

INFORMATION TO USERS

This was produced from a copy of a document sent to us for microfilming. While the most advanced technological means to photograph and reproduce this document have been used, the quality is heavily dependent upon the quality of the material submitted.

The following explanation of techniques is provided to help you understand markings or notations which may appear on this reproduction.

1. The sign or "target" for pages apparently lacking from the document photographed is "Missing Page(s)". If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting through an image and duplicating adjacent pages to assure you of complete continuity.
2. When an image on the film is obliterated with a round black mark it is an indication that the film inspector noticed either blurred copy because of movement during exposure, or duplicate copy. Unless we meant to delete copyrighted materials that should not have been filmed, you will find a good image of the page in the adjacent frame.
3. When a map, drawing or chart, etc., is part of the material being photographed the photographer has followed a definite method in "sectioning" the material. It is customary to begin filming at the upper left hand corner of a large sheet and to continue from left to right in equal sections with small overlaps. If necessary, sectioning is continued again—beginning below the first row and continuing on until complete.
4. For any illustrations that cannot be reproduced satisfactorily by xerography, photographic prints can be purchased at additional cost and tipped into your xerographic copy. Requests can be made to our Dissertations Customer Services Department.
5. Some pages in any document may have indistinct print. In all cases we have filmed the best available copy.

University
Microfilms
International

300 N. ZEEB ROAD, ANN ARBOR, MI 48106
18 BEDFORD ROW, LONDON WC1R 4EJ, ENGLAND

DRANEY, DANIEL ROBERT

CARBON-13 NMR STUDIES OF CONFIGURATION AND CONFORMATION

The University of Nebraska - Lincoln

PH.D.

1980

University
Microfilms
International

300 N. Zeeb Road, Ann Arbor, MI 48106

PREVIEW

CARBON-13 NMR STUDIES OF CONFIGURATION
AND CONFORMATION

by

Daniel R. Draney

A DISSERTATION

Presented to the Faculty of the
Graduate College of the University of Nebraska
In Partial Fulfillment of Requirements for
The Degree of Doctor of Philosophy

Major: Chemistry

Under the Supervision of C. A. Kingsbury

Lincoln, Nebraska

December, 1980

TITLE

Carbon-13 NMR Studies of Configuration and

Conformation

BY

Daniel R. Draney

APPROVED

DATE

Dr. James H. Looker

8/7/80

Dr. C. A. Kingsbury, Chairman

20 August '80

Dr. D. M. S. Wheeler

20 August 1980

Dr. George D. Sturgeon

Aug. 20, 1980

SUPERVISORY COMMITTEE

GRADUATE COLLEGE

UNIVERSITY OF NEBRASKA

Acknowledgements

The author wishes to express his profound appreciation to Dr. Charles Kingsbury for his thoughtful guidance, helpful attitude, and enormous patience displayed time and again over these occasionally traumatic years.

Thanks, also, to Dana Durham, Alan Sopchik, and my family for their assistance and support.

Special thanks to Maité Dubourg, and to Lisa Brown.

PREVIEW

INTRODUCTION

Since Karplus published his now famous paper (1) relating the dihedral angle between vicinal protons to their coupling constant (figure 1), ^1H NMR has found countless applications in conformational and configurational studies.

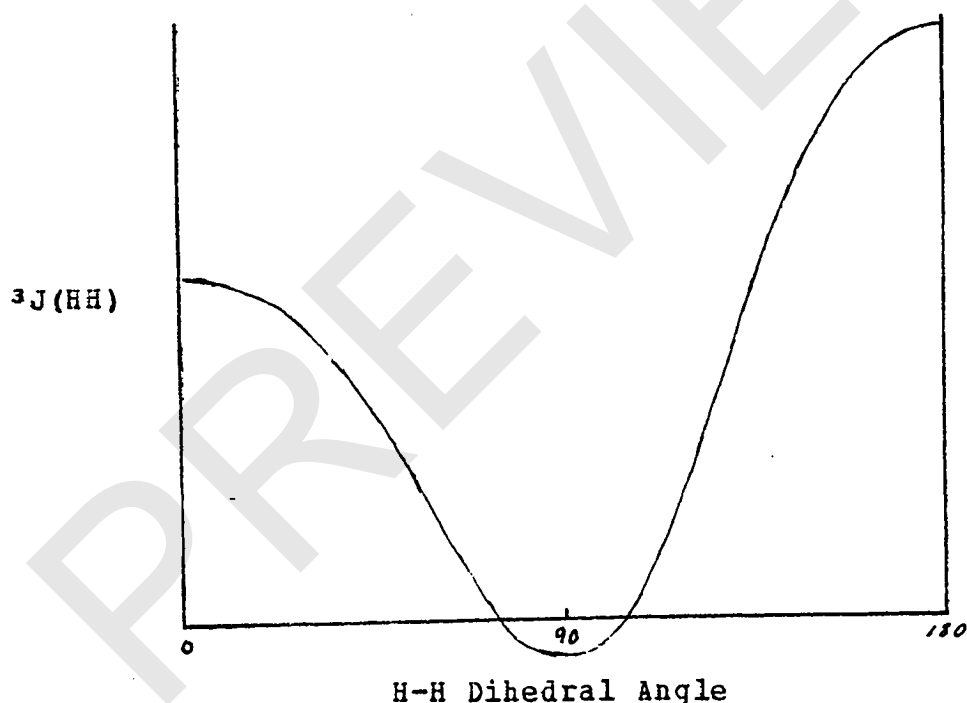


Figure 1, The Karplus Relationship

Three bond ^{13}C -H couplings offer a logical extension of this tool, and indeed a number of papers have emphasized

the parallelism between vicinal proton coupling constants and vicinal ^{13}C -H couplings (2-5). Vicinal couplings of protons to hetero atoms show this angular dependence, as well (6), and INDO calculations by Wasylishen and Schaefer (7) predict that ^{13}C -H couplings will also follow the pattern.



1 2

Unfortunately, the vicinal ^{13}C -H couplings are more dependent upon electronic factors, such as electronegativity, hybridization, and/or the presence of hetero atoms, than the corresponding proton-proton couplings (8). In fact the electronic factors may even be more important than dihedral angle in determining the magnitude of the coupling. In order to evaluate the variations possible in the coupling constants due to electronic factors, it was necessary to go to a rigid system: olefins. Since proton-proton coupling constants in alkenes such as 1 have been used for years to distinguish between E and Z isomers, the question arises

whether ^{13}C -H coupling constants might not be of similar use with more highly substituted alkenes such as 2. The primary purpose of this study is to determine the effects of cis and trans geometries on $^3J(\text{CH})$, in order to determine the configuration of alkenes such as 2. Von Philipsborn and Vogeli (2d) have also addressed this question, drawing similar conclusions.

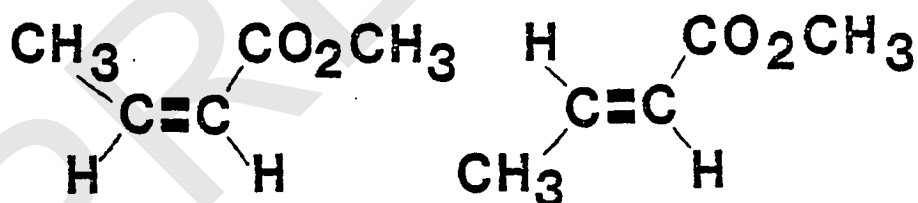
De Haan and van de Ven and Roberts et al. have advanced a useful method of determining alkene configuration based upon ^{13}C chemical shifts (9). However, this method seems best applied in cases where both the E and Z isomers are available. If only a single isomer is available, the assignment of configuration would be difficult, if unusual steric or electronic effects were present (10,11).

The use of additivity relationships, based on substituent effects on ^1H chemical shifts, seems to be an even more powerful method for determining alkene configuration (9). However, deviations from additivity predictions for carbonyl and other alkene substituents have been noted.

It was hoped that ^{13}C -H coupling constants would show sufficient regularity so that these data also could be used to identify E or Z isomers. Studies of chemical shifts and of coupling constants would complement one another, and provide the researcher with a battery of techniques for

configuration assignment (12).

Marshall and Seiwel have reported that a large $^3J(\text{CH})$ value (14.5 Hz) is found between carbonyl and trans hydrogen in 3, and a smaller value (6.8 Hz) is found for cis nuclei in 4, rather similar to the variation in H-H coupling constants with geometry in other molecules (13,14). This coupling constant for trans ^{13}C -H nuclei was substantially higher than for certain α,β -unsaturated ketones briefly investigated in our laboratory. However, our determination for (E)-crotonic acid agrees well with that of Marshall and Seiwel for 4. A second objective of the present study was to observe the range in coupling constants as structure was varied.



3

4

In other studies, Karabatsos and Orzech suggested that bond angle variations imposed by steric constraints gave rise to sizable variations in ^{13}C -H (2), but electronegativity effects were not considered to be very important (2c). Perlin's data, however, could be

interpreted in terms of a sizable electronegativity effect (15). Lemieux and co-workers also emphasized the importance of stereo-electronic factors on variations in $^3J(CH)$ (8). In studies of proton couplings in alkenes, several other factors were shown to affect the magnitude of the coupling constant. Thus Rummens and de Haan (16a) discussed certain $J(HH)$ variations in terms of rehybridization of the sp^2 carbon atoms. Schiebe and co-workers (16b) showed that increasing sp^2-sp^2 single bond distance in butadienes gave smaller values of 3J . Yalymova and Samitov (16c) also examined electronegativity effects, while Cooper and Manatt (16d) considered the effect of bond angle variations on $^3J(HH)$.

In earlier studies, H-H coupling constants in alkenes were shown to vary over a twofold range for trans nuclei and over a fivefold range for cis nuclei, depending upon the type of alkene substitution (17). The effects of electronegativity, as determined by Banwell and Shephard and by Schaefer, are given in eq 1 and eq 2:

$$J(cis) = 11.71\{1 - 0.34E(x)\} \quad (1)$$

$$J(trans) = 19.0\{1 - 0.17E(x)\} \quad (2)$$

Where $E(x)$ is an electronegativity parameter for the substituent x (18). If $^{13}C-H$ coupling constants indeed parallel H-H couplings, similar electronegativity effects

would be expected (19).

In considering the various factors that may affect the magnitude of $^3J(\text{CH})$, the hybridization of carbon deserves special mention. This factor, of course, is not present in H-H coupling constants. Karabatsos pointed out that $^3J(\text{CH})$ should decrease in the order: $sp^1 > sp^2 > sp^3$, if the Fermi contact mechanism of spin coupling is dominant (18,20,21). Since a Fermi contact interaction requires a finite value for the square of the wave function at the nucleus (that is, an s orbital), the interaction increases proportionately with increasing s character in the coupling path, particularly at the ^{13}C nucleus. A third objective of this study was to observe the effect of hybridization on $^3J(\text{CH})$, although these effects are hard to differentiate from electronegativity effects in certain cases. Another factor to consider is the possibility that steric effects of substituents on the double bond may affect the observed coupling for carbonyl and other sp^2 carbons by forcing the p orbitals of the ^{13}C to twist out of the plane of the double bond, reducing overlap. The combination of pi and sigma pathways for spin coupling in alkenes, in comparison to sigma only in Karabatsos' cases (20), represents an unknown factor. Murrell and Ditchfield (21b) suggested that pi contributions to $^3J(\text{HH})$ are small, but it may not be possible to ignore these effects for $^3J(\text{CH})$.

RESULTS AND DISCUSSION

Table I lists the ^{13}C NMR data for thirty-nine alkenes of known configuration (there is some doubt concerning 25, see ref. 40). The coupling constants quoted in Table I and elsewhere in this section are line separations (LS) rather than true coupling constants [$^3J(\text{CH})$], which must be derived from the LS by computer simulation of the spectrum. The LS values should be of more use to the practicing chemist. In Table I, the data for trisubstituted alkenes are of foremost interest. In such alkenes, couplings between cyanide or carbonyl and hydrogen represent an AX spin system, and thus, LS and $^3J(\text{CH})$ are identical. For methyl substituted alkenes, an AM_3X spin system is present, where M are the methyl protons; LS should again be very close to $^3J(\text{CH})$.

The deviation of LS from $^3J(\text{CH})$ should be most serious for disubstituted alkenes. These alkenes were investigated in order to observe the variation of LS with structure in compounds whose configuration is firmly established by other means. For disubstituted alkenes such as (E)-cinnamic acid (28), the carbonyl ^{13}C nucleus represents X of an AEX spin system, where the alkene hydrogens are A and B. Owing to the large difference in chemical shift of

Table I

Line Separations Due to Coupling of the ^{13}C Nucleus with
the ^1H Nucleus Indicated

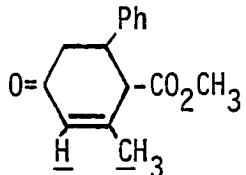
Cmpd.	Isomer	Structure	Orientation of Coupled Nuclei	LS (Hz)
5	<u>E</u>	$i\text{-C}_3\text{H}_7\text{CH}=\text{CH}-\text{CH}_3$	cis	~6
6	<u>E</u>	$t\text{-C}_4\text{H}_9\text{CH}=\text{CH}-\text{CH}_3$	cis	6.9
7	<u>E</u>	$\text{Cl}-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_3$	cis	6.0
	<u>E</u>	$\text{Cl}-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_3$	cis	~7
8	<u>Z</u>	$\text{Ph}-\text{CH}=\text{CH}-\text{CH}_3$	trans	10.0
9	<u>E</u>	$\text{Ph}-\text{CH}=\text{CH}-\text{CH}_3$	cis	6.6
10	<u>E</u>	$\text{Ph}-\text{CH}=\text{CH}-\text{CH}_2\text{OH}$	cis	6.8
11	<u>E</u>	$\text{Ph}-\text{CH}=\text{CH}-\text{CH}_2\text{Cl}$	cis	8.0
12	<u>E</u>	$\text{Ph}-\text{CH}=\text{C}(\text{CH}_3)\text{Ph}$	trans	8.3
13	-	$\text{H}_2\text{C}=\text{C}(\text{CH}_3)\text{Ph}$	cis	6.6
			trans	11.1
14	-	$\text{HO}_2\text{C}-\text{CH}=\text{C}(\text{CH}_3)_2$	cis	7.1
			trans	8.4
15	-	$\text{CH}_3-\text{CO}-\text{CH}=\text{C}(\text{CH}_3)_2$	cis	7.0
			trans	8.0
16	<u>Z</u>	$\text{Ph}-\text{CO}-\text{CH}=\text{C}(\text{CH}_3)\text{Ph}$	cis	6.7
17	<u>E</u>	$\text{PhCO}-\text{CH}=\text{C}(\text{CH}_3)\text{Ph}$	trans	7.8
18	<u>Z</u>	$\text{CH}_3\text{CO}-\text{CH}=\text{C}(\text{CH}_3)\text{NHCH}_2\text{Ph}$	cis	6.1
19	-		cis	6.2

Table 1 (continued)

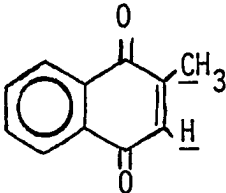
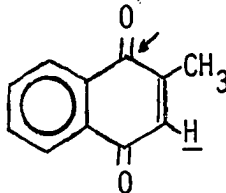
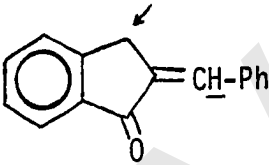
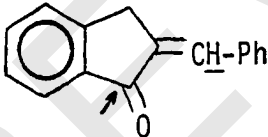
Cmpd.	Isomer	Structure	Orientation of Coupled Nuclei	LS (Hz)
20	-		cis	5.7
			trans	~10
21	<u>E</u>		trans	8.5
	<u>E</u>		cis	~6
22	<u>E</u>	Ph-CH=C(CH ₃)-CO-Ph	trans	8.5
	<u>E</u>	Ph-CH=C(CH ₃)-CO-Ph	cis	6.4
23	<u>E</u>	CH ₃ -CH=CH-CHO	cis	6.0
	<u>E</u>	CH ₃ -CH=CH-CHO	cis	8.8
24	<u>E</u>	Ph-CH=CH-CHO	cis	8.8
25	<u>Z</u>	Ph-CH=C(Br)-CHO	cis	7.8
26	-	Ph-CH=C(CO ₂) ₂	cis	7.3
			trans	10.8

Table I (continued)

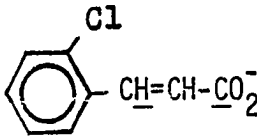
Cmpd.	Isomer	Structure	Orientation of Coupled Nuclei	LS (Hz)
<u>27</u>	-	$\text{CH}_3\text{-CH=C}(\text{CO}_2\text{CH}_3)_2$	cis	7.0
		$\text{CH}_3\text{-CH=C}(\text{CO}_2\text{CH}_3)_2$	trans	12.2
<u>28</u>	<u>E</u>	$\text{Ph-CH=CH-CO}_2^-(\text{D}_2\text{O})$	cis	6.3
	<u>E</u>	$\text{Ph-CH=CH-CO}_2\text{H}(\text{CDCl}_3)$	cis	7.0
<u>29</u>	<u>Z</u>		trans	12.0
<u>30</u>	<u>Z</u>	$\text{Ph-CH=C}(\text{Cl})\text{CO}_2^-$	cis	5.0
<u>31</u>	<u>Z</u>	$^-\text{O}_2\text{C-CH=CH-CONH}_2$	trans	11.5
	<u>Z</u>	$^-\text{O}_2\text{C-CH=CH-CONH}_2$	trans	12.2
<u>32</u>	<u>Z</u>	$^-\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH-CO}_2^-$	trans	10.8
	<u>Z</u>	$^-\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH-CO}_2^-$	cis	7.3
<u>33</u>	<u>E</u>	$^-\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH-CO}_2^-$	cis	6.7
	<u>E</u>	$^-\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH-CO}_2^-$	trans	8.3
<u>34</u>	<u>E</u>	$^-\text{O}_2\text{C-C}(\text{Br})=\text{CH-CO}_2^-$	trans	9.5
<u>35</u>	<u>Z</u>	$^-\text{O}_2\text{C-C}(\text{Br})=\text{CH-CO}_2^-$	cis	4.3
<u>36</u>	-	$\text{CH}_3\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH}_2$	cis	~6.5
		$\text{CH}_3\text{O}_2\text{C-C}(\text{CH}_3)=\text{CH}_2$	trans	~10
<u>37</u>	<u>E</u>	$\text{CH}_3\text{O}_2\text{C-C}(\text{CN})=\text{CH-CH}(\text{CH}_3)_2$	cis	~6
	<u>E</u>	$\text{CH}_3\text{O}_2\text{C-C}(\text{CN})=\text{CH-CH}(\text{CH}_3)_2$	trans	13.8
<u>38</u>	<u>E</u>	$\text{CH}_3\text{O}_2\text{C-C}(\text{CN})=\text{CH-Ph}$	cis	~7
	<u>E</u>	$\text{CH}_3\text{O}_2\text{C-C}(\text{CN})=\text{CH-Ph}$	trans	14.0

Table I (continued)

Cmpd.	Isomer	Structure	Orientation of Coupled Nuclei	LS (Hz)
39	<u>E</u>	$\text{NC}-\text{CH}=\text{CH}-\text{Ph}$	cis	8.7
40	-	$(\text{NC})_2-\text{C}=\text{CH}-\text{Ph}$	cis	8.4
		$(\text{NC})_2-\text{C}=\text{CH}-\text{Ph}$	trans	14.4
41	<u>E</u>	$\text{NC}-\text{C}(\text{CH}_3)=\text{CH}-\text{Ph}$	cis	8.8
	<u>E</u>	$\text{NC}-\text{C}(\text{CH}_3)=\text{CH}-\text{Ph}$	trans	8.2
42	<u>Z</u>	$\text{Ph}-\text{C}\equiv\text{C}-\text{CH}=\text{CH}-\text{Ph}$	trans	15.0
43	<u>E</u>	$\text{Ph}-\text{C}\equiv\text{C}-\text{CH}=\text{CH}-\text{Ph}$	cis	8.2

A and B among other factors, the deviation of LS from $^1J(\text{CH})$ is small (~ 0.2 Hz). For propenylbenzene, the methyl ^{13}C represents X of an ABM₃X spin system. For the Z isomer, (8) computer simulation shows that LS is again very similar to $^3J(\text{CH})$, within the error in data acquisition, ± 0.25 Hz. However, for the E isomer, LS does not correspond to $^3J(\text{CH})$ because of the small chemical shift difference between A and B, and large $J(\text{AB})$ and $|J(\text{AX}) - J(\text{BX})|$ terms. For simplicity, the terms "LS" and "coupling constant" will be used interchangeably to indicate line separations, whether or not the LS also correspond to true coupling constants.

Table II
Ranges of LS, Hz
(Common Values)

<u>Hybridization</u> <u>of Carbon</u>	<u>Cis Nuclei</u>	<u>Trans nuclei</u>
sp^1 (CN, C-C)	8.2-8.7	14-15 (~ 14)
sp^2 (CO)	4.3-10	9.5-16.9
sp^3 (CH ₂ X)	5.7-8.0 (~ 6)	7.7-11.0 (~ 8)

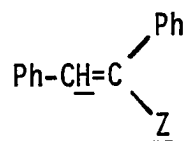
In Table I, the compounds are grouped in the order sp^3 , sp^2 , sp with regard to the hybridization of the carbon coupled to the alkene proton. Table II shows a summary of these results. For cis and trans nuclei the LS roughly

follow the predicted order of $sp > sp^2 > sp^3$, although considerable overlapping of ranges occurs (21a). Note, for example, the small difference (1.4 Hz) between the cis and trans couplings in mesityl oxide (15).

Table III illustrates the effect of varying the type of ^{13}C nucleus coupled to H in an otherwise constant hydrocarbon skeleton. The configurations of these compounds are known from other work and/or from the configurations of their precursors. The acid chloride and the aldehyde groups show the largest LS values for carbonyl groups. In fact these values are even larger than that of the sp hybridized nitrile carbon in this series. In Table I, the aldehydes 23, 24, and 65 exhibit similarly large values. Carboxylic acid, ester, and amide groups are not well differentiated (compare also 26-33, 36-39, and 57-59). That is the variations from compound to compound for the same type of carbonyl are as great as the variations from group to group, when the rest of the molecule is the same. Ketones consistently have the smallest LS values for carbonyls (cf. 57, 58, page 16)

The presence of a conjugating group, such as phenyl, substituted at carbonyl (e. g., 55) has little effect compared to alkyl groups (e. g., 55, 56, 58, 59). It is noteworthy that rigid (21) and nonrigid (22) ketone groups have similar LS values (22) (compare also 20 and 59). Thus, apparently, π overlap is not that important in the

Table III

LS of Substituted Stilbenes

Z^a	Cmpd ^b	LS (trans)	Cmpd ^b	LS (cis)
CN	<u>44</u> (Z)	14.2	<u>45</u> (E)	9.0
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{Cl} \end{array}$	<u>46</u> (Z)	16.9	<u>47</u> (E)	9.9
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{OH} \end{array}$	<u>48</u> (Z)	12.5	<u>49</u> (E)	7.3
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{OCH}_3 \end{array}$		<i>c</i>	<u>50</u> (E)	7.4
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{N} \begin{array}{l} \nearrow \text{Ph} \\ \searrow \text{CH}_3 \end{array} \end{array}$	<u>51</u> (Z)	11.5	<u>52</u> (E)	6.8
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{H} \end{array}$			<u>53</u> (E)	10.0
$\begin{array}{c} \text{N}-\text{OH} \\ \parallel \\ \text{C}-\text{H} \end{array}$			<u>54</u> (E)	9.2
$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{Ph} \end{array}$			<u>55</u> (E)	6.0

Table III (continued)

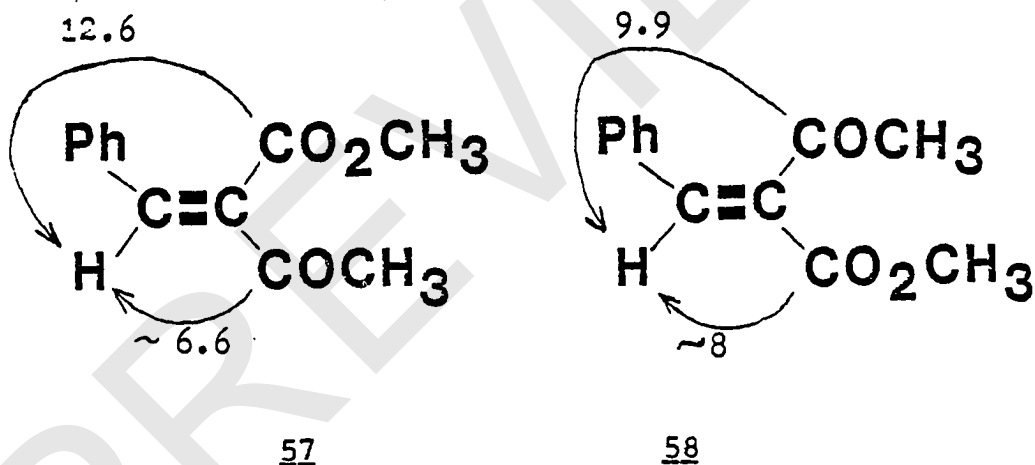
\underline{Z}^a	Cmpd ^b	LS (trans)	Cmpd ^b	LS (cis)
$\begin{array}{c} \text{O} \\ \\ \text{C}-\text{CH}_3 \end{array}$			56(E)	~6

^aStilbene substituent.

^bThe letter in parentheses refers to the configuration of the compound.

^cData for a slightly impure compound are 12.5 Hz.

transmission of spin information from H to ketone carbonyl. Except for the aldehyde and oxime groups (an aldoxime), the LS values are arranged such that sp^2 ^{13}C nuclei that have large LS values lie upfield in chemical shift and vice versa (23). The LS values parallel $^1J(CH)$ values for $H-CO-X$, again except for $X = H$. Lichter and Roberts and others have emphasized the possible importance of changes in excitation energy on coupling constants. Parallel changes were found for J and chemical shift in their systems.

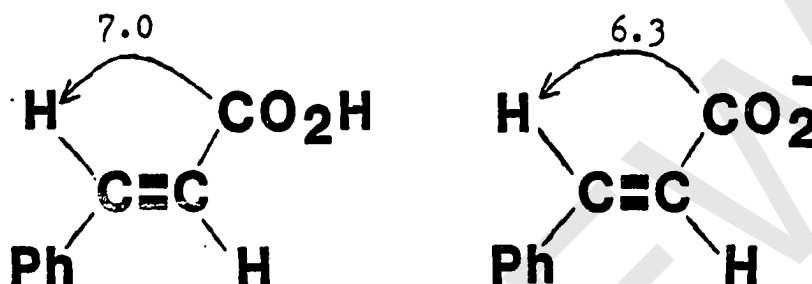


As with H-H couplings, the effects of electronegative groups appear to be quite large. Comparison of bromomaleic (34) and citraconic acids (32) shows that the former has the lower LS [$J(\text{trans})=9.5$ vs. 10.8 Hz]. The difference between 35 and 33 is even greater [$J(\text{cis})=4.3$ vs. 6.7 Hz], similar to H-H couplings, where the electronegative group is *trans* to one proton (cf. Eq 2 vs. Eq 1). This series involves substituents of similar size, and thus

differential steric effects are not likely to be important. The bromo aldehyde 25 shows a lower LS than 24 or 53. Chlorocinnamic acid (30) has a lower LS than phenylcinnamic acid (49). Although steric effects are variable in these compounds, the pattern is consistent: The presence of an electronegative group along the coupling path decreases the magnitude of the coupling constant. This is as expected, since the electronegative substituent would decrease the electron density along the coupling path, and the coupling information is carried through bonds by electron-electron and electron-nucleus correlation.

Electronegative substituents substituted on the carbon coupled to hydrogen appear to have the opposite effect, that is they increase the LS values for sp^3 carbons. The series 9, 10, and 11 shows an increasing LS as the electronegativity of the substituent increases from H (LS 6.6 Hz), OH (6.8 Hz), to Cl (8.0 Hz). In 7 the chloromethyl group has an apparently larger LS than the methyl (21a,25). Moving from 2-methyl-1,3-diphenyl-2-propen-1-one (22) to its bromomethyl analogue results in an increase in LS from 8.5 to 10 Hz. This is again consistent with the Fermi contact mechanism of spin coupling. The presence of the electronegative group on the ^{13}C nucleus draws electrons from that carbon. This increases the effective electronegativity of the carbon toward the electrons

carrying the coupling information. This change in the carbon's effective electronegativity is probably a reflection of a hybridization change (s orbitals are more electronegative than p orbitals).



28

The reverse is also true: Increasing electron density at the carbon-13 nucleus decreases the coupling. This is illustrated by the comparison of the neutral and anionic forms for 28. The carboxylate group has its fill of electrons due to the negative charge, and it is much more difficult for the electrons bearing the coupling information to "get in". However comparison of 39 and 43 indicates only a slightly larger LS for cyanide than alkyne (26), and the trans coupling for the sp^1 carbon in the alkyne 42 was the largest coupling for an sp^1 carbon in the present study (although the difference was not large; see for example 44). Furthermore there is no apparent relationship between the electronegativity of substituent X and coupling to carbonyl for $-COX$ in Table III. Evidently

the simple model of changes in effective electronegativity of carbon breaks down in the presence of pi bonds to the carbon-13 nucleus. With regard to the effect of substitution on the CC double bond, disubstituted alkenes appear to have larger LS than trisubstituted alkenes for trans CH₃-H couplings (the difference would be still larger if $^3J(\text{CH})$ values were calculated, as $^3J(\text{CH})$ is greater than LS). Thus 8 and 13 show LS of 10-11 Hz, whereas 12, 14, 15, and 17 show LS of ca. 8 Hz. However, for couplings to carbonyl groups, disubstituted alkenes have larger LS in some cases, but not in others.

The LS values discussed above show significant variation with structure, but these variations are by no means worse than the variations in $^3J(\text{HH})$ previously used to assign configuration in compounds of general structure 1 (17). Using the data of Table I, certain molecules were investigated whose state of isomerism could not be assigned in any other way. Compounds 57 and 58 (page 16) were obtained as an inseparable mixture upon condensation of methyl acetoacetate with benzaldehyde. The major component, 57, showed a large LS for the ester carbonyl and a smaller LS for the ketone; 57 is thus the Z isomer. Compound 58 shows the reverse LS characteristics, and is therefore the E isomer.

In contrast the difference in ketone carbonyl chemical shift was -7.5 ppm, whereas the difference for ester