spectrum of 2-hydroxy-5,6-dihydronaphthalene has maxima at 262 mμ, 270 mμ and 304 mμ with extinction coefficients of 6125, 4980 and 2400 respectively.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 82.16; H, 6.90.
Found: C, 82.07; H, 7.23.

19. 7-Methoxy-1-tetralone (LXXXIII)

A finely divided precipitate of amine-sulfate was produced by dissolving 32.4 g. (0.20 mole) of 7-amino-1-tetralone in 120 ml. of 6 N sulfuric acid in a 1-l. beaker with vigorous hand stirring and cooling the resulting solution to 0° in an ice-salt bath. A solution of 14.2 g. (0.20 mole) of 95 per cent sodium nitrite in 60 ml. of water was added slowly down the side of the beaker. The temperature was kept between 0° and 3° by adding ice directly to the reaction mixture. The diazonium salt solution was added dropwise to a stirred solution of 1500 ml. of 10 per cent sulfuric acid which was heated on the steam bath. The reaction mixture was heated for thirty minutes after the addition

was complete and then cooled overnight in the refrigerator. The crude crystalline product was collected on a Büchner funnel, washed with water and dried. The yield was 26 g. or 80 per cent of the theoretical yield.

To a solution of 31 g. (0.19 mole) of the crude 7-hydroxy-1-tetralone and 10.8 g. (0.19 mole) of potassium hydroxide in 100 ml. of water in a 500-ml., three-necked flask equipped with mechanical stirrer, dropping funnel and reflux condenser was added dropwise 24.5 g. (0.19 mole) of dimethyl sulfate. The reaction mixture was stirred for one hour at room temperature after addition was complete. The reaction mixture was made basic and steam distilled to give 21.7 g. (65 per cent yield) of white crystalline material. One recrystallization from hexane gave 18.5 g. of 7-methoxy-1-tetralone, m.p. 60-62°. Evaporation of the mother liquor gave an additional 2.3 g. of material melting 50-55°. Melting points of 61°, 62°, 63° and 67° are recorded in the literature.[84,85,86,87]

20. 1-Hydroxy-7-methoxytetralin (LXXXIV)

A solution of 18.5 g. (0.104 mole) of 7-methoxy-1-tetralone, m.p. 60-62°, was dissolved in 100 ml. of dry ethyl ether and added dropwise to 3.8 g. (0.10 mole) of lithium aluminum hydride in 50 ml. of dry ether in a 500-ml. flask equipped with mechanical stirrer and dropping funnel. After three hours the excess lithium aluminum hydride was decomposed with wet ether and the inorganic hydroxides were dissolved by addition of dilute hydrochloric acid. The ether layer was separated and the aqueous solution remaining was extracted twice with ether. The

ether extracts were combined, washed with aqueous sodium bicarbonate and dried over sodium sulfate. Evaporation of the ether left 13.2 g. of white crystalline material melting 31-33°. No further purification was effected.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92.
Found: C, 74.55; H, 7.93.

21. 2-Methoxy-5,6-dihydronaphthalene (LXXXV)

The 13.2 g. of 1-hydroxy-7-methoxytetralone was vacuum distilled, b.p. 125°/0.2 mm., in an attempt to purify it. Instead 7.9 g. of a non-viscous liquid was obtained. This liquid rapidly became discolored although stored in a sealed ampule in a cold room. A redistillation, b.p. 105°/0.15 mm., N_D^{29} 1.5715, gave 3.3 g. of a clear liquid. The remaining 4.6 g. polymerized in the distillation pot to form a hard transparent resin. The liquid, 2-methoxy-5,6-dihydronaphthalene, has an ultraviolet spectrum with maxima at 261 mμ and 302 mμ with extinction coefficients of 6090 and 2340 respectively.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55.
Found: C, 81.40; H, 7.24.

22. 7-Chloro-1-tetralone (LXXXVI)

Fresh cuprous chloride was prepared by adding a solution of 9.5 g. (0.050 mole) of sodium bisulfite and 8.4 g. (0.150 mole) of potassium hydroxide in 75 ml. of water in portions to a warm solution of 43.0 g. (0.170 mole) of hydrated copper sulfate and 36.0 g. (0.062 mole) of sodium chloride in 150 ml. of water. The supernatant liquid was de-

canted and the white cuprous chloride was washed several times with cold water by decantation. The cuprous chloride was dissolved in a mixture of 180 ml. of water and 180 ml. of concentrated hydrochloric acid and cooled in an ice-bath.

A paste of amine hydrochloride was formed by dissolving 16.1 g. (0.10 mole) of 7-amino-1-tetralone in a warm mixture of 45 ml. of concentrated hydrochloric acid and 45 ml. of water in a 500-ml. beaker and cooling it to 0° in an ice-bath. A solution of 7.10 g. (0.10 mole) of 95 per cent sodium nitrite in 25 ml. of water was added down the side of the beaker. The reaction mixture was stirred by hand and ice was added to the beaker to keep the temperature below 2°. The diazonium salt solution was stirred into the previously prepared cuprous chloride solution and the resulting complex was allowed to stand overnight. Steam distillation of the reaction mixture yielded 14.4 g. of crystalline solid. Recrystallization from hexane gave 11 g. (61 per cent) of 7-chloro-1-tetralone, m.p. 97-98°. Melting points of 94° and 97° are recorded in the literature.[83,81]

23. 1-Hydroxy-7-chlorotetralin (LXXXVII)

To 2.0 g. (0.053 mole) of lithium aluminum hydride in 100 ml. of anhydrous ethyl ether in a 1-l., three-necked flask equipped with mechanical stirrer and dropping funnel was added 11.0 g. (0.061 mole) of 7-chloro-1-tetralone, m.p. 97-98°, in 200 ml. of anhydrous ether. After three hours the excess lithium aluminum hydride was decomposed by adding wet ethyl ether dropwise. Dilute hydrochloric acid was added to dissolve the inorganic hydroxides. The ether layer was separated, washed

with aqueous sodium bicarbonate and dried over sodium sulfate. The ether was evaporated in a current of air and the residue was dissolved in hexane and placed in an ice-bath. The yield of white crystals of 1-hydroxy-7-chlorotetralin, m.p. 40-41°, was 10.4 g. (92 per cent of the theoretical yield).

Anal. Calcd. for $C_{10}H_{11}OCl$: C, 65.75; H, 6.07; Cl, 19.41.
Found: C, 65.73; H, 6.03; Cl, 19.68

24. Phenylurethan of 1-Hydroxy-7-chlorotetralin (XC)

A mixture of 10.4 g. (0.057 mole) of 1-hydroxy-7-chlorotetralin and 8.0 g. (0.060 mole) of phenyl isocyanate was heated on the steam bath for fifteen minutes in an Erlenmeyer flask equipped with a calcium chloride drying tube. One recrystallization from benzene-hexane gave 18.7 g. (88 per cent yield) of the phenylurethan of 1-hydroxy-7-chlorotetralin as a white powder melting 115-116°.

Anal. Calcd. for $C_{17}H_{16}O_2ClN$: C, 67.66; H, 5.35; N, 4.64; Cl, 11.75.
Found: C, 68.06; H, 4.85; N, 4.15; Cl, 11.62.

25. 2-Chloro-5,6-dihydronaphthalene (XCII)

A vacuum distillation apparatus was set up containing 16.0 g. of the phenyl urethan of 1-hydroxy-7-chlorotetralin. A vacuum distillation, 160-185°C/50 mm., gave 2-chloro-5,6-dihydronaphthalene contaminated with diphenylurea and basic organic material. The distillate was dissolved in ether, washed with dilute hydrochloric acid, aqueous sodium bicarbonate and water and dried over sodium carbonate. The ether was evaporated and the residue was dissolved in hexane and fil-

tered through 10 cm. of activated alumina. A vacuum distillation gave 3.6 g. (45 per cent yield) of 2-chloro-5,6-dihydronaphthalene as a non-viscous colorless liquid, N_D^{33} 1.5868, b.p. 164°/65 mm. The ultraviolet spectrum of 2-chloro-5,6-dihydronaphthalene has maxima at 2625 mμ, 293 mμ and 304 mμ with extinction coefficients of 8330, 1430 and 1125 respectively.

Anal. Calcd. for $C_{10}H_9Cl$: C, 72.95; H, 5.51; Cl, 21.54.
Found: C, 73.16; H, 5.39; Cl, 21.25.

26. 7-Bromo-1-tetralone (LXXXVIII)

Fresh cuprous bromide was prepared by adding a solution of 19.0 g. (0.10 mole) of sodium bisulfite and 16.8 g. (0.30 mole) of potassium hydroxide in 100 ml. of water in portions to a warm solution of 86.0 g. (0.34 mole) of hydrated copper sulfate and 50 g. (0.48 mole) of sodium bromide in 250 ml. of hot water. The supernatant liquid was decanted and the white cuprous bromide was washed several times with cold water by decantation. The cuprous bromide was dissolved in 100 ml. of water and 150 ml. of 48 per cent hydrobromic acid and cooled in an ice bath.

A paste of amine-hydrobromide was prepared by dissolving 32.2 g. (0.20 mole) of 7-amino-1-tetralone in 130 ml. of water and 70 ml. of 48 per cent hydrobromic acid in a 500-ml. beaker and cooling to 0° in an ice-salt bath. A solution of 14.2 g. (0.20 mole) of 95 per cent sodium nitrite in 50 ml. of water was added down the side of the beaker. The reaction mixture was stirred by hand and ice was added to the beaker to keep the temperature below 3°. The diazonium salt solution was stirred into the previously prepared cuprous bromide solution and the

resulting complex was allowed to stand overnight. A steam distillation of the reaction mixture yielded 31.6 g. of white crystalline 7-bromo-1-tetralone. Recrystallization from hexane gave a first crop of 25 g. (56 per cent yield) of white needles, m.p. 78-79°. A melting point of 77° is reported in the literature.[88]

27. 1-Hydroxy-7-bromotetralin (LXXXIX)

To 2.0 g. (0.053 mole) of lithium aluminum hydride in 100 ml. of anhydrous ethyl ether in a 1-l., three-necked flask equipped with mechanical stirrer and dropping funnel was added 18.7 g. (0.083 mole) of 7-bromo-1-tetralone, m.p. 78-79°, in 200 ml. of anhydrous ether. After three hours the excess lithium aluminum hydride was decomposed by adding wet ethyl ether dropwise. Dilute hydrochloric acid was added to dissolve the inorganic hydroxides and the ether layer was separated. The water layer was extracted twice with ether and the combined ether extracts were washed with aqueous sodium bicarbonate and dried over sodium sulfate. Evaporation of the ether left 17.9 g. (96 per cent yield) of white crystalline 1-hydroxy-7-bromotetralin which melted 51-52° after one recrystallization from hexane.

Anal. Calcd. for $C_{10}H_{11}OBr$: C, 52.88; H, 4.88; Br, 35.19.
Found: C, 53.19; H, 4.77; Br, 35.2.

28. Phenylurethan of 1-Hydroxy-7-bromotetralin

A mixture of 4.95 g. (0.022 mole) of 1-hydroxy-7-bromotetralin and 3.0 g. (0.025 mole) of phenyl isocyanate was placed in an Erlenmeyer flask equipped with a calcium chloride drying tube and heated for fifteen

minutes on the steam bath. The mixture was cooled, washed with benzene and recrystallized from hexane to give 6.5 g. (85 per cent yield) of the phenylurethan of 1-hydroxy-7-bromotetralin as silken needles, m.p. 129-131°.

Anal. Calcd. for $C_{17}H_{16}O_2NBr$: C, 58.97; H, 4.66; N, 4.05; Br, 23.08

Found: C, 59.34; H, 4.42; N, 4.49; Br, 22.3.

29. 2-Bromo-5,6-dihydronaphthalene (XCIII)

A solution of 35.7 g. of 1-hydroxy-7-bromotetralin, 250 ml. of dry pyridine and 125 ml. of acetic anhydride was heated for twenty minutes on the steam bath in an Erlenmeyer flask equipped with a calcium chloride drying tube. The reaction mixture was poured into 600 ml. of ice water and extracted with ether. The ether extract was washed with dilute hydrochloric acid, aqueous sodium bicarbonate and water, dried over magnesium sulfate and evaporated. The liquid residue was placed in a distillation apparatus and heated to 270-295° until no further acetic acid distilled. The residue was dissolved in hexane, washed with aqueous sodium bicarbonate, dried over potassium carbonate and filtered through a column of activated alumina. Evaporation of the hexane and vacuum distillation of the residue gave 24.3 g. (74 per cent yield) of 2-bromo-5,6-dihydronaphthalene as a colorless non-viscous liquid, N_D^{33} 1.6122, b.p. 175°/0.55 mm. The ultraviolet spectrum of 2-bromo-5,6-dihydronaphthalene has maxima at 263 mμ and 304 mμ with extinction coefficients of 6540 and 790 respectively.

Anal. Calcd. for $C_{10}H_9Br$: C, 57.44; H, 4.34; Br, 38.22

Found: C, 57.33; H, 4.27; Br, 38.44.

30. 1,2,7-Tribromotetralin

To an ice-cold solution of 1 g. (0.0048 mole) of 2-bromo-5,6-dihydronaphthalene in 5 ml. of dry ether was added in the dark 0.72 g. (0.0048 mole) of bromine in 15 ml. of ether. The ether was evaporated and the crystalline residue was recrystallized twice from hexance to give white cubes, m.p. 76-78°, of 1,2,7-tribromotetralin.

Anal. Calcd. for $C_{10}H_9Br_3$: C, 32.56; H, 2.46; Br, 64.99.
Found: C, 32.83; H, 2.66; Br, 64.53.

31. 5,6-Dihydro-2-naphthoic Acid (XCIV)

A 250-ml., three-necked, round-bottomed flask containing 1.7 g. (0.070 mole) of magnesium turnings and equipped with magnetic stirrer, dropping funnel and reflux condenser was placed under a head of nitrogen and flamed to remove moisture. A solution of 10 g. (0.048 mole) of 2-bromo-5,6-dihydronaphthalene and 3 g. (0.021 mole) of methyl iodide in 100 ml. of dry ether was added dropwise to the flask with stirring. When addition was complete the reaction mixture was refluxed for forty-five minutes and then poured onto powdered Dry Ice in 100 ml. of dry ether. The Dry Ice was allowed to evaporate and the ether solution was shaken with 60 ml. of 10 per cent hydrochloric acid. The ether solution was extracted twice with aqueous potassium hydroxide. The potassium hydroxide solution was warmed to expel ether, treated with norite, filtered and acidified with hydrochloric acid. The white precipitate of 5,6-dihydro-2-naphthoic acid was collected on a Büchner funnel, washed with water and dried. The yield was 2.6 g. or 31 per cent of the theoretical yield. The crude material was dissolved in hot benzene-hexane, treated

with norite, filtered and cooled to give 5,6-dihydro-2-naphthoic acid as white needles which sublime at 120° and melt 136-137°. Evaporation of the original extracted ethereal reaction solution yielded 3.7 g. of recovered 2-bromo-5,6-dihydronaphthalene.

Anal. Calcd. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79.

Found: C, 75.75; H, 6.08.

32. 1,2-Dihydronaphthalene

To 20 ml. of refluxing absolute ethanol protected by a calcium chloride drying tube was added in small pieces 4 g. of potassium. When the potassium and ethanol had completely reacted, ethanol was distilled until the temperature of the residual solution reached 145°. To the hot potassium ethoxide solution was added 15 g. of 1,4-dihydronaphthalene which had been purified *via* its mercuric acetate derivative.* The reaction mixture was refluxed for sixteen hours, poured into ice-water and extracted with ether. The ether extract was washed with dilute hydrochloric acid, aqueous sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated. The residue was distilled, b.p. 122°/55 mm., to give 11 g. of a colorless liquid. The 1,2-dihydronaphthalene has a maximum at 259 mμ with a molar extinction coefficient of 9240. Huckel has reported an extinction coefficient of 9449 at 259 mμ.[59]

*Graciously donated by H. Secor.

D. Time Duration of Reaction Experiments

1. Determination of the Reaction Times of Some Simple Reactions in Liquid Ammonia

a. Preliminary experiments. To 25 ml. of liquid ammonia in a Dewar flask were added 2.50 ml. of tert.-amyl alcohol and 0.27 g. of potassium. When the initial reaction between potassium and alcohol was complete, 1.0 g. of 1-naphthol was added to the flask to give a solution of potassium 1-naphthoxide. In another Dewar flask 0.55 g. of potassium was dissolved in 25 ml. of liquid ammonia. The potassium 1-naphthoxide solution was poured into the potassium metal solution. The time taken for the blue color of the potassium to disappear after addition was complete was measured. Representative times required in these and the following experiments are given in Table IV.

In other experiments solutions of 2.50 ml. of tert.-amyl alcohol dissolved in 25 ml. of liquid ammonia were poured into 25 ml. of ammonia containing 0.55 g. of potassium metal. The time taken for the disappearance of the blue color was measured.

A final series of runs were made by pouring solutions of 0.55 g. of potassium dissolved in 25 ml. of ammonia into solutions of 1.5 g. of potassium 1-naphthoxide in 25 ml. of ammonia.

b. Refined experiments with the small reactor. In order to maintain a dry atmosphere and to obtain more precision an apparatus (Figure 3) was constructed in which the contents of two compartments could be forced simultaneously into a third compartment by nitrogen pressure. This apparatus was dried, filled with nitrogen and placed in

an acetone bath (C, Figure 3) maintained at -38°. In one compartment (A, Figure 3) was placed 12 ml. of liquid ammonia, 1.0 ml. of tert.-amyl alcohol and 0.510 g. of potassium 1-naphthoxide. In another compartment (A', Figure 3) was placed a solution of 0.23 g. of potassium in 11 ml. of liquid ammonia. The reaction time was taken as the time required for disappearance of the blue color after the two solutions were forced through a T-bore stopcock into the third compartment (B, Figure 3). Representative times required for this and other experiments parallel to those described in (a) above are given in Table IV.

c. Refined experiments with the large reactor. A larger reactor (Figure 3) identical with the one described in (b) above was constructed in which compartments A and A' could hold 50 ml. of solution. This apparatus was dried, filled with nitrogen and placed in a liquid ammonia bath (C, Figure 3) at -33°. In one compartment (A, Figure 3) was placed 36 ml. of liquid ammonia, 3.0 ml. of tert.-amyl alcohol and 1.59 g. of potassium-1-naphthoxide. In another compartment (A', Figure 3) was placed a solution of 0.68 g. of potassium in 36 ml. of liquid ammonia. The reaction time was taken as the time required for disappearance of the blue color after the two solutions were forced through a T-bore stopcock into a third compartment (B, Figure 3). The effect of additives such as ether, water and alkoxide ion and of a different alcohol, ethanol, on the reaction times of this and other reactions parallel to those described in (a) above are given in Tables IV and V.

2. Limit of Reaction Time for Potassium 5,6-Dihydro-1-naphthoxide

The reduction of the double bond conjugated with the benzene ring proceeds very rapidly. It was observed that when the potassium-in-ammonia solutions were mixed with the potassium-5,6-dihydro-1-naphthoxide-ethanol-ammonia solutions of the T-bore stopcock (Figure 3) that the blue coloration disappeared when the reaction solution had traveled 12 mm. through the tube connecting the stopcock with the middle compartment (B, Figure 3). This tube was 2 mm. in diameter and the total volume of reaction solution, 80 ml., traveled through it in six seconds. From these facts the time required for the disappearance of the blue coloration can be calculated to be approximately 0.003 second.

The reaction time is the time required for the solution to travel 1.2 cm. down the capillary tube.

$$\text{Volume of capillary tube} = 1.2 \times (0.1)^2 \times 3.14 = 0.038 \text{ ml.}$$

$$\text{Flow rate} = \frac{80 \text{ ml.}}{6 \text{ sec.}} = 13 \text{ ml./sec.}$$

$$\text{Reaction time} = \frac{\text{Volume of capillary tube}}{\text{flow rate}} = \frac{0.038 \text{ ml.}}{13 \text{ ml./sec.}} = 0.003 \text{ sec.}$$

3. Reaction of Potassium 5,6-Dihydro-1-naphthoxide With Potassium Superoxide in Ammonia

A large reactor (Figure 3) with a glass enclosed magnetic stirring bar in the center compartment (B, Figure 3) was immersed in a liqud ammonia bath. A rapid stream of dry oxygen was passed through a solution of 1.44 g. (0.037 mole) of potassium in 40 ml. of ammonia in the center compartment. Within fifteen minutes a yellow precipitate of potassium superoxide had formed. A solution of 3.2 g. (0.017 mole) of potassium

1-naphthoxide and 4 ml. (0.07 mole) of absolute ethanol in 40 ml. of ammonia was added from arm A (Figure 3) and the resulting reaction mixture was stirred for two hours. The ammonia was allowed to evaporate and the residue was diluted with ice, acidified and extracted with ether. The ether extract was dried over magnesium sulfate and evaporated to leave a residue which was vacuum sublimed. The sublimate was shown to be starting material, 1-naphthol, by its melting point, 96-97°, and ultraviolet spectrum.

E. Relative Rate Study

1. Reduction of 2-Substituted-dihydronaphthalene With an Excess of Potassium

a. 1,2-Dihydronaphthalene. A solution of 1.0 g. of 1,2-dihydronaphthalene, 20 ml. of dry ether and 5 ml. of ethanol was dissolved in 100 ml. of liquid ammonia in a 200-ml. flask equipped with Dry Ice condenser and magnetic stirrer. To this solution was added potassium metal in small portions until the blue coloration persisted for one minute, about 1 g. being required. After the ammonia had evaporated, the residue was diluted with ice-water and extracted with ether. The ether extract was dried over magnesium sulfate and the ether was evaporated. The residue from the ether extract was vacuum distilled twice. The product, tetralin, N_D^{35} 1.5368, had an ultraviolet spectrum with maxima at 266.5 mμ and 273.5 mμ with molar extinction coefficients of 1035 and 900 respectively.

b. 2-Methoxy-5,6-dihydronaphthalene. 2-Methoxy-5,6-dihydronaphthalene was reduced and worked up in precisely the same manner as described for 1,2-dihydronaphthalene in part (a) above. The product, 6-methoxytetralin, N_D 1.5342, has an ultraviolet spectrum with maxima at 279 mμ and 287.5 mμ with molar extinction coefficients of 1870 and 1710 respectively.

c. 2-Amino-5,6-dihydronaphthalene. 2-Amino-5,6-dihydronaphthalene was reduced and worked up in precisely the same manner as described for 1,2-dihydronaphthalene in part (a) above. The product, 6-aminotetralin, m.p. 36-38°, has an ultraviolet spectrum with a maximum at 293 mμ with a molar extinction coefficient of 1795.

d. 2-Bromo-5,6-dihydronaphthalene. 2-Bromo-5,6-dihydronaphthalene was reduced and worked up in precisely the same manner as described for 1,2-dihydronaphthalene in part (a) above. An elemental analysis showed that there was no bromine in the product. The product, tetralin, N_D^{36} 1.5332, has maxima at 266.5 mμ and 274 mμ.

e. 2-Chloro-5,6-dihydronaphthalene. 2-Chloro-5,6-dihydronaphthalene was reduced and worked up in precisely the same manner as described for 1,2-dihydronaphthalene in part (a) above. An elemental analysis showed that there was no bromine in the product. The product, tetralin, N_D^{34} 1.5313, has maxima at 266.5 mμ and 274 mμ.

2. Reduction of the 2-Halodihydronaphthalene With a Limited Amount of Potassium

a. 2-Bromo-5,6-dihydronaphthalene. To a solution of 2.10 g. (0.01 mole) of 2-bromo-5,6-dihydronaphthalene, 10 ml. of dry ether and

2 ml. of absolute ethanol in 100 ml. of ammonia in a 200-ml. flask equipped with magnetic stirrer and Dry Ice condenser was added 0.80 g. (0.02 mole) of potassium. After the ammonia had evaporated, the residue was diluted with ice-water and extracted with ether. The ether extract was dried over magnesium sulfate and the ether was evaporated. The residue from the ether extract was vacuum distilled twice. An elemental analysis showed that the product contained 14.5 per cent bromine which corresponds to 72 per cent reduction of the nuclear bromine.

b. 2-Chloro-5,6-dihydronaphthalene. 2-Chloro-5,6-dihydronaphthalene (1.65 g., 0.01 mole) was reduced and worked up in precisely the same manner as described for 2-bromo-5,6-dihydronaphthalene in part (a) above. An elemental analysis showed that the product contained 10.1 per cent chlorine which corresponds to 41 per cent reduction of the nuclear chlorine.

3. Relative Rate Experiments

A large reactor of the type depicted in Figure 3 was constructed in which compartments A and A' would hold up to 50 ml. of solution and compartment B up to 100 ml. A typical run was made in the following manner. The reactor was cleaned, dried, and heated in an oven to 90°; dry nitrogen was then passed through it while it was cooling. When it had cooled to room temperature it was immersed in liquid ammonia and 30 ml. of ammonia was condensed into each of arms A and A' (Figure 3). To the ammonia solution in arm A was added 10 ml. of dry ether and 160 mg. (4.0 m. mole) of potassium wire. To the other arm (A', Figure 3) was added 2 ml. (34 m. mole) of absolute ethanol and 140 mg. (3.5 m.

mole) of potassium wire. When the reaction of the potassium and ethanol in arm A' was complete, to it was added a solution of approximately 400 mg. each (ca. 3 m. mole) of 5,6-dihydro-1-naphthol and a 2-substituted-5,6-dihydronaphthalone in 10 ml. of dry ether. Both ammonia solutions were stirred and then forced through the "T-bore" stopcock into the center compartment (B, Figure 3) by a pressure of nitrogen. The reaction was over almost immediately and the reaction solution was poured into an Erlenmeyer flask. As soon as the ammonia had evaporated 50 ml. of 5 per cent potassium hydroxide solution was added to the residue which was then extracted twice with ether. The combined ether extracts were extracted four times with 5 per cent potassium hydroxide solution.* The potassium hydroxide extracts were combined, cooled, and acidified and extracted twice with ether. There were now two ether extracts, one containing the naphthol and the other containing the 2-substituted-dihydronaphthalene. Each extract was heated on the steam bath in a stream of air until the ether was driven off. Each residue was carefully dried and the per cent reduction of each sample determined by ultraviolet spectrophotometry.

As an example, for one reduction in which the 2-substituted-dihydronaphthalene was the parent compound,1,2-dihydronaphthalene, the per cent reductions were determined as follows. A sample of the par-

*Potassium 1-naphthoxide can be extracted from a dilute potassium hydroxide solution with ether. It was therefore not too surprising then to find that four extractions with dilute aqueous alkali were required to completely extract the partially reduced 5,6-dihydro-1-naphthol from ether solution.

tially reduced 1,2-dihydronaphthalene, isolated as described above, was found to have a molar extinction coefficient, E, of 5150 at the maxima, 259 mμ. The E values for the sample of the 1,2-dihydronaphthalene used in this work and for the product, tetralin, at 259 mμ are 9240 and 400 respectively.

$$\text{Fraction of 1,2-dihydronaphthalene remaining} = \frac{4760 - 400}{9240 - 400} = 0.494$$

The E values for partially reduced 5,6-dihydro-1-naphthol taken from the same reaction mixture, 5,6-dihydro-1-naphthol and 5-hydroxytetralin at 265 mu are 6660, 8010 and 30 respectively.

$$\text{Fraction of 5,6-dihydro-1-naphthol remaining} = \frac{6660 - 30}{8010 - 30} = 0.835$$

With this data a ratio of rate constants was calculated.

$$\frac{k_1}{k_2} = \frac{\log (\text{Fraction of 1,2-dihydronaphthalene remaining})}{\log (\text{Fraction of 5,6-dihydro-1-naphthol remaining})} =$$

$$\frac{\log 0.494}{\log 0.835} = \frac{1-0.694}{1-0.922} = \frac{0.306}{0.078} = 3.93$$

Other rate constant ratios were obtained in an analogous manner.

Some difficulties in experimental technique which had to be overcome were encountered in this work. The most serious difficulty was an unequal rate of delivery of solutions from the two side compartments (A and A'). This was usually due to small quantities of solids in or near the "T-bore" stopcock. This trouble was eliminated from side A' by adding the organic substrates to it in ether solution. The difficulty was alleviated in side A by blocking the constricted bottom portion of the compartment with a glass rod so that no potassium wire could settle

near the stopcock at which place it dissolved very slowly and left a small residue from the original wire's surface. The potassium was used in the form of a calibrated wire so that any desired weight could be conveniently obtained by measuring out the correct length. This largely avoided the formation of insoluble oxides through exposure of the potassium to the atmosphere in weighing. The weights of potassium obtained in this manner were accurate within 1 per cent.

Some difficulties were also encountered in working up the organic substrates. The 5,6-dihydro-1-naphthol was susceptable to dimerization so that it was necessary to exercise care in evaporating its ether extract to dryness in preparing the samples for spectrophotometric analysis. No precision could be obtained with 1,2-dihydronaphthalene because the dihydronaphthalene is noticeably more volatile than tetralin. The analyses varied greatly, depending upon the amount of evaporation of the dihydronaphthalene which occurred when the ether solvent was removed. The results of runs made at the same time under identical conditions agreed with one another but not with other runs. Variations in the results with other less volatile substrates were not too great.

The spectrophotometric analysis could not be applied to the two halodihydronaphthalenes because the halogen was also reduced. The extent of double bond reduction in these compounds was estimated from the amount of alkali metal consumed by them (i. e., total metal consumed in a run minus that consumed by the naphthoxide) and an analysis of their residual halide content. That is, the assumption was made that the metal not consumed by reduction of naphthoxide or halide was consumed by the styrene-

type double bond.

The rates of reduction of the 2-substituted dihydronaphthalenes relative to potassium 5,6-dihydro-1-naphthoxide are tabulated in Table VI.

CHAPTER IV

SUMMARY

Two lines of evidence were adduced to support the electron addition or "ionic" mechanism (c. f. equations, page 19) for the reduction of carbon-carbon unsaturation by alkali metal and alcohol in liquid ammonia. First it was shown that the reduction itself is extremely fast, much faster than the reaction between alkali metal and alcohol in liquid ammonia to produce hydrogen. The rate of reaction of the metal with the alcohol was decreased immensely (by adding alkoxide ion or changing alcohols) without effecting the rate at which carbon-carbon unsaturation is reduced. Second, competitive reactions showed that an organic substrate with a net negative charge was reduced more slowly than were neutral substrates. These facts were taken as evidence that the rate-controlling process in the reduction is the reversible pick up of electrons from the solvent by the organic substrate to form carbanions; these then add protons irreversibly.

As a correlary of the above work, the properties of the dihydronaphthalenes were extensively investigated. 5,8-Dihydro-1-naphthol and its methyl ether were shown to be isomerized by alkali predominately to the 5,6-dihydroisomers, although the production of some 7,8-dihydroisomer in the isomerization was demonstrated. The structure of the 5,6-isomer was proven by degradation and that of the 7,8-isomer by both degradation and synthesis. A logical method of predicting the direction of isomerization of substituted-5,8-dihydronaphthalenes

was presented and the ultraviolet spectra of ortho and meta substituted styrenes were discussed and compared.

Also as a correlary of this work, a number of organic compounds were synthesized. An unequivocal synthesis of 1-amino-7,8-dihydronaphthalene was accomplished but the overall yield was small. No simple method of producing 1-substituted-dihydronaphthalenes in good yield was found although several synthetic schemes were tested. A good, general synthesis for 2-substituted-dihydronaphthalenes from a commercially available compound, 1-tetralone, was devised and exploited.

The following compounds, which have not been previously reported, were prepared and characterized during the course of this work.

1-Methoxy-5,6-dihydronaphthalene

1-Methoxy-5,8-dihydronaphthalene

8,8'-Dimethoxy-1,2,3,4,3',4'-hexahydro-1,2'-binaphthyl

1-Acetoxy-5,6-dihydronaphthalene

1-Acetoxy-5,8-dihydronaphthalene

1-Hydroxy-2,5-dibromo-8-methoxytetralin

2,8-Dimethoxy-1-hydroxy-5-bromotetralin

2,5-Dibromo-8-methoxy-1-tetralone

1,8-Dimethoxy-4-bromonaphthalene

cis-1,2-Dihydroxy-5-methoxytetralin

2-(2-Methoxy-6-carboxyphenyl)-propanoic Acid

Methyl-2-(2-methoxy-6-carbomethoxyphenyl)-propanoate

Lactone of 3-(2-Hydroxy-6-carboxyphenyl)-propanoic Acid

Lactone of 3-(2-Hydroxy-6-carbomethoxyphenyl)-propanoic Acid

5-Methoxy-2-hydroxytetralin

5-Methoxy-2-benzoxytetralin

1-Methoxy-7,8-dihydronaphthalene

1,6-bis-Methoxymethoxynaphthalene

5-Methoxymethoxy-2-tetralone

5-Hydroxy-2-tetralone

2,5-Dihydroxytetralin

7,8-Dihydro-1-naphthol

1,4-Dihydro-2-methoxy-5-naphthylamine Hydrochloride

1,4-Dihydro-5-acetamido-2-methoxynaphthalene

5-Acetamido-2-tetralone

5-Acetamido-2-hydroxytetralin

7,8-Dihydro-1-aminonaphthalene

7,8-Dihydro-1-acetamidonaphthalene

1-Hydroxy-5-nitrotetralin

1-Chloro-5-nitrotetralin

6,6'-Dinitro-1,2,3,4,1',2',3',4'-octahydro-1,1'-binaphthyl

6-Amino-1-tetralone

1-Hydroxy-7-aminotetralin

1-Acetoxy-7-acetamidotetralin

2-Amino-5,6-dihydronaphthalene

2-Acetamido-5,6-dihydronaphthalene

1-Methylene-6-aminoindane or 3-Methyl-5-aminoindene

1-Methylene-6-acetamidoindane or 3-Methyl-5-acetamidoindene

2-N,N-Dimethylamino-5,6-dihydronaphthalene

2-Hydroxy-5,6-dihydronaphthalene

1-Hydroxy-7-methoxytetralin

2-Methoxy-5,6-dihydronaphthalene

1-Hydroxy-7-chlorotetralin

Phenylurethan of 1-hydroxy-7-chlorotetralin

2-Chloro-5,6-dihydronaphthalene

1-Hydroxy-7-bromotetralin

Phenylurethan of 1-Hydroxy-7-bromotetralin

1,2,7-Tribromotetralin

5,6-Dihydro-2-naphthoic Acid

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