Carbon-13 Nuclear Magnetic Resonance Spectroscopy. Substituted Vinyl Ethers and Acetates[1a]

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The ^{13}C NMR spectra of a number of substituted methyl vinyl ethers and vinyl acetates have been determined. In both series the polar substituent induces a large downfield shift of the directly bound olefinic carbon. This α shift varies in only a minor way with changes in the substitution pattern of alkyl groups on the double bond, except for bulky *geminate substitution*, which decreases the magnitude of this effect substantially. On the contrary, the substituent shift on the β-olefinic carbon is strongly shielding and depends significantly on the substitution pattern. Thus, alkyl groups cis to the methoxy function decrease this shielding in methyl vinyl ethers, whereas substitution at the geminate position causes a decrease in the β effect for vinyl acetates. The upfield shift of γ_{cis} and γ_{trans} carbons are also dependent on the structure of the molecule. These substituent effects are rationalized on the basis of steric and conjugative interactions in the substituted olefins.

The idea of substituent effects has proven to be an extremely useful tool in the study of organic molecules by ^{13}C NMR spectroscopy.[2] Substituent parameters have been derived for a number of functional groups on aliphatic and aromatic frameworks, but relatively little work has been done with olefinic compounds.[3] The effect of substitution at vinylic positions has been studied extensively only for simple alkenes, for which attention has been focused mainly on the unsaturated carbons.[4] In the present work, enol ethers and enol acetates are examined in order to probe the changes in chemical shifts in both the saturated and unsaturated portions of olefins provoked by substitution with the strongly interacting methoxy and acetoxy groups.

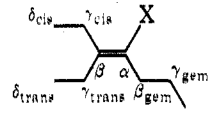
Experimental Section

Spectra. Carbon-13 NMR spectra were obtained using a modified high-resolution NMR spectrometer consisting of a Varian 14.1K Gauss electromagnet with an external ^{19}F lock, a Hewlett-Packard frequency synthesizer operating at 15.1 MHz, and an Ortec time-controlling device for gating the pulses. The free-induction decay signal was accumulated with a Fabri-Tek 1074 time-averaging computer. Fourier transformations were conducted with a Digital Electronics Corp. PDP 8/I computer. The limiting precision of the chemical shift data is ±0.12 ppm (4K data points in the time-domain spectra for a 250-ppm spectral window). Measurements were performed on ca. 10–30% (v/v) solutions in CCl_4. The solvent was used as an internal standard, and chemical shifts were converted to internal Me_4Si reference by the relation $\delta_{CCl_4} = 96.0$ ppm. This relationship was verified in several instances.

Materials. Most of the enol acetates were prepared from the corresponding carbonyl compounds by reaction with acetic anhydride or isopropenyl acetate.[5,6] The enol ethers were prepared from the corresponding carbonyl compounds in the usual manner via the intermediate dimethoxy acetals and ketals.[6] Mixtures of isomers were separated by preparative GLC using a 20-ft column of 20% Carbowax 20M on Chromosorb W, or a 20-ft column of 30% SE-30 on Chromosorb W. Infrared and NMR spectra are consistent with the structures assigned. Proton NMR shifts for olefinic hydrogens were used to differentiate between *E* and *Z* isomers.[7] The structures assigned in this fashion are substantiated by the ^{13}C NMR data.

Results

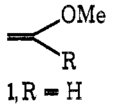
The chemical shifts for the series of vinyl ethers and vinyl acetates are listed in Tables I and II. The signals corresponding to the olefinic carbons are easily distinguished because of their low-field chemical shifts. In appropriate cases assignments were confirmed by single-frequency off-resonance spectra.[8] Assignments of signals to aliphatic carbons are more difficult and, in many cases, are based solely on analogy with the corresponding carbon in the parent alkane. However, possible ambiguities in these assignments are not of major significance for the conclusions given below. The validity of the concept of substituent effects for these compounds was confirmed by reasonable linear correlations (slopes approximating unity) for plots of the shifts of given carbons in the vinyl derivatives against the corresponding carbons of the parent olefins. The correlation for the β carbon for both types of compounds is improved by subdividing the data (see Figures 1 and 2). For vinyl ethers the two subgroups are compounds with alkyl substitution cis to the methoxy function and compounds without this feature. Vinyl acetates give a better correlation when separated into compounds possessing and compounds devoid of substituents geminate to the acetoxy-bearing carbon. The conventions indicated in I have been adopted to identify the different carbons.



I (X = H, OMe, OAc)

Discussion

I. Vinyl Ethers. α Effect. The α carbons of enol ethers (I, X = OMe) are shifted ca. 30 ppm downfield with respect to the corresponding carbon of the unsubstituted olefin (I, X = H). This shift is considerably larger than the ca. 17 ppm deshielding promoted by a similar substitution of the nonpolar ethyl group. Vinyl ethers without geminate substitution show substituent shifts in the range 31.4 ± 1.1 ppm. (Owing to the limited data available, *maximum* deviations from the average values are used throughout this paper.) However, geminate substitution causes a decrease in the α shift which is related to the size of this substituent as illustrated by the series 1 (30.6 ppm), 4 (27.4 ppm), 6 (23.8 ppm). The larger cyclic compounds 11 and 12 appear



1, R = H
4, R = CH_3
6, R = i-C_3H_7

to behave like other geminate-substituted examples, although five-membered compound 10 shows a larger α effect. This variance in substituent shift is probably related primarily to differences in the polarization of the double-bond electrons caused by the *gem*-alkyl group in the parent alkene,[9] and to nonbonded interactions between the methoxy group and the *gem*-alkyl moiety.[10]

Table I
^{13}C Chemical Shifts for Some Methyl Vinyl Ethers[a]

Compd	(No.)	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	OCH_3
Methyl vinyl ether[b]	(1)	153.2	84.1							52.5
		(30.6)[c]	(−38.5)							
(*E*)-1-Methoxypropene	(2)	147.5	96.0	12.5						54.9
		(31.8)	(−36.8)	(−6.8)						
(*Z*)-1-Methoxypropene	(3)	146.4	100.2	8.8						58.5
		(30.7)	(−32.6)	(−10.5)						
2-Methoxypropene	(4)	80.4	160.2	20.4						53.9
		(−35.3)	(27.4)	(1.1)						
1-Methoxy-2-methylpropene	(5)	141.4	109.0	14.3[d]	18.9[e]					58.0
		(30.9)	(−31.7)	(−9.0)	(−4.4)					
2-Methoxy-3-methyl-1-butene	(6)	76.8	168.9	33.1	20.2					53.5
		(−34.3)	(23.8)	(1.4)	(−1.5)					
(*E*)-1-Methoxy-1-heptene	(7)	147.0	101.8	27.7	30.5[f]	31.1[f]	22.4	13.7		54.6
		(32.5)	(−37.3)	(−6.8)	(1.1)	(1.1)	(−0.9)	(−0.7)		
(*Z*)-1-Methoxy-1-heptene	(8)	145.6	106.6	23.5	29.3	31.2	22.3	13.7		58.4
		(31.1)	(−32.5)	(−11.0)	(−0.1)	(−1.0)	(−1.0)	(−0.7)		
(*E*)-4-Methoxy-3-heptene	(9)	14.2[f]	18.3[f]	94.3	154.8	30.3	18.8[f]	12.0[f]		52.5
		(−0.1)	(−2.6)	(−37.6)	(25.6)	(0.7)	(−4.5)	(−1.6)		
1-Methoxycyclopentene	(10)	161.1	92.3	28.6	21.1	31.4				55.6
		(30.9)	(−37.9)	(−3.6)	(−1.5)	(−0.8)				
1-Methoxycyclohexene[g]	(11)	155.5	92.0	22.7	23.3	22.7	27.2			54.0
		(28.7)	(−34.8)	(−2.7)	(0.8)	(−1.5)	(1.8)			
1-Methoxycyclooctene[g]	(12)	158.3	93.5	24.3	31.0	25.8	25.8	29.5	28.3	53.3
		(28.6)	(−36.2)	(−2.3)	(−0.5)	(−0.1)	(−0.1)	(−0.3)	(1.7)	

[a] In parts per million downfield from Me_4Si. [b] Data from ref 21 (neat). Converted to the Me_4Si scale using δ_c (CS_2) = 193.7 ppm. [c] $\Delta\delta = \delta^i_{ROMe} - \delta^i_{RH}$, the difference between the chemical shift of the carbon in the vinyl ether and that of the corresponding carbon in the parent olefin. [d] Carbon cis to the methoxy function. [e] Carbon trans to the methoxy group. [f] Assignment not unambigously established. [g] Assignments are tentative both in the vinyl ether and in the corresponding cycloalkane.

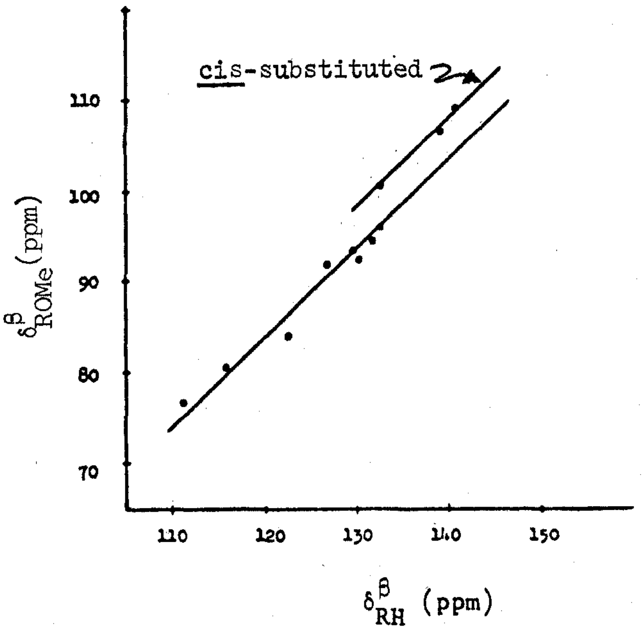


Figure 1. Correlation between ^{13}C chemical shifts of β carbons in methyl vinyl ethers (ROMe) and the corresponding alkenes (RH).

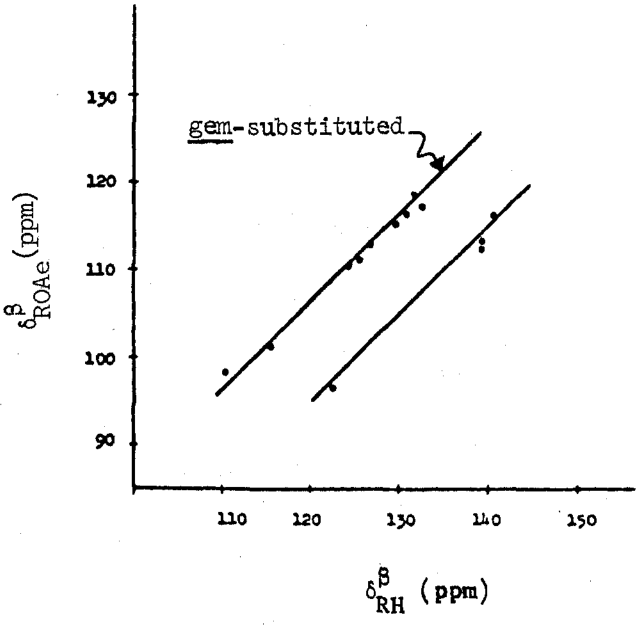


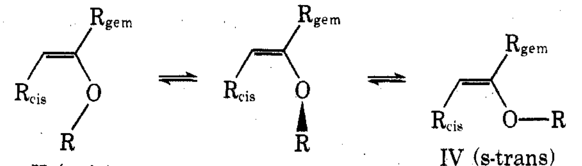
Figure 2. Correlation between the ^{13}C chemical shifts of β carbons in vinyl acetates (ROAc) and the corresponding alkenes (RH).

β Effect. An olefinic carbon β to the methoxy group suffers a large upfield shift. The magnitude of this effect appears to depend on substitution at the β carbon cis to the functional group (see Figure 1). Thus, cis-substituted compounds are shielded by −32.3 ± 0.6 ppm, whereas vinyl ethers without cis substituents show a β shift of −36.5 ± 2.2 ppm. (The scatter in these values appears to result from minor systematic differences with substitution patterns.) For comparison, an ethyl group introduces a β shift of only ca. −10 ppm.[4a] The large shielding effect on the β carbon is rationalized on basis of conjugative interaction between the double bond and the oxygen which increases electron density on the β carbon.[11,12] The difference between the two types of vinyl ethers may be attributed to a decrease in electron transfer in the cis-substituted compounds, since substituting at R_{cis} with an alkyl group modifies the conformational equilibrium II ⇄ III ⇄ IV so as to increase gauche conformation III which is not important for conju-

Table II
^{13}C Chemical Shifts for Some Vinyl Acetates[a]

Compd	(No.)	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C=O	CH_3
Vinyl acetate	**(13)**	141.2	96.6							166.1	20.1
		(19.6)	(−25.0)[b]								
2-Acetoxypropene	**(14)**	101.2	152.8	19.3[c]						167.4	20.5[c]
		(−14.5)	(20.0)	(−0.2)							
2-Acetoxy-3-methyl-1-butene	**(15)**	98.6	160.9	32.1	20.1					167.0	20.5
		(−12.5)	(15.8)	(0.4)	(−1.6)						
1-Acetoxy-2-methylpropene	**(16)**	130.2	116.3	15.2[d]	19.2[c,e]					166.4	19.9[c]
		(19.7)	(−24.4)	(−8.1)	(−4.1)						
(*E*)-2-Acetoxy-2-butene	**(17)**	14.6	110.8	145.7	11.4					167.4	20.3
		(3.2)	(−12.5)	(21.5)	(0.0)						
(*Z*)-2-Acetoxy-2-butene	**(18)**	18.8	110.0	145.2	9.9					166.6	19.7
		(2.2)	(−15.2)	(20.0)	(−6.7)						
2-Acetoxy-3-methyl-2-butene	**(19)**	15.5	116.8	138.8	18.0[d]	16.8[e]				167.4	20.5
		(2.8)	(−14.0)	(20.7)	(−6.8)	(0.3)					
(*E*)-1-Acetoxy-1-heptene	**(20)**	135.5	113.5	27.1	29.1	31.1	22.3	13.8		166.0	20.1
		(21.0)	(−25.6)	(−7.4)	(−0.3)	(−1.2)	(−1.0)	(−0.6)			
(*Z*)-1-Acetoxy-1-heptene	**(21)**	134.0	112.8	24.3	28.8	31.3	22.3	14.0		165.8	20.3
		(19.5)	(−26.3)	(−10.2)	(−0.6)	(−0.9)	(−1.0)	(−0.4)			
(*E*)-4-Acetoxy-3-heptene	**(22)**	14.4	19.8[e]	119.0	147.9	30.7	19.8[e]	13.5		167.4	20.5[e]
		(0.1)	(−1.1)	(−12.9)	(18.7)	(1.1)	(−3.5)	(−0.1)			
(*Z*)-4-Acetoxy-3-heptene	**(23)**	13.4	18.6	117.2	147.5	35.3	19.6[e]	13.4		166.5	20.1[e]
		(−0.6)	(−7.4)	(−15.2)	(18.1)	(0.2)	(−3.6)	(−0.1)			
1-Acetoxycyclohexene[f]	**(24)**	148.4	113.0	21.5	23.5	22.5	27.0			167.4	20.5
		(21.6)	(−13.8)	(−3.5)	(1.0)	(0.0)	(2.0)				
1-Acetoxycyclooctene[f]	**(25)**	150.3	115.3	24.5	29.3	25.5	27.5	26.0	29.3	167.8	20.5
		(20.6)	(−14.4)	(−2.1)	(0.2)	(0.2)	(2.2)	(−3.1)	(3.2)		

[a] Chemical shifts reported in parts per million downfield from Me_4Si. [b] $\delta^i_{RX} - \delta^i_{RH}$, the difference between the chemical shift of the *i* carbon in the enol acetates and that of the corresponding carbon in the parent olefin. [c] The assignments are not unambigously established. [d] Carbon cis to the acetate function. [e] Carbon trans to the acetate function. [f] Except for C_1 and C_2, the assignments for the other carbons in both the acetate and the parent alkene are tentative.



II (s-cis) III (s-gauche) IV (s-trans)

gation.[13,21] In addition a shielding contribution for compounds without cis substituents may come from steric interaction between the methoxy function and the hydrogen at R_{cis}.[22] Support for the operation of this mechanism is derived from the chemical shift behavior of the methoxy group (vide infra).

γ_{cis} and γ_{trans} Effects. Generally, substitution of a vinylic hydrogen affects both cis and trans carbons attached to the other olefinic carbon. For instance, a methyl group shields a γ_{cis} carbon by ca. −5 ppm, whereas the effect at a γ_{trans} position is smaller and variable in sign.[23,24] In vinyl ethers both types of carbons experience an upfield shift suggestive of an increase in negative charge. The γ_{cis} carbon is shielded by −10.2 ± 1.2 ppm, considerably more than the −4.2 ± 2.6 ppm shift of the γ_{trans} carbon. These values vary appreciably with substitution pattern, especially γ_{trans}, which is smaller in the presence of a geminate substituent. The shielding at the γ carbons appears to reflect the β effect and, therefore, parallels the transfer of electron density to the β carbon. In addition, the γ_{cis} carbon is shielded by a through-space steric interaction with the added methoxy group. For simple cis–trans isomers, the through-bond contribution appears to predominate, as evidenced by shifts of ca. −11 and −7 ppm at the γ carbons of isomeric cis and trans compounds, respectively (e.g., compare **3** with **2**, and **8** with **7**).

Other Carbons. Carbons of the *gem*-alkyl chain appear to follow the general trends observed for straight-chain alkyl derivatives, namely, deshielding at β_{gem} (1.3 ± 0.6 ppm) and shielding at γ_{gem} (−1.6 ± 2.9 ppm).[4] Long-range effects, such as those at remote carbons in the alkyl chains of the isomeric 1-methoxy-1-heptenes (**7** and **8**), are noteworthy.

The Methoxy Carbon. The methyl carbon of the ether function falls in the chemical shift range of 52.5–58.5 ppm and depends on the structure of the molecule analogously to the β shifts. Thus, in compounds without cis substitution this carbon is found at higher field (52.5–55.6 ppm) than in cis-substituted ethers (58.0–58.5 ppm).[25] Steric interaction between the methyl and the β-vinylic hydrogen in s-cis conformation II (R_{cis} = H; R = CH_3) helps to account for the observed chemical shifts of both the methoxy carbon and the β carbon (vide supra).

II. Vinyl Acetates. α Effect. The acetate function deshields the α-olefinic carbon of enol acetates by ca. 20 ppm. The magnitude of the shift does not depend to a large extent on the alkyl substitution pattern of the double bond, although geminate substituents larger than methyl decrease the α effect as shown by the significantly smaller values for compounds **15**, **22**, and **23** (see Table II). The cyclic compounds do not show this behavior, suggesting that the decrease in the deshielding effect is caused by steric interactions between γ_{gem} carbons and the acetoxy group. For compounds differing only in the stereochemistry of the alkyl chain relative to the acetate function (i.e. pairs of *E* and *Z* isomers), the α carbon is consistently at ca. 1 ppm higher field for the isomer with cis-alkyl substitution. (Compare **17** vs. **18**, **20** vs. **21**, and **22** vs. **23**.)

β Effect. The dependence of the shielding of this carbon on the structure of the molecule is evident from Figure 2, which shows a clean separation into groups of compounds *with* and *without* substitution at the geminate position. The β carbon of the double bond in geminate-substituted vinyl acetates (β shift of -14.0 ± 1.5 ppm) is less shielded by more than 10 ppm relative to compounds lacking this type of substitution (β shift of -25.6 ± 1.2 ppm). The general upfield shift at the β carbon is again ascribed to conjugation between the double bond and the attached oxygen.[26] The smaller shift for geminate-substituted vinyl acetates is associated with less conjugative transfer of electron density to the β carbon, alkyl substitution at the geminate position sterically hindering attainment of conformer IV (R = OAc) and forcing the molecule into the s-gauche conformation III. In both of the subgroups compounds with cis substituents are upfield of those with trans groups.

γ_{cis} and γ_{trans} Effects. As with vinyl ethers, both carbons bonded to the β-olefinic position show upfield substituent effects. The magnitudes of these shifts parallel those of the β shift. Both γ_{cis} and γ_{trans} carbons are strongly shielded in vinyl acetates that do not bear alkyl substitution at the geminate position (γ shifts of -9.2 ± 1.0 and -5.8 ± 1.7 ppm, respectively). However, a geminate substituent causes the shielding of the γ_{trans} carbon to drop considerably (ca. -1.0 ppm), whereas the shift of the γ_{cis} carbon (-7.0 ± 0.4 ppm) decreases only slightly. The *gem*-alkyl group decreases electron transfer to the β carbon and also retards charge relay to γ_{trans} by virture of its cis steric interaction with this carbon. However, steric interactions between the γ_{cis} carbon and the acetate group are increased by a butressing effect of the geminate substituent and presumably lead to a compensating shielding at γ_{cis}.

Other Effects. The β carbon in the *gem*-alkyl chain is, in general, deshielded and the magnitude of this effect appears to depend on the nature of the β-carbon moiety and on the substitution pattern of the double bond. Thus, methyl groups are deshielded relative to methylene groups in the β_{gem} position (compare **17** and **18** vs. **22** and **23**). Furthermore, in pairs of *Z* and *E* isomers, compounds with alkyl chains cis to each other show a larger downfield shift than those with a trans arrangement of these groups. Interestingly, remote carbons in the *cis*- and *trans*-alkyl chains of compounds **20** and **21** show upfield shifts.

The Acetate Group. Both carbonyl and methyl carbons fall into relatively narrow ranges (166.1–167.8 and 19.7–20.5 ppm, respectively). The failure of the carbonyl chemical shift to parallel the large changes of the β carbon is consistent with a lack of conjugative interaction between these two moieties. However, the chemical shifts of the carbonyl carbons in compounds without *gem*-alkyl substitution (166.1 ± 0.3) are consistently ca. 1 ppm upfield of compounds with *gem*-alkyl groups (167.2 ± 0.7 ppm), probably because of steric interactions in the latter.

Summary

The results of this study are in general accord with the correlations of ^{13}C chemical shifts with electron densities for monosubstituted ethylenes.[12] The large downfield α shift is attributed to inductive withdrawal by the highly electronegative substituents, the methoxy group being substantially more effective than the acetoxy function. The β shift is upfield and usually quite large also. The major factor here is undoubtedly conjugative transfer of electron density to the β carbon from the oxygen, although double-bond polarization[9] probably also plays a significant role. The larger shifts for methoxy relative to acetoxy are in agreement with the relative abilities of these functions to donate electron density by resonance.[27] Alkyl substituents which change the conformational situation of the methoxy or acetoxy group so as to decrease conjugation also lower the magnitude of the upfield β effect. This accounts for the smaller β shifts for cis-substituted enol ethers and geminate-substituted acetates. The much larger difference between the two subgroups of acetates reflects the greater difficulty the larger acetate group has in achieving a suitable alternative to conformation IV capable of conjugation, whereas methoxy can modify its conformational distribution toward form IV when the normally favored conformer II is destabilized. The γ carbons on the double bond also appear to be shielded by an increase in electron density at the β carbon suggesting a relay of charge to these centers. Other steric interactions (especially those involving geminate groups) can cause significant changes in substituent shifts, usually decreasing the magnitudes of these effects relative to those of molecules without such interactions. Thus, steric stress generally decreases the ability of a substituent to play its usual role, regardless of whether this is shielding or deshielding.

Registry No.—**1**, 107-25-5; **2**, 4188-69-6; **3**, 4188-68-5; **4**, 116-11-0; **5**, 17574-84-4; **6**, 51776-45-5; **7**, 55373-78-9; **8**, 55373-79-0; **9**, 55373-80-3; **10**, 1072-59-9; **11**, 931-57-7; **12**, 50438-51-2; **13**, 108-05-4; **14**, 108-22-5; **15**, 3814-40-2; **16**, 14478-14-9; **17**, 15984-02-8; **18**, 15984-03-9; **19**, 3814-41-3; **20**, 17574-85-5; **21**, 17574-86-6; **22**, 55373-81-4; **23**, 5780-51-8; **24**, 1424-22-2; **25**, 14478-13-8.

References and Notes

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(2) See, for example, (a) J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, N.Y., 1972; (b) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, New York, N.Y., 1972; (c) G. E. Maciel in "Topics in Carbon-13 NMR Spectroscopy," G. C. Levy, Ed., Wiley-Interscience, New York, N.Y., 1974, pp 53–77.

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(9) The efficacy of a substituent in modifying the electronic structure of an olefin undoubtedly depends on the electron distribution in the reference compound which is formally being substituted. Calculations indicate that replacement of a hydrogen in ethylene by a methyl group causes a polarization of the π-electron density away from the substituted olefinic carbon towards the unsubstituted one: L. Libit and R. Hoffman, *J. Am. Chem. Soc.*, **96**, 1370 (1974). Consequently, a substituent effect operating in the same sense would be expected to be diminished by a geminate group.

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(13) Evidence from dipole moment data,[14] infrared,[15] microwave,[16] and electron diffraction spectra[17] are consistent with the existence of s-cis and s-gauche conformers in methyl vinyl ether. Proton NMR data for vinyl ethers[18] and trans-alkyl substituted compounds[19] are consistent with a preference for the s-cis conformation, whereas cis-substituted enol ethers are suggested to prefer the s-trans conformation IV.[19] However, a recent infrared study of the 1-methoxy-1-propenes has been interpreted in terms of a preferred nonplanar conformation for the *Z* isomer.[20]

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Carbon-13 Nuclear Magnetic Resonance Spectra of the Vitamin B-6 Group

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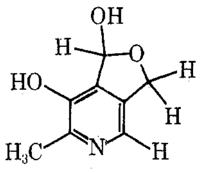
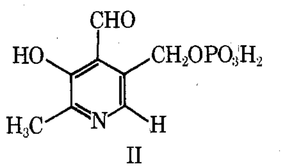
The Fourier transform natural abundance carbon-13 spectra of pyridoxal, pyridoxal 5′-phosphate, pyridoxamine, pyridoxamine 5′-phosphate, and pyridoxine are reported. Resonances are assigned by chemical shift analogies and by spin–spin coupling to adjacent protons. Chemical shifts are strongly pH dependent owing to the deprotonation of the various functional groups. Chemical shift analogies are interpreted as indicating a zwitterionic structure at neutrality. The detailed pH dependence of the carbon-13 chemical shifts of pyridoxal 5′-phosphate, pyridoxamine 5′-phosphate, and pyridoxine are reported. Long- and short-range proton-to-carbon coupling constants are also reported and are not found to be strongly pH dependent.

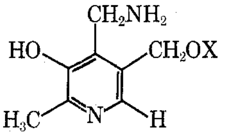
The vitamin B-6 group is comprised of pyridoxal (PL, I), pyridoxal 5′-phosphate (PLP, II), pyridoxamine (PM, III), pyridoxamine 5′-phosphate (PMP, IV), and pyridoxine (PN, V). These substituted pyridines are essential cofactors to a large number of enzymes involved in the metabolism of amino acids. The reactions they catalyze proceed through Schiff base formation of the amino acid with the substituted 4-pyridine aldehyde form of the vitamin. The Schiff base may undergo any one of a number of electron shifts transforming the amino acid moiety into the various observed products.[1] A particular type of enzyme apparently participates in the reaction by selectively catalyzing only the desired electron shift and by inhibiting all the other types of shifts. In order to understand the means by which enzymes can control the electron shifts in these Schiff bases, it is necessary to understand the factors which influence electron densities in the aromatic ring of the vitamin B-6 Schiff bases. The sensitivity of carbon-13 nuclear magnetic resonance (^{13}C NMR) to electronic structure is well known. We are in the process of carrying out a complete study of the ^{13}C NMR spectroscopy of the vitamin B-6 Schiff bases and their metal complexes, but, as a prelude, it has been necessary to study the vitamin B-6 group itself. Herein we report the ^{13}C NMR spectral assignments, pH dependence, and coupling constants for the vitamin B-6 group and some related pyridine derivatives.



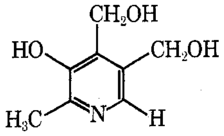
I



II



III, X = H
IV, X = PO$_3$H$_2$



V

Experimental Section

Pyridoxal hydrochloride and pyridoxal-5′-phosphate were purchased from Sigma Chemical Co., and pyridoxamine dihydrochloride was obtained from Mann Research Laboratories. Picoline was from Reilly Tar and Chemical Corp. Pyridoxine, pyridoxamine 5′-phosphate, and the remaining monosubstituted pyridines were from Aldrich. Deuterium oxide was 99.8% from Thompson-Packard; NaOD (40% in D_2O) and DCl (20% in D_2O) were from Diaprep Inc.

Carbon-13 nuclear magnetic resonance spectra were obtained at 40° in Fourier transform mode with a Jeol PS/FFT-100 spectrometer and Jeol EC-100 data system. Chemical shifts were recorded in parts per million relative to an external capillary of dioxane; these values were adjusted to the tetramethylsilane (Me_4Si) scale by adding 67.4 ppm to the observed shift. This ignores a small (<0.2 ppm) correction due to diamagnetic susceptibility.[2] Typically a 6250-KHz range and 16K words of memory were used, giving a digital resolution of 0.76 Hz. The D_2O solvent was the source of an internal deuterium lock. Broad band decoupled (2 KHz), single frequency decoupled, and undecoupled spectra were recorded.

Solutions (1 *M*) of pyridoxal-related compounds (except pyridoxine) in D_2O were maintained at constant ionic strength with sodium chloride (3 *M*); in cases where 1 *M* solutions could not be prepared, saturated solutions were used. The pD (negative logarithm of deuterium ion activity) was recorded by adding 0.41 to the reading of a Brinkmann Model E512 pH meter standardized against aqueous buffers;[3] this method is valid only in the range $2 < \mathrm{pD} < 9$, and values outside this range are approximate. No correction was made for sodium ion effects. Acidity was varied by the addition of DCl or NaOD. At these conditions of high salt and reagent concentration, observed pH becomes an ill-defined concept and reported pD values must be viewed as approximate measures of pH.

Results and Discussion

Resonance Assignments. Despite the structural similarity of compounds I–V, complete assignment of their resonances is an arduous task because many fall in a narrow