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The nuclear magnetic resonance analyses of some geometric isomers.

Thomas H. Crawford

University of Louisville

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NAME OF STUDENT: THOMAS H. CRAWFORD

TITLE OF THESIS: THE NUCLEAR MAGNETIC RESONANCE
ANALYSES OF SOME GEOMETRIC ISOMERS

APPROVED BY READING COMMITTEE COMPOSED OF THE
FOLLOWING MEMBERS:


NAME OF DIRECTOR: ________________________________

DATE: May 17, 1961
UNIVERSITY OF LOUISVILLE

THE NUCLEAR MAGNETIC RESONANCE ANALYSES
OF SOME GEOMETRIC ISOMERS

A Dissertation
Submitted to the Faculty
Of the Graduate School of the University of Louisville
In Partial Fulfillment of the
Requirements for the Degree
Of Doctor of Philosophy

Department of Chemistry
By
Thomas Crawford
May, 1961
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T.H.C.
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INTRODUCTION
The research problem presented herein involved the structural determination of several \( \alpha,\beta \)-unsaturated acids and esters. The solution to this problem was sought in the nuclear magnetic resonance (n.m.r.) spectra of these compounds. The n.m.r. approach to structural problems in organic chemistry has been investigated extensively in the past ten years and it has proven to be an extremely powerful tool for this type of analysis.

The data used in the structural determinations are presented in tabulated form, and in the appendix tracings of the original spectra may be found. Each compound is discussed separately with respect to its probable structure and its recorded spectrum. Two brief sections follow the discussion of the spectra. One of these concerns a stereospecific solvent effect and the other relates to the effect of an anisotropic neighboring double bond on proton \( \tau \)-values.

The configurational assignments for the various compounds were made possible by observing the changes in chemical shift for particular protons in different isomers and by comparison of the observed spin coupling constants with those reported in the literature. Almost all of the compounds discussed in this thesis were of such a nature that their spectra could be interpreted on a simple first order basis. In the limited number of cases which involved more complex spectra, some approximations were attempted which made possible the assignment of configuration at several
bonds. In some cases the assignments were not conclusive, but they found strong support in the approximate treatments given the complex splitting patterns.
HISTORICAL
Historical

The purpose of this discussion is to summarize the available information relevant to the studies described in the following sections. Nuclear magnetic resonance effects were first detected in 1945 by two independent groups: Purcell, Torrey and Pound\textsuperscript{1} at Harvard University and Bloch, Hansen and Packard\textsuperscript{2} at Stanford University. These earliest experiments were directed toward the development of a method which could detect environmental changes at the nuclear level. At the time of these investigations perhaps little thought was given to the potential of the method as a tool for structural organic chemistry.

Many workers followed these initial observations with their own contributions but it was not until 1951 that Arnold, Dhamatti and Packard\textsuperscript{3} detected a separation in the resonance frequencies for the three different types of protons in ethanol. The separation between the resonance signals for each of the three protons is referred to as the chemical shift. The realization that such small differences in environment could be detected by the n.m.r. method opened a new avenue of investigation of organic compounds which could tell how the various groups in the molecule were linked together.

The step from the first detection of n.m.r. effects to the differentiation of chemically unlike protons in a molecule spanned only six years. During that relatively
short time, however, the instrumentation had to be greatly refined to make possible the examination of such systems under, what are called today, high resolution conditions. The introduction of high resolution techniques and the accompanying multiplet splitting of the resonance lines required a more thorough investigation of the theoretical concepts underlying the n.m.r. experiment.

Since 1951 many compounds have been examined and numbers of interesting and useful correlations have been made between resonance frequency and structural arrangements. There are several good reviews, \textsuperscript{4,5,6} books \textsuperscript{7,8} and a monograph \textsuperscript{9} all of which facilitate bringing these data together for the analysis of new spectra. The interpretation of spectra, which will lead to a structural assignment, is in many cases reduced to a problem of correlating the peak positions in an observed spectrum with those reported in the literature. It should be pointed out, however, that complicating factors such as complex splitting of the peaks or overlapping of resonance lines may reduce the reliability of simple first order correlations of line position. Such systems may require a rigorous mathematical analysis to achieve a reliable structural assignment.

**Units of Chemical Shift**

Chemical shift data may be presented in several ways. They may be measured directly in cycles per second (c.p.s.) by introducing into the spectrum at known frequencies, side
bands of any desired line.\textsuperscript{10} This may be done by modulating the field with a variable frequency oscillator. The separation between lines in a spectrum is usually measured with respect to some reference material added to the solution directly; this method is referred to as the internal standard method. Some workers have found it desirable to keep the reference material separate from the compound under study by placing the reference in a capillary inside the n.m.r. sample tube. Either method is satisfactory, but recently more workers are adopting the internal standard technique. The most common reference material for this latter method is tetramethylsilane (TMS) which was suggested by Tiers\textsuperscript{11} as a good reference material because the resonance line for all nine methyl hydrogens occurs at very high frequency, generally well beyond the resonance lines of the usual protons examined. Tiers has reported that chemical shift data measured with respect to TMS give good results without extrapolation of the results to infinite dilution. This is somewhat dependent on the system being examined, however.

The $\tau$ unit was suggested by Tiers as an acceptable way to report chemical shift data. The $\tau$ value for any line in the spectrum may be calculated by measuring the separation in c.p.s. between the desired line and the TMS line. This is converted to parts per million (ppm) by dividing the c.p.s. value by the frequency at which resonance
was observed. This is fixed in most spectrometers and is the operating frequency of the radio frequency generator. As indicated the TMS line occurs at high field. It has also been observed that most other protons will experience a resonance condition somewhere over a spread of 10 p.p.m. With this in mind the TMS line was given arbitrarily a value of 10.00, since it will usually be the highest field peak in the spectrum. The $\tau$ value for a given line is taken as the difference between the TMS value, 10.00, and the p.p.m. value for that line. This is satisfactory in another way, too, since the $\tau$ value increases as the spectrum runs from low to high values of field strength.

The $\tau$ unit of chemical shift will be used throughout this paper, except where the literature references use some other system. In such a case the data will be reported in the units selected by those workers.

Analysis of Simple Olefinic Systems

The simplest system one can have for an n.m.r. analysis of cis and trans configurations is a disubstituted ethylene, \( \text{RCH=CHR'} \), where \( \text{R} \) and \( \text{R}' \) differ significantly in the way they influence the magnetic environment of the olefinic protons. If these two protons are different because of their environment, they will experience a resonance condition at different field strengths. Where \( \text{R} \) and \( \text{R}' \) are groups that do not have a spin-spin coupling interaction with these protons, the arrangement may be referred to as an AX system, using the notation suggested by Pople.\(^7\)
If the two protons in this system are labeled $H_A$ and $H_X$, where $H_A$ has a chemical shift different from $H_X$, it is expected that there will be a spin interaction between them. Such a coupling between these nuclei results in splitting the resonance line of each proton into a doublet. Each doublet will be symmetrical provided the difference in chemical shift ($\Delta$) between $H_A$ and $H_X$ is large compared with the separation of peaks in each doublet. This separation between the peaks of each doublet is a measure of the coupling constant ($J$) and is reported in cycles per second. The quantum mechanical considerations of such a system, where $\Delta$ is large compared with $J$, are not complicated by the mixing of wave functions which are found in the matrix solution of the Hamiltonian. The coupling may be interpreted as a first order interaction and explained in terms of simple spin orientations of the two nuclei. The chemical shift data may be measured directly from the mid-point of each doublet since the "center of gravity" of the pair is located at the exact center.

In a system where R and R' do not differ greatly in the influence they exert on the magnetic properties of the olefinic protons, so that $\Delta$ is of the same magnitude as $J$, the appearance of the doublets is altered and the system is referred to as an AB system. The spin-spin interactions may no longer be considered simply as a function of spin orientations, and a closer look must be taken at certain
matrix elements which in the former AX case had been unim-
portant. The pair of doublets is no longer symmetrical. The 
inner peaks of the pair increase in intensity and the outer-
most lines decrease. Accompanying this change in symmetry 
is a corresponding shift of the center of gravity for each 
doublet toward the inner peak. Pople has derived the follow-
ing relationship which will facilitate the calculation of 
the "weighted chemical shift,"
\[ C = \frac{1}{2}(\Delta^2 + J^2)^{\frac{1}{2}} \]
where \( \Delta \) and \( J \) have been previously described and \( C \) is 
defined in Fig. No. 1.

As \( \Delta \) approaches \( J \), the doublets become more and more 
unsymmetrical; the two central peaks continue to increase 
while the two outer lines diminish in intensity. In the 
limiting case as \( \Delta \) goes to zero, the two central lines 
coalesce while the outer ones disappear. This situation is 
best described as an \( A_2 \) system where both protons are equiva-
ient and their resonance is a single line.

Fig. No. 1
As the value of $\Delta$ was varied from the AX through the AB system, it should be noted that the coupling constant, $J$, remained essentially constant. If the olefinic protons were fixed in a cis configuration, $J$ would measure between 8 and 12 c.p.s. If a trans configuration prevailed, the coupling constant would have values between 15 and 16 c.p.s. This difference in cis-and trans-coupling constants is usually a very good method of establishing the configuration in dissubstituted olefins.

Effects of Anisotropic Neighboring Groups

It has been observed that a neighboring group having large anistropic magnetic susceptibilities may very noticeably influence the resonance of other groups held in its vicinity by a fixed configuration at a double bond. Jackman and Wiley\textsuperscript{12,13,14} noticed such an effect in several pairs of cis- and trans- $\alpha,\beta$-unsaturated carboxylic esters. Using a 40 mc. spectrometer they observed a separation of 10 c.p.s. between the two C-methyl resonance lines of methyl senecioate and an 11 c.p.s. separation in mesityl oxide. The $\beta$-methyl protons in dimethyl citraconate and mesaconate were separated by 6 c.p.s. In each case the $\beta$-methyl which was in a cis-configuration with the methoxycarbonyl group experienced a resonance condition at lower field than the trans-isomer.

This characteristic shift to low field proved useful in establishing the configuration of the cis- and trans-isomers.
of 3-methylglutaconic acid. The substance reported in the literature, m.p. 115-116° and long accepted as the trans-isomer of this acid, was shown to be a mixture of the cis- and trans-isomers. The presence of such a mixture was well established by the appearance of a resonance line for the 3-methyl and methylene groups of each isomer comprising the mixture. Isolation of the pure trans-isomer from this complex was accomplished, and the spectra of the pure isomers agreed with the lines present in the spectrum of the complex.

Using this same approach, Elvidge 15 examined the 2-trans-4-trans-and 2-cis-4-trans-isomers of the methyl esters of 3-methylmuconic acid. The separation between the lines of the 3-methyl groups in the two isomers was 10 c.p.s. The chemical shift data were recorded on a 40 mc. spectrometer and reported in c.p.s. relative to toluene as an internal standard. (See Fig. No. 2)

It should be noted that the C4-proton experienced a large shift to low field (967 to 916) in the 2-cis-4-trans-isomer. This interaction has been examined in the unsubstituted

---

Fig. No. 2

It should be noted that the C4-proton experienced a large shift to low field (967 to 916) in the 2-cis-4-trans-isomer. This interaction has been examined in the unsubstituted
muconic ester series and reported by Jackman and in the 2,2'-dimethylmuconic esters. A similar C4-proton-methoxy-carbonyl interaction is observed in the work reported later in this thesis.

Morris, Vernon and White applied this technique to confirming the structures of some substituted crotonic acids. Their observations of shifts to low field for protons in the vicinity of the methoxycarbonyl group led them to propose the existence of partial hydrogen bond formation between the 3-methyl protons and the carbonyl group. Protons which are involved in hydrogen bonds are generally found at abnormally low field. The presence of a partial hydrogen bond could account for the deshielding effect of the methoxycarbonyl group. Jackman has suggested that the large anisotropy of the carbonyl group is quite capable of explaining this shift and that it is not necessary to postulate the formation of hydrogen bonds.

A cis-C3-proton may also experience a shift to low field through the deshielding effect of the carbonyl group. In this case the shift is of greater magnitude than that observed for a 3-methyl group. The deshielding of the C3-proton is more extensive because the deshielding effect on the three 3-methyl protons is reduced by the free rotation of this group, which effectively distributes the influence of the carbonyl group over all three protons. The C3-proton may have \( \tau \)-values which differ from 0.55 to 0.94.
for a cis-trans-pair, while the difference for the 3-methyl proton signal is less pronounced, 0.10 to 0.30 \( \tau \) units.\textsuperscript{14}

Nair and Adams\textsuperscript{18} demonstrated this strong shift to low field for the C3-proton in a series of tri-substituted 2,3-unsaturated esters. (See Fig. No. 3)

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CO}_2\text{R} \\
\text{H} & \quad \text{X} \\
\tau & = 3.70 \\
\text{TO} & 4.30
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{X} \\
\text{H} & \quad \text{CO}_2\text{R} \\
\tau & = 3.00 \\
\text{TO} & 3.30
\end{align*}
\]

FIG. NO. 3

In all instances the isomer with the C3-proton and the carbonyl group in a cis- relationship presented the lower field line for the C3-proton.

Barber, Jackman, and Weedon\textsuperscript{19} have studied the effect of a double bond lying in the proximity of a proton attached to a carbon atom other than those involved in the double bond. They observed this deshielding influence in the carotenoid, bixin. The "all trans" methyl bixin gave a pair of doublets at \( \tau = 2.61 \) and 4.12, which were assigned to the protons on the terminal carbon-carbon double bond. From the examination of "natural methyl bixin" they obtained a similar spectrum with doublets appearing at \( \tau = 4.14 \) and 2.63, plus an additional doublet at 2.07. The doublets at 2.63 and 2.07 were half the intensity of the 4.14 doublet. The appearance of the 2.07 doublet and the reduction in the
intensity of the pair at 2.63 was ascribed by these workers to be due to a difference in the stereochemistry of one of the penultimate double bonds. By assigning a cis- configuration to the C4-5 double bond, the C-3 proton will be in the proximity of the C6-7 double bond. This could act as a deshielding group through the anisotropic magnetic susceptibility associated with the $\pi$-electrons of the double bond.

To verify the effectiveness of a double bond as a deshielding agent, these workers studied methyl 2,7-di-methyl-octatrienoate with a cis- configuration at the C4-5 double bond. This system is much like that proposed for natural methyl bixin. As expected, the C3 proton gave a resonance peak at 0.42 p.p.m. lower frequencies than the C3 proton in the all trans isomer of methyl 2,7-dimethylocatatrienoate.

Bates and Gale have made some rather precise measurements of chemical shift by using a double internal standard technique. Tetramethylsilane was used as the primary internal standard and the nine methyl protons of t-butyl alcohol were used as the secondary standard. The $\tau$-value for these t-butyl protons is well known in carbon tetrachloride to be 8.793, and in deuterochloroform to be 8.755. This second peak was used to correct the spectrum for any nonlinearity in the sweep rate. Application of this correction factor permitted measurement of $\tau$-values accurate to 0.01 in the 8.2 to 8.5 $\tau$-region. The system studied by Bates and Gale was
A-CH₂C(CH₃) = CHCH₂-B

where A and B were varied to include the isoprene unit, the hydroxyl group, and/or a proton. The differences in chemical shifts between the cis- and trans-isomers were of the order of 0.07 p.p.m., a small but measurable value by this method.

Several workers have reported anomalous chemical shifts in the spectra of systems having an aromatic group present.²¹,²² Pople has accounted for these shifts by suggesting the presence of a secondary magnetic field arising from the circulation of π-electrons in the aromatic ring.²³ These electronic circulations through the closed conjugated loop of the benzene ring are induced by the applied magnetic field. This secondary field will vary in direction. At the edge of the ring its direction is the same as the applied field according to the model of Pople. This means that the ring protons would be expected to reach a resonance condition at a lower applied field strength than ordinary olefinic protons. Above the plane of the ring the secondary field is directed oppositely to the applied fields; this results in a diminution of the applied field experienced by protons in this region. The resonance condition for such protons would be found at higher field strength.

Waugh and Fessenden examined a series of 1,4-poly-methylenebenzenes to substantiate a shift to high field for protons located over the plane of the benzene ring.²⁴ In this
series of compounds the central methylene groups are located over the plane of the benzene ring and should be differenti­ated from the other methylene protons by their high field resonance appearance. The observed chemical shifts for these central methylene groups are in good agreement with the chemical shifts calculated on the basis of the Pople model, after a few refinements had been made.

Curtin, Gruene and Shoulders\textsuperscript{25} have shown in their examination of cis- and trans- stilbene, that the olefinic protons of the trans isomer (3.01\textit{T}) are deshielded because of their orientation with respect to the phenyl groups which are coplanar with the double bond. The protons of the cis-isomer (3.51\textit{T}) show a decrease in the magnitude of deshielding since the phenyl groups do not have the same orientation with the protons and the molecule is no longer coplanar.

Examination of the cis- and trans- isomers of 1,2-diphenylcyclopentane showed that the protons which were \textit{\alpha} to the phenyl groups in the trans- isomer were shielded (7.11\textit{T}) because they lay above the plane of the vicinal phenyl group.\textsuperscript{25} The cis- isomer requires that the \textit{\alpha}-protons be further removed from the vicinal phenyl groups and thus the effectiveness of the magnetic shielding is reduced (6.71\textit{T}).

**Solvent Effects**

The effect of the ring currents in the aromatic nucleus has been discussed up to this point by considering
only those examples in which the ring was attached to the molecule under study. It has been shown that benzene when used as a solvent also produces a chemical shift and it is always to higher field.\textsuperscript{26,27} Schneider, \emph{et al.}, have attributed this solvent effect to a preferred orientation of the solvent to the solute molecules.\textsuperscript{28,29,30} They classified benzene as a "disk shaped" solvent as opposed to a "rod shaped" solvent, e.g., carbon disulfide.

By suggesting that the benzene ring orients itself over the proton as indicated in A, and not B, (Fig. No. 4) it is obvious that the ring currents in the aromatic nucleus would shield the hydrogen atom on the solute molecule, resulting in a shift to high field.

![ORIENTATION A](image1)

ORIENTATION

A

![ORIENTATION B](image2)

B

FIG. NO. 4

Acetone and carbon disulfide, which are classified as "rod shaped" solvents, tend to promote a shift to low field for most protons. These shifts to low field are explained in terms of partial hydrogen bond formation.

Several workers have investigated the interesting solvent effects of pyridine. This is a solvent with aromatic properties and a "disk shape" but which, in spite of these similarities to benzene, causes a solvent shift to low field.
Several acids have been reported to give a resonance shift to high field in benzene but a shift to low field in pyridine. Some Japanese investigators have examined MeCO$_2$H, CHCl$_2$CO$_2$H, EtCO$_2$H, BuCO$_2$H and iso-BuCO$_2$H in benzene and pyridine as the solvents. Benzene caused a characteristic shift to high field and pyridine caused a shift of the resonance lines to low field. The shift to low field in pyridine for the methyl proton resonance signal was thought by these workers to be caused by the methyl protons acting as a weak acid and thus forming a N-H bond. They also suggested that the acidic OH formed a bond with the nitrogen atom of the pyridine giving a N···H-O- type of complex.

Reeves reported that addition of trimethylamine to acetylacetone converted the keto-enol mixture entirely to the enol form. He attributed that shift in equilibrium to a complex formed between the enolic OH and the amine nitrogen, N···H-O-. French workers have found that by using pyridine as the base in acetylacetone, no such shift in equilibrium is observed. This difference in reactivity may find its explanation in the fact that pyridine ($pK_b=8.8$) is a much weaker base than trimethylamine ($pK_b=4.2$).

Freyman reported a shift to low field for the N-hydrogen in pyrole when pyridine was added. He attributed this shift to the formation of a hydrogen bond between the N-proton of pyrole and the unshared pair of electrons of the pyridine nitrogen atom.
One more useful observation concerning the solvent shift by pyridine was reported by Slomp. He found that in using pyridine as a solvent for several steroids, certain methyl resonance lines were shifted from their position when observed in deuterochloroform. This is of particular interest in the study of steroids because the methyl resonance lines often are superimposed. Some of the work to be reported in this thesis will deal with a solvent effect of pyridine on some aliphatic $\alpha:\beta$-unsaturated acids. It would appear that the use of various solvents on a system can greatly facilitate the interpretation of the spectrum and aid in the establishment of absolute configurations.
EXPERIMENTAL
Sample preparation:

All of the compounds examined in this research were prepared in the Department of Chemistry of the University of Louisville. These compounds were received for n.m.r. analysis as pure samples so no further attempts to increase the purity were necessary before examination. The esters were studied in some instances as the pure liquid ester and then in a dilute solution with carbon tetrachloride as the solvent. Solid esters were always examined in carbon tetrachloride.

The insolubility of the acids in carbon tetrachloride necessitated the use of another medium, except in one instance where this solvent was used. Pyridine was found to be the most effective in dissolving these acids. The aromatic type proton of the pyridine ring interferes with the olefinic portion of the spectrum, but the C-methyl region is free from any pyridine lines. In some instances where it was desirable to examine the olefinic portion of the spectrum and where solubility of the acid permitted, piperidine was used as the solvent. The protons of this solvent interfered with the C-methyl region but gave no peaks in the olefinic proton region.

In some instances the samples were weighed quantitatively and solutions of exact concentration prepared. In general, from studies carried out with these compounds,
there appeared to be a negligible concentration effect on the chemical shift. In the discussion of several compounds this effect is noted and any changes in chemical shift included. The concentrations of the solutions examined in carbon tetrachloride were in the 15 to 25% concentration range. Acids in pyridine were examined at about this same concentration.

The n.m.r. sample tube was made of 5 mm. o.d. pyrex glass tubing about 6 inches long and sealed and rounded on one end. Ordinary pyrex tubing was used for this purpose after a thorough cleaning. Immediately prior to the addition of the sample to the tube, the internal standard, tetramethyldisiloxane (TMS), was added with a capillary medicine dropper. The tube was shaken one time to remove any excess TMS, leaving only a film on the tube walls. It was found that this gave an adequate amount of internal standard in the sample. The sample was then added to the tube which was placed in a beaker of powdered dry-ice and allowed to cool. It was then sealed by heating the tube near the top with a torch and pulling off the top portion. Some caution was taken to keep the seal very near the center of the tube to minimize the wobble of the sample tube when spinning in the spectrometer.

**Description of Spectrometer**

The spectrometer used in these experiments was a Varian Associates V-4302 Dual Purpose, 60 mc., N.M.R. Spectrometer.
This system included a VK-3506 Super-stabilizer and a VK-3519 field homogeneity control assembly. The magnet cooling water was controlled to within $\pm 0.1^\circ$ C by the Varian model V-3520 Magnet Coolant Control System. The room housing this equipment was air conditioned with the temperature maintained at $24^\circ$ C$\pm 2^\circ$ C. The spectra were recorded on a Varian G-10 Graphic Recorder.

**Calibration Technique:**

The side band technique of calibration was employed throughout this research. A Hewlett Packard 200 CD Wide Range Oscillator was used for this purpose. The frequency readings were taken directly from the scale on the oscillator; no frequency counter was used to monitor the output of this oscillator. Two different methods were used; each gave reproducible results. In one case the entire spectrum was reproduced on either side of the parent spectrum by modulating the field with a side band frequency set high enough to keep the three sets of peaks from overlapping. The separation between the respective peaks in each curve established a good calibration for the spectra. Adjustments could be made for long term instability in the sweep rate by interpolating.

The alternate procedure for calibration involved field modulation with the side band oscillator at different frequencies. This method introduced side bands of the TMS peak at different places in the spectrum. The sample
was first examined with no side band imposed on the curve, and the regions where no lines appeared were approximately determined. The next run was made with the side bands placed at the selected frequencies. The preferred locations of the side bands were also determined by superimposing side bands on different lines of the spectrum when the curve was displayed on the oscilloscope.

The center of each peak in the spectrum was determined and measured with respect to the center of the TMS peak. The values obtained for the chemical shifts were reproducible to within ±0.017 T units (±1 c.p.s.), and coupling constants were reproduced consistently within ±0.5 c.p.s. The system used to report the chemical shift data is that of Tiers. The TMS peak is assigned a value of 10.00 and all line positions are measured relative to that. All coupling constants are reported in c.p.s. units.
DISCUSSION
DISCUSSION

It has been the object of this study to establish the geometrical configurations of several unsaturated aliphatic acids and esters. The interpretation of the n.m.r. spectra of these several compounds has been the main source of information for the solution of these structural problems. In this section the isomers of each compound are discussed separately in some detail. Some of the isomers were available for examination only in isomeric mixtures; the mixtures are discussed under one heading. The isomers are numbered consecutively I through XIX. The suffix A given several of the compounds denotes an acid; the absence of a suffix denotes an ester. If the n.m.r. data did not permit a conclusive configuration assignment, the drawing at the beginning of that discussion represents what is thought to be the most likely structure.

All chemical shift values are given in $\tau$-units (±0.017), unless otherwise stated. The symbol $\tau$ does not precede each value used in the discussion but must be implicitly understood, unless otherwise stated. All coupling constants are reported in cycles per second (c.p.s.). Table No. I gives a complete listing of all of the compounds examined, with chemical shifts for each type of proton and coupling constants when available. A compilation of the spectra of all the compounds reported may be found in the
Appendix. These are tracings of the actual spectra at a reduced scale.

The final two sections included in the discussion deal with two observations made in analyzing the spectra of several of the compounds. The first is a treatment of the data concerning a solvent effect and the second takes up briefly the deshielding ability of the double bond.
<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>C2</th>
<th>C3</th>
<th>C4</th>
<th>C5</th>
<th>Other</th>
<th>J-coup.</th>
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**Chemical shifts given in T-units; J coupling constants given in c.p.s.**

*Indicates values taken from isomeric mixtures only.
<table>
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<th>Other</th>
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**Chemical shifts given in $\tau$-units; J coupling constants given in c.p.s.**

*Indicates values taken from isomeric mixtures only.
Methyl 3-methyl-5-phenyl-2-cis-4-trans-pentadienoate (I)

There are four possible isomers in the 3-methyl-5-phenylpentadienoic acid system. The 2-cis-4-trans-methyl ester (m.p. 36-37°) is discussed first in this series since such a configuration places the 3-methyl protons as remotely from the methoxycarbonyl group and the aromatic ring as can be accomplished by configuration differences. The resonance frequency of the 3-methyl group in this isomer is referred to as the "normal" position for such a 3-methyl group, inasmuch as it is neither deshielded by the methoxycarbonyl group nor shielded by the phenyl ring. Either or both of these forces must be considered in the interpretation of the spectra of the other three isomers in this series.

The spectrum of the pure ester of the 2-cis-4-trans-isomer presented a peak at 8.00 which was assigned to the 3-methyl protons. This line was split into a doublet by spin-spin coupling with the C2-proton (J=1-2 c.p.s.). The C2-proton had a resonance signal at 4.30 which split into a quartet. The coupling is the same as that observed for the 3-methyl line.
The C4- and C5- protons gave a pair of doublets at 1.40 and 3.13. The coupling constant for these doublets was 16 c.p.s. which establishes a 4-trans-configuration. The appearance of the 1.40 doublet requires that a deshielding group be near either the C4- or the C5- proton, since olefinic hydrogens do not usually experience a resonance condition at such low field strength. Examination of the possible structural arrangements of this ester shows that only a 2-cis-configuration places the deshielding methoxycarbonyl group in the vicinity of the C4- and C5-protons with the 4-trans-configuration. A similar type of deshielding of a C4-proton has been reported by Elvidge in his study of the 3-methylmuconic acids. The T-value of the C4-proton in the muconic acid could not be expected to agree well with the analogous proton shift in the 3-methyl-5-phenyl-isomer being studied here, since the 5-phenyl group also exerts a deshielding influence on the C4-proton giving it an anomalously low field resonance position.

Structural models reveal that the molecule (I) cannot assume a planar conformation when the methoxycarbonyl group is moved by rotation about the C3 single bond into the vicinity of the C5 proton. Jackman has suggested that a planar structure is required for maximum deshielding. A 3-s-cis conformation resulting from the above mentioned rotation does not meet this requirement of planarity (Fig. No. 5). The unhindered 3-s-trans conformation does permit
a planar structure and has the C4 proton in the region of the deshielding cone of the methoxycarbonyl group. The low field doublet must therefore be assigned to the C4 proton.

3-s-trans

3-s-cis

FIG. NO. 5

The work by Elvidge\textsuperscript{15} on the 3-methylmuconates also helps substantiate this assignment. The C4-proton in the 2-cis-4-trans-isomer of methylmuconate is shifted 1.27 p.p.m. to low field while the C5-proton seems to experience no shift to low field caused by this methoxycarbonyl. The absolute configuration of this 3-methyl-5-phenyl isomer (I) is unequivocally established by these data to be 2-cis-4-trans.

Other lines in the spectrum, which were not involved in the above configurational assignments were at 6.34, assigned to the methyl protons of the ester group, and a complex multiplet in the vicinity of 2.90 assigned to the aromatic ring protons.

The 2-cis-4-trans- acid was examined as a molecular complex (m.p. 124-126\degree), previously reported to be the pure 2-cis-4-trans-isomer\textsuperscript{38} and later shown to be a complex.\textsuperscript{39} The solvent used for this complex was pyridine. The spectrum showed two lines of approximately equal intensities
in the methyl region. The 3-methyl protons of the 2-cis-4-trans-isomer were assigned to the line at 7.95 and 3-methyl protons of the 2-trans-4-trans-isomer were assigned to the line at 7.42. These assignments have been verified by examining the pure 2-trans-4-trans- acid in pyridine and by studying the solvent effect of pyridine on 3-methyl protons with a 2-cis-configuration in α-β-unsaturated acids. The substance (m.p. 124-126°) was therefore shown by the n.m.r. data to be a molecular complex with approximately equal parts of both isomers present.
The liquid ester was prepared from the acid (m.p. 160°) using diazomethane and examined in the n.m.r. spectrometer as the pure liquid. Dilution with carbon tetrachloride had negligible effect on the chemical shifts. This acid (m.p. 160°) had been previously shown by Wiley to have a 2-trans-4-trans- configuration. The n.m.r. spectrum gave the expected number of peaks and established the purity of the compound. This simple observation of the number of peaks in the spectrum removes any possibility of the substance being a molecular complex.

The 3-ethyl protons were assigned to the doublet at 7.67 (J=1.2 c.p.s.). This resonance frequency is 0.33 7-units (20 c.p.s.) lower than the 3-methyl resonance in the 2-cis-4-trans-isomer (I). A shift to lower frequency of such magnitude has been correlated with the geometrical configuration existing between the 3-methyl and methoxy-carbonyl groups in similar α-β-unsaturated esters and indicates a 2-trans configuration. The C2- proton was assigned to a line at 4.22 which was split into a quartet.
through coupling with the 3-methyl protons (J=1-2 c.p.s.).

The C4- and C5-protons appeared to be in equivalent environments and therefore gave a sharp singlet at 3.32. A structural model of this isomer shows that this equivalence may well be expected. The spectrum of trans-β-methylstyrene shows the two olefinic protons in this compound to be nearly equivalent. This isomer has its olefinic protons in an environment similar to that proposed for the 2-trans-4-trans-isomer at the C4-5 double bond. Referring to structural models again, one can see that the C4- and C5-protons in a 2-trans-4-cis-configuration could not be equivalent to each other since the C4-proton is quite removed from the shielding range of the aromatic ring. Such a 4-cis-arrangement would lead to two unsymmetrical doublets with coupling constants of about 10 to 12 c.p.s. The structural arrangement at the C4-5 double bond is therefore established as trans. The 4-trans configuration is also confirmed by ultraviolet and infrared spectra.

The equivalence of the C4- and C5-protons also points to the absence of any deshielding influence on the C4-proton.
by the methoxycarbonyl group. This is in agreement with the 2-trans- assignment made earlier and based on the chemical shift of the 3-methyl group only. These data conclusively establish the 2-trans-4-trans-configuration for this isomer.
Methyl 3-methyl-5-phenyl-2-trans-4-cis-pentadienoate (III)

The liquid ester (n_d^25 = 1.5685) was examined in carbon tetrachloride at approximately 20% concentration. This particular sample showed a small peak at 8.27. This is the position expected and later verified for the 3-methyl protons of the 2-cis-4-cis-isomer. Comparison of the line intensities of this contaminant with those of the 2-trans-4-cis-isomer indicated less than 5% impurity. Such a small percentage of this other isomer did not give any detectible lines in the olefinic region of the spectrum, so the measurement of coupling constants of the 2-trans-4-cis-isomer was not interfered with.

The 2-trans-4-cis- structure proposed for the predominant isomer placed the 3-methyl protons in the deshielding region of the carbonyl group, as observed in the 2-trans-4-trans-isomer (II) (pg. 31). A chemical shift to low field would be expected for the 3-methyl proton absorption comparable in magnitude to that observed in II, i.e., about 0.33 τ. This shift of 0.33 τ to low field is relative to
the position observed for the 3-methyl line in I, or the "normal" position as it was defined (pg. 27).

The $\tau$-value which was actually observed for the 3-methyl group of this proposed 2-trans-4-cis-isomer (III) was 7.88; this represents a shift from the "normal" (8.00) position to lower field of only 0.12 $\tau$. This diminished deshielding effect can be explained by assuming the presence of another anisotropic group in the vicinity of the 3-methyl protons which exerts an opposite or shielding effect. The aromatic ring attached to the 5-carbon can, if properly oriented, function as such a group which will produce a shielding effect on protons with a resultant shift to high field. The effects of the induced ring currents in the aromatic nucleus have been discussed previously (pg. 14).

It should be restated that hydrogen atoms situated over the plane of the ring must experience a shift to high field to satisfy their resonance conditions since the secondary field produced in this vicinity by induced circulations of the $\pi$-electrons is opposed to the applied magnetic field.

Examination of a structural model of the 2-trans-4-cis-isomer reveals that such a relationship between the phenyl ring and the 3-methyl protons is possible. The diminished deshielding effect by the carbonyl group in this isomer is therefore readily explained as a simple cancelling out of part of the effect of one anisotropic group by another.
There should be some freedom of rotation about the C-3 single bond. If this were so, the phenyl group would spend some time average in the proximity of the 3-methyl group, shielding it and also some time average in the vicinity of the C2-proton where it should also act as a shielding agent. Structural models can again be used to show that by rotation about the C3-4 bond, the 3-methyl protons and the C2-proton have almost identical spatial relationships with the phenyl group; these considerations should lead to a similar shielding for each group. A difference in the intensity of shielding would be predicted, since the effect for the methyl group is averaged over the three protons.

![Chemical structures](image)

Fig. No. 6

The position of the C2-proton resonance line indicates no shielding effect present. Its $T$-value is 4.23, which is in good agreement with the position of the C2-proton line (4.22) in the 2-trans-4-trans-isomer (II), in which the C2-proton can not possibly be shielded by the phenyl ring. This lack of shielding at the C2-proton leads to the conclusion that there must be a favored conformation at the
C3-4 bond which holds the 3-methyl protons over the plane of the 5-phenyl group. Some workers have suggested the formation of a \( \pi \)-electron-hydrogen bond to explain the anomalous shifts to high field when aromatic solvents are used.\(^{22}\) The protons on the methyl group are not nearly so tightly bound to their carbon atom as is the C2-proton bound to the C2-carbon. Hyperconjugation possibilities at the 3-methyl group and not at the C2-proton would substantiate this. It would seem likely then, that the 3-methyl hydrogens are much more susceptible to formation of a \( \pi \)-electron-hydrogen bond than is the olefinic C2-hydrogen. Such a "bond" formation between these two groups may account for the hindered rotation about the C-3 bond.

These observations concerning the preferred conformation are in agreement with the work of Aston\(^ {41}\) and Mulliken\(^ {42}\) who predicted a preference for the 3-s-trans conformation in conjugated diene systems. Aston calculated the 3-s-trans form to be more stable by 2 KCal/mole over the 3-s-cis form in the unhindered 1,3-butadiene system. The system being studied here, compound III, is a butadiene substituted with bulky groups which cause severe steric hindrance to rotation at the C3-single bond. The following scale drawings made according to the suggestions of Braude\(^ {43}\) indicate the different steric relationships for the two conformers, 3-s-trans and 3-s-cis.
A favored conformation at the C3-4 single bond implies an energy barrier to rotation, which at room temperature appears to be sufficient to cause hindered rotation. This energy barrier could probably be overcome at elevated temperature. The spectrometer used in these experiments was not equipped with a temperature probe which makes possible the study of chemical shifts as a function of temperature. The ester being considered here was heated in hot water and then inserted into the regular n.m.r. probe for examination. The spinning sample no doubt cooled rapidly so there is no way of knowing the temperature of the sample when the spectrum was taken. It can only be said that there were no obvious changes in the appearance of the spectrum as the temperature varied.

To further substantiate the 2-trans-4-cis-structure for this isomer, reference is made to the olefinic portion of the spectrum. The C4- and C5-protons were assigned to a pair of unsymmetrical doublets with coupling constants of 12 c.p.s. which indicate a 4-cis- configuration. The actual chemical shifts must be calculated for these two
doublets because their unsymmetrical appearance shifts their center of gravity from the mid-point of the doublet toward the inner, larger peaks. The olefinic portion of the spectrum is presented schematically in Fig. No. 8.

A discussion of the equation used to calculate the chemical shift may be found on page 8. The coupling constants, $J$,

$$
\begin{align*}
\text{WEIGHTED CHEMICAL SHIFT POSITION } &\tau = 3.78 \\
\text{WEIGHTED CHEMICAL SHIFT POSITION } &\tau = 3.57 \\
\text{WEIGHTED CHEMICAL SHIFT POSITION } &\tau = 3.99
\end{align*}
$$

have been measured to be 12 c.p.s., and the separation between the two inner peaks is 16 c.p.s. The value of $C$ in the equation

$$
(1) \quad C = \frac{1}{2} (\Delta^2 + J^2)^{\frac{1}{2}},
$$

may be calculated from the relationship

$$
(2) \quad 2C - J = 16.
$$

Substitution of $C$ and $J$ into equation (1) enables the calculation of the chemical shift between the pair of doublets. This value is 25.2 c.p.s.
The mid-point between the two doublets was measured to be 3.78. The $T$-value for each doublet is then 0.21 units, to either side of this mid-point or at 3.99 and 3.57. This calculation shows the center of gravity of each doublet shifted toward the large inner peak by 1.5 c.p.s. The chemical shift data presented in this work are accurate to only 1 c.p.s. It is doubtful that calculation of the weighted chemical shifts for unsymmetrical doublets is significant, where the difference is not greater than this.

The assignment of these doublets to either the C4- or C5-protons is based on a comparison with work done with cis-$\beta$-methylstyrene. 40

In this system the olefinic protons appear in the spectrum as a pair of unsymmetrical doublets ($J = 11.4$ c.p.s.). The low field doublet was assigned to the hydrogen on the same carbon as the phenyl group. This is reasonable since this proton lies in the region which is deshielded by the ring currents associated with the aromatic ring. The doublet appearing at 3.57 in the 2-trans-4-cis-isomer would accordingly be assigned to the C5-proton. The 3.92 pair must then result from the C4-proton resonance.
A sample of the crude liquid 2-trans-4-cis-acid was examined in carbon tetrachloride and in pyridine. The sample contained impurity but a large peak at 7.88 when examined in carbon tetrachloride was in good agreement with the 3-methyl line of the ester in the same solvent. The olefinic portion of the spectrum was not too well defined but coupling constants measured between 11 and 12 c.p.s. When the acid was examined in pyridine the 3-methyl resonance line shifted 0.27 \( \tau \) to lower field (7.61). Such a shift to low field in the presence of pyridine requires a cis-relationship between the 3-methyl and methoxycarbonyl group (i.e., 2-trans-configuration).
Methyl 3-methyl-5-phenyl-2-cis-4-cis-pentadienoate (IV)

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
3.56 \\
3.07 \\
2.85 \\
2.85 \\
8.27 \\
4.30 \\
6.50 \\
\text{CO}_2\text{CH}_3
\end{array}
\]

This isomer has not been isolated in its pure form. Its presence was detected in the product formed when a mixture of the cis- and trans-isomers of methyl 3-methyl-5-phenyl-2-pentene-4-ynoate was hydrogenated over a Lindlar catalyst. This mixture of acetylenic esters was examined with n.m.r. previous to the hydrogenation. The intensities of the 3-methyl lines indicate a cis:trans ratio of 1.56/1.00. The liquid product obtained from the hydrogenation reaction was also examined in the n.m.r. spectrometer; two large peaks appeared in the methyl region (7.88 and 8.27), and a complex splitting pattern was present in the olefinic portion of the spectrum.

The peak occurring at 7.88 has the same position as that observed for the 3-methyl protons of the 2-trans-4-cis-isomer (III) reported earlier (pg. 34). The line at 8.27 is also in the correct region for a H_3C-C= grouping. The ratio of intensities of the 8.27 to the 7.88 peaks is 1.46/1.00. The similarity of the intensity ratios of the 3-methyl protons for the acetylenic esters and the hydro-
genation products indicates that the two different environments at the C2-3 double bond still exist in approximately the same proportion. The 7.88 line is accordingly attributed to the presence of the 2-trans-4-cis-isomer (III) in the mixture; the 8.27 is assigned to the 3-methyl protons in the 2-cis-4-cis-isomer (IV).

The protons of the 3-methyl of the 2-cis-4-cis-isomer (IV) find their resonance condition at higher field than those of the other three isomers in this series. This is readily understood by referring to a structural model. It can be seen that the methoxycarbonyl group is too far removed from the 3-methyl protons to exert any deshielding influence. The phenyl group, however, is in position to assume a conformation in which it acts as a shielding group. The result should be and is observed as a shift to high field for the 3-methyl line.

It is interesting to attempt a prediction for the position of the 3-methyl line for the 2-cis-4-cis-isomer (IV). The prediction is based on the observed shielding and deshielding efficiencies of the phenyl and carbonyl groups as they acted separately and in concert in the other three isomers of this series. It was observed that the methoxycarbonyl group in the 2-trans-4-trans-isomer (II) shifted the resonance line of the 3-methyl protons 0.33 τ to low field from the "normal" position in the 2-cis-4-trans-isomer (I). The 2-trans-4-cis-isomer (III) had a 3-methyl line
at 0.12 \( \tau \) lower field than the "normal" position. This small shift was interpreted to mean that the phenyl group was effectively cancelling out part of the low field shift caused by the methoxycarbonyl group. If these shielding effects are additive (it has been shown that some shielding effects are \(^4\)) then it would appear that the methoxycarbonyl group is more effective in its deshielding than the phenyl ring is in shielding by 0.12 \( \tau \). This leads to a predicted value of 0.21 \( \tau \) for the shift to high field of the 3-methyl when influenced by the phenyl ring only. Relative to the "normal" position this would call for a \( \tau \)-value of 8.21 for the 3-methyl line in the 2-cis-4-cis-isomer (IV). The observed value of 8.27 is in close agreement with the predicted value.

The olefinic portion of the spectrum indicates two lines for the C2 protons. The smaller of these two at 4.23 is assigned to the 2-trans-4-cis-isomer (III) and the other occurring at 4.30 to the 2-cis-4-cis-isomer (IV). The positions of these two resonance lines correlate well with the observation that the C2 proton in similar \( \alpha-\beta \)-unsaturated esters was shifted to a lower field when it was cis to an unsaturated linkage at the 4-5 carbons (see pg. 102). The 4.30 line is in excellent agreement with \( \tau \)-value of the C2 proton in the 2-cis-4-trans-isomer (I), as would be expected.

The remainder of the olefinic spectrum is complicated by overlapping of lines from the C4 and C5 protons of each
The olefinic portion of the spectrum of the mixture of 2-cis-4-cis and 2-trans-4-cis isomers of methyl 3-methyl-5-phenylpentadienoate.

- 2-trans-4-cis-isomer III
- 2-cis-4-cis-isomer IV
isomer (see Fig. 9). A doublet \((J=12\ \text{c.p.s.})\) at 4.02 was assigned to the C4 proton of the 2-trans-4-cis-isomer (III) in agreement with the spectrum of the pure isomer. The other doublet for this isomer, resulting from the C5 proton resonance, should be found at 3.56. A study of structural models shows that the C5 proton in both the 2-cis-4-cis-(IV) and the 2-trans-4-cis-(III) isomers should be in the same environment, since modifications at the C2-3 double bond are too far removed to influence it. The resonance doublet for this proton should be found at the same position in both isomers. An unsymmetrical doublet is present at 3.56. Its area appears great enough to represent two protons when compared with the 4.02 doublet. The coupling constant is also 12 c.p.s.

The C4 proton of the 2-cis-4-cis-isomer (IV) must still be accounted for. Its resonance should be shifted to low field through the deshielding effect of the methoxycarbonyl group. There is a singlet occurring at 3.16 which is believed to be the large line of the unsymmetrical doublet expected for the C4 proton. A coupling constant of 12 c.p.s. places the small line of this doublet under the phenyl resonance peak. At the point where this line should occur there is definite evidence of a shoulder on the phenyl peak.

It should be pointed out that the C4-proton of the 2-cis-4-trans-isomer (I) was shifted to a quite low field (1.40). This represents a shift of 2.59 \(\tau\) from the 3.99
position in the 2-trans-4-cis-isomer (III) where it is not
deshielded by any neighboring groups. Structural models
show that in the 2-cis-4-trans isomer (I) the C4 proton is
"sandwiched" in between the methoxycarbonyl group and the
phenyl ring, which in this instance acts as a deshielding
agent because of its co-planar orientation with respect to
the C4 proton. Thus, two groups are acting in concert to
shift the resonance to lower field. Jackman\(^9\) has reported
for dimethyl 2-cis-4-cis-muconate a shift for the C4 proton
of 1.27 \(\tau \) from the shielded position in the 2-cis-4-trans-
isomer.

\[
\begin{align*}
\text{H}_3\text{CO}_2\text{C} & \quad \text{H} \\
& \quad \text{co}_2\text{CH}_3
\end{align*}
\]

Fig. No. 10

The shift observed for the C4 proton in the 3-methyl-5-
phenyl-isomer (IV) under study here was only 0.95 \(\tau \). It is
believed that a lack of co-planarity in this isomer may
inhibit electron withdrawal from the C4 position and thus
increase the local diamagnetic shielding. Such an effect
would reduce the magnitude of the deshielding by the methoxy-
carbonyl at the C4 position.
The mixture which had a 3-methyl line intensity ratio of 1.46/1.00 was heated in an oil bath for two hours at 160°-185° C. The material was examined with n.m.r. after this treatment. Four lines were present in the 3-methyl region of the spectrum. The 8.27 peak (of IV) had almost disappeared after heating while the 7.88 line (of III) was still relatively as strong. A line appeared at 8.00 after heating and is in agreement with the 3-methyl line observed in the 2-cis-4-trans-isomer (I); its intensity surpasses the line which appeared at 7.88. Another small peak appeared at 7.67 and coincides with the 3-methyl resonance of the 2-trans-4-trans-isomer (II), making it seem that all four isomers were certainly present.

This accumulation of spectral and chemical evidence points very definitely to the presence of the 2-cis-4-cis-isomer (IV) and points out, as well, its unstable nature which may account for the difficulty encountered in attempts to isolate the pure isomer.
Methyl 2-trans-3-methyl-5-phenyl-2-pentene-4-ynoate (V)

The pure trans isomer \( (n^2_D = 1.5910) \) was examined as the liquid ester and also in a dilute solution with carbon tetrachloride. The chemical shift values did not change with the concentration. The 3-methyl resonance line occurred at 7.63 as a large doublet. The splitting arises from the spin coupling interactions between the C2 proton and the 3-methyl protons. The methoxycarbonyl group is the only group in this compound which can be moved into position to influence the 3-methyl resonance frequency by differences in cis and trans configurations. The relatively low frequency of the 3-methyl line (7.63) indicates a cis configuration for the methoxycarbonyl and 3-methyl groups. This value is in close agreement with the frequency of the 3-methyl resonance of methyl 3-methyl-5-phenyl-2-trans-4-trans-pentadienoate (II); in this isomer, too, the 3-methyl is influenced only by the methoxycarbonyl.

The C2 proton is assigned to the small quartet at 3.95. The coupling constants for this splitting may be found at the end of the discussion on this compound. The protons of the methoxycarbonyl group gave a resonance singlet at 49.
6.43, which is the usual range for such protons. The aromatic protons presented a complex splitting pattern, the approximate center of which was 2.83.

A mixture of the methyl esters of the 2-trans (V) and 2-cis (V') isomers of this compound was examined as the pure liquid and also with carbon tetrachloride present as a diluent. The chemical shift values were essentially the same in both cases. A doublet at 7.63 was assigned to the 3-methyl group of the 2-trans-isomer (V), in agreement with the spectrum of the pure isomer. Another doublet present at 8.00 and of greater intensity, indicating a predominance of this isomer, was assigned to the 3-methyl group of the 2-cis-isomer (V').

The C2 protons of the trans and cis isomers were assigned to the quartets occurring at 3.95 and 4.13 respectively. These assignments were made on the basis of the intensities of the quartets and on the $T$-value for the C2 proton in the pure 2-trans-ester (V). This is in agreement with the finding that the C2 proton occurs at a lower frequency when cis to the unsaturated linkage at the C4-5 bond (see pg. 102).

The methoxycarbonyl resonance appeared as two peaks. The 6.37 line was associated with the 2-cis-isomer and the smaller 6.43 line was assigned to the 2-trans-isomer. These assignments were based on the intensities of the two peaks and also on the position of the corresponding line.
in the pure 2-trans-isomer (V). The aromatic protons had a very complex splitting arrangement, and no attempt was made to separate and assign the various peaks. The approximate center was at 2.78.

The ethyl esters of a similar mixture of these two isomers were examined first as the undiluted liquid esters and then in four different concentrations using carbon tetrachloride as the solvent. There was a change in chemical shift for the 3-methyl group of the trans isomer of 0.05 \( \tau \) to higher frequency; the 3-methyl of the cis isomer was shifted by 0.05 \( \tau \) to lower frequencies. The C2 protons in both isomers experienced a shift to lower frequencies of 0.05 \( \tau \). Although these shifts in peak position are significant and show a definite concentration dependence for this ester, the magnitude of the shift was not enough to cause any problem in differentiating the cis- and trans-isomers.

The coupling constants for the spin interaction between the C2 proton and the 3-methyl protons were studied under high resolution and slow sweep conditions on the spectrometer. The side band technique of calibration was used by imposing three side bands on the spectrum at 20 c.p.s. separation. The coupling constants at the quartet and the doublet were measured in both the methyl and the ethyl ester mixtures. The values of the coupling constant for the 2-trans-isomers were 1.38 c.p.s.; the 2-cis-isomers had
a constant of 1.37 c.p.s. These are average values taken from eight determinations with standard deviations of 0.07 and 0.04 c.p.s. respectively. It appears from these data that the long range coupling constants do not afford a technique for differentiating cis and trans isomers in this particular instance.
Methyl 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoate (VI).

This pure ester (m.p. 66-67°) was dissolved in carbon tetrachloride at an approximate concentration of 25%. The 3- and 4-methyl groups give resonance lines at 7.60 and 8.02. The higher frequency resonance line of these two is in the region for a 3-methyl group trans to the methoxy-carbonyl, while the lower frequency peak is correct for a 3-methyl in a cis configuration with the ester group. Although a methyl group in an arrangement such as the 4-methyl would not be expected to give a resonance line at as low a frequency as 7.60, the assignments could not be positively made at this point. The locations of the C2 or C5 proton lines do not establish the configuration, since there seems to be no direct correlation between the absolute position of proton resonance lines and their configurations in the compounds studied.
The stereo-specific solvent effect of pyridine on the 3-methyl group in the acid (m.p. 127.5-8°) was used to verify which of the two resonance lines, 7.60 or 8.02, should be assigned to the 3-methyl protons. If the configuration at the C2-3 double bond were cis, to give the 3-methyl value of 8.02, pyridine should cause a shift to low field of about 0.05 T. If, however, the configuration were trans, the 7.60 line of the cis-3-methyl should shift to a new position 0.20 to 0.25 T units lower in the spectrum.

At approximately 25% solution of the acid in pyridine was examined. The solution gave resonance lines at 8.02 and 7.42. This solvent shift unequivocally shows the 7.60 line of the ester to be associated with the cis 3-methyl group.

This position for the 3-methyl, of 7.60, establishes the configuration at the C2-3 bond as trans. Since the peak position of the 3-methyl group in the methyl ester of 3-methyl-5-phenyl-2-trans-4-trans-pentadienoic acid (II) is found at 7.67, the 7.60 position for the 3-methyl of the 3,4-dimethyl compound (VI) establishes the configuration at the C4-5 double bond as being trans. The alternative cis-configuration at this double bond would cause the resonance line of the 3-methyl to be shifted to a higher frequency by the phenyl (ca. 7.81) as in methyl 3-methyl-5-phenyl-2-trans-4-cis-pentadienoate (III).
2,3-dimethyl-5-phenyl-2-cis-4-trans-pentadienoic acid (VII A)

The 2-cis-4-trans-acid (VII A) was examined in two different solvents. An approximately 25% solution of the acid in pyridine was studied to determine the configuration of the C2-3 double bond. The pyridine spectrum occurs at low field and does not interfere with the 2 and 3-methyl resonance lines. The two methyl groups were assigned to the peaks occurring at 7.83 and 8.03. The position of the two methyl groups' resonance lines make a specific assignment difficult at this point. To determine the configuration of the C4-5 double bond, the acid was studied, using piperidine as the solvent. The solubility of the acid in piperidine is slight, so a saturated solution was used. The piperidine spectrum occurs at high field and does not interfere with the olefinic proton region of the spectrum. The presence of two doublets, 2.22 and 3.68, with coupling constants of 16 c.p.s. indicates a trans configuration at the C4-5 double bond. Also the occurrence of one doublet at such low fields can only be explained by the nearness of the methoxycarbonyl group to the C4 proton. This arrangement is consistent only with the cis configuration at the C2-3 bond.
Ethyl 2,3-dimethyl-5-phenyl-2-cis-4-trans-pentadienoate (VII)

Ethyl 2,3-dimethyl-5-phenyl-2-trans-4-trans-pentadienoate (VIII)

2,3-dimethyl-5-phenyl-2-trans-4-trans-pentadienoic acid (VIIIA)

Fig. No. 11

56
If the configuration of the acid is 2-cis-4-trans (VII), the 3-methyl group can be assigned to the 8.03 peak by analogy to the position of the 3-methyl group in methyl 3-methyl-5-phenyl-2-cis-4-trans-pentadienoate (I). The line at 7.83 can thus be assigned to the 2-methyl group.

To substantiate these assignments, the sample was examined for long range coupling interactions under slow sweep, and high resolutions conditions. The 8.03 peak shows a definite splitting into a doublet with a coupling constant of about 1-2 cycles per second. The 7.83 peak only broadens but shows no well defined splitting. The spin-spin coupling interaction between the C4 proton and the 3-methyl gives rise to this splitting in the 8.03 peak. The splitting observed is in agreement with the peak assignments made. It would appear from the spectrum that the long range coupling constants for the 2- and 3-methyl protons is quite small and causes only a broadening of the lines.

A mixture of 2-cis-4-trans (VIIA) and 2-trans-4-trans (VIIIA)-isomers of the 2,3-dimethyl-5-phenylpentadienoic acid was examined in pyridine. The concentration was varied by approximately 50% in two different runs. There was no apparent change in the chemical shift values. The lines at 7.83 and 8.03 are in good agreement with the 2- and 3-methyl lines observed in the spectrum of the pure 2-cis-4-trans-isomer (VIIA). The other lines occurring in the spectrum of the
mixture at 7.70 and 7.62 may be assigned respectively to the 2- and 3-methyl groups of the 2-trans-4-trans-isomer (VIIIA).

High resolution examination of this mixture (VIIA and VIIIA) showed the 8.03 line splitting into a doublet, while the 7.83 line was only broadened. The fine structure of the 8.03 line was in agreement with the assignments made for these peaks. The 3-methyl line should be split into a doublet by the spin coupling interaction between this group and the C4 proton. The 2-methyl group resonance line might have been expected to show a long range coupling interaction with the 3-methyl protons and be split into some multiplet of peaks. The lack of this hyperfine splitting indicates a very slight interaction between these two methyl groups which are in a cis configuration. The 7.70 and 7.62 lines have a complex splitting pattern; this indicates a spin coupling interaction between the trans 2- and 3-methyl protons. The methyl groups are trans to each other in the 2-trans-4-trans-isomer (VIIIA). The 7.62 line has a more complex splitting pattern than the 7.70 peak; it may be concluded from this, that the additional splitting is caused by a coupling between the 3-methyl and the C4-proton. This supports the assignment of the 7.62 line to the 3-methyl group of the 2-trans-4-trans-isomer (VIIIA).

The mixture was also examined in piperidine, but solubility difficulty prevented obtaining a good spectrum.
There were present, however, two doublets at low field (2.24 and 3.68) in good agreement with the spectrum of the pure 2-cis-4-trans-isomer (VIIA). A single resonance line at 3.43 indicated the presence of the C4 and C5 protons in the 2-trans-4-trans isomer (VIIIA). These protons were expected to give a single resonance line, since they are magnetically equivalent to one another. The equivalence of two protons in such an environment was demonstrated in the spectrum of methyl 3-methyl-5-phenyl-2-trans-4-trans-pentadienoate (II). (See pg. 31).

A solution of the ethyl esters of this mixture of isomers was examined, first as the pure mixture of esters and then diluted approximately 50% with carbon tetrachloride. The change in concentration had no effect on the line positions for the methyl protons. The spectrum of the mixture had two singlets of equal intensity occurring at 8.15 and 8.10. Another pair of singlets, equal to each other in intensity but less than the other pair, occurred at 7.98 and 7.86. The appearance of an unsymmetrical doublet at 2.08 with coupling constants of 16 c.p.s. indicated the presence of the 2-cis-4-trans-isomer (VII). The other doublet associated with this one through a spin coupling interaction was found at 3.43. There was a singlet at 3.25 which was assigned to the C4 and 5 protons of the 2-trans-4-trans-isomer (VIII).
These configurations assigned to the two isomers present in the mixture require the following peak assignment of the C-methyl lines. The high field pair at 8.10 and 8.15 must be assigned respectively to the 3- and 2-methyl protons of the 2-cis-4-trans-isomer (VII). The 7.98 and 7.86 lines were assigned to the 2- and 3-methyls of the 2-trans-4-trans-isomer (VIII).

It should be noted that the 3-methyl resonance lines for these two isomers came at higher frequencies than the 3-methyl lines in the esters of the 3-methyl-5-phenylpentadienoic acids. The difference in chemical shift between the 3-methyl resonance lines of the two 2-cis-4-trans-compounds (I and VII) was 0.10 ppm; the 2-trans-4-trans-compounds (II and VIII) showed a slightly greater difference of 0.19 ppm. It is suggested that the presence of an electron releasing group, such as the 2-methyl group, may give rise to this shift to high field experienced by the 3-methyl protons in the 2,3-dimethyl compound. Not in agreement with this suggestion, however, is the fact that no such shift of the 3-methyl resonance to higher frequencies was experienced in methyl 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoate (VI). The 3-methyl resonance, in the case of VI was in agreement with that of methyl 3-methyl-5-phenyl-2-trans-4-trans-pentadienoate (II).

The specific solvent effect of pyridine was also used to establish the configuration at the C2-3 double bond. The
peak assigned to the 3-methyl group of the 2-cis-4-trans-isomer differed by 0.07 $\tau$ when examined as the acid in pyridine (8.03) and as the ester in carbon tetrachloride (8.10). The 2-trans-4-trans-isomer exhibited a chemical shift difference for the 3-methyl of 0.25 $\tau$ (7.62 to 7.87). This shift was large as expected for the isomers with the methyl and the methoxycarbonyl group in a cis configuration relative to each other.

The 2-methyl peaks also experienced a solvent effect, but it did not seem to be too sensitive to configuration. Pyridine promoted a shift to lower frequencies of 0.30 $\tau$ for the 2-methyl group of the 2-cis-trans-isomer and for the 2-trans-4-trans a very similar 0.28 $\tau$ shift to lower frequencies.
2,3-dimethyl-5-p-tolyl-2-trans-4-trans-pentadienoic acid (IXA)

The pure 2-trans-4-trans-acid (IXA) (m.p. 192-193°) was examined in a 25% solution of pyridine. Three lines occurred in the methyl region of the spectrum at 7.59, 7.71 and 7.76. The assignment of these lines to the various methyl protons was based on the splitting of the 7.59 and 7.71 lines. The multiplet appearance of these peaks is caused by the spin-spin coupling interaction between the 2- and 3-methyl protons. The 7.76 line was a sharp singlet and assigned to the para-methyl group.

The 7.59 position for a methyl group is in close agreement with the 3-methyl line (7.62) of the 2-trans-4-trans-isomer (VIIIA) of 2,3-dimethyl-5-phenylpentadienoic acid (pg. 57). The assignment of the 7.59 line to the 3-methyl fixes the configuration as 2-trans-4-trans. The 2-methyl must be assigned to the 7.71 line which also agrees with that of VIIIA (7.70). Piperidine and triethylamine were both tried as solvents since the protons in these solvents would not interfere with the olefinic portion of the spectrum. The acid was insoluble in both, however.
2,3-dimethyl-5-p-tolyl-2-cis-4-trans-pentadienoic acid (XA)

The pure 2-cis-4-trans-isomer (XA) (m.p.167.5-169°) was examined in a 25% solution of pyridine. Only two lines appeared in the methyl region of the spectrum, one at 7.85 and another at 8.05 of half the intensity. These \(T\)-values are in good agreement with those given for the 2- and 3-methyl peaks respectively of the 2,3-dimethyl-5-phenyl-2-cis-4-trans-pentadienoic acid (VIIA). The 8.05 line showed some indication of splitting.

The larger line at 7.85 indicates an equivalence of the para-methyl and 2-methyl protons. A slow sweep rate on the spectrometer did not resolve these two groups. Solubility difficulties prevented examination of this acid in either piperidine or triethylamine which would have permitted a study of the olefinic proton region of the spectrum. Such an examination was not necessary, however, to fully establish the absolute configuration as 2-cis-4-trans.
2,3-dimethyl-5-(p-methoxy)-phenyl-2-trans-4-trans-(XIA) and 2-cis-4-trans-(XIIA) pentadienoic acids

These two isomers were not examined as separate pure isomers but rather as a mixture of the acids dissolved in pyridine. The concentration was approximately 25%, and a later dilution caused no change in the chemical shift data. The peak positions observed for the C-methyl protons are in good agreement with those values observed for the 2-cis-4-trans (VIIA) and 2-trans-4-trans (VIIIA) isomers of the 2,3-dimethyl-5-phenylpentadienoic acid.

High resolution studies of these four methyl resonance lines indicate a difference in the cis and trans long range coupling constants. The 7.72 and 7.60 lines of the 2-trans-4-trans-isomer (XIA) split in a similar manner indicating a noticeable spin coupling interaction between the 2- and 3-methyl protons. It was not possible to determine the coupling constants for this interaction between the two methyl groups because the small separation of their resonance lines prevented a simple first order interpretation. The 8.02 peak of the 2-cis-4-trans-isomer (XIIA) was slightly split
but the 7.83 line was not. It must be concluded that the spin interaction involving the 8.02 line does not arise from a coupling between the 2- and 3-methyl protons since both these peaks are not split. The splitting of the 8.02 peak must arise from the coupling between the C4-proton and the 3-methyl group.

The methoxy resonance signal is of some interest in this compound since it appeared as a doublet at 4.50 with a separation between the peaks of about 0.05 \( \tau \). The presence of a doublet for these protons can not be readily explained. It seems that the configurational difference at the C2-3 double bond in the two isomers present must be the cause, since this is the only difference between the two isomers. The mechanism of this chemical shift or splitting is, however, not immediately obvious.
Methyl 2-trans-2,3-dimethyl-5-phenyl-2-penten-4-ynoate (XIII)

This compound ($n^2_\text{D} = 1.5879$) was examined first as the pure liquid ester and then diluted with carbon tetrachloride to approximately 50% and 10% concentrations. The chemical shift data remained constant throughout these variations. The spectra contained two peaks in the C-methyl region as expected for the pure isomer. A line at 7.76 was assigned to the 3-methyl group and is typical of a cis relationship between a 3-methyl and a methoxycarbonyl group. The remaining C-methyl line at 7.83 must be assigned to the 2-methyl protons. Since only 0.07 $\tau$-units separate these two lines it is possible to reverse the assignments, but the required configuration would still involve a cis relationship between the 3-methyl and the methoxycarbonyl group to account for a 7.83 peak for a 3-methyl group. A trans relationship between these two groups would be expected to shift the 3-methyl resonance to 8.0 or higher.

Other evidence which points to the correctness of the assignment may be found in the splitting interaction of the 2- and 3-methyl protons. Their resonance lines show definite indications of splitting. It was observed in the
2,3-dimethyl-5-phenylpentadienoic acids (VIIA and VIII A) that the two C-methyl bands showed a definite splitting pattern when trans to each other but showed only a broadening effect when in a cis relationship. The splitting of the 7.76 and 7.83 lines in the spectrum of XIII indicates a trans relationship.
Methyl 4-methoxycarbonyl-3-methyl-5-phenyl-2-cis-4-cis-pentadienoate (XIV)

The purified diester (b.p. (0.3 mm.) = 125°) was examined in a 15% solution with carbon tetrachloride as the solvent. The presence of a single peak at 8.12 indicated a pure isomer and established a 2-cis- configuration. This $T$-value falls well within the limits observed by Wiley and Jackman for similar $\alpha$-$\beta$-unsaturated esters with this same geometrical configuration. The C2-proton was assigned to the line at 4.16. This, too, is evidence for a 2-cis configuration since if the C2-3 bond were trans, the C2 proton would lie in the vicinity of the 4-methoxycarbonyl group and its resonance line would be shifted to low field (ca., 3.0).

The C4-5 bond configuration must be cis also. The singlet occurring at 2.63 was assigned to the C5-proton. Its low field resonance is attributed to the nearness of the 4-carboxyl group, a relationship only possible with a 4-cis configuration. The assignments of the C2 and C5-protons to the 4.16 and 2.63 lines respectively can be made with some confidence. It would not be logical to reverse the assignments.
In all of the phenyl substituted olefinic compounds studied throughout this research problem, a proton attached to an unsaturated carbon with a vicinal phenyl group has not been observed at a $\tau$-value higher than 3.57.

The 3-methyl line at 8.12 is believed to be at high enough field to indicate a strong shielding by the phenyl group. The peak comes at a slightly lower value than observed for the 3-methyl peak in methyl 3-methyl-5-phenyl-2-cis-4-cis-pentadienoate (IV) which was observed at 8.27. This difference in chemical shift for these two similar isomers is not surprising since there is an additional electron withdrawing group present in the diester. The work by Jackman and Wiley\textsuperscript{14} presents the following useful information concerning the effect on the 3-methyl group resonance by addition of a second methoxycarbonyl group. It was found in each case in going from the mono to the diester, other structural features being held constant, that the 3-methyl resonance line consistently appeared at lower fields (0.12 to 0.16 $\tau$-units) in the diester (see Fig. No. 12). The 8.12 line of the diester being studied here is 0.15 p.p.m. lower than the 3-methyl line of the corresponding monoester (IV) which is found at 8.27; this is in agreement with the observations of these other workers.

These data indicate that the phenyl group is acting in the diester (XIV) very much as it did in the mono-ester (IV), i.e., as a strong shielding group at the 3-methyl site.
Fig. No. 12

The effect on the chemical shift of a 3-methyl peak by addition of a Cl \( \text{CO}_2\text{R} \) group to the molecule.
This shielding requires a 3-s-trans conformation at the C3-4 single bond since only in this conformation is the phenyl group in the vicinity of the 3-methyl protons. The drawing below illustrates the different spatial relationships in the two possible conformations, 3-s-trans and 3-s-cis.

![3-s-trans and 3-s-cis](image)

Fig. No. 13

Cawley\textsuperscript{38} has described this compound and assigned a 4-cis configuration, leaving the C2-3 double bond open for discussion. He suggested that the diacid molecule assumes the energetically favored 3-s-trans conformation even though it is more hindered. Wiley\textsuperscript{39} has also reported this diacid and presented evidence for a 2-cis-4-cis-configuration. The n.m.r. data on this compound confirm the total configuration assigned by Wiley. Cawley's suggestion of a 3-s-trans conformation is supported by these data also.
Methyl 4-methoxycarbonyl-3-methyl-7-phenyl-2-cis-4-cis-6-trans-heptatrienoate (XV)

\[
\begin{align*}
&\text{H} & \text{H} & \text{H} & \text{H} & \text{H} \\
&\text{CO}_2\text{CH}_3 & \text{CO}_2\text{CH}_3 & \text{H}_3\text{C} & \text{H} \\
&\text{2.85} & \text{3.31} & \text{6.35} & \text{6.52}
\end{align*}
\]

The pure ester (m.p. 99.5-96\(^\circ\)) was examined in carbon tetrachloride at a concentration of approximately 25\%. A single resonance line at 7.95 indicated the purity of the compound but did not give conclusive evidence to the configuration of the C2-3 bond. This value is at the lower limit for 3-methyl protons trans to a methoxycarbonyl group, according to a compilation of n.m.r. data on similar \(\alpha,\beta\)-unsaturated esters by Wiley and Jackman.\(^1\) The range for a trans-methyl to methoxycarbonyl relationship was reported to be 8.27 to 7.96 by these workers. The position of the C2-proton line (4.13) does, however, conclusively establish a 2-cis configuration. This \(\tau\)-value agrees well with that of the C2-proton of methyl 4-methoxycarbonyl-3-methyl-5-phenyl-2-cis-4-cis-pentadienoate (XIV). A 2-trans configuration would place the C2-proton in the deshielding range of the methoxycarbonyl group and result in a shift to low field (Ca., 3.0) for the C2-proton peak.
A 4-cis-6-trans-configuration was easily established by comparing the portion of the molecule from the methoxycarbonyl group to the C7-carbon with the 2-trans-4-trans isomer of methyl 3-methyl-5-phenylpentadienoate (II) (pg. 31). The only difference is the lack of a "3-methyl" group in the isolated portion of the heptatrienoate molecule. The appearance of a large peak at 3.32 in the spectrum of the pentadienoate (II) was attributed to the equivalence of the C4 and C5 protons. The appearance of a similar peak in the heptatrienoate spectrum at 3.31 must be attributed to a configuration which will give equivalent environments at the C6 and C7-positions, i.e., trans.

The configuration at the C4-5 double bond must be cis. If it were not, the 4-methoxycarbonyl group would be in position to deshield the C6 proton, and its resonance would be expected to come well below the phenyl peak as in the 2-cis-4-trans-isomer of methyl 3-methyl-5-phenylpentadienoate (I) (pg. 27). The lack of such a low field doublet establishes a 4-cis configuration. This assignment requires that the 4-methoxycarbonyl group deshield the C5-proton. The absence of a peak in the deshielded proton region, which overlaps the aromatic proton region, must mean the C5-proton peak is obscured by the aromatic proton band.

It is interesting to observe that the equivalence of the C6 and C7 protons was not entirely expected since the configuration at the C4 bond was cis. It was observed in
methyl 2, 7-dimethyl-2-trans-4-cis-6-trans-octatrienoate\(^1\) that the C3 proton was shifted to low field from its position in the all trans isomer, by the nearness of the C6-7 double bond.

\[
\begin{align*}
\text{H}_3\text{C} & \text{H} \quad \text{H} \quad \text{CO}_2\text{CH}_3 \\
\text{H}_3\text{C} & \text{H} \quad \text{H} \quad \text{CH}_3
\end{align*}
\]

**Fig. No. 14**

The C3-proton in the all trans isomer gave a line at 0.42 \(\tau\) higher field. The equivalence of the C6 and C7-protons in the heptatrienoate (XV) indicates that the C2-3 double bond is ineffective in deshielding the C6-proton. This may be due to the presence of the 3-methyl group but is more probably due to the fact that the two bulky methoxycarbonyl groups prevent a co-planar configuration. This would, in effect, reduce the deshielding influence of the double bond by increasing the local diamagnetic shielding at the site of the C6-proton.

High resolution examination of the olefinic portion of this spectrum revealed the presence of some small lines on either side of the 3.31 peak. An attempt was made to calculate the line positions and intensities on the basis of an ABX system. No correlation could be achieved, and it was concluded that the best interpretation might be an ABC
system, where A and B are nearly equivalent. The mathematical treatment of such a system requires an electronic computer to carry out the trial and error evaluation of two third order secular determinants arising in the problem; this was not attempted. Without the calculated spectrum, however, the absolute configuration is well established as 2-cis-4-cis-6-trans.
Methyl 3-methyl-7-phenyl-2-cis-4-trans-6-trans-heptatrienoate (XVI)

\[
\begin{array}{c}
\text{H} & \text{H} & \text{C} & \text{H} & \text{CO}_2\text{CH}_3 \\
3.34 & 8.08 & 4.47 \\
2.85 & 3.34 & 2.18 & 6.43
\end{array}
\]

The pure ester (m.p. 46.5°) was examined in carbon tetrachloride. A single peak in the C-methyl region (8.08) indicated a pure 2-cis-configuration. This value agrees closely with the 3-methyl peak position of methyl 3-methyl-5-phenyl-2-cis-4-trans-pentadienoate (I) (pg. 27). A 2-cis configuration requires the methoxycarbonyl group to lie in the region of the C4-proton; this causes a shift to low field for its signal. Such a low field doublet (J=15 c.p.s) was observed at 2.18 and assigned to the C4-proton. The 15 c.p.s. coupling constant established a 4-trans-configuration. The other doublet expected for an AB spin system, as represented to a first approximation by the C4 and C5-protons, was obscured by the peak for the protons on the C6-7 double bond. The C5 proton signal would also be expected to show some complex splitting, caused by the spin coupling interaction with the C6-proton; this would also tend to obscure its position.
The protons on the C6-7 double bond are assigned to a doublet at 3.34 with a separation between the peaks at 6 c.p.s. This is interpreted as meaning these protons are nearly equivalent and represent essentially an AB system in which $J_{AB}/\Delta_{AB}$ is greater than one. This large band at 3.34 is somewhat characteristic of the large singlet (3.32) which appeared in the spectrum of the 2-trans-4-trans isomer of methyl 3-methyl-5-phenylpentadienoate (II) and which was assigned to the equivalent C4 and C5 protons (pg. 31). The total appearance of this part of the spectrum, which is made up of the peaks for the C5, C6, and C7-protons, is similar to the pattern expected for an AB$_2$ system. This can not be the whole picture, however, since the "A" proton in such a system would correspond to the C5-proton in this compound (XVI) which would be further split by the C4-proton. This would give a system more complicated than one designated AB$_2$.

The assignments may seem vague at this point, but some confidence may be had in the configuration suggested for the molecule, particularly at the C2-3 and C4-5 bonds; these are well established by the $\tau$-values for the 3-methyl and the C4-proton, as well as the 15 c.p.s. coupling constant for the C4-proton. The C6-7 double bond is probably trans; if it were not the large doublet would not be expected at 3.34, but rather a pair of unsymmetrical doublets with coupling constants of 10-12 c.p.s. would appear. The configuration
of this last bond should not be considered as conclusive, however.

A sample of the pure acid (XVIA) (m.p. 193.5-194°) was examined in pyridine. The pyridine spectrum obscured the olefinic region, but a single line in the methyl region (7.98) indicated a pure 2-cis-configuration. The 7.98 position represents a shift of 0.10 $\tau$ to low field from its position in the methyl ester examined in carbon tetrachloride. This is in the expected range for the stereospecific solvent effect of pyridine on a methyl group which is trans to an $\alpha$-$\beta$-unsaturated carboxylic group, i.e., in this acid the carboxyl group is cis to the chain.

There is a total of eight geometrical isomers for the compound being discussed here as shown in Fig. No. 15. Forms B, C, E and G may be precluded as acceptable structures since the 2-trans configuration of each does not place the methoxycarbonyl group in the proximity of the C4-proton as is required by the presence of the 2.18 doublet in the observed spectrum. D and H each have a 4-cis configuration which is not consistent with the 16 c.p.s. coupling constant observed. F would not be expected to give a large band in the spectrum at 3.43, since a 6-cis configuration would not make the C6 and C7-protons nearly equivalent as they have been interpreted to be from the appearance of the spectrum. Structure A only is compatible with the observed spectrum.
Fig. No. 15
Methyl 3-methyl-7-phenyl-2-trans-4-trans-6-trans-heptatrienoate (XVII)

The pure ester (m.p. 64°) was examined in carbon tetrachloride. A single line in the methyl region (7.72) indicated a pure 2-trans configuration. This δ-value is in good agreement with that found for the 3-methyl protons of the 2-trans-4-trans-isomer (II) of methyl 3-methyl-5-phenylpentadienoate, in which the 3-methyl protons are influenced only by the methoxycarbonyl group (pg. 31).

The olefinic portion of the spectrum was somewhat more complicated and an absolute assignment for all the lines cannot be made. Several things can be said, however, about the probable configuration of the remaining two double bonds from the general appearance of the spectrum. A rather large peak occurring at 3.43 is characteristic of the C4- and C5-proton line in the 2-trans-4-trans-isomer (II) of methyl 3-methyl-5-phenyl-pentadienoate (pg. 31) and similar to the spectrum observed for trans-β-methylstyrene. A cis-configuration in these latter two reference
compounds resulted in two unsymmetrical doublets, characteristic of an AB system. The appearance of a strong band at approximately the same field strength for the heptatrienoic ester (XVII) being studied here, leads to the assumption that the configuration at the C6-7 double bond is trans also.

In this same region of the spectrum, there are two doublets (J=16 c.p.s.) at 3.80 and 3.43; the latter one is superimposed on the singlet at 3.43. The 16 c.p.s. coupling constant established a 4-trans-configuration. The appearance of a doublet at 3.43 is in good agreement with the value that can be predicted for the resonance line of the C4-proton based on the following considerations. It has been shown that the C4-proton of the 2-cis-4-cis-isomer of dimethyl muconate was shifted 1.27 \text{~mT} to low field by one of the methoxycarbonyl groups. In the discussion of the methyl 3-methyl-7-phenyl-2-cis-4-trans-6-trans-heptatrienoate (XVI) spectrum, just preceding this, it was well established that the C4-proton resonance line occurred at 2.18. The C4-proton and the methoxycarbonyl group have a relationship in the 2-cis-isomer (XVI) similar to that in the muconate described. Measuring 1.27 \text{~mT} to higher field from the 2.18 position of the C4-proton of the 2-cis-4-trans-6-trans-isomer (XVI) gives a predicted value of 3.45 for the C4-proton when not deshielded by the methoxycarbonyl, as in the 2-trans-isomer (XVII). This agrees with the observed value.
It should be pointed out that the interpretation of this spectrum based on a simple first order analysis cannot be entirely justified. The coupling constants and the chemical shifts are not greatly different in magnitude and spin interactions for these four protons attached to consecutive carbons should be expected to cause a rather complex fine structure of the olefinic peaks. Even with these approximations, however, it seems reasonable to conclude that the isomer examined has a 2-trans-4-trans-6-trans-configuration.

In case some reservations may be held about assigning these rather ambiguous doublets to a 4-trans-configuration, another approach may be taken. Jackman\(^{19}\) has observed in his study of bixin and methyl-2,7-di-methyl-2-trans-4-cis-6-trans-octatrienoate a shift to low field for protons which must lie in the proximity of a double bond, such as the C3-proton lying close to the C6-7 double bond as indicated in the drawing of the octatrienoate (pg. 74). Its resonance is found at 0.427 lower field than in the all trans isomer. In the heptatrienoate studied here (XVII), a 4-cis-configuration would have been expected to produce a definite non-equivalence in the C6 and C7 protons. This would have altered the appearance of the spectrum of these protons from the large band at 3.43 to a pair of unsymmetrical doublets. This configuration seems likely, therefore, to be 2-trans-4-trans-6-trans. It must be stressed,
however, that the data presented here are not conclusive. The interpretation based on the singlet and the doublets can be at best only a rough approximation. The multiplet splitting observed in the olefinic region may possibly be analyzed as an $A_2B_2$ system. The phenyl peak is close to the observed splitting, however, and it is difficult to ascertain the limits of the olefinic band.

The pure acid (m.p. 202-3) (XVIIA) was examined in pyridine. A single methyl resonance line at 7.47 indicated a pure 2-trans-configuration. The presence of pyridine shifted the 3-methyl resonance line 0.25 ppm to low field from its position in the ester in carbon tetrachloride. This is characteristic of a 3-methyl group cis to an $\alpha,\beta$-unsaturated carboxylic group, i.e., in this acid the carboxyl group is trans to the chain.
Methyl 3,6-dimethyl-7-phenyl-2-cis-4-trans-6-trans-heptatrienoate (XVIII)

The pure ester (m.p. 33°) was examined in a 15% solution, using carbon tetrachloride as solvent. Dilutions were made to study the effect of concentration. The 3-methyl was found to shift its resonance to low field by 0.05 \( \tau \) at the most dilute concentration; other lines shifted only about 0.02 \( \tau \). These concentration effects are well within the limits of the chemical shifts affected by configurational differences and did not interfere the structural determination.

The 3- and the 6-methyl groups were assigned to two peaks at 7.90 and 7.95 respectively, and the configuration at the C2-3 double bond was established as cis. The assignment of either of these two peaks to the 3-methyl group would require a 2-cis-configuration. A specific assignment was attempted to considering the effect of pyridine on the two C-methyl peaks of the acid. The stereospecific solvent effect of pyridine causes only a
slight change, ca. 0.05 \( \Delta \), in the position of the resonance line of the 3-methyl group when a cis configuration at the C2-3 bond exists. (See pg. 102.) Examination of the pure acid (m.p. 170-171\(^\circ\)) in pyridine showed a change in chemical shift for the 7.90 peak of 0.03 \( \Delta \) (7.87); the 7.95 peak stayed the same, within the limits of the experiment. This established the configuration at the C2-3 bond as cis and confirmed the peak assignments as given.

To further establish a cis configuration at the C2-3 bond, the position of the C4-proton must be observed. This proton gave a resonance doublet at 2.15, well below the aromatic protons. The only possibility for a C4-proton to acquire such a low resonance condition is in having the methoxycarbonyl group in its proximity. Such a spatial arrangement can exist only when the C2-3 double bond has a cis-configuration.

The configuration at the C4-5 double bond was easily established as being trans by the appearance of two doublets with coupling constants of 16 c.p.s. The C4-proton, already mentioned, was assigned to the low field doublet at 2.15 and the C5-proton was assigned to the 3.42 doublet.

The configuration at the C6-double bond was concluded to be trans. This assignment was based on the appearance of the C6-methyl line at 7.95, which is in good agreement with the C4-methyl resonance line (at 8.02) in the
methyl ester of 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoic acid (VI).

![Chemical structure of methyl ester of 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoic acid](image)

Fig. No. 16

The C7-proton was assigned to a singlet at 3.53. This appeared in the middle of the C5-proton doublet and partially overlapped one line of the doublet. No attempt was made to calculate a weighted chemical shift for the pair of doublets. The total configuration of this isomer was established, therefore, as being 2-cis-4-trans-6-trans.
Methyl 3,6-dimethyl-7-phenyl-2-trans-4-trans-6-trans-heptatrienoate (XIX)

3.48 3.33 7.66
H H H3C
2.87
4.32

The pure ester (m.p. 54°) was examined in a 15% solution, using carbon tetrachloride as the solvent. Two dilutions with additional solvent were made, each approximately reducing the concentration by 50%. The effect of this was to cause a slight shift of the 3- and the 6-methyl resonance lines to lower field. The effect was more pronounced on the 6-methyl peak which was shifted 0.05 τ to lower field; the 3-methyl line was shifted only 0.03 τ to lower field. The other lines remained essentially the same within the limits of the experimental error (±0.017).

The 3- and 6-methyl groups were assigned to the 7.68 and 7.98 peaks respectively. These assignments were based on the positions of other lines in the spectrum as well as τ-values taken from the spectra of model compounds. It was evident that the configuration of the C2-3 double bond was trans; if it were not the C4-proton would be deshielded by the methoxycarbonyl group and experience a
resonance condition at a frequency lower than the aromatic protons. This type of deshielding was observed in the 2-cis-4-trans-6-trans-isomer (XVIII) of methyl 2,6-dimethyl-7-phenylheptatrienoate; the $\tau$-value for the C4-proton in this isomer was 2.15 (pg. 85). The appearance of the C4-proton line as a doublet at 3.82 on the high field side of the aromatic proton signal indicates a lack of deshielding and requires a trans assignment for the C2-3 double bond. The 3-methyl resonance line at 7.68 is in agreement with this assignment.

In order to substantiate this assignment, the pure acid (m.p. 181-182°) (XIXA) was examined in pyridine. The stereospecific solvent effect of pyridine on the 3-methyl group shifted its resonance line to 7.43, a shift of 0.25 $\tau$. This is characteristic of a 2-trans-configuration. The 6-methyl line stayed at 7.98, indicating a complete independence from this solvent effect.

The configuration of the C4-5 double bond was well established by the appearance of a pair of doublets at 3.82 and 3.33, each having coupling constants of 16 c.p.s.; this requires the configuration at the C4-5 bond to be trans. The specific assignment of the C4 and C5-protons to either of these doublets is not necessary to complete the argument for a 4-trans configuration, but it is, perhaps, ideal to complete the assignment. The 2-cis-4-trans-6-trans-isomer (XVIII) of this compound is reported on
Its C4-proton is shifted to low frequencies and is easily identified, leaving the C5-proton at 3.42 also easily identified. The C5-proton should be essentially unaffected by a change in configuration at the C2-3 bond. It would be expected to have a resonance line at about the same frequency in both the 2-cis and the 2-trans isomers, provided the remaining bonds have the same configuration in both isomers. On this argument then, the 3.35 doublet of (XIX) may be assigned to the C5-proton and 3.82 doublet must be associated with the C4-proton.

The configuration at the C6-7 double bond was established by comparing the position of the 6-methyl line with the resonance position of the 4-methyl group in the methyl ester of 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoic acid (VI). (See Fig. No. 16.) The 6- and the 4-methyl protons of these two different compounds have resonance lines at about the same place, 7.98 and 8.02 respectively; this should establish the configuration at the C6-7 bond as trans, since the \( \tau \)-values of the methyl groups indicate similar environments at both sites. A cis configuration at this bond would be expected to shift the 6-methyl resonance to a different frequency.

The C7-proton has a resonance line at 3.48 and unfortunately overlaps one of the lines making up the doublet assigned to the C5-proton. This did not interfere with the interpretation of the spectrum, but it did prevent
any calculation of weighted chemical shifts for the two unsymmetrical doublets.

The C2-proton was assigned to a peak at 4.32. Comparing this line position with that of the C2-proton in the 2-cis-4-trans-6-trans-isomer (XVIII), one finds it to be at 0.13 lower field. This is in agreement with data from the spectra of other \( \alpha-\beta \)-unsaturated esters which show the C2-proton resonance to occur at lower frequencies when cis- to the unsaturated bond at C4-5. (See pg. 102.) The aromatic protons gave a sharp singlet at 2.28. The total configuration for this isomer is established as being 2-trans-4-trans-6-trans.
Stereospecific solvent effect of Pyridine

The medium surrounding the molecule plays a large role in determining the chemical shifts experienced by the protons of that molecule. Schneider, et al., have examined some aspects of this "solvent shift" effect and have attempted to explain it by the following considerations. There is for any molecule a screening constant $\sigma$. This screening constant may be thought of as having two components: $\sigma_{\text{gas}}$ which is the screening constant for the isolated molecule and $\sigma_{\text{solvent}}$ which is a screening contribution due to the presence of a solvent.

The contribution from the solvent may be further discussed by assuming it to be composed of four factors,

$$\sigma_{\text{solvent}} = \sigma_b + \sigma_w + \sigma_a + \sigma_e$$

where $\sigma_b$ is proportional to the bulk magnetic susceptibility of the solvent molecules; $\sigma_w$ arises from the van der Waals forces between the solute and solvent, $\sigma_a$ is an anisotropic magnetic susceptibility factor, and $\sigma_e$ may be attributed to a "polar effect" or a perturbing of the electronic structure of the molecule, caused by an electric field set up by the charge distribution of the neighboring solvent molecules.

Schneider reports that the $\sigma_e$ contribution may be either positive or negative depending on the orientation of the solvent molecule with respect to the nucleus whose resonance is being studied. Bothner-By and Glick have
also investigated solvent effects and have found that aromatic solvents tend to produce shifts to high field for the solute. They explain this shift in terms of a preferred orientation between the solvent and solute molecules due to the "disk" shape of the aromatic solvent. The large diamagnetic anisotropies of the aromatic solvents give rise to secondary magnetic fields, which through this preferred orientation can cause a diminution of the applied field at the solute proton, resulting in a shift to high field. This interpretation stresses both $\sigma_e$ and $\sigma_a$ contributions.

The particular solvent effect observed in the series of $\alpha - \beta$-unsaturated acids in pyridine reported in this paper has to do with what may be termed a "stereospecific solvent shift." Table No. 2 contains a listing of the various acids examined in pyridine and shows the $\tau$-values for the 3-methyl group in both the cis- and trans- configurations. It also shows the 3-methyl $\tau$-value when examined as the methyl ester, either as the pure liquid ester or in carbon tetrachloride. It can readily be seen that a cis relationship between the 3-methyl and the carboxyl group of an acid examined in pyridine results in a shift of 0.18 to 0.25 $\tau$ to lower field, relative to the 3-methyl line of the ester. A trans relationship shows only a 0.05 to 0.07 $\tau$ shift to low field.

To verify the observation that pyridine appeared to cause shifts to low field, chloroform was studied as the
Chemical shift data for the 3-methyl peak under different solvent conditions.

<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>Ester in CCl₄</th>
<th>Acid in Pyridine</th>
<th>Acid in CCl₄</th>
<th>△ 3-methyl**</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>8.00</td>
<td>7.95</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>120 c.p.s.</td>
<td>123 c.p.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>7.67</td>
<td>7.42</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>140 c.p.s.</td>
<td>155 c.p.s.</td>
<td>151 c.p.s.</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>7.88</td>
<td>7.61</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>126 c.p.s.</td>
<td>143 c.p.s.</td>
<td>17 c.p.s.</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>8.27</td>
<td>8.18</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td></td>
<td>104 c.p.s.</td>
<td>109 c.p.s.</td>
<td>5 c.p.s.</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>7.60</td>
<td>7.42</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>144 c.p.s.</td>
<td>155 c.p.s.</td>
<td>11 c.p.s.</td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>8.10</td>
<td>8.03</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>114 c.p.s.</td>
<td>118 c.p.s.</td>
<td>4 c.p.s.</td>
<td></td>
</tr>
</tbody>
</table>

* τ- and c.p.s. units are given for each peak.

** △ 3-methyl is the difference in chemical shift between the 3-methyl peak observed in the ester in CCl₄ and the acid in pyridine.
### TABLE NO. 2 (continued)

Chemical shift data for the 3-methyl peak under different solvent conditions*

<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>Ester in ( \text{CCl}_4 )</th>
<th>Acid in Pyridine</th>
<th>( \Delta ) 3-methyl**</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIII</td>
<td>7.86 128 c.p.s.</td>
<td>7.62 143 c.p.s.</td>
<td>0.24 15 c.p.s.</td>
</tr>
<tr>
<td>XVI</td>
<td>8.08 116 c.p.s.</td>
<td>7.98 122 c.p.s.</td>
<td>0.10 6 c.p.s.</td>
</tr>
<tr>
<td>XVII</td>
<td>7.72 137 c.p.s.</td>
<td>7.47 152 c.p.s.</td>
<td>0.25 15 c.p.s.</td>
</tr>
<tr>
<td>XVIII</td>
<td>7.90 126 c.p.s.</td>
<td>7.87 128 c.p.s.</td>
<td>0.03 2 c.p.s.</td>
</tr>
<tr>
<td>XIX</td>
<td>7.68 139 c.p.s.</td>
<td>7.43 154 c.p.s.</td>
<td>0.25 15 c.p.s.</td>
</tr>
<tr>
<td></td>
<td>8.07 116 c.p.s.</td>
<td>7.92 125 c.p.s.</td>
<td>0.15 9 c.p.s.</td>
</tr>
<tr>
<td></td>
<td>7.83 130 c.p.s.</td>
<td>7.49 151 c.p.s.</td>
<td>0.34 21 c.p.s.</td>
</tr>
</tbody>
</table>
solute molecule in benzene, carbon tetrachloride and pyridine at 5% concentrations. The aromatic solvent benzene caused a shift of 0.917 \( \tau \) to high field for the chloroform proton, relative to its position in carbon tetrachloride. This effect has been previously reported\(^4\) and attributed to a selective orientation of the aromatic nucleus over the chloroform proton (Orientation A, Fig. 4 pg. 17). The pyridine solution showed a shift to low field of 1.13 for the chloroform peak relative to the carbon tetrachloride position.

It is interesting to speculate on the cause of this low field shift in general and in particular on the stereospecific solvent effect brought about, curiously enough, by a disk shaped, aromatic molecule. It can be concluded that in the chloroform-pyridine system, the pyridine molecules do not assume an orientation with the chloroform protons in the same manner the benzene molecules do. Rather, it would seem that the lone pair of unshared electrons on the nitrogen atom takes the predominant role and forms an N...H-CCl\(_3\) type complex. Such an association would be expected to promote a shift to low field as observed for O...H association.

This type of orientation of the pyridine nucleus with the solute, places the proton at the edge of the ring. Such an orientation of a proton with a benzene ring results in a shift to low field caused by the secondary magnetic
fields associated with the ring currents of the π-electrons. Since the pyridine molecule has definite aromatic character and has similar resonance stabilized π-electron bonds, similar types of circulations would be expected. The low \( \tau \)-values of the pyridine ring protons require the presence of some type of deshielding mechanism as was true for the benzene ring protons. It is very likely that similar secondary magnetic fields exist in the neighborhood of pyridine as in benzene and that they contribute to the deshielding observed for the ring protons of pyridine and for the proton of chloroform also.

The suggestion was put forth by Tsubomura\(^{46}\) that compounds having hetero-atoms with a lone pair of electrons be called n-donors and those olefinic or aromatic in nature be referred to as π-donors. Some studies by Mullikan\(^{47}\) have shown pyridine to be an n-donor type molecule in complex formation with I\(_2\). The low field shift observed in the spectra of these acids would support the n-donor properties of pyridine when it is used as a solvent.

The stereospecific nature of this shift requires a further examination of the pyridine-RCOOH interaction. It would be instructive to determine whether the acid group loses its proton to the pyridine solvent molecule leaving behind an anion RCOO\(^-\), or if a partial N...H bond formation occurs between the pyridine nitrogen and the carboxyl proton. The latter would leave the pyridine molecule.
specifically oriented near the 3-methyl when a cis-relationship existed between the 3-methyl and the carboxyl groups.

A mixture of the cis- and trans- isomers of 3-methylglutaconic acid was examined in one normal sodium hydroxide and in 15 normal ammonium hydroxide. Under these conditions it was supposed that the acid would give up its proton to the base. There are at least two possibilities that could occur when an anion is left behind. The extra pair of unshared electrons on the oxygen might be expected to increase the electron density at the 3-methyl site thus increasing the local diamagnetic shielding at this location. This would result in a shift to high field. An alternate scheme would be to expect an increased possibility of H...O bonding between the 3-methyl protons and the anion group; this would result in a shift to low field. Such an interaction would explain the stereospecific nature of the solvent effect since the cis-relationship would allow the 3-methyl group to take part in hydrogen bond formation while the trans-relationship would hold the 3-methyl group too far away from the anion to permit a noticeable interaction.

The difference in chemical shift for the cis- and trans-3-methyl protons of 3-methylglutaconic acid examined in pyridine was 0.43 p.p.m. (7.49 and 9.92) and for the ester in carbon tetrachloride was 0.24 p.p.m. (7.83 and 8.07). Examination of the acid in the sodium hydroxide
gave a difference of 0.13 p.p.m. (8 c.p.s.) and in ammonium hydroxide a difference of 0.12 p.p.m. (7 c.p.s.). The chemical shift data taken in the aqueous media could not be directly related to the \( T \)-values observed in the non-aqueous media so it is difficult to know if the the methyl lines were found at relatively higher field. The significant point is that the large difference in 3-methyl shifts observed in pyridine was not observed in either sodium hydroxide or ammonium hydroxide. These data force the conclusion that hydrogen bonding between the 3-methyl protons and the anion is not the explanation for the large shift observed in pyridine. In fact, there seems to be a diminution of the deshielding effect on the cis-3-methyl protons by the carbonyl group, reducing it below what it is in the ester. This effect may find its explanation in the additional resonance structure possible when the anion is involved.

![Chemical Structure](image)

**Fig. No. 17**

This additional canonical form should cause considerable delocalization of the electrons of the carbonyl double bond. Such a delocalization would be expected to reduce
the magnitude of the deshielding cone associated with the carbonyl group, and result in a diminished difference in chemical shift for the cis- and trans- isomers.

The explanation of the stereospecific shift must lie in the presence of a N...H bond, and the group responsible for the large shift to low field for the cis-3-methyl must be the pyridine ring. A trans-relationship places the 3-methyl protons too far from the pyridine ring to be very strongly influenced.

A mixture of the 2-cis-4-cis-(IVA),2-trans-4-cis-(IIIA) and 2-trans-4-trans (IIA)-isomers of 3-methyl-5-phenylpentadienoic acid was examined in carbon tetrachloride to prove the increased deshielding observed in pyridine was related to the presence of pyridine and not simply attributable to the difference in the ester and the acid. The peaks for the 3-methyl protons in the isomeric mixture of acids were in excellent agreement with the values observed for the esters. The carbon tetrachloride was removed from this mixture by reduced pressure evaporation at room temperature and pyridine was added. Table No. 2 shows the chemical shift data for the 3-methyl protons of the esters in carbon tetrachloride and the acids in carbon tetrachloride and pyridine. It must be concluded that the shift to low field in pyridine solution is definitely dependent on the presence of pyridine.
Table No. 2 indicates that 3-methyl groups trans to the carbonyl group, when examined as the acid in pyridine, generally experience a shift to low field of 0.05 to 0.07 \( \tau \)-units (3 to 4 c.p.s.) relative to their \( \tau \)-value when examined as the ester in carbon tetrachloride. This slight shift may well be attributed to the n-donor properties of pyridine. This would involve the solvolysis of the acid along the chain, and the orientation of the solute to solvent would be expected to be,

\[
\begin{array}{c}
\text{O} \\
\text{---H--C--R} \\
\text{H} \\
\end{array}
\]

Fig. No. 18

which is typical of an n-donor solvent-solute complex. Other workers\textsuperscript{31} have reported a shift to low field for the C-methyl groups of some saturated acids in pyridine. They have suggested a similar type of partial bond formation.

The 4-methyl protons of 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoic acid had the same \( \tau \)-value in pyridine as they did for the ester in carbon tetrachloride. A model shows that there is severe steric hindrance between this methyl group and the aromatic ring. It is highly possible that the independence from solvent effect demonstrated by this methyl peak may result from the inability
of the pyridine solvent molecule to attack at this hindered site.

The 2-methyl protons in 2,3-dimethyl-5-phenyl-pentadienoic acid in pyridine experienced a shift of 0.28 \( \tau \) (17 c.p.s.) to low field relative to their position when studied in the ester in carbon tetrachloride. The shift to low field was independent of the configuration at the C2-3 double bond. This would be expected for a 2-methyl group proton since its position, relative to the carboxyl group, is not a function of the configuration.
Influence of neighboring double bond

The effect of a double bond on the chemical shift of a nearby proton has been reported by Jackman, et al., and previously discussed (pg. 13). It should be recalled that these workers observed this effect in an octatrienoate system, in which case the deshielded proton was four bonds removed from the effective double bond but oriented in such a manner that they were as close together as possible. In the series of olefinic esters discussed in the preceding sections of this thesis a similar type of deshielding was observed. The C2-proton peak was found at lower field when cis to the C4-5 unsaturated bond than when a trans configuration existed between these two groups. This effect can readily be seen in Table No. 1 (pg. 25) where the chemical shift data for all the compounds studied are listed.

The effect of this bond on the chemical shift was more subtle (0.07 to 0.17 \( \tau \) shift to low field) than the deshielding observed in the octatrienoate (0.42 \( \tau \) shift to low field). A structural model shows the deshielded C3-proton in the octatrienoate to be closer to the anisotropic C6-7 double bond, than the C2-proton is to the anisotropic C4-5 double bond in the pentadienoates. This difference in separation between the two interacting groups would account for the difference in the magnitude of the deshielding effect. This stereo-dependent shift
is a useful aid in establishing the configuration of the C2-3 double bond when there is a C4-5 double bond in conjugation with it.
Interpretation of the n.m.r. spectra of several isomeric unsaturated acids and esters has made possible the assignment of their correct geometric configurations. The four isomers (see text I, p. 27; II, p. 31; III, p. 34; IV, p. 42) of the 3-methyl-5-phenylpentadienoic acid series were examined and their structures established. The presence of the previously unknown 2-cis-4-cis isomer (IV) of this series was clearly demonstrated and its structure assigned, although it was not isolated from a mixture with the 2-trans-4-cis isomer (III). One isomer of the methyl 4-methoxy-carbonyl-3-methyl-5-phenylpentadienoate series was shown to have 2-cis-4-cis configuration (XIV) (see text p. 68). The data for compounds III and XIV establish that there is a favored conformation in which the 3-methyl protons are held over the plane of the 5-phenyl group. The aromatic ring, so oriented, acts as a shielding group and the 3-methyl resonance is shifted to high field.

The structures of several chain and ring substituted 3-methyl-5-phenylpentadienoic and 3-methyl-7-phenylhepta-
triencoic acids and esters were assigned on the basis of their n.m.r. spectra. Two isomers (XVI, p. 76; and XVII, p. 80) of the 3-methyl-7-phenylheptatrienoic acid series were examined and assigned structures of 2-cis-4-trans-6-trans and 2-trans-4-trans-6-trans respectively. The assignments were made by correlating the n.m.r. data of these two isomers with those of simpler model compounds. Only approximate treatments of the olefinic regions of the spectra were possible because of the complex nature of the spin interactions of the olefinic protons. The configurations assigned for the C2-3 and C4-5 bonds of XVI and the C2-3 bond of XVII were well established. The C6-7 bond of XVI and the C4-5 and C6-7 bonds of XVII should not be considered as conclusive. A rigorous structural assignment was made for the 2-cis-4-trans-6-trans and the 2-trans-4-trans-6-trans isomers (XVIII, p. 84 and XIX, p. 87) of the 2,6-dimethyl-7-phenylheptatrienoic acid series. The olefinic region of the spectra of these two isomers is considerably simplified and the interpretation was carried out as a simple first order analysis.

A method for establishing the configuration of the C2-3 double bond has been developed on the basis of a stereo-dependent solvent effect on the resonance peak of the 3-methyl protons of \( \alpha, \beta \)-unsaturated acids in a pyridine medium. This solvent effect is stereo-dependent in that the magnitude of the change in chemical shift value of the 3-methyl group is
considerably larger for a cis 3-methyl-carboxyl relationship than for a trans 3-methyl-carboxyl relationship. An \(\alpha,\beta\)-unsaturated acid having a 3-methyl group cis to the carboxyl group examined in pyridine has its 3-methyl proton resonance peak shifted to low field about 0.25 \(T\)-units. This shift to low field is relative to the \(T\)-value of the 3-methyl protons of the acid or the ester in carbon tetrachloride solution. The 3-methyl peak in the trans relationship is shifted only 0.07 \(T\)-units to low field. Since this effect was not noticed in solutions of the acids in aqueous bases (sodium hydroxide and ammonium hydroxide), it is believed to result from complex formation between the acid proton and the pair of unshared electrons of the pyridine nitrogen. Such a complex formation would place the pyridine nucleus and the 3-methyl protons near each other in the cis configuration; the trans configuration could not produce this same effect as shown below.

The configurations at the C2-3 bond of the esters studied in this research were further established by observing the relative positions of the C2-proton peaks of the 2-cis
and the 2-trans isomers. The C2-proton was always found to have a lower $\tau$-value when it and the C4-5 bond were in a cis relationship. The deshielding effect of the unsaturated bond on the cis C2-proton resulted in a chemical shift to low field of about 0.1 $\tau$. The steric relationships are shown below.

![Chemical Diagrams]

The results of this research on the application of n.m.r. methods to some structural problems involving unsaturated aliphatic acids and esters may be summarized as follows:

1. The geometric configurations of twenty unsaturated compounds have been assigned using the method by Jackman and Wiley$^{12}$ of observing the shielded and deshielded chemical shift values of the 3-methyl protons in $\alpha,\beta$-unsaturated esters. The olefinic proton spin-spin coupling constants were used where applicable to establish geometric configuration.

2. Pyridine was observed to cause a shift to low field (0.25 $\tau$) for the resonance peak of the 3-methyl
protons of $\alpha,\beta$-unsaturated acids having a cis 3-methyl-carboxyl configuration. A trans relationship resulted in only a slight shift ($0.07\,\tau$). These shifts to low field are relative to the $\tau$-value for the 3-methyl protons examined in carbon tetrachloride solutions.

3. The deshielding nature of the magnetically anisotropic double bond was observed and used as a means of verifying geometric configurations.
The following drawings are tracings made to one half scale from the original spectra of the esters examined in this research. The chemical shift data are given in $\tau$-units for each peak.
Methyl 3-methyl-5-phenyl-2-cis-4-trans-pentadienoate (I)

Methyl 3-methyl-5-phenyl-2-trans-4-trans-pentadienoate (II)
Methyl 3-methyl-5-phenyl-2-trans-4-cis-pentadienoate (III)

Mixture of

Methyl 3-methyl-5-phenyl-2-trans-4-cis-pentadienoate (III) and Methyl 3-methyl-5-phenyl-2-cis-4-cis pentadienoate (VI)
Methyl 2-trans-3-methyl-5-phenyl-2-pentene-4-ynoate (V)

Mixture of Methyl 2-trans-3-methyl-5-phenyl-2-pentene-4-ynoate (V) and Methyl 2-cis-3-methyl-5-phenyl-2-pentene-4-ynoate (V')
Methyl 3,4-dimethyl-5-phenyl-2-trans-4-trans-pentadienoate (VI)

Mixture of

Ethyl 2,3-dimethyl-5-phenyl-2-cis-4-trans-pentadienoate (VII) and Ethyl 2,3-dimethyl-5-phenyl-2-trans-4-trans-pentadienoate (VIII)
Methyl 4-methoxycarbonyl-3-methyl-5-phenyl-2-cis-4-cis-pentadienoate (XIV)

Methyl 4-methoxycarbonyl-3-methyl-7-phenyl-2-cis-4-cis-6-trans-heptatrienoate (XV)
Methyl 3-methyl-7-phenyl-2-cis-4-trans-6-trans-heptatrienoate (XVI)

Methyl 3-methyl-7-phenyl-2-trans-4-trans-6-trans-heptatrienoate (XVII)

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Methyl 3,6-dimethyl-7-phenyl-2-cis-4-trans-6-trans-heptatrienoate (XVIII)

Methyl 3,6-dimethyl-7-phenyl-2-trans-4-trans-6-trans-heptatrienoate (XIX)
36. R. H. Wiley and P. Nau, University of Louisville, unpublished results.
37. R. H. Wiley and C. Staples, University of Louisville, unpublished results.