1. Correlations of Electronic Effects of Substituents With Nmr Spectra. 2. Addition Reactions of Cis, Trans-1,5-Cyclodecadiene and Cis-Cyclodecene and Trans-Cyclodecene.

George Albert Knesel III

Louisiana State University and Agricultural & Mechanical College

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   AND CIS- AND TRANS-CYCLODECENE

A Dissertation

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Louisiana State University and
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by

George Albert Knesel, III
B.S., Southeastern Louisiana College, 1962
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ABSTRACT

Part 1: Correlation of Electronic Effects of Substituents With N.M.R. Spectra

Several series of compounds in dimethyl sulfoxide solutions have been studied by nuclear magnetic resonance spectroscopy. The data show definite correlations with electronic effects. In the first series, the substituted phenols, the chemical shifts for the phenolic protons were found to be strongly dependent on the electronic nature of the substituent and are linearly correlated to Hammett sigma constants. A few sigma constants are not well correlated by the chemical shifts. This non-correlation is attributed to various solvent effects peculiar to dimethyl sulfoxide. This method presents a convenient way of determining sigma constants for new substituents. In a similar study on a series of substituted benzaldehydes, there is general correlation between chemical shifts of the aldehydic protons and electronic effects of the substituents. No quantitative correlation exists, however, with sigma constants. The n.m.r. spectra of a series of substituted alcohols in dimethyl sulfoxide showed loss of the multiplicity which had been obtained with unsubstituted alcohols. This difference is attributed to the higher acidities of the hydroxyl protons due to the electro-negative character of the substituents.

Part 2: Addition Reactions of cis,trans-1,5-Cyclodecadiene and cis- and trans-Cyclodecene

Additions of various reagents to cis,trans-1,5-cyclo- decadiene and cis- and trans-cyclodecene have been studied.

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Those reactions which give normal 1,2-addition products (epoxidation, methylenation, hydroboration, diimide reduction, and catalytic hydrogenation) show a high selectivity for the trans double bond. This high selectivity is attributed to the relative freedom of the transition state from steric factors when the trans rather than the cis double bond is attacked.

Three reactions (bromination, ozonization, and acetoxylation) have been found to give products formed by transannular reactions: hydrogen migration across the ring in the case of the cyclodecenes and electron shift in the case of cis, trans-1,5-cyclodecadiene. One of these reactions, bromination, has been studied extensively. In the case of cis, trans-1,5-cyclodecadiene study of models shows that the stereochemistry of the product is dependent on the conformation of the ethylenic pi clouds when the reagent makes its initial attack. Analysis of the reaction products does not reveal selectivity of initial attack at the trans double bond by bromine or lead tetraacetate.
INTRODUCTION

This dissertation is divided into two parts. The first part deals with the correlation of nuclear magnetic resonance spectra with electronic effects of substituents in three series of compounds. The second part is concerned with the addition of various reagents to some medium ring olefins, namely, cis- and trans-cyclodecene and cis,trans-1,5-cyclo-decadiene. The diene has received major attention. The two parts are not directly related in any way, but both are concerned with the general field of electronic effects and physical-organic chemistry.

In the first part of the dissertation, the correlation of the chemical shifts of meta and para substituted phenols with Hammett sigma constants is of interest to physical-organic chemists. It provides the best correlation to the Hammett sigma constants obtained from n.m.r. data and is a convenient way of obtaining new sigma constants with high accuracy. The chemical shifts of the aldehydic protons of a series of meta and para substituted benzaldehydes, although not well correlated to sigma constants, provide insight into the nature of the experiments with the substituted phenols. A point of pragmatic importance to the organic chemist is the loss of multiplicity in the n.m.r. spectra of some substituted alcohols from the results obtained for unsubstituted alcohols.

In the second part of the dissertation, the purpose of the study is to find out more about medium ring compounds,
addition reactions and their mechanisms, and reaction intermediates in general. Accordingly, addition reagents with different modes of addition were used. The trans double bond is selectively attacked in the cis addition reactions studied. These reactions are epoxidation, methylenation, hydroboration, diimide reduction, and catalytic hydrogenation. The products obtained in these reactions are normal 1,2-addition products. Three reactions, namely, bromination, ozonization, and acetoxylation give transannular products, resulting from transannular electron shift or hydrogen migration depending on the olefin being used.
PART 1: CORRELATIONS OF ELECTRONIC EFFECTS OF SUBSTITUENTS WITH N.M.R. SPECTRA

CHAPTER I

INTRODUCTION

Since this part of the dissertation concerns n.m.r. spectra, a brief explanation of n.m.r. data is included here.¹

The nuclear magnetic resonance spectra arise from transitions between different energy states of nuclei. A necessary requirement for an isotope to be measurable by n.m.r. is that it have a spin number, I>0. Having I>0 simply means that a nucleus has magnetic properties and thus can interact with external magnetic field. The proton fulfills this requirement with I=1/2. With I=1/2, a nucleus can assume two spin orientations, one lower in energy than the other by hν. When a sample is placed between the poles of a magnet and 2μH₀=hν, where H₀ is the strength of the external magnetic field and μ is the gyromagnetic constant, transition can occur from the lower to the higher energy state.

If the transitional, or resonance, frequencies for all protons in a molecule were the same, only one peak would be observed, and n.m.r. would be of no use to the organic chemist. Its usefulness resides in the fact that this resonance frequency is dependent on the electronic, structural environment of the nucleus. The surrounding electrons themselves have magnetic properties and thus interact with the external magnetic field, lessening its effectiveness on

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the nucleus. The effective magnetic field, \( H_{\text{eff}} = H_0 - \sigma H_0 \), where \( \sigma H_0 \) is the induced field due to the shielding electrons, must equal \( h \nu / 2 \mu \) for a transition to take place. Hence every proton which is in a different electronic, structural environment will have a different resonance frequency and will produce a different peak on the spectrum. The separation of resonance frequencies of nuclei in different structural environments from some arbitrary standard is termed the "chemical shift". In this paper tetramethylsilane is the internal standard. The chemical shift is measured in delta units, which are dimensionless. Delta is defined as \( \left( H_r - H_s \right) / H_r \), where \( H_s \) and \( H_r \) are the field strengths corresponding to resonance for a particular nucleus in the sample \( H_s \) and reference standard \( H_r \).

Tetramethylsilane (TMS) possesses very highly shielded protons. When TMS is used as an internal standard, the less electron shielding a proton experiences the larger is its chemical shift. Thus the chemical shift of \(-\text{C}-\text{OH}\) is greater than \(-\text{C}-\text{H}\), which is greater than \(-\text{C}-\text{OH}\), greater than \(-\text{CH}_2-\), greater than \(-\text{CH}_3\), greater than TMS which is zero by definition.

Another phenomenon of n.m.r. is that the single peak which is due to protons in the same electronic environment is sometimes split into multiplets. The spectrum of ethanol is usually used as an illustrative example. There are three sets of equivalent protons in ethanol, \( \text{CH}_3-\text{CH}_2-\text{OH} \): the three methyl (1.17\( \delta \)), the two methylene (3.62\( \delta \)), and the hydroxy (5.32\( \delta \)). This value for the hydroxy proton is
for acidified ethanol. With acid present the methyl peak is split into a triplet, the methylene is a quartet, and the hydroxy is a singlet. With highly purified ethanol, the methyl peak remains a triplet, the methylene quartet is split into an octet and the hydroxy singlet becomes a triplet (5.28E). Explaining these facts will account for multiplicity and its disappearance.

Multiple absorption is due to interaction between protons on adjacent atoms. Each proton may have either of two spin values. Considering all the combinations of the different types of spin arrangements of the protons on the adjacent atoms explains what multiplet will appear and the relative heights of each peak. Generally, if there are "n" equivalent protons on adjacent carbons, the proton peak will be split into "n+1" peaks, the peak heights being equal to the binomial coefficients of the "nth" order. Thus the methyl peak is split into three peaks with relative heights 1,2,1 because the adjacent carbon has two equivalent protons.

The reason the multiplicities of the methylene protons and the hydroxy proton are different when acid is present is that the hydroxy-methylene interaction is not observed. This loss of multiplicity is attributed to a rapid "chemical exchange". Chemical exchange is a term used to describe the fact that in a given period of time a single proton may be attached to a number of different ethoxy groups. In a given period of time, if chemical exchange is rapid enough, a particular proton will be attached to many different ethoxy
groups, and the spin orientations of the methylene protons that the hydroxy proton would otherwise experience will be averaged into one peak. The methylene protons likewise average the spin orientations on the hydroxy protons that become attached to it, and the methylene absorption remains a quartet.

Dimethyl sulfoxide causes the acidic protons of interest in this paper to have a larger chemical shift than they have in usual solvents or in the pure state. It also causes multiplicity to be observed in molecules where it is not observed under usual conditions. How are these solvent properties explained? Dimethyl sulfoxide is a very good hydrogen bonding molecule, and hydrogen bonding produces the large chemical shifts and slows down chemical exchange, bringing back unobserved multiplicity. Hydrogen bonding causes a large chemical shift because it causes the proton to be further removed from the electrons bonding it to the parent molecule. It is true that the electrons of the dimethyl sulfoxide come into the neighborhood of the bridging proton, but all of the environmental electrons are further from it than the original bonding electrons. The proximity of the electrons, rather than the number is most important as far as the chemical shift is concerned.

As will be seen, dimethyl sulfoxide plays a different role in each of the series of compounds studied: substituted phenols, substituted benzaldehydes, and substituted alcohols.
A. Acidity of Phenols

Phenols are much more acidic than alcohols. The $K_a$'s of phenols are about $10^{-10}$, whereas the $K_a$'s for alcohols are in the neighborhood of $10^{-16}$ to $10^{-18}$. This enhanced acidity of phenols can be explained by studying the structures of the ionization products of phenols, the phenoxide ions. The phenoxide ion is stabilized by resonance structures such as II-IV. Phenol itself is only slightly stabilized by resonance forms such as V. The acidity of phenols is even further increased by the presence of electron-withdrawing substituents at the meta and para positions of the benzene ring. And the acidity decreases with electron-releasing substituents. This change in acidity is due to the effect of these substituents on the phenoxide ion. These effects are known to be twofold, inductive and mesomeric. To a large extent the same effects influence the data in this experiment and the ionization of phenols.

B. Results

In this n.m.r. spectral study of a series of substituted phenols in dimethyl sulfoxide (DMSO), the chemical shifts of phenolic protons have been found to be strongly
dependent on the nature of the substituent and are linearly correlated to Hammett sigma constants. Substituents with strong electron-withdrawing resonance character behave in a manner intermediate between that predicted by $\sigma$ and by $\sigma^-$. Deviations are also obtained for substituents which undergo a solvent effect that is not encountered with the usual conditions of obtaining sigma constants.

C. Hammett's Sigma-Rho Relationship

What are Hammett sigma constants and why are they important? A short section on the Hammett equation will answer this question. The Hammett equation relates structure and the reactivity in the side chain reactions of meta and para substituted benzene derivatives; $\log(K/K_0) = \sigma\rho$, where $K$ and $K_0$ are the equilibrium or rate constants for the substituted and unsubstituted benzene derivatives respectively, $\sigma$ is a constant related only to the substituent and $\rho$ is a constant measuring the susceptibility of a particular reaction to substituent effects. By definition, $\sigma = \log K - \log K_0$, where $K$ and $K_0$ are the ionization constants of the benzoic acids in water at $25^\circ$. Rho is therefore defined as unity for this reaction. Sigma for hydrogen is zero since $\log K_0 - \log K_0 = 0$. Thus, sigma is, by definition a measure of the effect of a substituent (different in the meta and para positions) relative to hydrogen on the ionization of benzoic acid. In this ionization the substituent effects are mainly inductive, and the Hammett treatment would be expected to work best for those reactions which also involve mainly inductive effects.
The ionization of phenols, however, is greatly enhanced by the resonance effect of para electron-withdrawing groups, through the stabilization of the phenoxide ion. This is illustrated below for the case of the nitro group. For reactions such as these, a different substituent constant has been proposed, $\sigma^-$, for strong para electron-withdrawing resonance substituents. Many other sigma constants have been proposed for varying situations. The only other sigma to be used in this study is the $\sigma^O_R$ constant, which is a measure of the resonance electronic effect of a substituent as distinct from the inductive effect. The $\sigma^-$ constants do not come from a defining reaction, but values are taken that best fit all reactions for which they are used. More will be said about $\sigma^O_R$ when it is discussed later.

What about the purpose of Hammett relationships? First of all, it permits the correlation of a vast body of data. It is normally used to obtain sigma values for new substituent groups and rho values for new reactions. These parameters are then useful in giving information concerning the electronic characteristics of substituents and the electron demand of reactions.

D. Experimental Conditions

The spectra of the substituted phenols were obtained
for dimethyl sulfoxide solutions approximately 5-20% in phenol with a Varian Associates HA-60 spectrometer. The solid phenols were in the 5-10 weight % range and the liquid phenols were approximately 10 volume %. The chemical shifts of the phenolic protons of phenol and \( m \)-fluorophenol were identical for 10% and 20% solutions, indicating that there is no concentration dependency of the chemical shifts. The age of the solution does not affect the chemical shift. However, with the strong electron-withdrawing groups \( p \)-CHO and \( p \)-NO\(_2\), the phenolic proton peaks spread over two to four delta units when old solutions were used. In order to be certain of the center of gravity of the peaks, freshly prepared solutions had to be used. Table 1 contains the chemical shift data of the phenolic protons, with the compounds listed in decreasing order of chemical shift. In the column of sigma values are undesignated, and \( \sigma^- \) and \( \Sigma \sigma^- \) are used to designate these values when listed. For the points that deviate from the correlation line the values calculated from the slope of the line are included and are designated \( \sigma_f \).

**E. Role of Dimethyl Sulfoxide (DMSO)**

It should be pointed out that dimethyl sulfoxide favors reproducible and meaningful data in two ways. Firstly, it produces a large chemical shift which is quite susceptible to substituent effects. For instance, in a 10% solution of phenol in carbon tetrachloride, the phenolic proton chemical shift is \(-6.45\) p.p.m., whereas in DMSO it is \(-9.32\) p.p.m. As pointed out in the introduction it is the
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<td>p-NO₂</td>
<td>-10.98</td>
<td>σ = 1.270</td>
<td>1.66</td>
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<tr>
<td>p-CHO</td>
<td>-10.54</td>
<td>σ = 1.126</td>
<td>1.32</td>
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<tr>
<td>m-NO₂</td>
<td>-10.34</td>
<td>σ = 1.02</td>
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<td>m-Cl</td>
<td>-9.84</td>
<td>σ = 0.52</td>
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<tr>
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<td>p-Br</td>
<td>-9.66</td>
<td>σ = 0.34</td>
<td></td>
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<tr>
<td>p-Cl</td>
<td>-9.62</td>
<td>σ = 0.30</td>
<td></td>
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<tr>
<td>4-Cl,3-CH₃</td>
<td>-9.50</td>
<td>σ = 0.18</td>
<td></td>
</tr>
<tr>
<td>p-C₆H₅</td>
<td>-9.44</td>
<td>σ = 0.12</td>
<td></td>
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<tr>
<td>p-F</td>
<td>-9.36</td>
<td>σ = 0.04</td>
<td></td>
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<tr>
<td>H</td>
<td>-9.32</td>
<td>0</td>
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<td>m-CH₃</td>
<td>-9.16</td>
<td>-σ = 0.14</td>
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<tr>
<td>p-CH₃</td>
<td>-9.04</td>
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<tr>
<td>m-OH</td>
<td>-9.02</td>
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<tr>
<td>3,5-diOH</td>
<td>-9.00</td>
<td>-σ = 0.32</td>
<td></td>
</tr>
<tr>
<td>3,4-diCH₃</td>
<td>-8.98</td>
<td>-σ = 0.34</td>
<td></td>
</tr>
<tr>
<td>p-t-amyl</td>
<td>-8.96</td>
<td>-σ = 0.36</td>
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### TABLE I (cont'd)

<table>
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<tr>
<th>Substituent</th>
<th>Chemical Shift (ppm)</th>
<th>Sigma Values</th>
<th>Chemical Shift Relative to Phenol</th>
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<tr>
<td>$p$-OCH$_3$</td>
<td>-8.76</td>
<td>$\sigma_g = 0.268$</td>
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<td>$\sigma_g = 0.357$</td>
<td>$\sigma_g = 0.527$</td>
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<tr>
<td>$p$-nonyl</td>
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<td>$m$-benzoyloxy</td>
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<td>$\sigma_g = 0.329$</td>
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<td>$\sigma_g = 0.195$</td>
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<td>$m$-acetoxy</td>
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<td>$p$-acetoxy</td>
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### TABLE 2

**Chemical Shifts of Some Important Non-phenolic Protons**

<table>
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<tr>
<th>Proton Type</th>
<th>Chemical Shift (ppm)</th>
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<tr>
<td></td>
<td>HCCl$_3$</td>
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<td>$p$-t-amy1 C-H$_3$</td>
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<td>$p$-methyl C-H$_3$</td>
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</tr>
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<td>$m$-methyl C-H$_3$</td>
<td>-2.26</td>
</tr>
<tr>
<td>$p$-methoxy C-H$_3$</td>
<td>-3.78</td>
</tr>
<tr>
<td>nuclear proton</td>
<td>-6.94</td>
</tr>
<tr>
<td>Substituent</td>
<td>Chemical Shift</td>
</tr>
<tr>
<td>------------</td>
<td>---------------</td>
</tr>
<tr>
<td>o-Br</td>
<td>-10.14</td>
</tr>
<tr>
<td>o-Cl</td>
<td>-9.96</td>
</tr>
<tr>
<td>o-C₆H₅</td>
<td>-9.38</td>
</tr>
<tr>
<td>H</td>
<td>-9.32</td>
</tr>
<tr>
<td>o-CH₃</td>
<td>-9.14</td>
</tr>
</tbody>
</table>
strong hydrogen bonding ability of the DMSO that is responsible for this large chemical shift. Secondly DMSO minimizes the dependence of the chemical shift on concentration. Although in carbon tetrachloride the chemical shift of the phenolic proton varies from -5.95 to -6.75 p.p.m. in the 5-20% range (-4.37 to -7.45 p.p.m. in the 1-100% range),\textsuperscript{10} in DMSO there is no concentration dependence in the 5-20% range. This non-dependence on concentration is also due to the hydrogen bonding ability of the DMSO. In carbon tetrachloride solutions the concentration dependence is due to the varying amounts of intermolecular hydrogen bonding with varying concentrations. In DMSO, the solvent itself is such a good hydrogen bonding agent that there is no intermolecular hydrogen bonding between two phenol molecules. Perhaps it is more correct to say that intermolecular hydrogen bonding has no observably different effect on the phenolic proton chemical shift than the DMSO hydrogen bonding. This lack of concentration dependence eliminates errors due to sample preparation.

F. Related Work

The surprisingly good correlation between the chemical shift of substituted fluorobenzenes and Hammett's sigma constants,\textsuperscript{11} plus the fact that DMSO strongly hydrogen bonds to alcoholic protons,\textsuperscript{12} led to the inception of this study of substituted phenols in DMSO:

When one line is drawn to correlate the substituted fluorobenzene data, only a fair correlation is obtained, with the points scattered about the line. A better
correlation is obtained when different lines are used for the meta and for the para substituents. No reason is given in the paper why this should be so. However there is a mathematical examination of the Hammett relationship which shows that in certain cases separate lines should be needed for meta and for para substituents.13

Hammett sigma values in general correlate two types of data, equilibrium data and reaction rate data. The defining equation is for an ionization equilibrium. But it has been found that reaction rate data are equally well correlated. In the defining reaction sigma constants are a measure of electronic effects in the stabilization or destabilization of the benzoate ion relative to benzoic acid. In reaction rate treatments the relative effect on the stabilities of the transition state is being measured. The electronic effect of substituents would be expected to be called into play much more in the stabilization or destabilization of the benzoate ion than of the benzoic acid. Stabilization of transition states, likewise, is a more important factor than stabilization of ground states.

In the measurement of the chemical shifts of the substituted fluorobenzenes the ground state is observed, whereas sigma is evaluated from rate and equilibrium data and thus depends upon the substituent effect on the transition state or ionic species.

This factor might also be the reason that two lines do a better job of correlating the data. Since electronic
effects are greater in the para position, chemical shifts of the meta-substituted fluorobenzenes should be better correlated to sigma constants than would be the chemical shifts of the para-substituted fluorobenzenes. This hypothesis is supported by the fact that the meta correlation line goes through the origin and the para line does not.

G. Statistical Treatment of Data

Whatever the reason for the lines needed to correlate the substituted fluorobenzene data, Figure 1 clearly shows that only one line is needed to correlate the data with the substituted phenols. Except for certain deviations which will be dealt with later, it is a very good correlation. The correlation line in Figure 1 is obtained by a statistical treatment of the twelve well-correlated points. The p-iodo substituent, although well-correlated, is not included in the statistical study because p-iodophenol was not obtained until just before this writing. The calculations were done with an IBM Model 1620 computer. The "normal" regression model has been adopted for this statistical study. This model is a good one since the assumptions made are reasonable: (1) the chemical shifts of the different compounds are independent, (2) they all have the same standard deviation, (3) each has a "normal" distribution, and (4) there are constants $\rho$ and $\beta$ such that $E(\delta_i) = \rho \sigma_i + \beta$, where $i=1, \ldots, 12$, and $E(\delta_i)$ is the expectation of $\delta_i$. Maximum likelihood estimates $\hat{s}, \hat{\rho}, \hat{\beta}$ of the unknown parameters $s, \rho$, and $\beta$ have been computed, and $\hat{s}=0.0282, \hat{\rho}=1.496, \hat{\beta}=-0.0317$. "s" is the standard
Plot of Chemical Shifts of Phenolic Protons of Meta and Para Substituted Phenols Relative to the Chemical Shift of Phenol Versus Sigma Constants.

Slope $\rho = 1.496$
Intercept $\beta = .0317$
deviation. The correlation coefficient is 0.997. The arithmetic average difference of sigma values from the line is ±0.016 which is well within the standard deviation of sigma values obtained by other methods, which is ±0.03. The reason a "normal" regression model was used rather than a least squares fit of the data is that a confidence interval can be determined for rho. The regression lines from the two methods are essentially identical.

Performing a t-test on rho at the 90% confidence level gives $1.45 < \rho < 1.54$ and performing a chi-square test on the standard deviation at the 90% level gives $0.0245 < \sigma < 0.0444$. The significance of these tests is as follows. The fact that $1.45 < \rho < 1.54$ at the 90% confidence level means that given data such as those obtained in this experiment, ninety times out of a hundred the true value of rho will be between 1.45 and 1.54. This is quite a narrow $\Delta \rho$ region, which reinforces the good correlation coefficient and the good standard deviation obtained. The equation of the "normal" regression line is

$$\sigma = 0.667\delta + 0.0212.$$

At the end of the section on substituted phenols there is a calculation appendix defining the various statistical terms used in this statistical treatment.

The equations obtained for the correlation lines of the substituted fluorobenzenes are as follows: $^{11}$ (1) for one line correlating all the data points, $\sigma = 0.600\delta + 0.243$, with a residual sum of 2.38, (2) for two lines, one for meta points and one for para points, $\sigma_m = 1.69\delta_m$, and
\[ \sigma_p = 0.560 \delta_p^{+} .271, \] with residual sums .26 and .71 respectively.

H. Significance of Data

What, then, is responsible for such a good correlation in this experiment with the substituted phenols? It is not a matter of better data being taken, but rather a matter of more significant data. For the factor that makes these data so significant, we can again turn to the solvent, DMSO. Remembering that DMSO is a strong hydrogen bonding agent, we can clearly make the statement that the ordinary ground states of the substituted phenols are not being examined. The ground state of phenol is represented by the chemical shift of -4.37 p.p.m. in a 1% carbon tetra-chloride solution, \(^{10}\) where there is little or no hydrogen bonding. The value of the chemical shift for the phenolic proton of phenol in DMSO is -9.32 p.p.m. This signifies a much more acidic proton, a state of affairs somewhat closer to a solvated proton and a phenoxide ion. The presence of a more acidic proton does not mean a more rapid rate of chemical exchange. As a matter of fact, it is known that DMSO retards the rate of proton exchange. \(^{12}\) But the average position of the proton is much closer to that of a solvated proton, leaving at least a partial negative charge on the phenoxy group. In order for there to be good correlation

\[
\begin{align*}
\text{CH}_3 & \quad S=O \quad H \quad O \quad \text{X} \\
\text{CH}_3
\end{align*}
\]
between chemical shifts and sigma values, the various substituents must have the same relative effect on this intermediate position as they do on the equilibrium constants for the ionizations of the substituted benzoic acids. Examination of the deviating points will reveal that the breakdown of this relativity is the cause for the deviation of the strong electron-withdrawing resonance substituents.

I. Individual Data Points

Much of the chemical knowledge we possess today comes from data that do not correspond to predictions. The deviations obtained in this experiment have as much meaning as the well-correlated data. Without them there would be a much less complete picture of the actual situation.

Consider first of all that the regression line does not go through the origin; rather the intercept is -.0317. By definition, a Hammett sigma-rho plot is supposed to contain the origin. For some reason hydrogen as a substituent is more electron-withdrawing than predicted by its sigma value, causing the chemical shift of the phenolic proton to be .03 p.p.m. further downfield. A possible explanation is that this is due to a solvent effect. Examination of table 2 shows that whereas the ring protons do not have a change in chemical shift when the solvent is changed from chloroform to DMSO, the t-amyl and methyl protons show a change of .04 delta units. This change is in the direction of increased shielding, which can be explained by the fact that DMSO causes the environment of these protons to electron rich, thus making the substi-
tuents more electron releasing. It can only be assumed that the other substituents undergo the same solvent effect. The ring protons do not experience such a solvent effect.

The strong resonance electron-withdrawing groups $\text{p-CHO}$ and $\text{p-NO}_2$ deviate markedly from the regression line. Figure 1 shows that the $\sigma^-$ values for these two substituents correlate the chemical shifts better than the normal sigma values. Closer examination shows that the ratio $(\sigma^- - \sigma_\sigma)/(\sigma_\sigma - \sigma)$ is in the same range for both substituents, where $\sigma_\sigma$ is the sigma value corresponding to the regression line. For $\text{p-CHO}$ the ratio has the value 0.33 and for $\text{p-NO}_2$ has the value 0.40. Thus, whatever is controlling the one is also controlling the other. The fact that the regression line goes between the predicted points means that the substituents are more electron-withdrawing than predicted by $\sigma$ and less electron-withdrawing than predicted by $\sigma^-$. When the reasons for obtaining a good correlation were discussed earlier, a prime condition for good correlation was that each substituent must exhibit the same relative effect on the chemical shift as it does on the ionization constant of the substituted benzoic acids. And this effect on the ionization constant is primarily the effect a substituent has on the stability of the benzoate ion. Now, for most of the substituents the relative effects are the same in both cases—but not for $\text{p-CHO}$ and $\text{p-NO}_2$. Why? The other substituents have an electron-releasing resonance effect, when they have any at all. This effect is not particularly affected by the amount of negative charge to be stabilized. With the
electron-withdrawing resonance effect there is considerable
dependence on the amount of negative charge on the phenoxy
oxygen, since it is the presence of this charge that calls
the resonance effect into play. The substituent effects
for p-NO₂ and p-CHO are greater, in this experiment, than
in the ionization constants for benzoic acids, although
less than for the ionization constants for phenols, where
σ⁻ is used. This result means that these substituents
have an effect intermediate between that on the benzoate
ion, and on the phenoxide ion, and that there must, therefore, be some negative charge developed on the phenoxy
oxygen. This fact supports the explanation given as to why
the regression line for the substituted phenols is superior
to that for the substituted fluorobenzenes.

The point for p-phenyl is also quite a bit out of line
when the normal sigma constant (.009) is used. However a
sigma of 0.14 is reported from the ionization of ArNH₃⁺
and 0.18 from the ionization of ArOH.¹⁵ As with the p-NO₂
and p-CHO the p-phenyl is between the σ and σ⁻ values.
The fact that p-phenyl should behave like p-NO₂ and p-CHO
is due to the amphielectronic character of the phenyl
group. When an intermediate is electron-demanding, phenyl
is electron-releasing; and when an intermediate is electron
rich, phenyl is electron-withdrawing.

The hydroxy substituents, m-OH, p-OH, and 3,5-dihydroxy,
are much more electron releasing in this experiment than
their sigma values indicate. Again we find a solvent
effect. Figure 1 reveals a fact that is characteristic of
solvent effects. The m-OH and p-OH data points are very nearly the same distance from the regression line, and the 3,5-dihydroxy data point is very nearly twice as far displaced from the line as they are. This additivity and non-dependence on the position of the hydroxy group point very strongly to a solvent effect. The nature of the solvent effect is again that of hydrogen bonding. Hydrogen bonding to solvent has the effect of giving the OH group more O-character and thus more electron-releasing character than is indicated by its sigma constants. The sigma constants for meta and para-oxide are -0.708 and -0.519. The sigmas for m-OH and p-OH are -0.002 and -0.357 respectively, and their \( \sigma^a \)'s are -0.180 and -0.527.

The p-OCH\(_3\) group is also found to be more electron-releasing than predicted by its sigma constant. Table 2 shows that for alkyl groups the methyl protons are shifted upfield by 0.04 delta unit in DMSO compared to their chemical shifts in chloroform. However with p-OCH\(_3\) the shift is 0.12 delta unit upfield, that is, in the direction of greater shielding. This high electron density neighborhood is a sufficient condition for making p-OCH\(_3\) a more electron-releasing substituent. This solvent effect on the p-methoxy substituent is apparently dependent on the presence of the phenolic group. This high shielding of the methoxy protons is not observed for anisole or p-anis-aldehyde.

J. Inductive Order

The relative chemical shift values for highly branched
p-octyl and p-nonyl phenols are both -.30 p.p.m. This value is in between the values for p-methyl and p-t-amyl (-.20 and -.36 respectively). Since the carbon attached to the benzene ring in these highly branched compounds is at least primary and at most tertiary, the inductive order is followed by the chemical shifts of the p-alkyl groups. This order is not surprising since there is no reason to expect that the hyperconjugative order would be found.

K. New Substituents

As was stated in the introduction this technique can be used very conveniently to determine sigma constants of new substituents. Although almost all important types of substituents have been studied, sigmas have been determined for only two acyloxy substituents. The meta- and para-acetoxy sigma values have been measured as 0.39 and 0.31 respectively, each with an experimental error of 0.1. Two new substituents in this class have been examined with this new technique. For the meta-benzoyloxy substituent, a sigma of 0.329 is found, and for para-toluene sulfonyloxy, sigma is found to be 0.195. The sigma value determined by this technique ought to be as good as or better than those determined by conventional means (e.g., ionization data), since the deviations in this new method are only half what they are for the usual methods (±.016 compared to ±.03).

L. Correlation to $\sigma_R^0$

In Figure 2 the difference of the chemical shifts of the para and meta substituted phenols has been plotted against $\sigma_R^0$ values. $\sigma_R^0$ is a measure of the resonance
effect of a substituent separated from the inductive effect. The $\sigma^0_R$ values are obtained from a mathematical treatment which makes use of the different amounts of resonance effects for meta and para substituents. The correlation of data to this resonance effect parameter is very good except for NO$_2$, which would not be predicted to be correlated since m-NO$_2$ is well correlated on the sigma plot and p-NO$_2$ is not. The fact that hydroxy is well correlated to $\sigma^0_R$ supports the theory that the deviation of the m-OH and p-OH data from the sigma plot is due to a solvent effect, which is specific for OH. This good correlation of OH with its $\sigma^0_R$ value means that even in DMSO the effects of m-OH and p-OH are related in the same way as with usual conditions for obtaining sigma-rho plots.

M. Ortho Substituents

In addition to the meta and para substituted phenols four ortho substituted phenols have been studied. The chemical shift data are tabulated in Table 3. Simple observation of this table shows that there is no correlation between the chemical shift and $\sigma^*_x$, which is a measure used for ortho substituents in obtaining correlation to rate and equilibrium data. Figure 3 shows that the values obtained for the ortho substituted phenols bear a fair to good correlation to the values for the para substituted phenols, a phenomenon not observed with rate or equilibrium data. Again the experimental conditions spell the difference. Equilibrium and rate constants are strongly dependent on proximity effects, especially steric effects.
FIGURE 2

Plot of the Difference of the Chemical Shifts of Para and Meta Substituted Phenols Versus $\sigma^0_R$
Plot of Chemical Shifts of Phenolic Protons of Para-Substituted Phenols Versus the Corresponding Ortho-Substituted Phenols.

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Reaction rates are impeded sterically because the attacking reagent cannot easily approach the reaction site. In ionization equilibrium, involving, for example, the equilibrium is dependent on the solvation of the benzoate ion, which solvation is inhibited by steric factors. This inhibition of solvation is true in spite of the fact that the overall ortho effect in this ionization is to increase ionization.

Contrary to the solvation of benzoate ions which would utilize several solvent molecules at a time, hydrogen bonding between phenol and DMSO requires only one DMSO molecule at a time. Steric factors are not likely to be so great as to prevent even one solvent molecule from approaching as close to the phenolic proton as the acidity of the proton demands. Since these ortho data are correlated to the para data they must primarily represent the electronic behaviour of the ortho substituents rather than steric proximity effects. Sigma constants have been calculated for the ortho substituents by means of the regression line in Figure 1, which correlates the data from the meta and para substituents with their sigma constants. These calculated values appear in Table 3 and are designated as $\sigma^\circ_\delta$.

N. Comparison to Ionization of Phenol

One of the most surprising things about the correlation of the chemical shifts to Hammett sigma constants is that the correlation is better than for the ionization of substituted phenols. The explanation is to be found in the difference between the benzoate and phenoxyde ions. The
benzoate ion is not extensively stabilized by resonance with the benzene ring. The phenoxide ion, on the other hand, owes much of its stability to resonance with the benzene ring. In this experiment there is only partial charge developed on the phenoxy oxygen so that the phenolic chemical shift is not as susceptible to resonance effects as is the ionization of phenols. Thus this experiment better correlates with sigma constants.

O. Further Work

Valuable knowledge has been obtained from the experimental data obtained from the substituted phenols. There are other series of compounds, more difficult to obtain, which might give even better results, especially for substituents like $p$-NO$_2$. The series I intend to study are the substituted meta- and para-benzoyloxyphenols, with the substituents in the benzoyloxy ring. If the substituent effects are large enough to be successfully measured by n.m.r., these series should provide good electronic parameters (possibly sigma values) for substituents with strong electron-withdrawing mesomeric effects and for ortho substituents.

P. Calculations

The following set of equations are the equations used to calculate the various parameters in the statistical study.

\[
\hat{\rho} = \frac{\mathcal{L}}{\Delta \xi_0} \left[ \mathcal{L} \xi_0 \sigma^2 \left( \delta^2 - \alpha^2 \overline{\delta} \overline{\sigma} \right) \right],
\]

where $\hat{\rho}$ is the maximum likelihood estimate of the slope $\rho$. 

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$\sigma^a$ and $\delta^a$ are the sigma constants and the relative chemical shifts of the various substituents, $\bar{\sigma}$ and $\bar{\delta}$ are the mean values of the sigma constants and the relative chemical shifts respectively, and $S^a_{\sigma}$ is defined as $\frac{1}{n_a} \left( \sum_{i=1}^{n_a} \sigma^a_i \right) - \bar{\sigma}^a$.

$$\hat{\sigma}^a = S^a_{\sigma} - \hat{\beta}^a S^a_{\delta},$$

where $\hat{\sigma}$ is the maximum likelihood estimate for the standard deviation $s$, $\hat{\beta}$ and $S^a_{\delta}$ are as defined above, and $S^a_{\sigma}$ is defined as $\frac{1}{n_a} \left( \sum_{i=1}^{n_a} \sigma^a_i \right) - \bar{\sigma}^a$.

$$\hat{\beta} = \hat{\sigma} - \bar{\delta} \bar{\sigma},$$

where $\hat{\beta}$ is the maximum likelihood estimate of the intercept $\beta$; $\bar{\sigma}$, $\bar{\delta}$, and $\hat{\beta}$ are as defined above.

$$r = \frac{\hat{\beta} S_{\sigma}}{S_{\delta}},$$

where $r$ is the correlation coefficient, and the other parameters are as defined above.

$$A = \frac{1}{n_a} \sum_{i=1}^{n_a} \left| \delta_i^a / \hat{\beta} - \hat{\beta} / \hat{\beta} - \sigma^a_i \right|,$$

where $A$ is the average deviation of sigma from the regression line.

(6) The equation of the regression line is

$$\delta = 1.496 \sigma - .0317,$$

which can be rearranged to

$$\sigma = .667 \delta + .0212.$$

In this form the sigma values can be calculated for new substituents. For example, for m-benzoyloxy with a relative chemical shift of 0.46, $\sigma = (.667)(.46) + .0212 = .329$.

(7) The t-statistic involving rho has the value
\[ \sqrt{n-2} (\hat{\rho} - \rho) \frac{\sqrt{n} s^2}{\sqrt{n} \hat{s}^2} , \]

where \( n \) is the number of sample points, 12. In order to determine a 90% confidence interval for rho, we refer to the t-table with \( n-2=10 \) degrees of freedom and find that

\[ -1.372 < \sqrt{n-2} (\hat{\rho} - \rho) \frac{\sqrt{n} s^2}{\sqrt{n} \hat{s}^2} < 1.372. \]

Supplying the proper values for \( n, \hat{\rho}, s^2, \hat{s}^2 \) and solving, we obtain

\[ 1.448 < \rho < 1.543. \]

(8) The chi-square statistic involving \( s \) has the value

\[ n \hat{s}^2 / s^2. \]

This time the chi-square tables are referred to at the 90% confidence level with 10 degrees of freedom and we find that

\[ 4.87 < n \hat{s}^2 / s^2 < 16.0, \]

and \( .0245 < s < .0444. \)

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CHAPTER III
SUBSTITUTED BENZALDEHYDES

A series of seven substituted benzaldehydes has been studied with two purposes. The first purpose was to see if any information could be gained which would elucidate the electronic effect of the p-CHO group in the substituted phenol experiment. The second purpose, of course, was to study the behaviour of the substituted benzaldehydes per se. The experiment has shown (Table 4) that there is not a large change in the chemical shift of the aldehydic proton of benzaldehyde when the solvent is changed from chloroform to DMSO. The change is 0.04 delta unit in the direction of less shielding. It was seen that the methyl protons of cresol were shifted 0.04 unit in the direction of greater shielding with the same change in solvent. Some of the deviation of the p-CHO group in the phenol experiment from the behaviour predicted by $\sigma^-$ is probably due to a solvent effect. However this solvent effect cannot explain the large deviation that occurred. The major part of the deviation must be due to the fact that p-CHO is a strong electron-withdrawing resonance substituent.

The substituted benzaldehydes used were readily obtainable. The three electron-releasing substituents might be predicted to undergo a solvent effect in DMSO causing a deviation from any correlation line drawn for the other substituents. However, substituent effects on the chemical shift of the aldehydic proton of benzaldehyde are quite small both in chloroform and in DMSO, and deviations due to

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### TABLE 4

<table>
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<tr>
<th>Substituent</th>
<th>Chemical Shift HCl$_3$</th>
<th>Chemical Shift DMSO</th>
<th>Relative Chemical Shift, $\Delta - \delta_0$ p.p.m.</th>
<th>Sigma</th>
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<td>.778</td>
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<td>.10</td>
<td>.710</td>
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<td>0</td>
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<td>-.02</td>
<td>.257</td>
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<td>-9.94</td>
<td>-.14</td>
<td>-.268</td>
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<td>-9.78</td>
<td>-.30</td>
<td>-.357</td>
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<td>-9.76</td>
<td>-9.70</td>
<td>-.38</td>
<td>-.600</td>
</tr>
</tbody>
</table>
solvent would, therefore, be even smaller.

The correlation line in Figure 4 was drawn on the basis of visual approximation. No statistical study was made since it is obvious that the correlation is very poor for a Hammett plot. The slope of the line, rho, is .311 and the intercept is -.102. The value for rho is quite small compared to the rho for the phenol experiment, 1.496. This result confirms the earlier statement that the chemical shift of the aldehydic proton in benzaldehyde is much less susceptible to substituent effects than is the chemical shift of the phenolic proton.

What is the reason for the scatter in the correlation of the chemical shifts of the substituted benzaldehydes with sigma constants? Consider (Table 3) the difference in the chemical shifts when the solvent is changed from chloroform to DMSO. There is practically no change. There is very little interaction, therefore, between the aldehydic proton and the DMSO, relative to the interaction between DMSO and the phenolic proton. The result is that there is no charge introduced into the CHO group, and therefore the substituent effects would not be expected to be the same as in the ionization of benzoic acid. This dissimilarity to the ionization of benzoic acid was the same factor that caused the n.m.r. data of the substituted fluorobenzenes to give only a fair correlation to Hammett sigma constants.

SIGNIFICANCE OF RHO VALUES

The rho constant for the ionization of substituted
FIGURE 4

Plot of the Chemical Shifts of the Aldehydic Protons of Substituted Benzaldehydes Versus Sigma Constants

slope $\rho = .311$
intercept $\beta = -.102$
benzoic acids is defined as unity. Rho values obtained from other equilibrium data can be compared to this value. If a rho value greater than unity is obtained, then the equilibrium is more susceptible to substituent effects than is the defining reaction. If a rho is negative then the equilibrium constant is affected in a manner opposite to that in the defining reaction, that is, \( \log \left( \frac{K}{K_0} \right) \) becomes larger the greater the electron-releasing effect of the substituent. When the absolute value of rho is less than about 0.5, the substituent effect on a reaction is quite small and other, non-correlated factors become proportionately more important, causing greater scatter in the Hammett plot.

When rate data are plotted against sigma a different term is being plotted against sigma so that the rho values are no longer relative to that for benzoic acid ionization. Although it has been proven that kinetic data give Hammett plots as well as equilibrium data, this in no way implies that the rho values obtained from the plots will be of the same relative magnitude. However, rho values from rate data are usually compared to the scale defined by the ionization constants of substituted benzoic acids. It is plausible that the kinetic rhos, although not quantitatively related to equilibrium rhos, represent susceptibility of the same order of magnitude as that represented by equilibrium rhos of the same values. This plausibility stems from the fact that the ranges of rho values from both types of data are the same, and the fact that for both
types of data rho less than 0.5 is not significant.

Now in these two types of experiments it is the log K and log k that are linearly related to sigma. K and k are logarithmic functions of energy whereas the chemical shift is a linear function of energy. Therefore, the function \( \delta - \delta_0 \) was plotted versus sigma, rather than \( \log \delta - \log \delta_0 \). If the chemical shift had been measured in c.p.s. instead of p.p.m., a different numerical value would have been obtained for rho in the phenol and benzaldehyde plots. It so happens that a value for rho in the range of the rhos of equilibrium data is obtained if p.p.m. values are used. Here again the numerical value of rho does not quantitatively have the same meaning as it does in equilibrium plots. The fact, however, that the Hammett plot for the substituted benzaldehydes has a rho less than 0.5 and that the data are poorly correlated indicates that the rhos obtained using p.p.m. are of the same order-of magnitude as the rhos obtained from equilibrium data.
CHAPTER IV

SUBSTITUTED ALCOHOLS

Unless extreme measures are taken to rid an alcohol sample of traces of acid, the rate of the chemical exchange of the hydroxyl proton in the usual n.m.r. solvents is too rapid for observation of splitting due to the hydroxyl protons. It has been reported that in "dimethyl sulfoxide solution strong hydrogen bonding to the solvent shifts the hydroxyl resonance downfield (tau 6.0 or lower) and reduces the rate of proton exchange sufficiently to permit observation of hydroxyl proton splitting." This phenomenon becomes a handy tool for the organic chemist in the classification of alcohols. If a tertiary alcohol is being studied the hydroxyl peak will be a singlet. Similarly, secondary alcohols will produce doublets and primary alcohols triplets.

When routine analysis of methylenecyclohexane bromohydrin, a compound previously studied in Professor Traynham's laboratories, gave results that were not expected from its proposed structure, an investigation was made of the effect of electron-withdrawing substituents on the validity of the method. The experimental results are listed in Table 5. Several experimental conditions have been varied to see if they would have any effect on the results. These variations include changes in concentration, age of DMSO solution of the alcohols, treatment of alcohol with sodium or potassium carbonate, and fresh distillation of the alcohol. Table 5 shows that as often as not the variation of experimental
<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Chem. Shift p.p.m.</th>
<th>Multiplicity</th>
<th>K$_2$CO$_3$ or Na$_2$CO$_3$</th>
<th>Time in DMSO</th>
<th>Vol. % in DMSO</th>
<th>Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-ethoxyethanol</td>
<td>-4.55</td>
<td>t</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td>allyl alcohol</td>
<td>-4.71</td>
<td>t</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td>trans-2-chlorocyclooctanol</td>
<td>-4.92</td>
<td>d</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td>trans-2-bromocyclooctanol</td>
<td>-4.60</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td>ethylene bromohydrin</td>
<td>-5.20</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-4.46</td>
<td>s</td>
<td>yes</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-4.63</td>
<td>s</td>
<td>no</td>
<td>3 hrs.</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-3.97</td>
<td>s</td>
<td>yes</td>
<td>2 days</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-4.52</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.23</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>20</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.30</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>30</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.11</td>
<td>t</td>
<td>yes</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.11</td>
<td>t</td>
<td>yes</td>
<td>fresh</td>
<td>20</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.11</td>
<td>t</td>
<td>yes</td>
<td>1 hr.</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(poorly resolved)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>Chem. Shift</td>
<td>Multiplicity</td>
<td>K₂CO₃ or Na₂CO₃</td>
<td>Time in DMSO</td>
<td>Vol. % in DMSO</td>
<td>Purity</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------</td>
<td>----------------</td>
<td>------------------</td>
<td>--------------</td>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td>ethylene bromohydrin</td>
<td>-5.11</td>
<td>s (broad)</td>
<td>yes</td>
<td>2 hrs.</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td>ethylene chlorohydrin</td>
<td>-4.88</td>
<td>s</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-5.12</td>
<td>s (broad)</td>
<td>yes</td>
<td>2 days</td>
<td>10</td>
<td>Prep.</td>
</tr>
<tr>
<td></td>
<td>-5.05</td>
<td>t</td>
<td>yes</td>
<td>fresh</td>
<td>10</td>
<td>Prep.</td>
</tr>
<tr>
<td>ethylene cyano-hydrin</td>
<td>-4.88</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-5.21</td>
<td>s (broad)</td>
<td>yes</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-5.0</td>
<td>s (very broad)</td>
<td>yes</td>
<td>2 days</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-4.22</td>
<td>s (very broad)</td>
<td>1.5 hrs.</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-4.58</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.02</td>
<td>s (very broad)</td>
<td>3 days</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td>ethyl lactate</td>
<td>-5.45</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-5.28</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.22</td>
<td>s (very broad)</td>
<td>1.25 hrs.</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
</tbody>
</table>
TABLE 5 (cont'd)

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Chem. Shift p.p.m.</th>
<th>Multiplicity</th>
<th>K₂CO₃ or Na₂CO₃</th>
<th>Time in DMSO</th>
<th>Vol. % in DMSO</th>
<th>Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethyl lactate</td>
<td>-5.22</td>
<td>s (very broad)</td>
<td>3 days</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td>2,2,2-trichloro-ethanol</td>
<td>-6.7</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>A.O.</td>
</tr>
<tr>
<td></td>
<td>-6.74</td>
<td>s (broad)</td>
<td>no</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.71</td>
<td>s (broad)</td>
<td>1.25 hrs.</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
<tr>
<td></td>
<td>-5.72</td>
<td>s (broad)</td>
<td>3 days</td>
<td>fresh</td>
<td>10</td>
<td>F.D.</td>
</tr>
</tbody>
</table>
conditions did alter the results.

The explanation for the loss of multiplicity of some of the alcohols follows. The strong electron-withdrawing substituents close to the hydroxy group apparently promote rapid proton exchange, even in dimethyl sulfoxide solution, with consequent loss of multiplicity of both hydroxyl and methylene proton resonances. The magnitude of the chemical shifts of the -OH resonances in the various alcohols suggests a definite correlation with the relative electron-attracting power of the substituent.

When no measures for purification were taken, the n.m.r. spectra of DMSO solutions of several of the alcohols studied showed loss of multiplicity of hydroxyl resonances. With added precautions for purity, fresh distillation and treatment with solid sodium or potassium carbonate, the predicted multiplicity was observed for some of the alcohols. The compounds tested can be put into three classes:

1) those giving expected multiplicity without special treatment: 2-ethoxyethanol, allyl alcohol, and trans-2-chlorocyclooctanol; 
2) those giving expected multiplicity only after prior treatment with carbonate: ethylene chlorohydrin and ethylene bromohydrin; 
3) those for which only singlet peaks are obtained, even after treatment with carbonate: ethylene cyanohydrin, ethyl lactate, and 2,2,2-trichloroethanol. Trans-2-bromocyclooctanol must be classed separately since there was only enough of it on hand for one run. It was not treated with carbonate, but the sample run without treatment showed no multiplicity.
in the hydroxyl proton peak.

The data show that for the ethylene bromohydrin samples not treated with carbonate there is considerable dependence of the chemical shift on concentration, whereas for the treated samples, chemical shift is not concentration dependent. The age of the DMSO solution is a factor of concern with some of the compounds. In the untreated samples, the chemical shift sometimes varies with the age of the sample. With the ethylene chloro- and bromohydrins the multiplicity gained by treatment with carbonate is lost after the DMSO solution is two hours old.

The reason these compounds have been studied so extensively is that the method is of pragmatic value to the organic chemist. As such, any factor that causes this lack of observation of multiplicity is of interest to him.

Conformational Equilibrium of Cyclohexanol

Among the compounds studied by Chapman\(^1^2\) are \textit{cis}-4-\textit{t}-butylcyclohexanol (-4.11 p.p.m.), \textit{trans}-4-\textit{t}-butylcyclohexanol (-4.45 p.p.m.), and cyclohexanol (-4.38 p.p.m.). The chemical shift values for the hydroxyl protons are in parentheses. Since the \textit{t}-butyl group locks the conformation of the cyclohexane ring,\(^1^8\) these data can be used to calculate the conformational equilibrium of cyclohexanol, from which the free energy difference between equatorial and axial -OH can be calculated. For this calculation to be done, it must be assumed that the \textit{t}-butyl group will not affect the chemical shift of the hydroxyl proton, a good assumption.\(^1^8\) Since n.m.r. data
are quite accurate, an accurate equilibrium constant should be obtained by linear interpretation of the chemical shift data. From the equation $K = \frac{\delta_a - \delta}{\delta - \delta_e}$, where $\delta_a$ is the chemical shift value for cis-4-tert-butylcyclohexanol, $\delta_e$ for the trans isomer, and $\delta$ for cyclohexanol, a value of $K=3.86$ is obtained. From the equation relating free energy to equilibrium constants $\Delta F^0 = -RT \log K$, with $T=298^0K$, $\Delta F^0$ is calculated to be $.829$ kcal/mole. This is in the range of $0.4$ to $0.9$ kcal/mole that has been obtained through various experiments.$^{20, 21}$
EXPERIMENTAL

All spectra in Part 1 of the dissertation were obtained with a Varian Associates HA-60 spectrometer. The compounds were in general obtained commercially. Trans-2-chloro- and trans-2-bromocyclooctanol were prepared by J. Schneller in Professor Traynham's laboratories. Ethylene chlorohydrin was prepared by adding dry hydrogen chloride to ethylene oxide in carbon tetrachloride and removing the solvent by rotary evaporation. Gas chromatography and infra-red analysis revealed no impurities in the residual chlorohydrin, which was used without further purification. The phenols were used as obtained; purity of samples were checked by melting point for each solid and gas chromatography for each liquid. All the melting point ranges were within two degrees of the reported values, and gas chromatography revealed no impurities in the liquids. The substituted benzaldehydes were also used as obtained. The treatments of the alcohol samples are briefly summarized in Table 5; "A.O." means used as obtained, and "F.D." means freshly distilled.
PART 2: ADDITION REACTIONS OF CIS, TRANS-1,5-CYCLODECADIENE AND CIS- AND TRANS-CYCLODECENE

CHAPTER I
INTRODUCTION

This part of the dissertation concerns addition reactions to the medium ring olefins cis- and trans-cyclodecene and cis,trans-1,5-cyclodecadiene, primarily the last. Medium rings are those with eight to eleven carbon atoms in the ring. This classification is not arbitrary. Medium ring compounds have several chemical characteristics which distinguish them from other compounds.

Perhaps the most striking difference in medium ring chemistry is that some reactions in rings of this size do not take place on the classically activated sites but involve atoms lying on opposite sides of the ring, leading to 1,4-, 1,5-, and 1,6-disubstituted products in the eight, nine, and ten membered rings respectively. The occurrence of such transannular reactions was reported independently by Prelog and by Cope and their coworkers in 1952,22,23 and the subject has been attracting considerable attention ever since. Transannular reactions are associated mainly with carbonium ion processes,24,25 although recent studies have uncovered some transannular free radical reactions.26,27

Another property of interest with medium rings and of importance to this work is that of the relative stabilities of the cis and trans isomers of the medium ring olefins. Trans-cycloheptene, a common ring, converts to
cis-cycloheptene so fast that it has never been isolated, although it has been detected. In the twelve membered ring, the trans olefin is more stable than the cis, as with acyclic compounds. These two rings are the immediate neighbors of the medium rings. Let us now examine the relative stabilities of the medium ring cis and trans olefins. The thermodynamic data are tabulated in Table 6.

<table>
<thead>
<tr>
<th>Ring Size</th>
<th>( \Delta \Delta H^\circ ) at 100(^\circ)</th>
<th>( \Delta \Delta F^\circ ) at 100(^\circ)</th>
<th>Equilibrium Constant at 100(^\circ)</th>
<th>% Cis at 100(^\circ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>-9.26(^{30})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>-2.87(^{30})</td>
<td>-4.04</td>
<td>232</td>
<td>&gt;99</td>
</tr>
<tr>
<td>10</td>
<td>-3.34(^{30})</td>
<td>-1.86</td>
<td>12.2</td>
<td>76</td>
</tr>
<tr>
<td>11</td>
<td>-0.12</td>
<td>.67</td>
<td>0.406</td>
<td>29</td>
</tr>
<tr>
<td>12</td>
<td>-0.41</td>
<td>.49</td>
<td>0.517</td>
<td>34</td>
</tr>
</tbody>
</table>

The \( \Delta \Delta H^\circ \) and \( \Delta \Delta F^\circ \) values are the values of the differences of the heats of hydrogenation and free energies of hydrogenation of the cis and trans olefins. No quantitative work on the \( \Delta \Delta F^\circ \) is available for cyclooctene, but the equilibrium constant is definitely much greater than 232, which is the value for cyclononene.

The instability of the trans isomer in the seven to ten membered rings is due to the angle strain introduced into the ring when the trans configuration is present. As the rings become larger, this strain decreases until the factors that cause the acyclic trans olefins to be more stable become the major factors. This factor becomes
the more important in the eleven membered ring; trans-cycloundecene is more stable than the cis isomer. Although no work has been done on the relative stabilities of the dienes, it is assumed that the stabilities of the cis and trans olefins are the same in these compounds as they are in the monoolefin compounds.

In this study both cis and trans addition reagents have been used. It is fitting that the difference in the mechanisms be discussed here, since the results obtained can be classified according to whether the addition reagent was cis or trans. What is it that makes a cis addition cis and a trans addition reagent trans? The answer lies in the mechanisms of the additions and the resulting stereochemistry of the addition products. An example of each type of addition will illustrate the difference. Bromine will be used as an example of a trans addition reagent, and diimide reduction will illustrate the cis addition mechanism.

In bromine addition, the initial attack on the olefin is by a cationic species, Br⁺, or its kinetic equivalent, to give a bromonium ion. Backside attack by bromide ion
on this bromonium ion gives product dibromide. As the illustration shows, bromine addition to \textit{cis}-2-butene gives racemic 2,3-dibromobutane. The term trans addition comes therefore from the stereochemistry of the addition product. A major characteristic of trans addition, whether electrophilic like bromine or not, is the stepwise addition of the addends.

Only recently has the olefin reduction by hydrazine been found to be due to the diimide species, N$_2$H$_2$.\textsuperscript{31} The addition of diimide is concerted, that is, one step. The diimide molecule approaches the olefin from one side of the pi cloud to form a cis transition state. Elemental nitrogen and the saturated product are then formed. The addends in the reaction product of a cis addition reaction are cis, or gauche, to each other. A concerted mechanism results in cis addition.

The cis addition reactions studied were: epoxidation, methylenation, hydroboration, diimide reduction, palladium catalyzed hydrogenation, or ozonation. Bromination and acetoxylation were the trans addition reactions studied. All of the cis addition reagents, except ozone, gave normal 1,2-addition products. In the case of \textit{cis},\textit{trans}-1,5-
cyclodecadiene, the trans double bond was preferentially attacked. With the trans addition reagents and with ozone, transannular products were obtained. For the bromination reaction, which was studied extensively, no preference for attack at the trans double bond was detected.

While this work was in progress, an article was published on the reactions of cis,trans,trans-1,5,9-cyclo-dodecatriene in which the relative reactivities of the cis and trans double bonds were compared for several addition reagents. From the data obtained, which largely corresponds to that obtained for cis,trans-1,5-cyclo-decadiene, some conclusions have been reached about the cause for the selectivity of the cis reagents.

It should be repeated at this point that the relative stabilities of the cis and trans double bonds are different in the twelve membered and ten membered rings. In both systems the trans double bond is preferentially attacked. Thus the controlling factor in the selectivity is not the relative stability of the trans double bond. It is due rather to steric factors which make cis addition more favorable at the trans than it is at a cis double bond.
CHAPTER II
RESULTS AND DISCUSSION.

In this section the results of each reaction will be reported and discussed; first the reactions yielding normal addition products, then those giving transannular products. The reactions will be discussed with respect to: (1) the normal mechanisms of the various addition reagents, (2) the corresponding results with cis,trans, trans-1,5,9-cyclododecatriene, (3) the chemical characteristics of cis,trans-1,5-cyclodecadiene. The reactions with cis- and trans-cyclodecene will be discussed with the corresponding reactions of cis,trans-1,5-cyclodecadiene.

In the reactions yielding normal addition products, the results of greatest interest are the relative amounts of addition to cis and trans double bonds. Reaction products were analyzed by capillary column gas chromatography to determine the relative quantities of the isomeric adducts. Gas chromatography peaks were assigned on the basis of the infrared spectra of the reaction products. Other methods of identification will be discussed when used. The relative amounts of the various products obtained in the reactions studied are tabulated in Table 7,8, and 9.

A. Addition Reactions Yielding 1,2-Addition Products

The reactions falling into this classification are epoxidation, methylenation, diimide reduction, hydroboration, and catalytic hydrogenation, all of which are
### TABLE 7

**Product Distribution of Reactions Yielding 1,2-Addition Products with cis,trans-1,5-Cyclodecadiene**

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Moles/Mole of Diene</th>
<th>% Conversion</th>
<th>Addition Products</th>
<th>Rel.% Addition Cis</th>
<th>Addition Trans</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. m-chloroperbenzoic acid</td>
<td>.85</td>
<td>76</td>
<td>5-epoxy cyclodecene</td>
<td>10-15</td>
<td>85-95</td>
<td>81.5</td>
</tr>
<tr>
<td>2. methylene iodide</td>
<td>1</td>
<td>&gt;95</td>
<td>bicyclo [8.1.0] undec-5-ene</td>
<td>3</td>
<td>97</td>
<td>48</td>
</tr>
<tr>
<td>Zn-Cu couple</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. diimide</td>
<td>excess</td>
<td>97</td>
<td>cis-cyclodecene, cyclodecane</td>
<td>1</td>
<td>99</td>
<td>73</td>
</tr>
<tr>
<td>4. hydrogen, palladium catalyst</td>
<td>excess</td>
<td>93</td>
<td>cis-cyclodecene, cyclodecane</td>
<td>19</td>
<td>81</td>
<td>93</td>
</tr>
<tr>
<td>5. diborane</td>
<td>2/9</td>
<td>&gt;90</td>
<td>cis-cyclodecene, trans-cyclodecene, cyclodecane</td>
<td>14</td>
<td>86</td>
<td>70</td>
</tr>
</tbody>
</table>

### TABLE 8

**Product Distribution of Reactions Yielding Transannular Products with cis,trans-1,5-Cyclodecadiene**

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Moles/Mole of Diene</th>
<th>% Conversion</th>
<th>Addition Products</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bromine in Acetic Acid</td>
<td>1</td>
<td>100</td>
<td>1-bromo-4-acetoxydecalin</td>
<td>91</td>
</tr>
</tbody>
</table>
**TABLE 8 (cont'd)**

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Moles/Mole of Diene</th>
<th>% Conversion</th>
<th>Addition Products</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Bromine in Acetic Acid</td>
<td>2</td>
<td>100</td>
<td>1-bromo-4-acetoxy-decalin</td>
<td>91</td>
</tr>
<tr>
<td>3. Lead tetraacetate</td>
<td>1</td>
<td>100</td>
<td>1,4-diacetoxydecalin</td>
<td>100</td>
</tr>
<tr>
<td>4. Ozone</td>
<td>1</td>
<td>80</td>
<td>a monoozonide</td>
<td>-</td>
</tr>
<tr>
<td>5. Ozone</td>
<td>2</td>
<td>100</td>
<td>a monoozonide</td>
<td>-</td>
</tr>
</tbody>
</table>

**TABLE 9**

Product Distribution of Reactions with cis- and trans-Cyclodene

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Reagent</th>
<th>Moles/Mole of Olefin</th>
<th>% Conversion</th>
<th>Addition Product</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cis</td>
<td>Bromine</td>
<td>excess</td>
<td>100</td>
<td>1,6-dibromo-cyclodene</td>
<td>10.5</td>
</tr>
<tr>
<td>Cis and Trans Mixture</td>
<td>Diborane</td>
<td>.14</td>
<td>54</td>
<td>27.5</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>72.5</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>32</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>68</td>
<td>54</td>
</tr>
</tbody>
</table>
cis addition reactions. As Table 7 indicates, addition to the trans double bond predominantly occurs in all of these reactions. This predominance was determined in the following manner. Cis,trans-1,5-cyclocdecadiene has strong absorption bands at 10.29 and 14.24 microns, corresponding to the trans and cis double bonds, respectively. The disappearance of the trans band in the addition product, but not the cis band, indicated that the trans double bond was attacked selectively.

1. Epoxidation

When m-chloroperbenzoic acid was added to an excess of cis,trans-1,5-cyclocdecadiene, gas chromatographic analysis of the resulting epoxide indicated it to be a mixture containing 85-90% of the trans oxide and 10-15% of the cis oxide. The reason such a large uncertainty in product distribution exists is that some of the epoxide was pyrolysed on the gas chromatographic column, causing poor resolution.

This selectivity towards the trans double bond was also found for the epoxidation of cis,trans,trans-1,5,9-cyclododecatriene with one mole of benzoyl peroxide. When two moles of peroxide were added to the triene, the reaction was no longer selective, i.e., the diepoxide product was not exclusively the trans,trans isomer but rather a mixture of trans,trans and trans,cis diepoxide. This loss of selectivity may be due to the strain in the twelve membered ring when two trans epoxy groups are introduced.
Epoxidation is a cis addition reaction since the reaction with a cis olefin yields a cis epoxide. It is obvious that the oxygen addend must approach from one side, since one atom could not add from two sides. However it is possible that the addition could be stepwise, allowing isomerization during the addition. That this does not happen is evidenced by the fact that a cis olefin yields a cis epoxide. So the addition is probably concerted with a symmetrical transition state.

2. Methyleneation

The methylation of cis,trans-1,5-cyclodecadiene with methylene iodide and zinc-copper couple is highly selective. The cyclopropyl derivative is 97% trans. The yield for the reaction after 23 hours was only 48%. This low yield was due in part to the conversion of cis,trans-1,5-cyclodecadiene to divinylcyclohexane, a thermal decomposition product. Methylation has been reported to be selective for cis,trans,trans-1,5,9-cyclododecatriene, the trans double bond reacting preferentially.

The formation of cyclopropyl compounds by this method was at first thought to involve the production of a divalent carbon species. There is now evidence that the reacting
species is an organic metallic compound resembling a Grignard reagent. Again the mechanism is cis and concerted, the evidence coming from the stereochemistry of the products obtained.

3. Diimide Reduction\textsuperscript{36}

This reaction was found to be the most selective of all. The diimide was produced in excess by the oxidation of hydrazine with air, with a copper sulfate catalyst. The extra high selectivity may be due to the fact that the diimide is generated internally which prevents local high concentrations of addition reagent. The reaction progress was followed by gas chromatography and was quenched when all the trans double bond had reacted, i.e., when gas chromatography showed that the cis,trans-1,5-cyclodecadiene was almost all reacted and that the product was almost exclusively cis-cyclodecene. The cis-cyclodecene formed was completely free of the trans isomer. There was about 1% of cyclodecane formed. The high selectivity of this reduction makes it very useful in the production of pure cis-cyclodecene. The mechanism of diimide addition was shown to be cis in the Introduction. This reaction was reported to be selective with cis,trans,trans-1,5,9-cyclo-dodecatriene also, trans double bond being reduced preferentially.\textsuperscript{32}

4. Hydroboration

The reaction of cis,trans-1,5-cyclodecadiene with diborane was also studied with respect to its value as a synthetic tool. However this reagent was not as selective
as the diimide. When the alkylborane was heated with excess propionic acid the products obtained were cis- and trans-cyclocdecene and cyclodecane in the proportions 86:11:3. The yield of products was 70%. The reaction of diborane with olefins is a cis addition reaction, involving a four-center transition state. The alkylborane

\[
\text{C} + \text{B}_2\text{H}_6 \rightarrow \text{C} \rightarrow \text{B} 
\]

product formed by reacting diborane to excess cyclodecadiene or cyclodecene is a dialkylborane rather than the trialkylborane obtained with most olefins. Cyclohexene is another olefin which does not form a trialkylborane. The reason for these olefins forming only dialkylboranes is the steric strain that would be introduced with the third alkyl group.

The structure of the cyclodecylborane was not determined by a degradative study of the alkylborane product. It is the conclusion drawn from the fact that when sufficient diborane had been generated to form tricyclocdecylborane with all the cyclodecene present, approximately one-third of the olefin remained unreacted. For a normal hydroboration reaction the balanced equation is found below.

\[
\text{When mixtures of cis- and trans-cyclocdecene (obtained }
\]

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by elimination of p-toluenesulfonic from cyclodecyl tosylate) were reacted with diborane (Table 9), the relative amount of trans-cyclodecene is seen to decrease, indicating a selectivity of diborane for the trans double bond. An interesting result is that in one case the total amount, not just the relative percentage, of cis-cyclodecene is greater at the end of the reaction than at the beginning. This is due to the fact that hydroboration is a reversible reaction. However, it cannot be concluded that elimination takes place in such a way as to produce only cis-cyclodecene. When a mixture of 90% cis- and 10% trans-cyclodecene was reacted with diborane, the amount of the trans isomer increased slightly until the amount of cis-cyclodecene was reduced to about that of trans-cyclodecene.

An explanation of the above phenomenon is as follows. Cis- and trans-cyclodecene form a single alkylborane. The resulting substituted cyclodecane has several different conformations (as does cyclodecane itself). Depending on the conformation of the carbon atoms to which the boron and hydrogen are connected, different olefins
are formed with the presumably cis elimination of boron and hydrogen. When there is a large excess of cis-cyclodecene over trans-, more cis-cyclodecene is reacting and the reverse reaction, elimination, causes the amount of trans-cyclodecene to increase. When present in about equal amounts, the trans reacts preferentially causing the amount of cis-cyclodecene to increase due to the elimination reaction.

One point conflicting with this interpretation is that with cis,trans-1,5-cyclodecadiene more than one isomer of cyclodecadiene (cis- and trans-1,4-, 1,5-, and 1,6-cyclodecadienes) would be expected with the elimination of boron and hydrogen. These isomers are not detected by gas chromatography. It is possible that they are not formed, or that they are formed in very small amounts, or that they are formed but not resolved on the gas chromatograph with the columns employed.

5. Catalytic Hydrogenation

Catalytic hydrogenation, like hydroboration, was studied not only with respect to the selectivity of the reaction, but also as a possible synthetic route to pure cis-cyclodecene. The synthetic potential of this reaction is not completely clear, although it is definitely not as good as diimide reduction. The reaction was unintentionally allowed to proceed too long. The reduction products obtained were cis-cyclodecene and cyclodecane in the ratio 77:23. Since no trans-cyclodecene was obtained it is possible that if the reaction had been stopped sooner cis-
cyclodecene might have been the only product. However the conversion of \textit{cis,trans}-1,5-cyclodecadiene was only 93\%, and its presence would be undesirable in the \textit{cis}-cyclodecene product. With diimide there is a 97\% conversion of the diene with only 1\% of cyclodecane formed. The addition of hydrogen in this experiment is 81\% to the trans double bond and 19\% to the cis.

Doubt has recently arisen as to the stereochemistry of catalytic hydrogenation. In some cases the addition of hydrogen is \textit{cis} and in other cases \textit{trans}. This is due to the stepwise addition of the hydrogen. However the adsorption to the catalyst has been shown to be \textit{cis}.\textsuperscript{41} \textit{Cis} addition of other reagents studied takes place selectively at the trans double bond in \textit{cis,trans}-1,5-cyclodecadiene. The trans double bond is thus more readily attached to the catalyst, and it is hydrogenated selectively, no matter what the overall stereochemistry of the hydrogenation is. The selectivity depends on the adsorption process being the rate controlling step for the hydrogenation.

6. 

\textbf{Selectivity of Cis Addition}

Similar results have been found for \textit{cis,trans}-1,5-cyclodecadiene and for \textit{cis,trans,trans}-1,5,9-cyclododecatriene when they are reacted with \textit{cis} addition reagents. Trans addition reagents have been found to be non-selective toward \textit{cis,trans,trans}-1,5,9-cyclododecatriene. The trans addition reactions with \textit{cis,trans}-1,5-cyclodecadiene lead to transannular products. From these products the
selectivity of initial attack is not easily determined. However, extensive degradative studies of the bromination reaction have led to the conclusion that bromine does not selectively attack the trans double bond in cis,trans-1,5-cyclodecadiene.

The fact that the trans double bond is less stable than the cis in the ten membered ring could possibly account for the selectivity of certain reagents for the trans double bond. But when the same selectivity is found with cis,trans, trans-1,5,9-cycloododecatriene where the trans double bond is presumably more stable, it must be concluded that the selectivity is not due to the relative stabilities of the double bonds but rather to the mechanism of addition of the reagent involved.

In the transition state of an olefin reacting with a cis addition reagent, there is a difference of energies due to eclipsing interactions with the cis and trans olefins. The transition state of a concerted, cis addition to cyclic cis and trans olefins can be represented by the figures below. When the cis double bond

\[
\begin{align*}
\text{cis,trans-1,5-cyclodecadiene} & \\
\text{cis,trans-1,5,9-cycloododecatriene} & \\
\end{align*}
\]

is attacked by a cis addition reagent, the mutual interference of the cis olefin substituents increases as the
bond angles contract from $120^\circ$ in the olefin toward the tetrahedral angle.\textsuperscript{32,42} These two references suggest that the normal tetrahedral angle is formed in the transition state. However the transition state does not represent an eclipsed ethane conformation, but rather a cyclobutane conformation (in the case of epoxidation and methylenation a cyclopropane conformation). In all three of these cases the cis olefin substituents are more highly eclipsed in the transition state than in the olefin. Models show that the eclipsed ethane would have the greatest eclipsing, followed by cyclobutane, cyclopropane, and cis alkene, in order of decreasing eclipsing. This observation does not change the argument that selectivity is due to higher eclipsing in the transition state, but does show that the eclipsing effect is not as great as stated earlier.

The selectivities of the foregoing reactions are quite high, even though there was not an excess of cis, \textit{trans}-1,5-cyclodecadiene in these reactions. The relative proportion of addition to the trans double bond would have been even higher if a large excess of the diene had been used. When one equivalent of addition reagent is added per mole of diene, the relative concentration of cis double bonds becomes much greater than that of the trans double bonds as the reaction nears completion, with the result that more cis addition product is formed than would have been if the relative amounts of cis and trans double bonds had been kept more in line by using a large excess of the
diene.

B. Reactions Yielding Transannular Products

1. Bromination

(a) Cis-cyclodecene

Bromine addition to cyclodecene has been studied carefully by Sicher and coworkers. A transannular reaction is reported with cis-1,6-dibromocyclodecane being formed in 17% yield from cis-cyclodecene and trans-1,6-dibromocyclodecane being formed in 25% yield from trans-cyclodecene. No 1,2-addition products were obtained. It was reported that hydrogen bromide evolution took place during the reaction. The problem was restudied using various bases (sodium acetate, pyridine, and calcium hydride) to prevent the accumulation of hydrogen bromide, in order to determine if the 1,2-dibromide might have been formed initially, only to be isomerized by the hydrogen bromide. The accumulation of hydrogen bromide was stopped, but the transannular product was still obtained.

(b) Cis,trans-1,5-cyclodecadiene

The addition to cis,trans-1,5-cyclodecadiene of bromine in acetic acid takes place in such a manner that only one equivalent of bromine is taken up when excess bromine is added. The infrared spectrum showed that both the cis and trans double bonds reacted. Infrared analysis also showed that the product is a bromo acetate rather than a dibromide. Gas chromatography showed that there are two major products, not completely resolved, of approximately equal amounts.
The bromo acetate was converted to the bromo alcohol with lithium aluminum hydride, and the alcohol was converted to a tosylate. Treatment of the bromo tosylate with lithium aluminum hydride yielded hydrocarbon which was identified on the gas chromatograph by comparison with authentic samples** as being 92.5% cis-decalin and 7.5% trans-decalin.

What is the significance of this product distribution? First of all the fact that decalin is formed is significant. A priori it is possible that perhydroazulene could have been formed or even bicyclo [6.2.0] decane, depending upon where the initial attack and the electron migration took place. The fact that decalin is formed means that initial attack is either at the 2 or the 5 position and the electron migration must result in the formation of a bond between carbon number 1 and carbon number 6.

![Decalin structure](image)

The relative amounts of 92.5% cis- and 7.5% trans-decalin do not account for the fact that two products of approximately the same amount are the main reaction products. Study of models reveal that four isomers of 1-bromo-4-acetoxy decalin can exist: cis-1-bromo-4-acetoxy-cis-decalin, cis-1-bromo-4-acetoxy-trans-decalin, trans-1-bromo-4-acetoxy-cis-decalin, and trans-1-bromo-4-acetoxy-
trans-decalin. The product formed depends upon the configuration of the cis,trans-1,5-cyclodecadiene at the time of initial attack.

Table 10 shows the result of this configurational study. The way the cyclodecadiene model is represented in Table 10 is as follows. First of all the molecule is being examined from the end on which there are four carbon atoms separating the double bonds, with the cis double bond on the right and trans double bond on the left, as illustrated above. The first two columns of Table 10 refer to the direction of the pi-clouds in various configurations. Each of these pi-cloud arrangements can be attained in two ways, each way depending upon whether the hydrogens attached to the trigonal carbons are "up" from the plane of the ring or "down" from the plane of the ring. These possibilities are tabulated in columns 3-6. Columns 7 and 8 tell which decalin is formed upon initial attack at either a cis or a trans double bond and also the relative position of the two substituents to each other. For instance, cis;e-e means that a 1,4-disubstituted cis-decalin is formed and that the substituents are both in the equatorial position.

The mechanism of the reaction is assumed to be almost
### TABLE 10

**Configurational Study of Bromine Addition to cis,trans-1,5-Cyclooctadiene**

<table>
<thead>
<tr>
<th>Double Bond</th>
<th>Cis</th>
<th>H&lt;sub&gt;5&lt;/sub&gt;</th>
<th>H&lt;sub&gt;6&lt;/sub&gt;</th>
<th>H&lt;sub&gt;1&lt;/sub&gt;</th>
<th>H&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Trans Attack</th>
<th>Cis Attack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trans</td>
<td>Cis</td>
<td>down</td>
<td>up</td>
<td>up</td>
<td>up</td>
<td>cis; e-e</td>
<td>cis; e-e</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>up</td>
<td>down</td>
<td>up</td>
<td>up</td>
<td>trans; e-a</td>
<td>trans; e-a</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>up</td>
<td>down</td>
<td>down</td>
<td>down</td>
<td>cis; e-e</td>
<td>cis; e-e</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>down</td>
<td>up</td>
<td>down</td>
<td>down</td>
<td>trans; e-e</td>
<td>trans; e-a</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>down</td>
<td>up</td>
<td>up</td>
<td>up</td>
<td>cis; e-e</td>
<td>cis; e-e</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>up</td>
<td>down</td>
<td>up</td>
<td>up</td>
<td>trans; e-a</td>
<td>trans; e-a</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>down</td>
<td>up</td>
<td>down</td>
<td>down</td>
<td>trans; e-a</td>
<td>trans; e-a</td>
</tr>
<tr>
<td>\</td>
<td>\</td>
<td>up</td>
<td>down</td>
<td>down</td>
<td>down</td>
<td>cis; e-e</td>
<td>cis; e-e</td>
</tr>
</tbody>
</table>

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concerted. The product formed was arrived at by going through the following sequence. For attack at a trans double bond, it was assumed that initial attack was at the lobe of the p-orbital of carbon number 5 that was pointing out of the ring. Formation of the bicyclic system was accomplished by overlap of the lobes of the p-orbitals on carbons number 6 and number 1 that were pointing into the ring. The acetoxy group was attached at the position of the lobe of the p-orbital on carbon number 2 that was pointing out of the ring. Cis attack used the same principle except that initial attack was at carbon number 2.

From the information in Table 10 it can be seen that there is equal chance of forming two isomers, cis-l-bromo-4-acetoxy-trans-decalin and trans-l-bromo-4-acetoxy-cis-decalin. Gas chromatography showed two major products of equal amounts. However these are not the two products, since reduction to hydrocarbon yielded a mixture of 92.5% cis-decalin and 7.5% trans-decalin, What, then, is the answer? Initial attack at the cis or at the trans double bonds yields the same product according to the conformational study in Table 10. However the illustration below shows that there are two isomers of trans-l-bromo-4-acetoxy-cis-decalin. One isomer has the hydrogen on the bromo substituted carbon trans to the hydrogen on the adjacent tertiary carbon. The other isomer has them cis to each other. The former is the isomer formed when initial attack is at the trans double bond and the latter
when initial attack is at the cis double bond. These two isomers have different physical properties and thus can be resolved on a gas chromatograph. These two isomers must then be the two main products of the reaction since they both yield cis-decalin upon removal of the substituent groups. This means also that there is no selectivity of attack at the trans double bond. This explanation is supported by the fact that acetoxylation, which will be discussed next, yields only one 1,4-diacetoxydecalin. In acetoxylation both substituents are the same, so that the same product is obtained whether initial attack is at the cis or at the trans double bond.

2. Acetoxylation

The recent report of Cope that the reaction of cyclooctene with lead tetraacetate leads to a large amount of 1,4-diacetoxy product suggested the possibility that this reagent would also give transannular products with cis,trans-1,5-cyclodecadiene. The mechanism of the reaction has been shown to be ionic, and a bridged intermediate has been proposed.

The reaction with cis,trans-1,5-cyclodecadiene not only gives transannular products but the reaction is much
more vigorous than that reported for cyclooctene. Gas

\[
\begin{align*}
\text{C} & \quad \text{C} \\
\text{Pb(OAc)}_3^+ & \quad \text{C} & \quad \text{C} \\
\text{Pb(OAc)}_2 & \quad \text{HOAc}
\end{align*}
\]

chromatography shows only one product formed and the infrared spectrum shows that both the cis and the trans double bonds react after only one equivalent of lead tetraacetate is added. The treatment of 1,4-diacetoxycyclooctadiene with lithium aluminum hydride produces an alcohol whose spectrum resembles that of 1,4-dihydroxy-cis-decalin.$^{53}$

The mechanism of the transannular addition of lead tetraacetate to cyclooctadiene is the same as that depicted for the transannular addition of bromine. The Pb(OAc)$_3^+$ species adds to either the cis or trans double bond in the manner indicated in the illustration above. The electrons from the double bond across the ring participate to open this bridged intermediate and form a decalin derivative. An acetate ion then completes the transannular addition across the ring, either before, after, or concurrent with the replacement of the Pb(OAc)$_3$ substituent by OAc.

The reaction of lead tetraacetate with cyclooctene at 64° for 2 hrs. gives only a 45% yield of the 1,4-diacetoxycyclooctadiene product. When lead tetraacetate was mixed with cis,trans-1,5-cyclooctadiene in acetic acid, the lead tetraacetate
immediately dissolved with reaction (lead tetraacetate is only slightly soluble in acetic acid) and the temperature rose to about 100°.

What is the explanation for this increased reactivity? With bromination there is no visually observable increase in reactivity when cis,trans-1,5-cyclooctadiene is used instead of a monoene. This is because the reaction is very rapid in both cases. With acetoxylation the reaction is not so rapid for a medium ring monene but is rapid for cis,trans-1,5-cyclooctadiene. The explanation is probably the following. The increased rate of reaction is accompanied by a large evolution of heat, which means that a much more stable system is present in the products than in the reactants. The only change that occurs in this reaction that does not occur in the reaction with cyclooctene is the formation of a bicyclic compound. From the study of the bromination of cis,trans-1,5-cyclooctadiene the bicyclic compound has been shown to be a decalin derivative. Decalin is a far more stable compound than cyclooctane. Decalin has normal dihedral angles whereas cyclooctane has dihedral angles of 116-117° which are considerably distorted from the normal tetrahedral angle of 109° 37'. Thus there is considerable angle strain in the cyclooctane ring which is not present in decalin. When cis,trans-1,5-cyclooctadiene reacts with a trans addition reagent to give a 1,4-disubstituted decalin, there is a large relief of strain.
There is more driving force for transannular effects in addition reactions with cis,trans-1,5-cyclodecadiene than with medium ring monoenes. With the monoenes the driving force is the added stability due to the formation of a more stable carbonium ion across the ring. With cis,trans-1,5-cyclodecadiene this factor is present, but there is the more important factor of relief of strain.

2. Ozonization

The transannular products obtained from bromination and acetoxylation are expected products since these reactions proceed through ionic intermediates. The addition of ozone to cis,trans-1,5-cyclodecadiene was definitely expected to give a normal ozonide. The normal mode of addition of ozone is the initial cis addition of the $O_3$ species which then rearranges to the ozonide. The fact that ozone addition yields transannular products is based on the fact that the addition of either one or two equivalents of ozone gives the same product. The infrared spectra of the reaction mixtures are identical, showing that both the cis and trans double bonds have reacted. The infrared spectrum of the ozone addition product has, in addition to the normal ozonide bands, a strong hydroxyl absorption band. Treatment
of the addition product with zinc in acetic acid yields a product whose infrared spectrum has the characteristics of an aldehyde. The strong hydroxyl band is not present in this spectrum. The carbon, hydrogen analysis of the 2,4-dinitrophenylhydrazone of this aldehyde indicates that there are two carbonyl groups. The treatment of the dicarbonyl compound with dilute neutral permanganate did not give a dicarboxylic acid but rather a product whose infrared spectrum is characteristic of a hydrocarbon.

Further studies on the ozonide by G. Franzen have shown that the solvent, ethanol and chloroform, react with the intermediate ozonide. A suggested sequence for the ozonization is illustrated below. Further analysis of the ozonide product and its reduction product will reveal whether these proposed structures are correct. The trans-annular route of the reaction is well-established in any case.
CHAPTER III
EXPERIMENTAL

Gas chromatographic analyses were carried out with a Barber-Coleman Model 20 instrument equipped with a hydrogen flame detector and a 100 ft. capillary column coated with GE-96 silicone. Infrared spectra were obtained with a Beckman IR-5 spectrophotometer. Capillary melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. The microanalysis reported was performed at L.S.U. by Mr. R. Seab. Ozonization was carried out with a Welsbach T-23 Ozonator.

A. Preparation of cis,trans-1,5-Cyclodecadiene

 cis,trans-1,5-Cyclodecadiene was prepared from the cyclooligomerization of 1,3-butadiene and ethylene through the action of nickel bis-cyclooctadiene. The synthetic process is shown below.

\[
\text{Ni(acac)}_2 + (\text{isobutyl})_2\text{AlH} \rightarrow \begin{array}{c}
\text{Ni} \\
\text{C}
\end{array}
\]

\[
\begin{array}{c}
\text{CH}_2=\text{CH}_2 \\
\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2
\end{array}
\]

1. Preparation of Nickel Acetylacetone

A mixture of 17.0 g. (0.175 mole) of nickel hydroxide, 36.0 g. (0.360 mole) of acetylacetone, and 500 ml. of benzene, in a 1 l. flask equipped with a Dean-Stark water trap, was refluxed for one hour, during which time more

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than 3 ml. of water was collected. After the solution had been refluxed overnight a residue which remained was filtered from the deep green solution. The residue, unreacted nickel hydroxide, weighed 10 g., corresponding to 19.4 g. (0.075 mole) of nickel acetylacetone in the benzene solution. The infrared spectrum of the benzene solution shows strong absorption at 6.30, 6.60, and 7.15 microns.

2. Preparation of Nickel Cyclooctadiene

To the benzene solution obtained above was added 40 g. (0.43 mole) of 1,5-cyclooctadiene. The solution was placed in a 3-neck, 1 l. flask, equipped with a stirrer and an addition funnel. The flask was flushed with nitrogen and a slight nitrogen pressure was maintained throughout the reaction. The reaction mixture was then cooled in an ice-water bath. Over a two hour period, 115 g. of a 20% toluene solution of diisobutylaluminum hydride (0.162 mole) was added. The solution was stirred overnight while the reaction vessel was allowed to warm slowly to room temperature. It was apparent at this time that all of the green color of the solution had not disappeared. The reaction vessel was again cooled and 95 ml. more of the diisobutylaluminum hydride solution (0.103 mole) was added. During this addition, a yellow precipitate formed. The solution was cooled to -20°, and the solution was taken off with a filter stick. Residual benzene was removed from the yellow precipitate by evaporation with a nitrogen stream. The yellow needles weighed 7.8 g. (0.0283 mole),
a yield of 21.3% of nickel bis-cyclooctadiene. No physical properties were taken since nickel bis-cyclooctadiene is reported to be sensitive to oxygen.36

3. Preparation of cis,trans-1,5-Cyclodecadiene36

The nickel bis-cyclooctadiene obtained above was placed into a nitrogen flushed, compressed gas cylinder. Into the cylinder was poured approximately 300 g. of liquid butadiene, and the cylinder was charged with ethylene to 450 p.s.i.48 The cylinder was allowed to stand at room temperature. After one week the pressure in the cylinder was only 300 p.s.i., and a strong medium ring diene odor was detected in the small amount of gas that was vented. After three weeks the pressure was still 300 p.s.i. The excess ethylene was bled off, and the liquid contents of the cylinder were separated from the catalyst (apparently destroyed) by filtration. The filtrate weighed 433 g. Gas chromatography revealed that cis,trans-1,5-cyclodecadiene accounted for 77-86% of the product. This large range is due to the thermal instability of cis,trans-1,5-cyclodecadiene above 70°, where it is converted to divinylcyclohexane.36 The operating conditions for the gas chromatograph are 90° for the column and 150° for the flash heater. The peak identified as divinylcyclohexane is 9.6% of the sample mixture. How much of it is in the product is unknown, but the infrared analysis indicates that there is a small amount from absorbance bands at 6.1, 10.1, and 11.0 microns.36 The other products consist of 3.6% n-decatriene, 1.2% of
cis,cis-1,5-cyclooctadiene, and 8.8% of 1,5,9-cyclo-
dodecatriene, mainly the all trans isomer, with a little of the cis,trans,trans isomer.

The divinylcyclohexane peak was identified as the one that grew when the gas chromatograph was operated at higher temperatures. The cyclooctadiene was compared to an authentic sample. The n-decatriene peak was assigned on the basis of being reported as a by-product and on the basis of the expected higher volatility of straight chain compounds. The trans,trans,trans-1,5,9-cyclo-
dodecatriene was based on the difference in the melting points of the isomers, the all trans isomer melting at 34° and the cis,trans,trans isomer melting at -16.8°.

The high boiling material obtained from the distillation consisted of a material that was a solid above 0°. The infrared spectrum of the high boiling material confirms this predominance of the all trans configuration by the strong absorption at 10.29 microns and the fairly weak absorption at the 14.25 microns, which are peaks assigned to the trans and the cis double bonds respectively.

The crude cyclodecadiene was distilled under vacuum, and the fraction distilling between 28.3° and 37.5° (0.8 mm.) was redistilled. The distillate collected at 30.6 - 33.2° (0.95 mm.) was 97% pure by gas chromatographic analysis, containing about 1.5% of both low boiling and high boiling impurities. The infrared spectrum showed strong absorbances at 10.29 and 14.24 microns, corresponding to the trans and cis double bonds respectively.
B. Preparation of cis-Cyclodecene from cis,trans-1,5-
Cyclodecadiene; The Reaction of cis,trans-1,5-Cyclo-
decadiene with Dihydrazine²⁹

In a 5 l. 3-neck flask 204 g. (1.5 moles) of undis-
tilled cis,trans-1,5-cyclodecadiene product and 441 g.
(7.5 moles) of 85% hydrazine hydrate were dissolved in
two liters of 95% ethanol. Copper sulfate (2 g.) was
added; the solid turned brown almost immediately upon
addition. Air was bubbled through the reaction mixture
vigorously and a condenser was used to prevent the loss
of material in the air stream. The reaction vessel was
immersed in a water bath in order to keep it at room
temperature.

The reaction progress was followed by gas chromato-
graphy. After 6 hr., the reaction was over 90% complete,
and after 8 hr., gas chromatography showed a trace of
cyclodecane and more than 95% reduction. After the air
stream had been stopped, the reaction mixture was diluted
with 2 l. of water, and the resulting solution was
extracted with four 400 ml.-portions of petroleum ether.
The ether extracts were washed with 125 ml. of 2 M hydro-
chloric acid, then with water. The extracts were dried
over magnesium sulfate, and the solvent was removed on
a rotary evaporator, leaving a residue of 144.4 g., a
73% yield of cyclodecene. Extraction of the product
from the alcohol-water solution was evidently incomplete.
The crude product was distilled at 6.4 mm and the middle
cuts were redistilled twice on a packed column, with a
high reflux ratio. A small cut, distilling at 61.0 -
62.3° (5.5 to 6.1 mm), was found to be 98+% pure cis-cyclo-
decene. Gas chromatography showed that there was no trans-
cyclodecene and less than 1% of cyclodecane in the product.

C. Reaction of cis-Cyclooctene with Bromine

1. In Acetic Acid with Sodium Acetate

To a solution of 3.003 g. (0.022 mole) of cis-cyclooctene
and 2.03 g. of sodium acetate in 50 ml. of acetic acid,
5.3 g. of bromine (0.033 mole) in 50 ml. of acetic acid
was added during 40 min. The reaction vessel was cooled
in an ice-water bath during the addition. The contents
were stirred for 5 min. more after the addition of all
of the bromine. Evolution of hydrogen bromide was not
observed. The excess bromine was consumed with sodium
thiosulfate. Water (100 ml.) was added to the acetic
acid solution, and the resulting solution was extracted
4 times, each with 50 ml. of pentane. The pentane extracts
were washed with sodium bicarbonate and then with water.
The extracts were dried over magnesium sulfate and the
solvent was removed on a rotary evaporator, leaving 6.0 g.
of residue. Some of the residue was a white solid, so the
residue was recrystallized from aqueous methanol to yield
0.682 g. of pure cis-1,6-dibromocyclooctene (10.5% yield)
with a sharp melting point at 93°. The literature value
is 93-94°.36 A potassium bromide pellet was made with
the 1,6-dibromide and the infrared spectrum in the finger-
print region (11-16 microns) is as follows: 11.30 microns,
medium to weak; 11.95, medium; 12.48, 12.74, weak; 13.39,
13.69, medium to strong; 14.28, strong; and 15.09, medium.
The liquid product (1.077 g, .00361 mole), remaining after removal of the solid, was dissolved with 2 g. of potassium iodide in 50 ml. of methanol, and the solution was refluxed overnight. The resulting iodine solution took up 6.0 ml. of 0.10 N sodium thiosulfate, which is equivalent to 8.3% of 1,2-dibromocyclodecane. A second bromination experiment yielded only 5.6% of the 1,2-dibromide. The infrared spectrum of the reaction product mixture indicates the presence of a bromoacetate.

2. In Carbon Tetrachloride with Pyridine

Into a 3-neck, 500 ml. flask, equipped with a stirrer and an addition funnel, was put 3.328 g. (0.0241 mole) of cis-cyclodecene and 1.95 ml. (0.0241 mole) of pyridine in 100 ml. of carbon tetrachloride. A solution 5.8 g. (0.0362 mole) of bromine in 50 ml. of carbon tetrachloride was added in 45 min. to the olefin solution which was maintained between -15° and -20°. No hydrogen bromide was evolved. The solution was allowed to warm to room temperature during an additional hour of stirring. Because gas chromatography showed some cyclodecene remained, 2.0 g. more of bromine was added to the solution at -10° to -15°. The pyridine-bromine complex was destroyed with sodium thiosulfate, and the carbon tetrachloride solution was washed with water and dried over magnesium sulfate. The solvent was removed on a rotary evaporator. The infrared spectrum was not the same as that of the product mixture obtained when the bromination was run in acetic acid. The product obtained from this experiment exhibited very strong
absorptions at 12.8 and 13.1 microns. Treatment of 0.779 g. of the product mixture with potassium iodide liberated only a small amount of iodine. Treatment of another portion of the product, 3.240 g., in 50 ml. of carbon tetrachloride with hydrogen bromide at 0° had no effect on the product mixture except that the trace of pyridine that remained was precipitated as pyridinium bromide.

3. In Carbon Tetrachloride with Calcium Hydride

In a 3-neck, 200 ml. flask equipped with a stirrer and an addition funnel was put 3.141 g. (0.0228 mole) of cis-cyclodecene in 100 ml. of carbon tetrachloride along with 0.944 g. (0.0228 mole) of calcium hydride powder. The calcium hydride did not dissolve in the carbon tetrachloride but was suspended in the solution. A solution of 5.5 g. of bromine in 50 ml. of carbon tetrachloride was added during one hour, the reaction vessel being maintained at -10° throughout the addition. The excess bromine disappeared as the flask was warming to room temperature. When the reaction flask was opened, hydrogen bromide came out profusely. Gas chromatography showed no remaining olefin. The calcium hydride was removed by filtration, and the solution was washed with water and dried over magnesium sulfate. The carbon tetrachloride was removed on a rotary evaporator. The calcium hydride particles, which appeared to have become coated with calcium bromide, may have become deactivated and incapable of removing hydrogen bromide. The infrared spectrum of the liquid reaction product was identical to that obtained when
pyridine was used instead of calcium hydride.

4. **With Bromine-pyridinium Hydrogen Sulfate**

Just before use, a solution containing 0.08 mole of bromine was prepared. The solution contained 12.8 g. of bromine, 12.8 g. of pyridine, 16 ml. of concentrated sulfuric acid, 50 ml. of chloroform, and enough acetic acid to bring the total volume to 180 ml.

To a solution of 2.769 g. (0.0200 mole) of cis-cyclodecene in 50 ml. of chloroform was added in 15 min., 45 ml. of the brominating solution (0.02 mole) prepared above. The reaction vessel, a 3-neck, 300 ml. flask, was cooled in an ice-water bath during the addition. When all the bromine had been added, the solution was allowed to warm up. There was a light green color to the solution. The reaction mixture was diluted with 100 ml. of water, and extracted three times, each with 50 ml. of petroleum. The extracts were washed with water, sodium bicarbonate solution, and water again. The extracts were dried over magnesium sulfate, and the solvent was removed on a rotary evaporator. A small sample, approximately 1 g., of the liquid residue was treated with potassium iodide in methanol. After several hours of refluxing, only a small amount of iodine was liberated; 5 ml. of 0.1 N sodium thiosulfate was required for titration. This result corresponds to less than 10% of a 1,2-dibromide.

D. **Reaction of cis,trans-1,5-Cyclodecadiene with Bromine-Pyridinium Hydrogen Sulfate**

The study of the reaction of **cis,trans-1,5-cyclo-**
decadiene with bromine involves first of all the addition reaction, which is followed by a series of degradative reactions chosen to reveal the structure of the addition product. The study is illustrated in the scheme below:

1. Reaction with Bromine

Into two 3-neck, 250 ml. flasks, equipped with stirrers and addition funnels were put separate solutions of cis-, trans-1,5-cyclodecadiene (2.72 g., .020 mole) in chloroform (50 ml.). To one solution was added 45 ml. (0.02 mole); and to the other 90 ml. (0.04 mole) of the brominating solution prepared in the last section, in 45 and 90 min. respectively. The solutions were worked up separately and analogously to the reaction with cis-cyclooctene. The infrared spectra of the two product mixtures were identical, the absorption bands for the cis and trans double bonds of the starting diene both being absent. There is a strong carbonyl band at 5.79 microns. Analysis by gas chromatography showed two products in about equal amounts from each preparation.

2. Reduction of 1-Bromo-4-acetoxydecalin with Lithium
Aluminum Hydride

An ether solution of 0.152 g. (4 mmoles) of lithium aluminum hydride in 25 ml. of anhydrous ethyl ether was prepared by refluxing mixture for 1 hr. in a 3-neck, 100 ml. flask equipped with a condenser with drying tube, an addition funnel, and a magnetic stirrer. The ether solution (actually a gray slurry) was cooled, and 1.2 g. of the bromoacetate (5.2 mmoles) in 10 ml. of ether was added dropwise with stirring. After addition, the mixture was refluxed for 30 min. The reaction vessel was then cooled in a water bath while 95% ethanol was added to destroy the excess lithium aluminum hydride. The alkoxide product was then hydrolyzed with 1 M hydrochloric acid. Petroleum ether (50 ml.) was added, and the organic layer was washed with water, sodium bicarbonate, and water again. The organic solution was dried over magnesium sulfate and concentrated by rotary evaporation to 0.9 g. of residue, a 91% yield if pure bromo alcohol. The residue was part solid and part liquid. Infrared analysis showed the disappearance of the carbonyl absorbance and the presence of an hydroxyl band at 3.09 microns. Gas chromatography showed two products in the same proportion as the original bromo acetate.

3. Conversion of the 1-Bromo-4-hydroxydecalin to the 1,4-Bromo-4-tosyloxydecalin

The bromo alcohol obtained above (0.9 g., 4.8 mmoles) was dissolved in 10 ml. of pyridine. p-Toluenesulfonyl chloride (1.5 g., 719 mmoles) was added, and the resulting
solution was allowed to stand overnight at room temperature. The solution was diluted with 100 ml. of water and extracted 4 times, each with 50 ml. of petroleum ether. The extracts were washed 3 times with water, dried over magnesium sulfate, and concentrated on a rotary evaporator. The residue of bromo tosylate weighs 1.5 g.

4. Degradation of the Bromotosyloxydecalin to Decalin

Tetrahydrofuran was dried in the following way:
1) stored over clean sodium for two days, 2) distilled over sodium, 3) treated with lithium aluminum hydride for ten minutes and filtered. The filtrate, which was then used, still contained a small amount of water. A tetrahydrofuran-lithium aluminum hydride slurry was prepared by refluxing a mixture of tetrahydrofuran (25 ml.) with lithium aluminum hydride (0.380 g., 10 mmoles) in a 100 ml. round bottom flask equipped with a magnetic stirrer and a condenser to which was attached a drying tub. The crude bromo tosylate (15 g., 4.4 mmoles) described above was added to the hydride slurry. The mixture was refluxed for 24 hr., and it was then worked up in exactly the same manner as was used in the conversion of the bromo acetate to the bromo alcohol. When the sample was analysed by gas chromatography and compared with authentic samples, the lower boiling products were identified as cis- and trans-decalin. The gas chromatograph showed that only a small amount of decalin was formed, most of the bromotosyloxydecalin remaining unreacted. The relative amounts of the
E. Epoxidation of cis,trans-1,5-Cyclodecadiene

A solution of 13.6 g. (0.1 mole) of cis,trans-1,5-cyclodecadiene in 10 ml. of ethyl acetate was prepared in a 200 ml. 3-neck flask equipped with a stirrer and a dropping funnel. A second solution of 17.2 g. (85% assay, 0.085 mole) of m-chloroperbenzoic acid in 60 ml. of ethyl acetate was added dropwise to the first solution during 30 min. The reaction flask was cooled in a water bath at 25° during the addition, and stirring was continued for 5 min. after addition was complete. Petroleum ether (100 ml.) was added to the reaction mixture in a 500 ml. separatory funnel and the solution was washed 3 times with sodium bicarbonate to separate the m-chlorobenzoic acid. The organic layer was then washed with water, dried over magnesium sulfate, and concentrated on a rotary evaporator. The residue weighed 15.2 g. The infrared spectrum showed some ethyl acetate remaining. The cis absorption band, at 14.25 microns, was much stronger than the trans absorption band at 10.29 microns. Gas chromatography showed the epoxide coming out in two sets of peaks, one of which had the appearance of a pyrolysis peak. The fact that the two sets of peaks are not resolved completely made measurement of the relative amounts of the cis and trans adducts difficult. The best estimate is 85-90% trans-epoxide and 10-15% cis-epoxide. Distillation at 0.45 mm yielded 10.5 g. of epoxide boiling from 49-50°, an 81.5% yield based on the amount of m-chloroperbenzoic
acid. Some cis,trans-1,5-cyclodecadiene (3.3 g.) was recovered, and 1 g. of material did not distill. The material balance is 99%.

F. Methylenation of cis,trans-1,5-Cyclodecadiene

Into a 150 ml. flask, equipped with a magnetic stirrer and a condenser with drying tube, was put 8.6 g. (0.132 g. at.) of zinc-copper couple 40 ml. of anhydrous ether. A small crystal of iodine was added, and the solution was stirred for ten minutes. Then 18 g. (.132 mole) of cis, trans-1,5-cyclodecadiene (90% pure) and 35 g. of methylene iodide were added. The reaction mixture was stirred (magnetic stirrer) and refluxed for 23 hr., after which time the white zinc iodide and the copper metal color were quite apparent. The solution was filtered; the filtrate was hydrolysed with 1 M hydrochloric acid and diluted with 150 ml. of water. The solution was extracted with three 75 ml. of petroleum ether, and the extracts were washed with water, dried over magnesium sulfate, and concentrated on a rotary evaporator. Analysis by gas chromatography showed one peak, with a very small shoulder (est. <3%). Since the infrared spectrum shows that the cis absorption band is very strong and the trans band almost non-existent, the larger gas chromatography peak was assigned to the adduct. Distillation of the residue at 1.5 mm. gave 6.1 g. boiling below 38°, 7.5 g. from 38-40°, 2.9 g. from 40-52°, and 3.8 g. of high boilers. By considering the gas chromatogram of each cut, the yield of bicyclo [8.1.0] undec-5-ene is calculated to be 8.5 g., a 48% yield. There was
very little \textit{cis,trans}-1,5-cyclodecadiene remaining. Gas chromatography showed that much of it was converted to divinylcyclohexane.

G. \textit{Hydroboration of cis,trans-1,5-Cyclodecadiene and Subsequent Treatment with Propionic Acid}

A 3-neck, 200 ml. flask was equipped with a stirrer and a dropping funnel; the flask was flushed with nitrogen, and a small flow of nitrogen was maintained throughout the subsequent reaction. Into the flask was put 27.2 g. (0.20 mole) of crude \textit{cis,trans}-1,5-cyclodecadiene (about 80\% \textit{cis,trans}-1,5-cyclodecadiene and 20\% mostly cyclododeca-trienes) and 1.9 g. (0.05 mole) of sodium borohydride in 55 ml. of diglyme (diethylene glycol dimethyl ether). A solution of 9.5 g. (0.067 mole) of boron trifluoride etherate in 25 ml. of diglyme was added during 1.5 hr. at room temperature. The reaction mixture was stirred for an additional hour. Gas chromatography revealed that only 2/3 of the cyclodecadiene had reacted. An additional 0.60 g. of sodium borohydride was added to the solution, and an additional 3.2 g. of boron trifluoride etherate in 10 ml. of diglyme was added dropwise. Gas chromatography showed that more than 90\% of the cyclodecadiene had reacted. At this point, 29.5 g. (0.41 mole) of propionic acid was added cautiously. The resulting mixture was refluxed for 2.5 hr. Petroleum ether (300 ml) was added to the solution, which was then washed five times with water to remove the propionic acid and diglyme. The petroleum ether solution was dried over magnesium
sulfate, and the solvent was removed on a rotary evaporator. The residue distilled at 63-66° (6.5 mm.), yielding 19.0 g. of product which gas chromatographic analysis showed to be 86% cis-cyclooctene, 11% trans-cyclooctene, and 3% cyclooctane.

H. Hydroboration of trans- and cis-Cyclooctene Mixture

The selectivity of hydroboration for the trans double bond in the ten-membered ring was further studied by hydroboring a mixture of cis- and trans-cyclooctene.\textsuperscript{53} This mixture was obtained by the following reaction sequence. First cyclooctanol was formed by hydroboring cis-cyclooctene and destroying the alkylborane with basic peroxide solution. The alcohol was then converted to the tosylate, which upon elimination gave a mixture of trans- and cis-cyclooctene in the ratio 3 to 1.

![Chemical Reaction Diagram]

1. Preparation of Cyclooctanol\textsuperscript{54}

A 3-neck 2 l. flask was equipped with a stirrer and a dropping funnel. The flask was flushed with nitrogen, and a small flow of nitrogen was maintained throughout the hydroboration. Into the flask was put 69 g. (0.50 mole)
of 92% cyclodecene (80% cis-cyclodecene, 12% trans-cyclodecene, and 8% cyclodecane)\(^5\), 9 g. (0.24 mole) of sodium borohydride and 800 ml. of diglyme. Boron trifluoride etherate, 42.5 g. (0.30 mole), in 200 ml. of diglyme was added dropwise. The reaction mixture was stirred for an hour after the addition was complete. Then 110 ml. of 3 M potassium hydroxide was added slowly, followed by the addition of 72 ml. of 30% hydrogen peroxide. The temperature of the reaction mixture rose to about 35-40\(^\circ\) during the addition of the peroxide. The reaction mixture was filtered, and the filtrate was extracted 4 times, each with 150 ml. of petroleum ether. The extracts were washed 4 times with water and dried over magnesium sulfate. The solvent was removed on a rotary evaporator, and distillation yielded 48 g. (0.31 mole, 62% yield) of cyclodecanol, b.p. 75-79\(^\circ\) (0.3 mm.).

2. Conversion of Cyclodecanol to Cyclodecyl Tosylate and Subsequent Elimination to cis- and trans-Cyclodecene

Into a 500 ml. 3-neck flask was placed 15 g. (0.097 mole) of cyclodecanol in 30 ml. of pyridine. To this solution was added 20 g. (0.11 mole) of p-toluenesulfonyl chloride. Dimethyl sulfoxide (100 ml.) was added, and the solution was allowed to sit at room temperature for 3 hours. The mixture was then heated to 50\(^\circ\) for 3 hours to speed up the elimination, which gas chromatography showed to be taking place at a slow rate but yielding a high percentage of trans-cyclodecene. The mixture was allowed to cool to
room temperature and to stand overnight (10 hr.). Petroleum ether (200 ml.) was added to the solution, which was washed with water until gas chromatography showed no dimethyl sulfoxide or pyridine remaining (about 6 washings). The petroleum ether solution was dried over magnesium sulfate, and the solvent was removed on a rotary evaporator, leaving 16.0 g. of crude material. Distillation yielded 9.9 g. (77% yield) of cyclodecene which gas chromatography showed to be 27.5% cis and 72.5% trans. The infrared spectra of the crude material and the distillate are quite different, which indicates that most of the elimination took place during the distillation. The infrared spectrum of the crude material shows the presence of the tosylate group and the absence of trans-cyclodecene, which absorbs strongly at 10.3 microns. The spectrum of the distillate is a composite of the spectra of cis- and trans-cyclo-cyclodecene.

3. Hydroboration

The 9.9 g. (0.072 mole) of cyclodecene obtained by the elimination reaction above was placed in a 250 ml. 3-neck flask equipped with a stirrer and a dropping funnel. Sodium borohydride (0.567 g., .015 mole) was added to the solution; the flask was flushed with nitrogen, and a small nitrogen flow was maintained throughout the reaction. The reaction mixture was cooled in an ice-water bath, and 2.81 g. (0.020 mole) of boron trifluoride etherate in 15 ml. of diglyme was added dropwise over a 20 min. period. Gas chromatography showed that the unreacted cyclodecene was

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61% cis and 39% trans.

When the reaction was repeated with another portion of cyclodecene, similar results were obtained. The quantities of reagents were 6.2 g. (45 mmoles) of cyclodecene (68% trans, 32% cis), 0.19 g. (5 mmoles) of sodium borohydride and 0.97 g. (3.07 mmoles) of boron trifluoride. Gas chromatography showed that the unreacted olefin was 54% trans- and 46% cis-cyclodecene.

I. Catalytic Hydrogenation of cis,trans-1,5-Cyclodecadiene

Into a hydrogenating bottle were put 27.2 g. (0.20 mole) of crude (about 80%) cis,trans-1,5-cyclodecadiene, 50 ml. of absolute ethanol, 20 mg. of palladium/carbon catalyst, and 0.5 ml. of pyridine. The bottle was connected to a Parr hydrogenator, flushed with hydrogen, and shaken under a hydrogen pressure of 39 p.s.i. In the first hour the pressure dropped 5 p.s.i. The shaking was continued overnight (18 hr.), and the total pressure drop for the reaction was 12 p.s.i. The catalyst was removed by suction filtration through a fine fritted glass filter. Gas chromatography showed that the relative percentages of products were 77% cis-cyclodecene, and 23% cyclodecane. No more than a trace of trans-cyclodecene was detected.

J. Ozonization of cis,trans-1,5-Cyclodecadiene

I. Calibration of Ozonator

The conditions for ozonization were as follows for all the ozonization experiments reported here. A Welsbach model T-23 Ozonator was used and the flow gas was oxygen.
The pressure regulator was set at 8 p.s.i., the flow rate was maintained at 0.04 cu. ft./min., and the voltage was set at 85 volts.

The rate of ozone production was determined as follows. A solution of 5 g. of potassium iodide in 75 ml. of water was put into a 150 ml. test tube. The filter stick delivery tube was flushed with the ozone-oxygen stream for two minutes and then it was immersed into the potassium iodide solution for 60 seconds. The solution was acidified with 10% sulfuric acid and titrated with 0.1 N sodium thiosulfate. The standardization was repeated for a 30 sec. time period, and the results checked within 1%. This result is considered acceptable since there is some error in the exact time of the ozonization. The oxygen stream was found to contain 1.63 mole % ozone. The time required for addition of 0.1 mole of ozone at these operating conditions is 114 min.

2. Ozonization of cis,trans-1,5-Cyclodecadiene

Into a 150 ml. test tube were placed 7.5 g. (0.55 mole) of cis,trans-1,5-cyclodecadiene (92.5% pure) and 20 ml. each of chloroform and 95% ethanol. The test tube was immersed in Dewar flask containing Dry Ice and acetone. The delivery tube was flushed for two minutes and then the ozone-oxygen stream was bubbled through the cyclodecadiene solution for 57 min. (0.05 mole of ozone). The solvent was removed on a rotary evaporator. Gas chromatography showed that about 10% of the cyclodecadiene had not reacted. The reaction was repeated with exact quantities
of organic reagents. This time the ozonization was carried on for 115 minutes (0.1 mole of ozone). The infrared spectra of this ozonide and of the previous one (half as much ozone added) are identical. The absorption bands due to both the cis and trans double bonds are absent. In addition to the usual ozonide absorption bands, there is a strong absorption at 2.92 microns. Both products react with potassium iodide solution to liberate iodine.

2. Reduction of Ozonide of cis,trans-1,5-Cyclodecadiene With Zinc In Acetic Acid

The ozonide resulting from 0.05 mole of cyclodecadiene was dissolved in 50 ml. of water and 50 ml. of acetic acid in a 250 ml. erlenmeyer flask and stirred with a magnetic stirrer. Zinc dust (10 g) was added, and an exothermic reaction took place immediately. Stirring was continued for 20 min. The solution was filtered, diluted with 200 ml. of water, and extracted with four 100 ml.-portions of petroleum ether. The extracts were washed with water and dried over magnesium sulfate. The solvent was removed on a rotary evaporator. The infrared spectrum showed the disappearance of the hydroxyl band and the appearance of carbonyl absorption (5.80 microns) and aldehydic hydrogen absorption (3.68 microns). Part of this product (0.9 g.) was treated with 1.2 g. of potassium permanganate in 100 ml. of water. The solution was stirred for 30 min., and then was filtered. The solution was strongly acidified with hydrochloric acid and extracted with petroleum ether. The solution was dried over magnesium sulfate and the
sovent was removed on a rotary evaporator. The infrared spectrum of the product showed no functional group, but had the appearance of a hydrocarbon spectrum. The rest of the carbonyl product was converted to its 2,4-dinitrophenylhydrazone derivative, which upon recrystallization from 95% ethanol decomposed at 93-98°. Anal. Calc. for C_{24}H_{27}N_{8}O_{9}: C, 50.0%; H, 4.7%. Calc. for C_{23}H_{23}N_{8}O_{8}Cl: C, 42.0%; H, 3.5%. Found: C, 47.3%; H, 5.1%.

K. Acetoxylation of cis,trans-1,5-Cyclodecadiene

l. Reaction of cis,trans-1,5-Cyclodecadiene with Lead Tetracetate

In a 100 ml. flask equipped with a condenser was placed 6.70 g. (0.50 mole) of cis,trans-1,5-cyclodecadiene in 50 ml. of acetic acid. Lead tetracetate (22.2 g., 0.05 mole) was added, and an extremely exothermic reaction took place (the temperature rose to 95° in less than a minute). The reaction flask was put into a water bath to cool. The solution was diluted with 250 ml. of water, and the solution was extracted 3 times with 100 ml. of petroleum ether. The extracts were washed with water, sodium bicarbonate solution, and water again. The extracts were dried over magnesium sulfate, and the solvent was removed on a rotary evaporator. The infrared spectrum of the residue showed that both the cis and trans double bonds had reacted. The spectrum is characteristic of an ester.

The reaction was repeated on a 0.025 mole scale with temperature control. The lead tetracetate was suspended in 25 ml. of acetic acid. The cyclodecadiene, dissolved
in 25 ml. of acetic acid, was added to the suspension, the temperature being maintained below 20°. By the time the addition was complete, all but a trace of the lead tetraacetate had disappeared. The reaction mixture was stirred for an additional 2 hours and then worked up in the same manner as the first reaction. The infrared spectrum of the product was completely identical to that of the first product. Gas chromatography showed only one peak for the reaction product.

2. Reduction of 1,4-Diacetoxydecalin with Lithium Aluminum Hydride

The diacetoxy product (0.025 mole) from the second acetoxylation reaction, in 50 ml. of anhydrous ether, was added dropwise to an ether slurry (75 ml.) of lithium aluminum hydride (1.0 g., 0.026 mole). After the addition, the slurry was refluxed for one hour. The reaction was worked up in the same manner as the other lithium aluminum hydride reactions: additions of methanol and acid, extraction, and evaporation of solvent. The infrared spectrum showed that the reaction was not complete. Some carbonyl absorption remained. There was a strong hydroxyl band at 2.92 microns. The spectrum (except for the carbonyl band) resembled the spectrum of 1,4-decalindiol.\(^{53}\)
SUMMARY

In the first part of the dissertation n.m.r. spectra were seen to be influenced strongly by electronic substituent effects. The chemical shifts of the substituted phenols in dimethyl sulfoxide are very well correlated to Hammett's sigma constants. This high correlation is attributed to the interaction between the solvent and the phenolic proton and the consequent susceptibility to substituent effects. In the classification of alcohols, the presence of strong electron-withdrawing groups close to the hydroxy group causes the absence of multiplicity in the hydroxy proton resonance signal.

In the second part of the dissertation addition reactions of cis,trans-1,5-cyclodecadiene and cis- and trans-cyclodecene were studied. Cis addition reagents were found to selectively attack the trans double bond and to yield normal 1,2-addition products. This selectivity is due to the high eclipsing strain in the transition state when the cis double bond is attacked. The two trans addition reactions studied, bromination and acetoxylation, yielded transannular products, 1,4-disubstituted decalins, with no selectivity of attack. Ozonization, which involves initial cis attack, also yields transannular products upon rearrangement and reaction with solvent.
REFERENCES


5 All chemical shifts are relative to internal tetramethylsilane.

6 H.H. Jaffe, Chem. Revs., 53, 191(1952);


9 This is the chemical shift value for one of the nuclear proton peaks. All of the nuclear proton peaks behaved the same.

10 Dyer, op. cit., p. 90.


14 The background for this statistical study may be found in H.D. Brunk, "An Introduction to Mathematical Statistics", Ginn and Company, Boston, 1960, Chapters 8, 10, 12, and 13.


17 Correspondence to Professor J.G. Traynham from Dr. Gordon H. Whitman, of the University of Birmingham, England, about the identity of methylenecyclohexane bromohydrin prompted this investigation.


33 These bands were reported for cis- and trans-cyclo-decene by A.T. Blomquist, R.E. Burge, Jr. and A.C. Sucsy, J. Am. Chem. Soc., 74, 3636(1952).

38 H.C. Brown, p. 106.
41 Obtained from my laboratory partner, John Dehn, who
42 separated the isomers on a preparative gas chromatograph.
47 Butadiene and ethylene obtained from Copolymer, Inc.,
48 Baton Rouge, La.
49 M. Ohno and M. Okamoro, Tetrahedron Letters, 35, 2423
50 (1964).
51 This is the method used for bromination of cyclo-
52 decadiene: Chem. Abs., 59, 11285c.
53 R.D. Smith and H.E. Simmons, Org. Synthesis, 41,
54 72-74.
55 H.C. Brown and K. Murray, J. Am. Chem. Soc., 81,
56 4108 (1959).
57 Obtained from Columbian Carbon Co., Lake Charles, La.
58 H.C. Brown, "Hydroboration", p. 70.
The use of pyridine to selectively poison the catalyst has been described by G. Wilke; information privately communicated to Professor Traynham by W.C. Baird, Sr.
VITA

George Albert Knesel, III was born on June 2, 1939 in New Orleans, Louisiana, where he attended parochial school. After two years at Jesuit High School, he entered St. Joseph Seminary to study for the priesthood, where he received his high school diploma and was graduated "summa cum laude" with an A.A. After deciding to leave the seminary he majored in chemistry in which he received the Bachelor of Science "with high honors" from Southeastern Louisiana College in 1962. He entered graduate school at Louisiana State University where he was a teaching assistant for one year. He was a NASA trainee during the 1963-1965 period. In September, 1965 he began his teaching career at Southeastern Louisiana College.

In August, 1960 he married Darleen Mae Mascair, and he has two daughters, Kimberlyn Ann, 3 years old, and Shelley Renée, 2 years old.


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Dean of the Graduate School

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Date of Examination:

January 11, 1966

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