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Conformational Study of Chiral Alkenes: The Influence of Protective Groups on the Relative Stability of Ground-State Rotational Isomers

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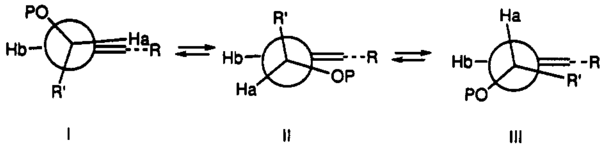
A variable temperature NMR study shows that a protective group on the hydroxy function of a chiral allylic alcohol can either enhance or counter the influence of the vinyl substituent on the ground-state (GS) conformations. If the allylic hydroxy is protected as a methyl ether, the CH-eclipsed form I becomes favored to a greater degree for normal chiral alkenes. Furthermore, conformer I becomes preferred even for the γ-hydroxy-α,β-unsaturated esters, which normally favor the CO-eclipsed form (II). On the other hand, the *tert*-butyldimethylsilyl (TBDMS) ether enhances the preference for conformer II for the γ-hydroxy-α,β-unsaturated esters and diminishes the preference for the CH-eclipsed form of normal chiral alkenes. These facts are explained by the size of the allylic oxygen lone pairs.

Introduction

It is known that the conformational preference of C1-oxygenated chiral alkenes depends on the property of the vinyl substituent (case a, eq 1).[1,2] Recently, we reported the results from a combined *ab initio* MO and variable-temperature (VT) NMR study of the conformations for chiral allylic alcohols.[3] Our study confirmed Hehre's theoretical predictions about the influence of the substituent at vinyl position on the ground state conformations of chiral alkenes.[3] We have now discovered that a protective group on the hydroxy function of a chiral allylic alcohol can either enhance or counter the influence of the vinyl substituent (case b, eq 1). This is significant since vinyl substituents cannot be changed easily in synthetic transformations, but hydroxy protective groups are routinely manipulated in organic synthesis.[4]

Use of protective groups as a means of controlling π-facial selectivity already attracts considerable attention.[5,6] Most notably is the study by Marshall, in which experimental investigation was coupled with a conformational analysis of the products. In most cases, the diastereoselectivity can be related to the conformational stabilities of the products. However, the silyl ether protected substrates give unusually high π-facial selectivity, Scheme I. Furthermore, the silyloxy group preferentially assumes the pseudoaxial position in the transition state, which is opposite to the prediction based on steric effects,[5] Scheme I. We approach the understanding of the origin of the selectivity by studying the fundamental differences in conformational isomerism. As a continuation of our recent report, we wish to report the results from our VT NMR study of the ground-state (GS) conformational preferences for chiral allylic alcohols with either *silyl* ether or *methyl* ether protective groups.



(1)

I II III

Estimated: $J_t = 10$ Hz $J_g = 2.5$ Hz $J_{g'} = 2.5$ Hz

Case a: I is favored when R = alkyl, II is favored when R = CO_2Et

Case b: I is favored when P = CH_3, II is favored when P = SiR_3

Among the three eclipsed rotamers around an alkene Csp2–Csp3 bond, the CH-eclipsed conformer was found to be more stable, especially for (*Z*)-alkenes.[7-9] From our recent VT NMR results,[3] the CH eclipsed form (I) is preferred for chiral allylic alcohols and the CO-eclipsed form (II) is preferred for γ-hydroxy-α,β-unsaturated esters (case a, eq 1). It is now found that if the allylic hydroxy is protected as a methyl ether, the CH-eclipsed form (I) becomes favored even for the γ-hydroxy-α,β-unsaturated esters (case b, eq 1). On the other hand, the *tert*-butyldimethylsilyl (TBDMS) ether diminishes the preference for conformer I.

Experimental Section

Most of the syntheses of the chiral alkenes for our NMR study follow known procedures.[10] They are summarized in Scheme II. The alcohols **2a–d** and **6a–c** were obtained by the reactions

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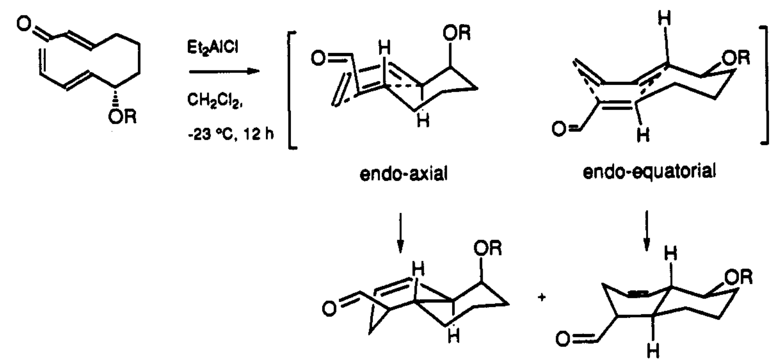
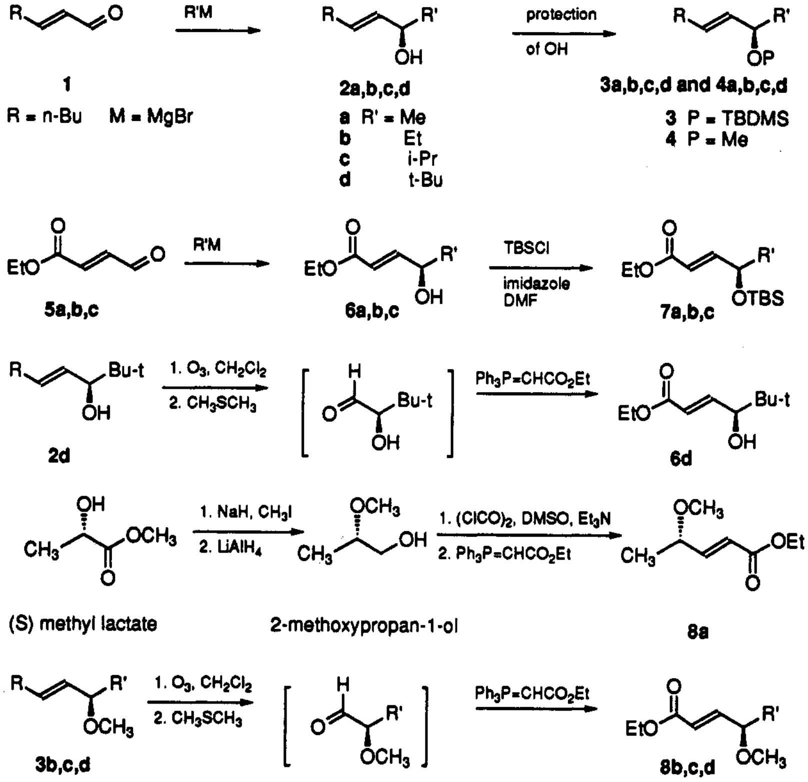
Scheme I



R	axial	equatorial
MOM	50	50
CH₂Ph	50	50
TBDMS	95	5

Reference 5

Scheme II



between an appropriate organometallic reagent and an aldehyde. An exception is alcohol **6d**, which was prepared from alcohol **2d** through a one-pot procedure of (1) ozonolysis, (2) dimethyl sulfide, and (3) Wittig reagent ($Ph_3P{=}CHCO_2Et$). The *tert*-butyldimethylsilyl (TBDMS) ethers **3a–d** were prepared by treating the alcohols in DMF with TBDMSCl and imidazole.[4] The allyl methyl ethers **4a–d** were prepared by the normal Williamson ether synthesis. However, attempted conversion of the γ-hydroxy-α,β-unsaturated ester, **6**, into the corresponding methyl ethers failed when the Williamson ether synthesis was followed. Consequently, **8a** was synthesized from methyl lactate through a sequence of reactions: (1) protection of the hydroxy group as a methyl ether (CH_3I, NaH), (2) reduction of the ester function with $LiAlH_4$, and (3) one-pot Swern–Wittig procedure.[11] The synthesis of the γ-methoxy-α,β-unsaturated esters **8b–d** was accomplished through the ozonolysis of the methyl allyl ethers **3b–d** followed by in situ Wittig reactions of the resulting aldehydes with $Ph_3P{=}CHCO_2Et$, Scheme II.

The NMR experiments involve measurements of the three-bond ($^3J_{ab}$) and the four-bond ($^4J_{ac}$) proton coupling constants at various temperatures (the J-averaging method).[12] The details of the experiments follow the early reports.[3] Briefly, the ^{1}H NMR spectra were recorded on a Bruker 300-MHz instrument with a variable temperature probe. The samples were degassed before each run, and the concentration was about 0.05 M. The variable-temperature data were reproducible to ±0.02 Hz in duplicate runs. Deuterated solvents including toluene, acetone, and chloroform were used in these experiments. Different solvents produced only small changes in the magnitude of the coupling

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Table I. Coupling Constants (Hz) and Chemical shifts (ppm) at Various Temperatures for Chiral Alcohols (CDCl₃)

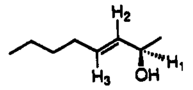
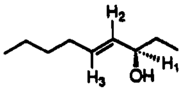
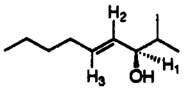
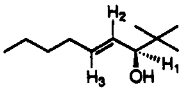
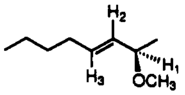
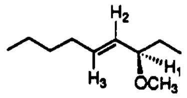
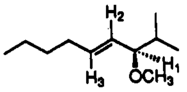
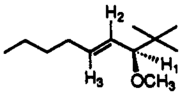
temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
						
223	7.02	15.54		4.21	5.42	5.57
243	6.94	15.27		4.22	5.44	5.58
263	6.74	15.36		4.23	5.46	5.59
273	6.63	15.34		4.23	5.46	5.60
295	6.46	15.31		4.23	5.48	5.61
325	6.18	15.40	0.70	4.23	5.49	5.62
						
223	7.84	15.43		3.90	5.34	5.57
243	7.61	15.29		3.91	5.37	5.58
263	7.37	15.33	0.64	3.92	5.39	5.60
273	7.27	15.34	0.68	3.93	5.40	5.60
295	7.07	15.38	0.69	3.94	5.41	5.61
325	6.80	15.41	0.80	3.95	5.44	5.63
						
223	7.87	15.25			5.33	5.52
243	7.79	15.36		3.68	5.36	5.54
263	7.54	15.34		3.70	5.38	5.56
273	7.44	15.34		3.71	5.39	5.57
295	7.30	15.38		3.72	5.41	5.58
325	6.99	15.38	0.81	3.74	5.43	5.60
						
223	7.88	15.36		3.61	5.41	5.54
243	7.66	15.44		3.62	5.42	5.55
263	7.55	15.34		3.63	5.44	5.57
273	7.47	15.34		3.64	5.45	5.58
295	7.45	15.38		3.65	5.47	5.59
325	7.15	15.36		3.66	5.49	5.62

Table II. Coupling Constants (Hz) and Chemical Shifts (ppm) at Various TEmperatures for Chiral Allyl Methyl Ethers 4a–d (CDCl₃)

temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
						
223	8.66	15.33		3.58	5.17	5.53
243	8.43	15.29		3.59	5.19	5.54
263	8.21	15.36		3.60	5.22	5.55
273	8.09	15.34		3.60	5.23	5.55
295	7.88	15.39		3.62	5.26	5.56
325	7.59	15.40	0.70	3.63	5.29	5.57
						
223	8.74	15.30		3.28	5.08	5.52
243	8.71	15.34		3.29	5.11	5.53
263	8.57	15.43		3.30	5.14	5.53
273	8.38	15.39		3.31	5.15	5.54
295	8.25	15.38		3.33	5.18	5.55
325	7.94	15.42	0.70	3.35	5.22	5.57
						
223	8.97	15.34		3.06	5.12	5.49
243	8.89	15.38		3.07	5.14	5.50
263	8.73	15.35		3.08	5.17	5.51
273	8.65	15.37		3.09	5.18	5.52
295	8.50	15.41		3.10	5.20	5.53
325	8.23	15.43		3.12	5.23	5.55
						
223	9.04	15.38		2.95	5.20	5.48
243	8.96	15.45		2.96	5.21	5.49
263	8.85	15.32		2.97	5.23	5.50
273	8.75	15.36		2.97	5.24	5.51
295	8.61	15.39		2.98	5.27	5.53
325	8.41	15.39		3.00	5.28	5.55

constants. Temperature change, however, did result in significant changes in $^3J_{ab}$.

Ethyl 4-Methoxy-2(*E*)-pentenoate (8a). To a solution of oxalyl chloride (22.4 mmol) in CH_2Cl_2 (187 mL) under nitrogen atmosphere at −78 °C was added DMSO (3.28 g, 44.8 mmol) with stirring. After 15 min, 2-methoxypropan-1-ol (1.66 g, 18.7 mmol in 23 mL of CH_2Cl_2) was added to the solution and the resulting mixture allowed to stir for 15 min. Triethylamine (9.45 g, 93.35 mmol) was added, and the reaction was brought to 22 °C. The resulting mixture was allowed to stir for an additional 2 h, after which time (carbethoxymethylene)triphenylphosphorane (19.51 g, 56.01 mmol) was added and the mixture allowed to stir for another 2 h. The reaction was diluted with diethyl ether and quenched with brine solution. The aqueous layer was extracted with ether. The organic layer was dried over $MgSO_4$. After the solvent was removed under reduced pressure, the product was purified over a column of silica gel to give 1.19 g (40%) of a colorless oil. ^1H NMR ($CDCl_3$) δ 6.77 (dd, J = 15.77, 6.19 Hz, 1H), 5.92 (dd, J = 15.78, 1.29 Hz, 1H), 4.15 (q, J = 7.14, 14.28 Hz, 2H), 3.85 (dq, J = 6.2, 6.2 Hz, 1H), 3.26 (s, 3H), 1.27–1.21 (m, 6H). HRMS: calcd for $C_8H_{13}O_3$ $(M - H)^+$ 157.0859, found 157.0861.

Ethyl 4-Methoxy-2(*E*)-hexenoate (8b). A steady stream of ozone was bubbled through a solution of (*E*)-3-methoxy-4-hexene (1.09 g, 9.53 mmol) in 17 mL of CH_2Cl_2 under nitrogen atmosphere at -78 °C until a light blue color persisted. Dimethyl sulfide (5.92 g, 95.3 mmol) was added, and the resulting mixture was allowed to stir for 3 h at 22 °C. The reaction was brought to 0 °C, and (carbethoxymethylene)triphenylphosphorane (4.32 g, 12.39 mmol) was added. The resulting mixture was allowed to stir for an additional 1.5 h at 0 °C, after which it was warmed to 22 °C and stirred for 30 min. The reaction was diluted with diethyl ether and quenched with water. The organic layer was washed with brine solution and dried over $MgSO_4$. After the solvent was removed under reduced pressure, the product was purified over a column of silica gel to give 0.49 g (30%) of a colorless oil. ^1H NMR ($CDCl_3$) δ 6.73 (dd, J = 15.78, 6.50 Hz, 1H), 5.93 (dd, J = 15.78, 1.24 Hz, 1H), 4.16 (q, J = 7.15, 14.29 Hz, 2H), 3.61 (q, J = 1.20, 6.34 Hz, 1H), 3.26 (s, 3H), 1.55 (m, 2H), 1.26 (t, J = 7.13 Hz, 3H), 0.86 (t, J = 7.43 Hz, 3H). HRMS: calcd for $C_7H_{11}O_3$ $(M - Et)^+$ 143.0703, found 143.0703.

Ethyl 4-Methoxy-5,5-dimethyl-2(*E*)-hexenoate (8d). The above procedure described for compound **8b** was followed starting with 1.98 g (13.9 mmol) of (*E*)-5-(ethoxycarbonyl)-3-methoxy-2,2-dimethyl-4-pentene, yielding 0.88 g (32%) of a colorless oil. ^1H NMR ($CDCl_3$) δ: 6.81 (dd, J = 15.77, 6.93 Hz, 1H), 5.92 (dd, J = 15.77, 1.20 Hz, 1H), 4.18 (q, J = 7.13, 14.27 Hz, 2H), 3.27 (d, buried, 1H), 3.24 (s, 3H), 1.27 (t, J = 7.13 Hz, 3H), 0.87 (s, 9H). HRMS: calcd for $C_7H_{12}O_3$ $(M - C_4H_8)^+$ 144.0781, found 144.0780.

The observed coupling constants at various temperatures for the chiral alkenes **3–8** are listed in Tables I–VI. For easy visualization, the temperature dependencies of the three-bond coupling constant for each set of the chiral alkenes are represented graphically in Figures 1–4. The interpretation of these data is discussed in the next several sections.

A. The steric size of the allylic substituents changes the isomeric composition of the three rotamer equilibrium. Why are greater values of coupling constants observed for the chiral alkenes with a larger allylic substituent R′? As the data in Tables I–VI and Figures 1–4 show, the observed coupling constants follow a consistent trend, i.e., $^3J_{obs}$ (*tert*-butyl derivatives) > $^3J_{obs}$ (*iso*-propyl derivatives) > $^3J_{obs}$ (ethyl derivatives) > $^3J_{obs}$ (methyl derivatives). This trend can be explained by considering the

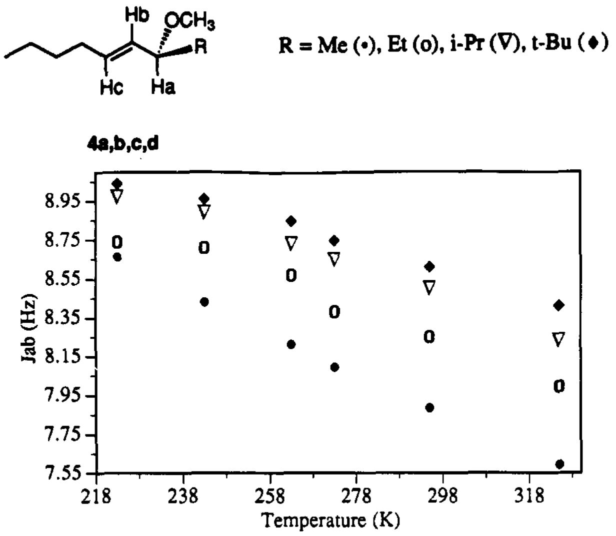
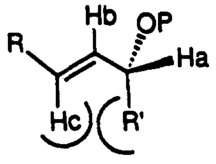


Figure 1. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for chiral allyl methyl ethers **4a–d**. The considerably larger coupling constants at lower temperatures indicate a preference (≃700 cal/mol) for the CH-eclipsed conformer **I**. Data were obtained in CDCl₃.

steric effects of the allylic substituent, R′. The CC-eclipsed conformer **III** suffers from steric repulsion between the allylic substituent R′ and the vinyl Hc. Thus, the *tert*-butyl derivatives **2–4d** and **6–8d** should have the smallest population of **III** (if there is any), while the methyl derivatives **2a–8a** should have a relatively significant population of **III**. Although **III** was not found to be a mimimum in an early theoretical study,[1] our recent *ab initio* MO calculations at the 6-31G* level have located the CC-eclipsed conformer for 3-buten-2-ol.[3] When the population of conformer **III** is negligible, the observed coupling constants are the average of two conformers, **I** and **II**, according to eq 2.



III

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

The p_i, p_{ii}, and p_{iii} are the fractional populations, and J_t, J_g, and $J_{g'}$ are the coupling constants characteristic of conformers **I–III**, respectively. The trans three-bond coupling ($J_t \approx 10$ Hz) is about four times as large as the gauche coupling (J_g or $J_{g'} \approx 2.5$ Hz) based on the Karplus type of relationship between torsional angle and vicinal coupling.[13] Consequently, the presence of **III** ($p_{iii} \neq 0$) will lead to smaller average coupling constants. The greater coupling constants observed for the *tert*-butyl derivatives **2–4d** and **6–8d** indicate the absence ($p_{iii} = 0$) or near absence of conformer **III**. Conversely, the smaller observed coupling constants for the methyl derivatives **2–4a** and **6–8a** (**Tables I–VI**) indicate the presence of **III** ($p_{iii} \neq 0$). The expected increasing steric interaction in the order of Me < Et < *i*-Pr < *t*-Bu is consistent with the VT NMR data, which show a progression of increasing coupling from methyl derivatives to *tert*-butyl derivatives, Figures 1–4.

B. Methyl Ether enhances the preference of chiral allylic alcohols for the CH eclipsed conformer. The first two figures include the chiral alkenes with a vinyl electron-releasing group (ERG, alkyl) or normal alkenes as opposed to conjugated alkenes.

Table III. Coupling Constants (Hz) and Chemical Shifts (ppm) at Various Temperatures for Chiral Allyl Silyl Ethers 3a–d (CDCl₃)

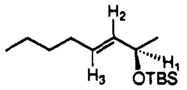
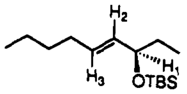
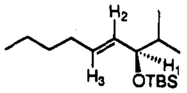
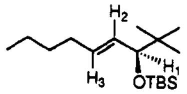
temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
						
223	5.41	15.54			5.38	5.48
243	5.58	15.53			5.39	5.49
263	5.50	15.36			5.40	5.50
273	5.53	15.33			5.40	5.51
295	5.66	15.37			5.41	5.52
325	5.60	15.38	0.71		5.43	5.53
						
223	6.76	14.85		3.93	5.35	5.49
243	6.72	15.35		3.87	5.32	5.46
263	6.66	15.28		3.89	5.33	5.48
273	6.67	15.35	0.70	3.90	5.34	5.49
295	6.60	15.36	0.76	3.93	5.35	5.50
325	6.52	15.35	0.72	3.96	5.37	5.52
						
223	7.43	15.44		3.58	5.28	5.42
243	7.24	15.26		3.63	5.30	5.43
263	7.13	15.43		3.67	5.32	5.45
273	7.09	15.43		3.68	5.32	5.46
295	7.01			3.71		
325	6.97	15.46	0.68		5.36	5.50
						
223	7.25	15.42		3.52	5.31	5.40
243	7.32	15.46		3.54	5.33	5.42
263	7.32	15.45		3.56	5.34	5.44
273	7.32	15.45		3.57	5.35	5.45
295	7.30	15.46		3.59	5.36	5.46
325	7.27	15.43		3.62	5.38	5.48

Figure 1 shows the temperature dependence of the chiral allyl methyl ethers **4a–d**, while Figure 2 displays the corresponding graph for the silyl ethers **3a–d**.

The methyl ethers **4a–d** give the largest three-bond (~8.5 Hz) and relatively small four-bond (~0.70 Hz) coupling constants as shown in Table II. The large three-bond coupling is consistent with a predominant CH eclipsed form. The small four-bond coupling is complementary to the information from the three-bond coupling. Previous reports have suggested that ^4J varies with rotamer population and is the smallest in magnitude when CH is eclipsed with C=C bond.[14] The current study confirms this proposal.

When the temperature is lowered, the observed coupling constants $^3J_{obs}$ for the allyl methyl ethers **4a–d** become greater. This indicates a shift of the population toward conformer **I** since it has a torsional angle $\tau_{H_1CCH_2}$ of ~180° and should have the largest coupling (≈10 Hz). According to Boltzman distribution law, eq 3, the more stable

$$\frac{N_2}{N_1} = e^{-(E_2-E_1)/kT} \qquad (3)$$

isomer becomes more populated at lower temperature. Thus, the VT NMR data show that the CH-eclipsed form is more stable for methyl ethers. Since the average $^3J_{obs}$'s are greater than those for the corresponding chiral allylic alcohols (Table I), the preference for the CH eclipsed form is enhanced for the methyl ethers.

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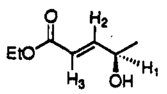
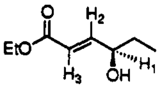
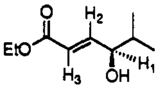
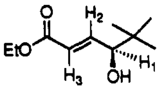
[13] (a) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11. Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. (b) Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783 and references cited therein. (c) Garbish, E. W. *J. Am. Chem. Soc.* **1964**, *86*, 5561.

[14] (a) Bothner-By, A. A.; Naar-Colin, C.; Gunther, H. *J. Am. Chem. Soc.* **1962**, *84*, 2748. (b) Whipple, E. P.; Goldstein, J. H.; McClure, G. R. *J. Am. Chem. Soc.* **1960**, *82*, 3811.

Table IV. Coupling Constants (Hz) and Chemical Shifts (ppm) at Various Temperatures for Conjugated Chiral Alcohols 6a–d ($C_6D_5CD_3$)

temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
						
273	4.37	15.61	1.75		6.82	5.94
245	4.46	15.61	1.74		6.78	5.87
315	4.59	15.65	1.72		6.75	5.85
335	4.66	15.64	1.69		6.73	5.83
355	4.74	15.68	1.69		6.72	5.81
373	4.80	15.68	1.68		6.70	5.74
						
273	4.59	15.62	1.74	3.69	6.86	5.99
295	4.70	15.64	1.72	3.68	6.82	5.95
315	4.82	15.65	1.71	3.68	6.79	5.91
335	4.87	15.68	1.69	3.68	6.77	5.88
355	4.95	15.68	1.67	3.67	6.75	5.86
373	5.01	15.70	1.67	3.67	6.73	5.84
						
273	4.84	15.61	1.72	3.59	6.91	6.02
295	4.92	15.62	1.71	3.56	6.87	5.97
315	5.02	15.64	1.71	3.55	6.84	5.94
335	5.10	15.66	1.70	3.55	6.81	5.91
355	5.18	15.67	1.67	3.55	6.79	5.89
373	5.23	15.68	1.66	3.56	6.78	5.87
						
273	5.26	15.63	1.58		7.05	6.02
295	5.37	15.60	1.65		6.99	5.97
315	5.44	15.62	1.65		6.95	5.94
335	5.51	15.62	1.62		6.92	5.92
355	5.58	15.65	1.60		6.90	5.90
373	5.62	15.66	1.60		6.88	5.88

The most surprising results are from the conjugated chiral alkenes. It is known that a vinyl EWG enhances the CO-eclipsed conformation in a C1-oxygenated chiral alkene.[1-3] The silyl ethers in Figure 3 follow this trend. However, the methyl ethers in Figure 4 show an increased coupling at lower temperature (except for **8d**), which indicates that the CH eclipsed form is preferred even for the chiral alkenes with an EWG at the vinyl carbon. This is surprising since, as far as we know, it is the first observation that an indirectly connected group overrides the influence of the vinyl substituent on the conformational preferences of a chiral alkene.

C. Silyl Ether enhances the preference of chiral allylic alcohols for the CO-eclipsed conformer. The coupling constants, $^3J_{obs}$, for the normal chiral alkenes with a silyl ether protective group **3a–d** remains relatively constant throughout the range of temperatures at which the NMR spectra were recorded, Figure 2. The original trend of increasing magnitude of coupling at lower temperature for the corresponding alcohols is diminished for the silyl ethers **3b** and **3c**. The silyl ether **3a** even exhibits a reversed trend. Its coupling constant decreased slightly as the temperature was lowered, which indicates that the CO-eclipsed form becomes slightly favored. The silyl ethers **3a–d** also show smaller three-bond coupling constants (5.41–7.43 Hz) than the methyl ethers **4a–d** and the corresponding alcohols **2a–d**, Table III. This is consistent with a predominant CO-eclipsed form. As for the conjugated chiral alkenes, the CO-eclipsed conformation is preferred for the alcohols (Table IV).[1-3] This is due to the electron-withdrawing effect of the $-CO_2R$ group. The silyl ethers in Figure 3 exhibit slightly smaller coupling constants than the alcohols (Tables IV and V), and they have the largest four-bond coupling constants (1.34–1.81 Hz, Table V). Both of these facts indicate an enhancement for the preference of the CO-eclipsed form. The decreased coupling at lower temperature is also consistent with a preferred CO-eclipsed form.

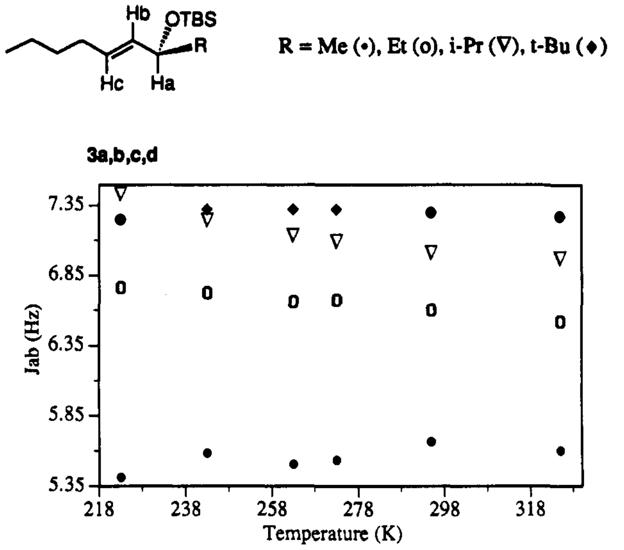


Figure 2. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for chiral allyl silyl ethers **3a–d**. The constant coupling constants indicate that there is little difference in the relative stabilities between conformers I and II for these silyl ethers. Data were obtained in $CDCl_3$.

Table V. Coupling Constants (Hz) and Chemical Shifts (ppm) at Various Temperatures for Conjugated Chiral Alkenes 7a–d ($CDCl_3$)

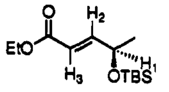
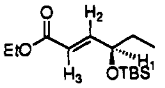
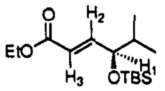
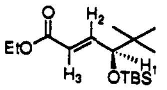
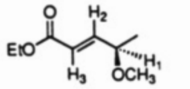
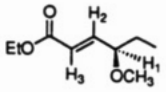
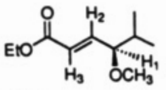
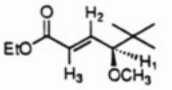
temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
						
223	3.37	15.39	1.87		6.94	5.96
233	3.47	15.39	1.88	4.43	6.93	5.96
243	3.57	15.43	1.83	4.42	6.92	5.96
253	3.69	15.42	1.89	4.42	6.92	5.96
263	3.78	15.42	1.87	4.42	6.91	5.96
273	3.87	15.44	1.86	4.42	6.91	5.96
295	4.06	15.47	1.81	4.42	6.90	5.96
						
223	3.93	15.44	1.78		6.93	5.94
243	4.13	15.47	1.79		6.91	5.95
263	4.31	15.49	1.77		6.90	5.95
273	4.43	15.50	1.75		6.90	5.95
295	4.63	15.50	1.70		6.89	5.95
325	4.83	15.56	1.63		6.88	5.95
						
223	4.09	15.54			6.92	5.92
243	4.39	15.54			6.91	5.93
263	4.65	15.56			6.90	5.93
273	4.81	15.53			6.90	5.93
295	5.02	15.57			6.89	5.93
325	5.29	15.62			6.88	5.93
						
223	5.00	15.54		3.80	6.98	5.89
243	5.37	15.58		3.79	6.96	5.88
263	5.79	15.65		3.80	6.94	5.88
273	5.88	15.63	0.87	3.80	6.93	5.88
295	6.13	15.67	1.34	3.81	6.92	5.88
325	6.43	15.70	1.32	3.82	6.91	5.88

Table VI. Coupling Constants (Hz) and Chemical Shifts (ppm) at Various Temperatures for Conjugated Chiral Allyl Methyl Ethers 8a–d ($CDCl_3$)



temp (K)	J_{12}	J_{23}	J_{13}	δ_1	δ_2	δ_3
223	6.61	15.73		3.86	6.75	5.92
243	6.48	15.77		3.85	6.76	5.92
263	6.35	15.77	1.22	3.85	6.76	5.92
273	6.30	15.76	1.25	3.85	6.77	5.92
295	6.19	15.78	1.29	3.85	6.77	5.92
325	6.07	15.78	1.32	3.85	6.78	5.92
						
223	6.87	15.79		3.59	6.71	5.92
243	6.74	15.76	0.92	3.60	6.72	5.92
263	6.65	15.77	1.18	3.59	6.72	5.92
273	6.60	15.78	1.20	3.61	6.73	5.92
295	6.50	15.79	1.24	3.61	6.74	5.92
325	6.39	15.79	1.26	3.61	6.74	5.93
						
223	7.05	15.77		3.42	6.75	5.93
243	6.97	15.75	1.03	3.41	6.76	5.93
263	6.89	15.78	1.17	3.42	6.76	5.93
273	6.85	15.78	1.19	3.42	6.76	5.94
295	6.78	15.78	1.21	3.42	6.77	5.94
325	6.70	15.79	1.23	3.44	6.77	5.94
						
223	6.97	15.74		3.26	6.82	5.92
243	6.88	15.77		3.26	6.82	5.92
263	6.89	15.74	0.81	3.25	6.81	5.92
273	6.94	15.76	1.18		6.81	5.92
295	6.93	15.76	1.20	3.26	6.81	5.92
325	6.92	15.78	1.19		6.81	5.93

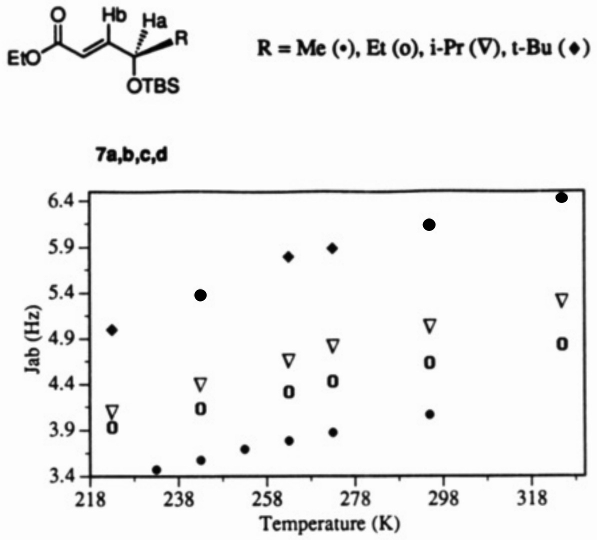


Figure 3. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for conjugated chiral allyl silyl ethers **7a–d**. The considerably smaller coupling constants at lower temperatures indicate a preference (≃700 cal/mol) for the CO-eclipsed conformer **II**. Data were obtained in $CDCl_3$.

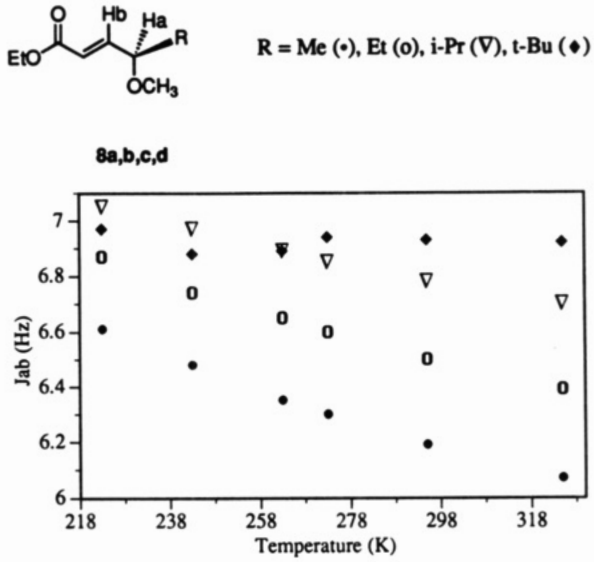


Figure 4. Spin–spin coupling constants ($^3J_{ab}$, Hz) as a function of temperature for conjugated chiral allyl methyl ethers **8a–d**. The relatively smaller change in coupling constants indicates that the preference for conformer **I** is relatively weak. However, it is significant that the methoxy group reverses the normal preference of a chiral α,β-unsaturated ester. Data were obtained in $CDCl_3$.

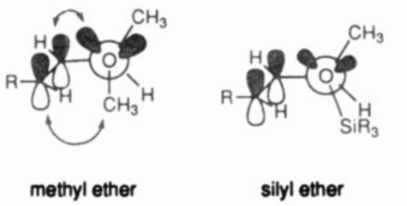


Figure 5. Schematic drawings show the larger allylic oxygen lone pairs in methyl ether causing unfavorable electrostatic and steric interactions.

In summary, the methyl ether enhances the preference for the CH-eclipsed form, and the silyl ether enhances the preference for the CO eclipsed form. What is the origin of the difference between methyl ethers and the silyl ethers? On the basis of our VT NMR data and recent literature reports, it appears to be the size of the allylic oxygen lone pairs. It is well known that the silyl ethers are less basic than the alkyl ethers.[15] Recently, a theoretical study showed that the oxygen lone pairs in silyl ethers are smaller than those in alkyl ethers.[16] The schematic drawing in Figure 5 shows the consequences of the lone pair size.

Although a TBDMS group is larger than a methyl group, the smaller lone pair on oxygen allows the torsional angle τ_{CCOSi} to widen, which leads to the relief of the steric strain and the stabilization of the CO-eclipsed form. Qualitatively, this may explain why the TBDMS derivatives in the Diels–Alder reactions give preferentially the endo-axial adduct, Scheme I, since the axial orientation corresponds to the CO-eclipsed conformation. One must address the Curtin–Hammett principle[17] before attempting to rationalize the product ratio by ground-state conformational preferences. A common generalization states: isomeric product ratio does not depend on the ground-state conformational equilibrium. A more correct description should be as follows: the isomeric product ratio depends only on the transition-state energy difference if the activation energy of the reaction is much higher than the barrier for conformational interconversion. Thus, if the activation energy of the Lewis acid catalyzed reaction is lower than the energy barrier required for the interconversion of the rotational isomers, kinetic quenching may result. This means that the ground-state conformational

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(15) (a) Sternbach, B.; Mac Diarmid, A. G. *J. Am. Chem. Soc.* **1961**, *83*, 3384. (b) West, R.; Wilson, L. S.; Powell, D. L. *J. Organomet. Chem.* **1979**, *178*, 5.

(16) Shambayati, S. L; Blake, J. F.; Wierschke, S. G.; Jorgenson, W. L.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 697.

(17) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

preference will be reflected in the product ratio. Although thermal Diels–Alder reactions require 110–250 °C heat for longer than 24 h, Lewis acid catalyzed Diels–Alder reactions usually proceeds rapidly at −78—20 °C. Therefore, the activation energy for the Lewis acid catalyzed reactions can be expected to be much lower than thermal reactions. We speculate that the ground-state conformational preferences control the diastereofacial selectivity in the Lewis-acid catalyzed Diels–Alder reactions.

Although our speculation needs further experimental evidence, it is clear that there is a difference in the conformational properties of *methyl* and *silyl* ethers. Our future efforts will involve the measurements of the activation energies for the Lewis acid catalyzed Diels–Alder reactions and the energy barrier for rotation around the C_{sp2}–C_{sp3} bond. The energy difference between conformers can be estimated by the *J*-averaging method.[12] Currently, methodologies are being developed in our laboratories to measure these energy differences quantitatively. Solvent effect is also being studied and will be reported in due course.

Acknowledgment. This research is supported by grants from the National Institutes of Health (1-R15-GM44260-01A1 and 1-R01-GM49745-01) and the Petroleum Research Fund (PRF#26684-AC4). 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: ^{1}H NMR spectra for compounds **8a**, **8b**, and **8d** (3 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.