Conformational Preferences of C1-Oxygenated Acyclic Chiral Alkenes: Evidence for the C–C Eclipsed Conformer

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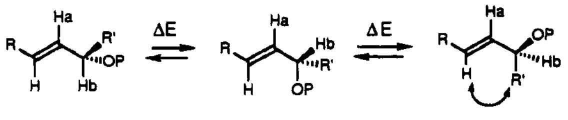
Received January 7, 1993

Three forms of conformational minima were found for 3-buten-2-ol by *ab initio* MO methods, including the conformers where the allyl methyl group eclipses the C═C bond. The computational results are corroborated by a VT NMR study of a variety of C1-oxygenated chiral alkenes. The experimental study indicates that chiral allylic alcohols and ethers with a formula of (*E*)-RCH═CHCH(OP)R′ can have either two or three stable rotamers depending on the size of the allylic substituent, R′. When R′ is a methyl group, the coupling constant, $^3J_{ab}$, is smaller than when R′ is a bulky group, indicating a three-rotamer equilibrium.

Introduction

Although rotational isomerism about a C_{sp2}–C_{sp3} bond has been studied extensively,[1,2] little is known about the influence of allylic substituents on conformational stability. For acyclic compounds, chiral (*Z*)-alkenes are known to be mainly in the C–H eclipsed form,[3] but there is still confusion in the literature about the relative conformational stability of asymmetric (*E*)-alkenes. Wilson et al. studied the conformations of 3-buten-2-ol by microwave spectroscopy and identified two stable conformations (**Ia** and **IIb**, Table I).[4] The C–H eclipsed conformation (**Ia**) was found to be ca. 520 cal/mol more stable than the C–O eclipsed form (**IIb**). They reported that some unassigned transitions in the microwave spectrum might have originated from either the C–O eclipsed form **IIa** or the C–C eclipsed form **IIIb**.[4] However, due to the complexity of the spectrum, the assignment was not straightforward. Khan and Hehre reported a theoretical study of the conformations of chiral alkenes, and they correctly predicted the influence of the vinyl substituents on conformational preference.[5] For example, conformer **I** is preferred when R = methyl while conformer **II** is favored when R = CN.[6] At the 3-21G level of theory, the C–C eclipsed conformer (**III**) was found for 2-methoxy-3-butene but was not found for 3-buten-2-ol.[5] The unassigned transitions in the previously reported microwave spectrum were suggested to be from conformation **IIa** (Table I).[5]

In a recent paper, we reported a study of the conformational preferences of chiral alkenes by the VT NMR method and described the influence of the vinyl substituents.[6] In this paper, we wish to report both experimental and computational results that indicate the presence of the third group of conformers (**IIIa–c**, Table I). The influence of the allylic substituents on the conformational preference of chiral alkenes is demonstrated through a gradual change in their steric size.



I II III

Favored when R = alkyl favored when R = CN or CO_2R'

Computational Methods and Results

Ab initio calculations were carried out by the Gaussian 88 and 90 programs[7,8] implemented on the Cray Y-MP/8 supercomputer. All structures in Table I were optimized using the STO-3G and 6-31G* theoretical models. No symmetry was imposed, and all parameters, including bond lengths, bond angles, and dihedral angles, were fully optimized. Harmonic frequencies were calculated for each equilibrium structure. The optimized structures have all positive frequencies, which is an indication of true minima on the 6-31G* potential surface. The conformational search was carried out by varying the torsional angles, $\tau_{CC\text{-}CO}$ and $\tau_{CC\text{-}OH}$, and nine minima were found for 3-buten-2-ol, **I–III**, Table I. In accord with previous reports,[4,5] the global minimum is a C–H eclipsed form (**Ia**), but in contrast to the previous report,[5] minima were located for the third group of conformers at both the STO-3G and the 6-31G* levels of theory. This discrepancy could have arisen from two factors: (1) the earlier calculations were performed using the 3-21G basis set, or (2) the alkene carbons were constrained as planar in the previous study. To examine the accuracy of the current calculations, we have explored the two-dimensional rotational potential surface, Figure 1. The energy contour map was constructed by systematic calculations (STO-3G) of 144 conformations, which were obtained by varying the torsional angles $\tau_{CC\text{-}CO}$

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[1] For theoretical studies, see: (a) Cremer, D.; Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1974**, *96*, 6900. (b) Hehre, W. J.; Pople, J. A.; Devaquet, A. J. P. *J. Am. Chem. Soc.* **1976**, *98*, 664. (c) Pross, A.; Radom, L.; Riggs, N. V. *J. Am. Chem. Soc.* **1980**, *102*, 2253. (d) Wiberg, K. B.; Martin, E. *J. Am. Chem. Soc.* **1985**, *107*, 5035. (e) Dorigo, A. E.; Pratt, D. W.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6589.

[2] For experimental studies, see: (a) Karabatsos, G. J.; Fenoglio, D. J. In *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1970; Vol. 5. (b) Bothner-By, A. A.; Castellano, S.; Ebersole, S. J.; Gunther, H. *J. Am. Chem. Soc.* **1966**, *88*, 2466.

[3] (a) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841. (b) Kishi, Y. *Aldrichim. Acta* **1980**, *13*, 23. (c) Gung, B. W.; Karipides, A.; Wolf, M. A. *Tetrahedron Lett.* **1992**, *33*, 713 and references cited therein.

[4] Smith, Z.; Carballo, N.; Wilson, E. B.; Marstokk, K.; Mollendal, J. *J. Am. Chem. Soc.* **1985**, *107*, 1951.

[5] Khan, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650.

[6] Gung, B. W.; Wolf, M. A.; Ohm, K. W.; Peat, A. J. Conformational Preferences of C1-Oxygenated Acyclic Chiral Alkenes: the Effect of Vinyl and Allyl Substituents. *Tetrahedron Lett.* **1993**, *34*, 1417.

[7] Hehre, W. J.; Radom, L.; Schleyer, P. v. P.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.

[8] Gaussian 90, Revision H: Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. Gaussan, Inc., Pittsburgh, PA, 1990.

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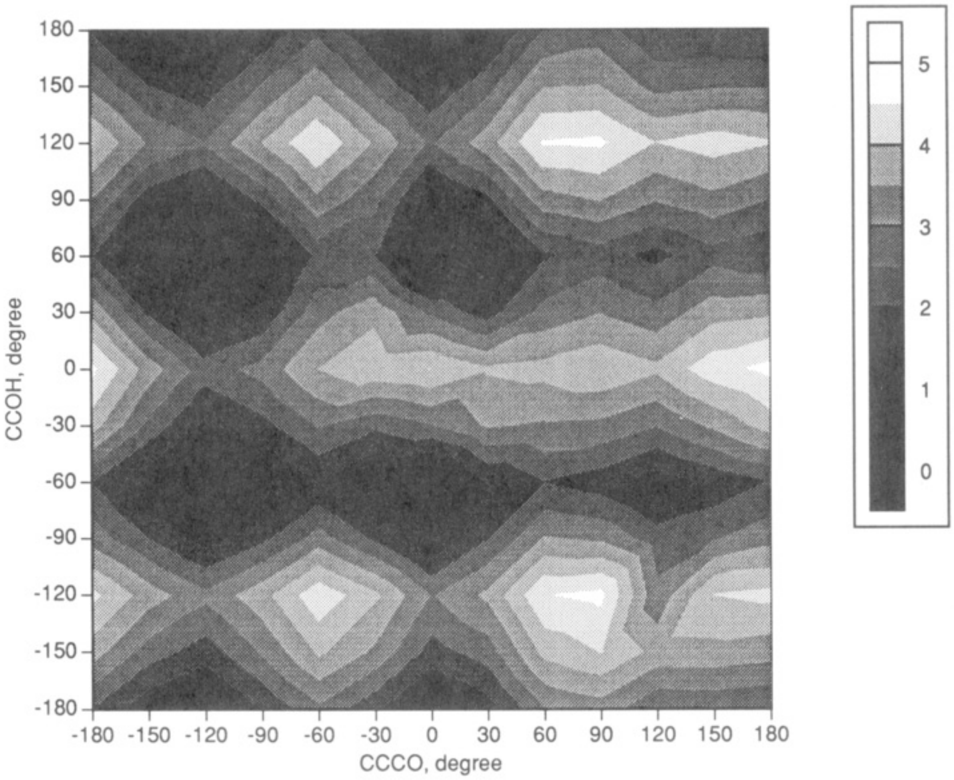
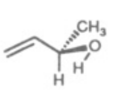
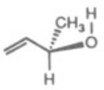
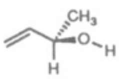
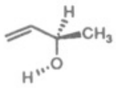
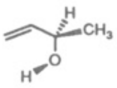
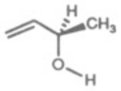
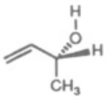
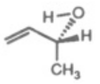
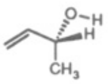


Figure 1. Rotational energy (kcal/mol) contour map for 3-buten-2-ol. The dark areas are potential wells, and the clear areas are energy maxima. The contour shades are in increments of 0.5 kcal/mol as indicated on the key bar. The energy contour map was constructed by a systematic calculation (STO-3G) of 144 conformations, which were obtained by varying the torsional angles τ_{CC-CO} and τ_{CC-OH}, at 30° intervals. All parameters except the two torsional angles being rotated are optimized.

Table I. Relative ab Initio Energies of the Conformations of 3-Buten-2-ol, I–III

	group I: C–H eclipsed			group II: C–O eclipsed			group III: C–C eclipsed		
									
	Ia	**Ib**	**Ic**	**IIa**	**IIb**	**IIc**	**IIIa**	**IIIb**	**IIIc**
STO-3G	0.0	0.33	0.66	0.29	0.25	0.68	1.84	1.21	1.94
3-21G[a]	1.0	3.0	2.6	0.0	0.2	1.3	*b*	*b*	*b*
6-31G*	0.0	1.96	1.57	0.38	0.77	1.52	2.95	1.53	2.57

[a] Reference 5. [b] Not a minimum, see ref 5.

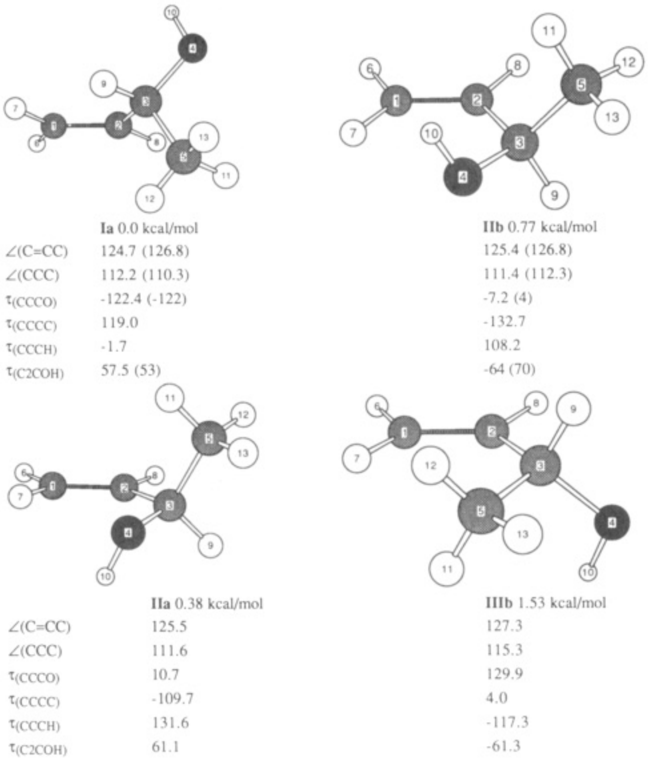
and τ_{CC-OH}, at 30° intervals. All parameters except the two torsional angles that are being rotated are optimized. The extended basis set (6-31G*) could have produced a more accurate energy map. However, the prohibitive expense in computer time is not justified at this time. Thus, Figure 1 shows a qualitative two-dimensional energy contour map while Table I lists the more accurate relative energies for the equilibrium structures.

The two conformations identified by microwave study are shown in the first row of Figure 2. The structural parameters calculated at the 6-31G* level are improved and closer to the experimental values than the previously reported calculations at the 3-21G level.[5] The greatest improvement is the dihedral angle of CCCO for structure **Ia** (microwave: −122.0°, 3-21G: −130°, and 6-31G*: −122.4°).

The two structures in the second row in Figure 2 represent the most stable conformations for the C–O and C–C eclipsed forms. It is interesting to note that the most stable C–O eclipsed form (**IIa**) at the 6-31G* level was not identified by the microwave study. The energy difference between **IIa** and **IIb** is small at all levels of theory, Table I. Both conformations have the hydroxylic H directly over the π-bond, but conformation **IIa** has the methyl group nearly perpendicular to the π-bond, while **IIb** has the C–H bond nearly perpendicular to the π-bond.

According to the microwave study, the energy difference between the C–H and the C–O eclipsed forms was about 520 cal/mol. Conformation **IIb**, which was previously assigned to represent the C–O eclipsed form, is 770 cal/mol higher in energy than the ground-state conformer **Ia** according to the current calculation. Conformation **IIa**, which according to the microwave study was also a possible isomer, is only 380 cal/mol higher in energy than the global minimum at the 6-31G* level of theory. The relative energy of either conformation can match the reported value within experimental error. However, a weighted average value from both conformations would give a near-perfect match. The existence of two energetically similar forms would also explain the complexity of the microwave spectrum, especially in the assignment of the transitions to the C–O eclipsed conformer.[4]

The C–C eclipsed form, **IIIb**, is 1.5 kcal/mol higher in energy than the global minimum (**Ia**) at the 6-31G* level



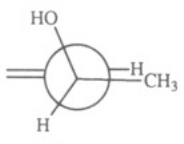
	Ia 0.0 kcal/mol	**IIb** 0.77 kcal/mol
∠(C=CC)	124.7 (126.8)	125.4 (126.8)
∠(CCC)	112.2 (110.3)	111.4 (112.3)
$\tau_{(CCCO)}$	-122.4 (-122)	-7.2 (4)
$\tau_{(CCCC)}$	119.0	-132.7
$\tau_{(CCCH)}$	-1.7	108.2
$\tau_{(C2COH)}$	57.5 (53)	-64 (70)

	IIa 0.38 kcal/mol	**IIIb** 1.53 kcal/mol
∠(C=CC)	125.5	127.3
∠(CCC)	111.6	115.3
$\tau_{(CCCO)}$	10.7	129.9
$\tau_{(CCCC)}$	-109.7	4.0
$\tau_{(CCCH)}$	131.6	-117.3
$\tau_{(C2COH)}$	61.1	-61.3

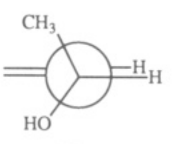
Figure 2. Selected conformations and their relative energies (6-31G*) of 3-buten-2-ol. The conformers in the first row were identified by the microwave study.[4] The second row shows the most stable conformation for the C–O and the C–C eclipsed forms. Selected parameters (6-31G*) are underneath each structure. The values in parentheses are from the microwave study.

of theory. This particular conformation was mentioned by Wilson et al. as the possible candidate for those unassigned transitions in the microwave spectrum. It will be shown later that the evidence from our VT NMR study is best accommodated by the presence of the C–C eclipsed forms (**III**). All nine conformations are slightly staggered because of the asymmetric allylic carbon. The bond angles of **IIIb** are larger than normal: $\angle_{(C=CC)} = 127.3°$ and $\angle_{(CCC)} = 115.3°$. The expansion of these bond angles reflects the repulsion between the methyl group and the vinyl H in conformation **IIIb**. However, the energy cost of the bond angle distortion apparently is not large enough to prevent it from being a local minimum.

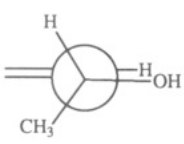
The barriers separating the minima can be seen in the energy contour map, Figure 1. The barriers around the torsional angle C$_{sp2}$–C$_{sp3}$ bond (τ_{CCCO}) are the "staggered" conformations **IV**, **V**, and **VI**. These forms correspond to the eclipsed conformation of ethane with respect to the single bond C$_{sp2}$–H, which is eclipsed with the C–C, C–H, or C–O in **IV**, **V**, or **VI**, respectively. The eclipsed conformations **VII**, **VIII**, and **IX** are the energy barriers separating the minima around torsional angle τ_{CCOH}. It is clear from inspection of the contour map that when both the C$_{sp2}$–H and the O–H bonds are eclipsed with a single bond (when $\tau_{CCCO} = -60, 60, 180°$, and when $\tau_{CCOH} = -120, 0, 120°$), maxima of conformational energy appear. On the other hand, when both the C$_{sp2}$–H and the O–H bonds are staggered with respect to single bonds ($\tau_{CCCO} = -120, 0, 120°$, $\tau_{CCOH} = -60, 60, 180°$), minima of conformational energy result. There are two types of interactions that have been suggested in the literature, which account for the stabilities in rotational isomers about a C$_{sp2}$–C$_{sp3}$ bond. One theory emphasizes the repulsive interactions.[1d] As pointed out by Wiberg for acetaldehyde,[1d] the energy barriers in a C$_{sp2}$–C$_{sp3}$ rotamer have the same origin as in ethane, which are the results of torsional strain. The other theory stresses hyperconjugative effects,[5] such as the overlap between $\pi_{C=C}$ and σ^*_{CO} and between σ_{CH} and $\pi^*_{C=C}$ orbitals. Both effects may contribute to the stabilities of individual conformers. However, the effect of torsional strain appears to be more obvious since conformations with eclipsed single bonds, such as **IV**–**IX**, are energy maxima.



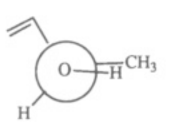
IV



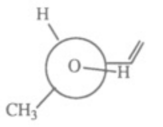
V



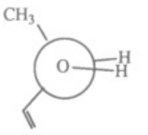
VI



VII



VIII

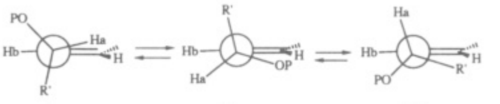


IX

The energy well for the CH and the CO eclipsed forms, **I** and **II**, have relatively deep and large area, Figure 1. Although the energy wells are shallow and small for the CC eclipsed form, **III**, they do exist on this energy contour map, which is also supported by our VT NMR experiments. The instability of **III** can be reasonably accommodated by considering the steric effects from the bulky methyl group.

Experimental Section

To provide samples for our VT NMR study, a group of chiral alkenes was prepared as depicted in Scheme I. This group of compounds includes a variation of substitution at both the vinylic and the allylic positions. Therefore, any specific trend attributed to allylic substitution would not be an isolated case. Several of the chiral allylic alcohols (**3a**–**d**) were produced by reactions between a commercially available α,β-unsaturated aldehyde (**1**) with an organometallic reagent,[9] Scheme I. The γ-hydroxy-α,β-unsaturated esters (**4a**–**d**) were prepared from the addition of a Grignard reagent to the known aldehyde, **2**,[10] Scheme I. Grignard reagents, including methyl-, ethyl-, and isopropylmagnesium bromide, reacted smoothly with the aldehyde, **2**, yielding hydroxy esters, **4a**–**c**. However, attempted addition of *tert*-butyllithium with **2** resulted in an unidentified mixture. Consequently, **4d** was prepared from the ozonolysis of **3d** followed by in situ Wittig reaction of the resulting aldehyde with $Ph_3P{=}CHCO_2Et$. The allyl methyl ethers **5a**–**d** were prepared by the normal Williamson ether synthesis.



(1)

Estimated ^{3}Jab:[16]	**I**	**II**	**III**
	Jt (≈ 10 Hz)	Jg (≈ 2.5 Hz)	Jg' (≈ 2.5 Hz)

The NMR experiments involve measurements of the proton coupling constants ($^3J_{ab}$, eq 1) at various temperatures (the

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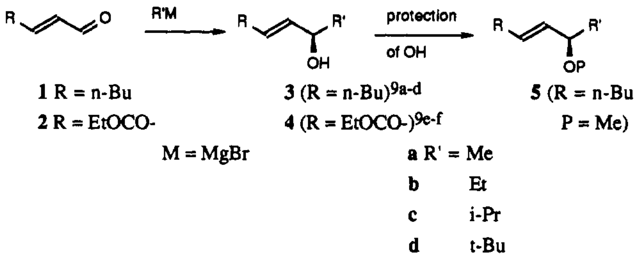
[9] (a) Metz, P.; Mues, C.; Schoop, A. *Tetrahedron* **1992**, *48*, 1071. (b) Martin, G. J.; Naulet, N.; Lefevre, F.; Martin, M. L. *Org. Magn. Reson.* **1972**, *4*, 121. (c) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525. (d) Linderman, R. J.; McKenzie, J. R. *J. Organomet. Chem.* **1989**, *361*, 31. (e) Tsuboi, S.; Sakamoto, J.; Kawano, T.; Utaka, M.; Takeda, A. *J. Org. Chem.* **1991**, *56*, 7177. (f) Tanikaga, R.; Nozaki, Y.; Nishida, M.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 729.

[10] Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180.

Scheme I



J-averaging method).[11-15] The ^{1}H NMR spectra were recorded on a Bruker 300-MHz instrument typically with a window of 1800–2200 Hz centered on the vinyl H and methine H resonance. A total of 128 000 data points were collected, and the digital resolution of all such measurements was ±0.017 Hz. The variable-temperature data were reproducible to ±0.02 Hz in duplicate runs. The samples were degassed before each run, and the concentration was about 0.05 M. Deuterated solvents including toluene, acetone, and chloroform were used in these experiments. Different solvents produced only small changes in the magnitude of the coupling constants. Temperature change, however, did result in significant changes in $^3J_{ab}$.

Results and Discussion

Our first goal was to qualitatively determine the relative conformational stabilities of these (*E*)-chiral alkenes that have different vinylic and allylic substituents. To do this, it is convenient to view the plots of J_{ab} vs temperature as shown in Figures 3–5. The substituent at the allylic position was changed from a methyl to a *tert*-butyl group for compounds in Figures 3–5. Consistent with the prediction made by Kahn and Hehre,[5] the variations of the observed coupling constants with temperature indicate two distinct trends according to the substituent at the vinyl position. For chiral alkenes with a vinyl electron-releasing group, Figures 3 and 4, the population of the conformation shifts toward the C–H eclipsed form as the temperature is lowered as indicated by the increasingly larger coupling constants, $^3J_{ab}$.

The chiral alkenes with an electron-withdrawing group at the vinylic position, Figure 5, show smaller coupling constants ($^3J_{ab}$) at lower temperature. This can be interpreted as an increase in the population of either the C–O eclipsed form, **II**, or the C–C eclipsed form, **III**, since both **II** and **III** should give smaller coupling. On the basis of the results from our *ab initio* calculations (Table I) and from the consideration of steric interactions, it is safe to assume that the C–O eclipsed form, **II**, was more stable and was responsible for the decreased magnitude of coupling at lower temperature.

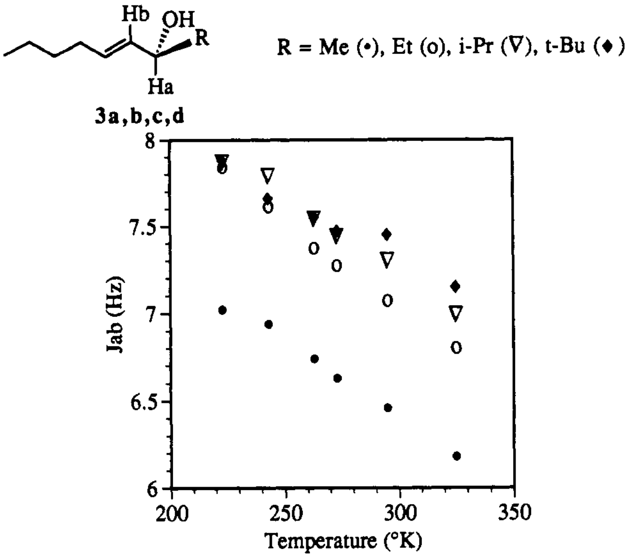


Figure 3. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for chiral allylic alcohols **3a–d**. Data was obtained in CDCl$_3$. 3-Octen-2-ol (**3a**) shows considerably smaller $^3J_{ab}$, which can be rationalized by assuming a three-rotamer averaging.

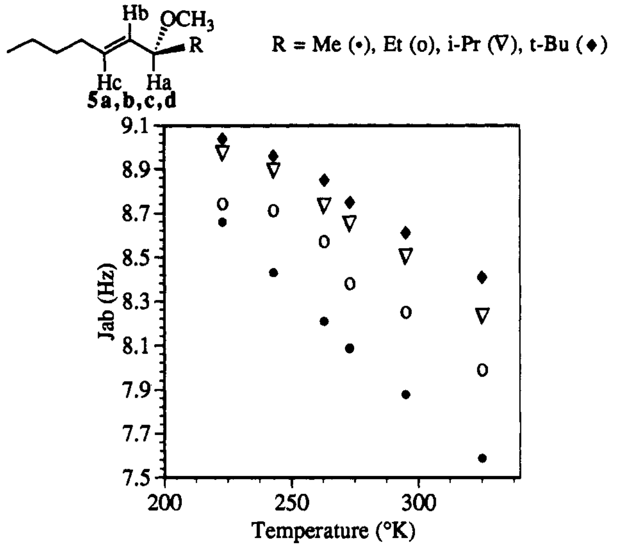


Figure 4. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for chiral allyl methyl ethers **5a–d**. Data was obtained in CDCl$_3$. 2-Methoxy-3-octene (**5a**) shows the smallest $^3J_{ab}$.

A new revealing trend is that the observed coupling constants increase with the size of the allylic substituent at any given temperature. This trend is shared by both classes of compounds and was first reported in our recent paper.[6] The coupling constants of the methyl derivatives are on an average 0.5–1.5 Hz smaller than those of the *tert*-butyl derivatives.

The magnitude of the three-bond coupling $^3J_{ab}$ depends upon two major factors: (1) the dihedral angle HaCR$_2$-CR$_2$Hb and (2) the electronegativity of the substituents, R. First, let us consider the change in the dihedral angle when the allylic substituent R' changes from a methyl group to a *tert*-butyl group. Upon larger allylic substitution, the magnitude of J_g might increase for conformation **II** due to the decreased torsional angle HaCCHb as a result of the repulsion between R' and Hb (see eq 1). However,

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[11] Copley, S. D.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 5008.

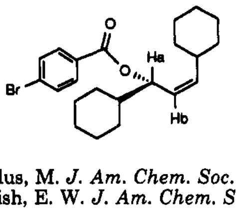
[12] Karabatsos, G. J.; Orzech, C. E., Jr.; Hsi, N. *J. Am. Chem. Soc.* **1966**, *88*, 1817.

[13] Cook, M. J. *Tetrahedron Lett.* **1969**, 2893.

[14] Bowmaker, G. A.; Calvert, D. J.; de la Mare, P. B. D.; Jones, A. J. *Org. Mag. Reson.* **1982**, *20*, 191.

[15] Jung, M. E.; Gervay, J. *Tetrahedron Lett.* **1990**, *31*, 4685.

[16] The J_t and J_g values were estimated from the Karplus[17] type of equation development by Garbish[18] and the consideration of a similar compound, such as **X**. Gonnella, N. C.; Nakanishi, K.; Martin, V. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 3775.



X, Jab = 9.4 Hz

[17] Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870.

[18] Garbish, E. W. *J. Am. Chem. Soc.* **1964**, *86*, 5561.

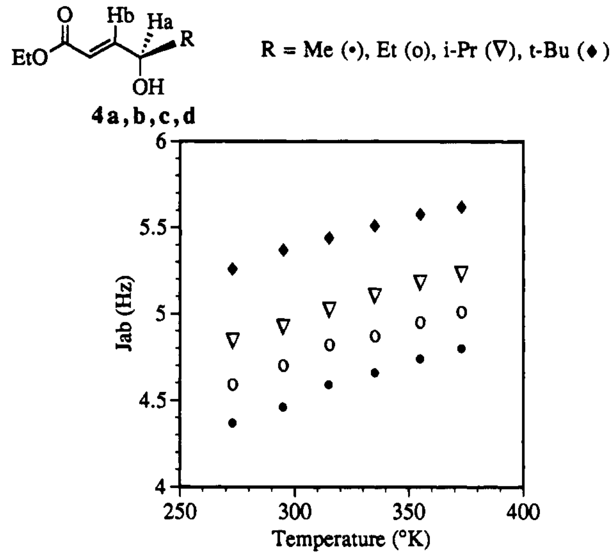


Figure 5. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for γ-hydroxy-α,β-unsaturated esters **4a–d**. Data were obtained in $CD_3C_6D_5$. Vinylic electron-withdrawing groups favor the C–O eclipsed form as indicated by the decreasing ($^3J_{ab}$) as temperature is lowered. Smaller allylic substituents in this class of compounds also lead to a smaller observed coupling constant.

this is true only if conformer **II** is predominant, since the same repulsion in conformer **I** should decrease the torsional angle in **I** yielding a smaller J_t. If the C–H eclipsed form is predominant, a smaller $^3J_{ab}$ should be observed upon increased size of R′. Since the observed coupling constants universally increase with the size of the allylic substituent for both classes of chiral alkenes, this explanation does not account for the fact that chiral alkenes **3a–d** and **5a–d** also exhibit the same phenomenon.

The electronegativity argument does not stand for obvious reasons, since alkyl groups are similar in their electron-withdrawing ability. On the other hand, the observed trend can be rationalized by a decrease in the population of conformer **III** when the allylic group, R′, becomes bulkier. We shall use the Newman projections of the three conformers in eq 1 and the *J*-averaging principle (eq 2) to illustrate the relationship between the observed coupling constants and the populations of individual conformers. Interconversion between rotamers is rapid even at −80 °C so that only weighted-average values of the coupling constants are observed (eq 2), where p_i, p_{ii} and p_{iii} are fractional populations and J_t, J_g, and J_g' are the coupling constants characteristic of forms **I**, **II**, and **III**, respectively. Each graph in Figures 3–5 shows a gradual increase in $^3J_{ab}$ as the steric demand of allylic R′ increases. As the steric size of R′ increases, so will its interaction with the vinyl H in conformer **III**. Consequently, the population of **III** (p_{iii}) will diminish, thereby $^3J_{ab}$ becomes a weighted average of only two conformers, i.e., **I** and **II**. This will yield larger observed coupling constants. Our data from solution NMR appear to be most consistent with a gradual change from a three-rotamer (**I**, **II**, and **III**, eq 1) equilibrium for the methyl derivatives (**3a**, **4a**, and **5a**, in Figures 3–5, respectively) to a two-rotatmer (**I** and **II** only) equilibrium for the *tert*-butyl compounds. Therefore, chiral alkenes with an allylic ethyl or an isopropyl group (**3bc**, **4bc**, **5bc**) appear to also have some population of **III** in solution, as indicated by their intermediate coupling constants at a given temperature.

$$^3J_{ab} = p_iJ_t + p_{ii}J_g + p_{iii}J_{g'} \qquad (2)$$

In conclusion, we have shown by both *ab initio* MO methods and the VT NMR technique that C1-oxygenated chiral alkenes can have either a three-rotamer or a two-rotamer equilibrium depending on the size of the allylic substituent. Although the significance of the conformational profiles of chiral alkenes has been recognized for some time, present experimental techniques are either difficult to interpret or cannot be applied to a wide range of examples. The effect of substituents on conformational preferences has received only scattered attention. The qualitative results presented here establish VT NMR as a viable method for the determination of the relative conformational stability of chiral (*E*)-alkenes. Currently, we are continuing our investigation with other chiral alkenes and will report our results in due course.

Acknowledgment. This research is supported by a grant from the National Institutes of Health (1-R15-GM44260-01A1). We are grateful to the National Science Foundation for Grants (CHE-9012532 and CHE-8951897) for the purchase of the 300-MHz Bruker FT-NMR and the HP GC-MS.

Supplementary Material Available: *Z*-matrix and total *ab initio* energies for conformations **I–III** (6-31G*) (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.