Conformational Studies of Chiral α,β-Unsaturated Aldehydes

Benjamin W. Gung,* Melinda S. Gerdeman, Rebecca A. Fouch, and Mark A. Wolf

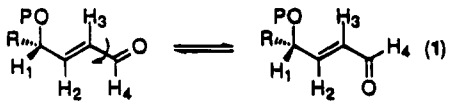
Department of Chemistry, Miami University, Oxford, Ohio 45056

Received January 31, 1994®

The conformational profiles for chiral α,β-unsaturated aldehydes have been studied by a combination of *ab initio* MO methods and the variable-temperature NMR technique. The s-trans rotational isomer around the C_{sp2}–C_{sp2} single bond is more stable than the s-cis conformer by ~500 cal/mol in chloroform. This difference is 950 cal/mol according to *ab initio* calculations at the MP2/6-31G* level of theory. The silyl ethers, **3a–d**, prefer the C–O eclipsed form while the methyl ethers, **6a–d**, favor the C–H eclipsed conformation for rotations around the C_{sp3}–C_{sp2} bond.

Introduction

The conformation around a C_{sp2}–C_{sp2} bond in α,β-unsaturated carbonyl compounds plays an important role in the diastereofacial selectivity of many synthetically useful reactions.[1,2] Consequently, in order to improve the diastereofacial selectivity in addition reactions to chiral α,β-unsaturated carbonyl compounds, it is important to understand the conformational profiles of the C_{sp2}–C_{sp2} single bond. It is known that acrolein prefers the s-trans form in the gas phase by ~2.0 kcal/mol.[3] Ab initio calculations give a difference of 2.2 kcal/mol at the MP3/6-31++G** level of theory.[4] However, little is known about more complex α,β-unsaturated aldehydes, such as those with a γ-chiral center, eq 1. Recently, we have

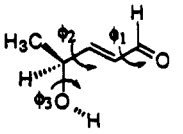


reported both variable-temperature NMR and *ab initio* studies of chiral allylic ethers and esters.[5] In addition to confirming the predictions (based on ab initio theory) of the substituent's effect on conformational stability,[6] we have also discovered that the allylic hydroxy protective group, -OP, influences the conformational preference. The chiral allylic methyl ethers prefer the conformation with the C–H linkage eclipsing the C=C bond, and the allyl silyl ethers prefer the form in which the C–O linkage is eclipsed with the C=C bond.[5]

Now we have extended our VT-NMR and computational studies to chiral α,β-unsaturated aldehydes. Computations are performed with the ab initio MO methods[7] on 4-hydroxy-2-pentenal, which serves as a prototype of γ-chiral α,β-unsaturated carbonyl compounds. The conformational search generates 16 rotational minima at the 6–31G* level of theory. According to our calculations, the most stable conformer is the s-trans isomer in which the allylic C–O bond eclipses the C=C double bond at the MP2/6–31G* level.[8]

We have also found that the VT-NMR technique is well suited for the study of the conformations of chiral α,β-unsaturated aldehydes. The rotation around the allylic C_{sp3}–C_{sp2} bond can be monitored by the couplings between the protons H1 and H2, and the distribution of the s-cis and s-trans isomers can be followed by the couplings between H3 and H4, eq 1. Like other electron-withdrawing groups (EWG), the -CHO function causes the C–O eclipsed form (as shown in eq 1) to be more stable unless the hydroxy group is protected with an alkyl group (P = alkyl, eq 1).[5] In accord with the conformational preference of acrolein in gas phase,[3] the s-trans isomer is found to be more stable for the α,β-unsaturated aldehydes. The protecting group for the γ-hydroxy appears to have no effect on the relative stability of the C_{sp2}–C_{sp2} single bond rotamers.

A. Conformational Study of 4-Hydroxy-2-pentenal with the *ab Initio* MO Methods. The *ab initio* calculations were carried out using the Gaussian 90 and 92 programs[9] implemented on the Cray Y-MP/8 supercomputer. All structures in Figure 1 were progressively optimized using the STO-3G, 3-21G, and 6-31G* theoretical models. All parameters, including bond lengths, bond angles, and dihedral angles were fully optimized. Harmonic frequencies were calculated for each equilibrium structure at the 6-31G* level. The optimized structures all have 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, ϕ_1, ϕ_2, and ϕ_3 and 18 minima



were found for 4-hydroxy-2-pentenal at the STO-3G level, **A–R**, Figure 1. However, four C–C eclipsed forms (**G**

® Abstract published in *Advance ACS Abstracts,* May 15, 1994.

(1) Oppolzer, W.; Loher, H. J. *Helv. Chim. Acta* **1981**, *64*, 2808.
(2) Suzuki, I.; Kin, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1993**, *115*, 10139.
(3) (a) Alves, A. C. P.; Christoferson, J.; Hollas, J. M. *Mol. Phys.* **1971**, *20*, 625. (b) DeGroot, M. S.; Lamb, J. *Proc. Roy. Soc. (London), Ser. A*, **1957**, *242*, 36.
(4) Wiberg, K. B.; Rosenberg. R. E.; Rablen, P. R. *J. Am. Chem. Soc.* **1991**, *113*, 2890.
(5) (a) Gung, B. W.; Wolf, M. A. *J. Org. Chem.* **1993**, *58*, 7038. (b) Gung, B. W.; Wolf, M. A.; Zhu, Z. *J. Org. Chem.* **1993**, *58*, 3350. (c) Gung, B. W.; Wolf, M. A.; Ohm, K.; Peat, A. J. *Tetrahedron Lett.* **1993**, *34*, 1417.
(6) Khan, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650.
(7) Hehre, W. J.; Radom, L.; Schleyer, P. v. P.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.
(8) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1972**, *66*, 217.
(9) 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. Gaussian, Inc., Pittsburgh PA, 1990. Gaussian 90, Revision H.

0022-3263/94/1959-4255$04.50/0

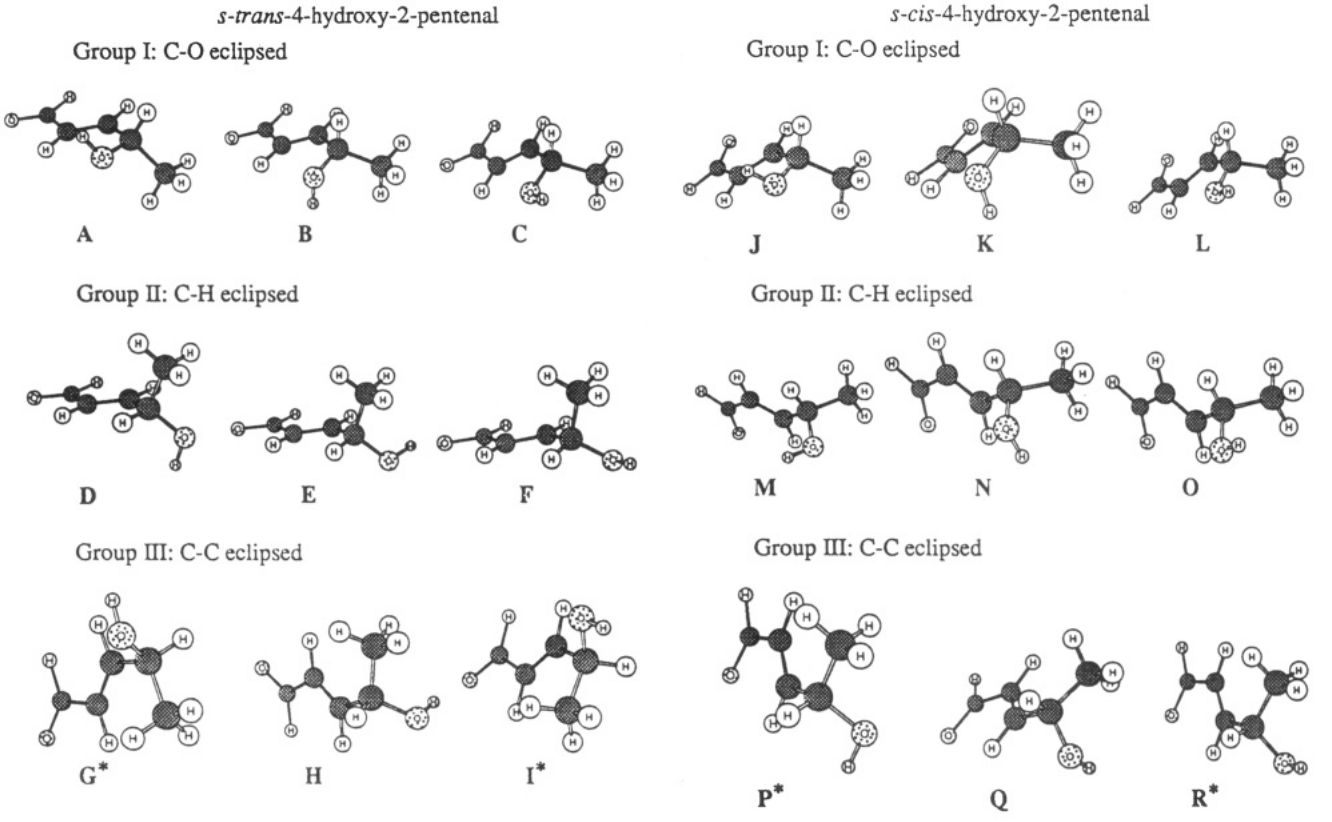
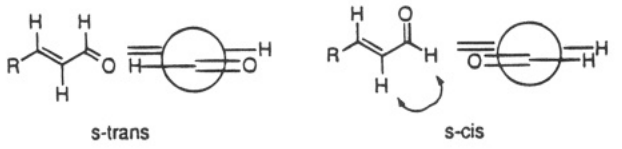


Figure 1. Molecular structures of the 18 conformational minima of 4-hydroxy-2-pentenal optimized at 6-31G* level of theory. These structures designated with an asterisk (*) are energy minima only at the STO-3G level.

and **I** from the s-trans isomers, and **P** and **R** from the s-cis isomers) are not minima at the 3-21G and the 6-31G* levels of theory. Single point Moller–Plesset electron correlation (MP2/6-31G*) are performed for all conformations optimized by the 6-31G* basis set.

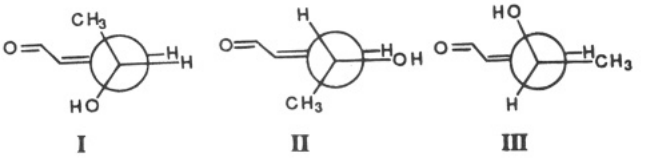
The calculated conformational minima can be divided into two major groups: the s-trans isomers where $\phi_1 = 180°$ and the s-cis isomers where $\phi_1 = 0°$. No gauche conformer was found (i.e., $\phi_1 = \sim 60°$). The global minimum conformer for 4-hydroxy-2-pentenal is the C–O eclipsed s-trans isomer **A**. The most stable s-cis isomer (**J**) is 0.95 kcal/mol higher in energy than **A** at the MP2/6-31G* level of theory. The energy difference can be attributed to the torsional strain in the s-cis isomers, which originates from the eclipsing C–H bonds illustrated below. It is interesting to note that every



s-trans isomer ($\phi_1 = 180°$, $\phi_2 = x°$, $\phi_3 = y°$) is more stable than its corresponding s-cis isomer ($\phi_1 = 0°$, $\phi_2 = x°$, $\phi_3 = y°$), by approximately 1 kcal/mol, Table 1. The rotational barrier for acetaldehyde is also ~1 kcal/mol,[10] which is about one third of the rotational barrier for ethane. Therefore, the CH–CH torsional interaction appears to be the only difference between the s-cis and the s-trans isomers.

At the MP2/6-31G* level of theory, the C–O eclipsed form (**A**) is the global minimum and is more stable than the lowest energy C–H eclipsed form (**D**) by 0.51 kcal/mol. This agrees with our experimental results very well (*vide infra*). The smaller basis sets (STO-3G and 3-21G) did not perform as well as the 6-31G* basis set, Table 1. The s-cis isomer, **J**, and the C–H eclipsed form, **D**, are predicted to be the global minimum by the 3-21G and the STO-3G basis sets, respectively. However, from our VT-NMR data, the most stable form has to be the C–O eclipsed, s-trans isomer (see part B).

To explore the barriers for rotation around the C_{sp3}–C_{sp2} bond, three "staggered" conformations were examined by constraining the CCCO torsional angle at 60°, 180°, −60°, respectively, and rotating the CCOH torsional angle at 60° interval, Table 2. These "staggered" rotamers actually correspond to the eclipsed conformations of ethane in that the C_{sp2}–H bond is eclipsed with the C–H, C–O, or C–C in **I**, **II**, or **III**, respectively.



The saddle point represented by structure **II** has a lower energy (2.32 kcal/mol, entry 9, Table 2) than either **I** (4.24 kcal/mol, entry 6, Table 2) or **III** (4.10 kcal/mol, entry 16, Table 2). It has been noted that the torsional strain between C–H and C–O bonds is not as high as that between C–H and C–H bonds.[10]

The origin of the conformational preference around a C_{sp3}–C_{sp2} bond can be attributed to two factors. The destabilizing effect of the torsional strain in the "staggered" conformations, such as **I**–**III**, and the stabilizing effect of the orbital interactions, such as the overlap

Table 1. Gaussian 92-Computed Relative Energies (kcal mol^{-1}) for (*S*)-4-Hydroxy-2-pentenal

entry	conformer	STO-3G	3-21G	6-31G*	MP2/6-31G*
			s-trans-4-Hydroxy-2-pentenal		
1	**A**	(−339.299502)[a]	(−341.770386)[a]	(−343.688747)[a]	(−344.673866)[a]
		0.19	0.61	0.00	0.00
2	**B**	0.15	0.94	0.44	0.37
3	**C**	0.41	1.61	0.87	0.88
4	**D**	0.00	2.08	0.40	0.51
5	**E**	0.34	3.96	1.90	2.21
6	**F**	0.42	3.00	1.08	1.62
7	**G**	1.84	*b*	*b*	*b*
8	**H**	1.17	3.28	1.44	1.60
9	**I**	1.66	*b*	*b*	*b*
			s-cis-4-Hydroxy-2-pentenal		
10	**J**	0.38	0.00	1.12	0.95
11	**K**	0.33	0.29	1.36	1.29
12	**L**	0.50	0.69	1.72	1.57
13	**M**	0.45	1.96	1.68	1.83
14	**N**	0.51	3.35	3.05	3.09
15	**O**	0.94	3.19	2.88	3.14
16	**P**	2.00	*b*	*b*	*b*
17	**Q**	1.64	3.18	3.19	3.10
18	**R**	2.22	*b*	*b*	*b*

[a] Total energy in atomic units. [b] Not a minimum.

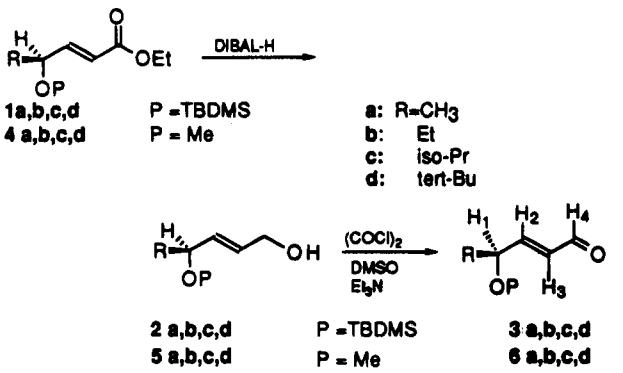
Table 2. Gaussian 92-Computed Relative Energies (kcal mol^{-1}) for Rotational Barriers in (*S*)-4-Hydroxy-2-pentenal (rigid rotor approximation)

entry	$\phi_{2(CCCO)}$	$\phi_{3(CCOH)}$	6-31G*//6-31G*
1	60	0	5.21
2	60	60	5.02
3	60	120	7.27
4	60	180	5.86
5	60	−120	5.93
6	60	−60	4.24
7	180	0	6.92
8	1809	120	4.98
9	180	180	2.32
10	180	−120	3.84
11	−60	0	11.1
12	−60	60	6.01
13	−60	120	14.5
14	−60	180	6.29
15	−60	−120	10.7
16	−60	−60	4.10

between $\pi_{C=C}$ and σ^*_{CO} and between σ_{CH} and $\pi^*_{C=C}$.[6,10] The electron-withdrawing group, -CHO, should raise the $\pi_{C=C}$ energy and lower the $\pi^*_{C=C}$ orbital energy. Consequently, the effect of the electron-withdrawing group is to reduce the orbital overlap between the $\pi_{C=C}$ and σ^*_{CO} and enhance the orbital interaction between the σ_{CH} and $\pi^*_{C=C}$. This effect is indeed observed since the CO bond prefers to eclipse the C=C bond in 4-hydroxy-2-pentenal. The CO eclipsed form **A** is more stable than the CH eclipsed form **D** by 0.51 kcal/mol for 4-hydroxy-2-pentenal. Without the EWG, -CHO, i.e., for 2-hydroxy-3-butene,[5b] the global minimum is the CH eclipsed form (which is more stable than the CO eclipsed form by 0.38 kcal/mol at the 6-31G* level). Thus, an EWG, such as the -CHO, can cause a reversal of conformational preference around a C_{sp3}—C_{sp2} bond by almost 1 kcal/mol.

B. Experimental Results and Discussion. The aldehydes needed for the VT-NMR experiments are prepared according to Scheme 1. The preparation of the corresponding esters (**1a–d** and **4a–d**) has been reported.[5] Those compounds (**1a–d** and **4a–d**) served as starting materials for the syntheses of the aldehydes (**3a–d** and **6a–d**). The esters (**1** and **4**) were reduced to

Scheme 1



allylic alcohols (**2** and **5**), which were then oxidized to the desired aldehydes via the Swern procedure.[11]

The details of the VT-NMR experiments have been described previously.[5] Normally, a freshly prepared sample (~0.05 M) in the desired solvent is degassed and the spectra taken at various temperatures on a 300-MHz Bruker instrument with a variable-temperature probe. In the temperature range of −50 °C to +52 °C, all peaks of the NMR spectra remain sharp, indicating rapid rotation around all single C—C bonds. The coupling constants measured are therefore weighted averages of all rotamers. Table 3 lists the important coupling constants and chemical shifts at different temperatures for aldehydes **3** and **6**.

1. General Trends for the Conformational Preferences of Chiral α,β-Unsaturated Aldehydes. To facilitate the analysis of the data in Table 3, we have introduced the $\Delta J/\Delta T$ values underneath each compound. The $\Delta J/\Delta T$ values are calculated by dividing the coupling constant change (ΔJ) over the temperature range (ΔT) at which the change in coupling was observed. Thus, a positive $\Delta J/\Delta T$ value means that the coupling constant increases as the temperature rises. On the other hand, a negative $\Delta J/\Delta T$ value indicates that the coupling constant decreases as the temperature rises. Graphically, one can plot the coupling change against the temperature, Figure 2 and 3. Thus the $\Delta J/\Delta T$ becomes

(10) Wiberg, K. B.; Martin, E. *J. Am. Chem. Soc.* **1985**, *107*, 5035.

(11) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

Table 3. Coupling Constants (Hz)[a] and Chemical Shifts (ppm)[a] at Various Temperatures for Conjugated Aldehydes 3 and 6 ($CDCl_3$)

temp (K)	$^3J_{12}$	$^3J_{23}$	$^4J_{13}$	$^3J_{34}$	δ_1	δ_2	δ_3	δ_4
			4-(TBDMSO)-2-Pentenal (**3a**)					
223	3.20	5.31	1.83	8.33		6.87	6.28	9.55
243	3.46	5.36	1.81	8.26	4.55	6.84	6.27	9.55
263	3.69	5.39	1.76	8.16	4.55	6.81	6.26	9.55
273	3.76	5.41	1.75	8.12	4.54	6.80	6.26	9.55
295	3.96	5.46	1.70	7.99	4.55	6.78	6.25	9.55
325	4.19	5.52	1.65	7.82	4.55	6.75	6.24	9.56
($\Delta J/\Delta T$)								
(10^3 Hz/K)	9.7	2.05	−1.76	−5.0				
			4-(TBDMSO)-2-Hexenal (**3b**)					
223	3.72	15.36	1.64	8.35	4.35	6.87	6.27	9.56
243	3.94	15.40	1.65	8.28	4.34	6.84	6.26	9.55
263	4.16	15.45	1.63	8.15	4.34	6.81	6.26	9.55
273	4.25	15.48	1.61	8.12	4.34	6.80	6.26	9.56
295	4.45	15.51	1.59	8.00	4.34	6.77	6.25	9.56
325	4.72	15.55		7.83	4.34	6.75	6.25	9.56
($\Delta J/\Delta T$)								
(10^3 Hz/K)	9.8	1.86	−0.69	−5.1				
			5-Methyl-4-(TBDMSO)-2-hexenal (**3c**)					
223	3.95	15.19		8.4	4.2	6.87	6.25	9.56
243	4.31	15.53		8.18	4.2	6.84	6.26	9.56
263	4.54	15.51	1.63	8.16	4.2	6.81	6.25	9.55
273	4.57	15.52	1.53	8.11	4.2	6.81	6.25	9.56
295	4.83	15.56	1.52	8.01	4.2	6.78	6.24	9.55
325	5.13	15.63	1.49	7.83	4.2	6.77	6.23	9.56
($\Delta J/\Delta T$)								
(10^3 Hz/K)	11.6	4.3	−2.3	−5.6				
			5,5-Dimethyl-4-(TBDMSO)-2-hexenal (**3d**)					
223	4.85	15.48		8.36	3.94	6.93	6.21	9.54
243	5.21	15.58	1.30	8.24	3.93	6.89	6.20	9.53
263	5.51	15.59	1.40	8.14	3.93	6.86	6.20	9.54
273	5.65	15.62	1.37	8.08	3.93	6.84	6.19	9.54
295	5.88	15.67	1.34	7.97	3.94	6.81	6.19	9.54
325	6.17	15.71	1.28	7.80	3.95	6.78	6.19	9.55
($\Delta J/\Delta T$)								
(10^3 Hz/K)	12.9	2.3	−0.2	−5.5				
			4-Methoxy-2-pentenal (**6a**)					
223	5.98	15.76		8.15	4.05	6.76	6.24	9.57
243	5.95	15.77		8.08	4.03	6.73	6.23	9.56
263	5.88	15.78	7.98	4.03	6.72	6.23	9.56	
273	5.86	15.82		7.95	4.02	6.71	6.23	9.56
295	5.80	15.83	1.25	7.85	4.02	6.70	6.22	9.57
325	5.73	15.82	1.29	7.68	4.01	6.68	6.22	9.57
($J/\Delta T$)								
(10^3 Hz/K)	−2.5	0.59	1.3	−4.6				
			4-Methoxy-2-hexenal (**6b**)					
223	6.36	15.77		8.25	3.81	6.72	6.24	9.58
243	6.23	15.81		8.13		6.70	6.24	9.57
263	6.17	15.77	1.11	8.01		6.69	6.23	9.58
273	6.20	15.80	1.14	7.96		6.68	6.23	9.58
295	6.13	15.81	1.21	7.86		6.67	6.24	9.58
325	6.07	15.52	1.21	7.70		6.65	6.23	9.58
($\Delta J/\Delta T$)								
(10^3 Hz/K)	−2.8	0.49	1.61	−5.4				
			4-Methoxy-5-methyl-2-hexenal (**6c**)					
223	6.46	15.78	1.07	8.21	3.59	6.73	6.24	9.59
243	6.45	15.77	1.08	8.16	3.58	6.71	6.23	9.58
263	6.44	15.79	1.10	8.05	3.58	6.69	6.23	9.58
273	6.42	15.79	1.15	8.00	3.57	6.69	6.23	9.58
295	6.39	15.81	1.17	7.89	3.57	6.67	6.23	9.59
325	6.37	15.83	1.15	7.73	3.56	6.66	6.23	9.59
($\Delta J/\Delta T$)								
(10^3 Hz/K)	−0.88	0.49	0.78	−4.7				
			4-Methoxy-5,5-dimethyl-2-hexenal (**6d**)					
223	6.59	15.8		8.16	3.45	6.80	6.24	9.60
243	6.62	15.9		8.14		6.78	6.24	9.59
263	6.57	15.73		8.03		6.76	6.24	9.59
273	6.52	15.75	1.02	8.08		6.75	6.23	9.59
295	6.63	15.78	1.17	7.91		6.73	6.23	9.60
325	6.63	15.84	1.12	7.76		6.71	6.23	9.60
($\Delta J/\Delta T$)								
(10^3 Hz/K)	0.39	0.39	1.9	−3.9				

[a] Protons are labeled in accordance with our earlier publication as shown in Scheme 1.

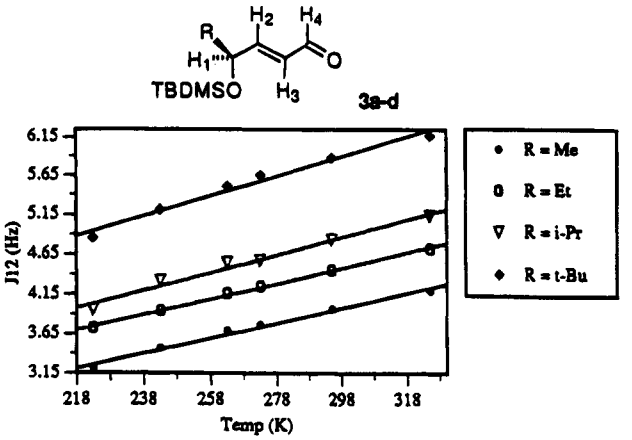


Figure 2. Spin–spin coupling constants ($^3J_{12}$, Hz) as a function of temperature for chiral α,β-unsaturated aldehydes **3a–d**. The considerably smaller couplings at lower temperatures indicate a preference for the C–O eclipsed form.

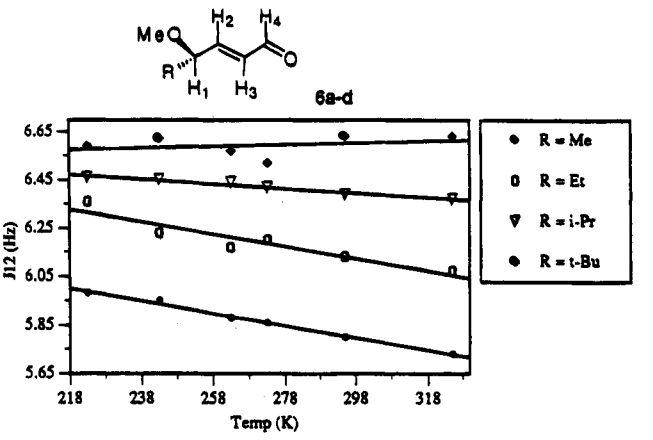


Figure 3. Spin–spin coupling constants ($^3J_{12}$, Hz) as a function of temperature for chiral α,β-unsaturated aldehydes **6a–d**. The larger couplings at lower temperatures indicate a preference for the C–H eclipsed form.

the slope of the graph. It is clear from the two figures that the silyl ethers (**3a–d**) give positive slope while the methyl ethers (**6a–d**) give negative slope. Physically, the positive slope or $+\Delta J/\Delta T$ indicates that the C–O eclipsed form is more stable than the C–H eclipsed form while the negative slope or $-\Delta J/\Delta T$ indicates the opposite.

Consistent with the observations on α,β-unsaturated esters,[5] the silyl ethers (**3a–d**) give rise to large changes in the three bond coupling $^3J_{12}$ as shown by the $\Delta J/\Delta T$ values (9.7 to 12.9 × 10^{-3} Hz/K). The methyl ethers (**6a–d**) show only small changes in $^3J_{12}$ ($\Delta J/\Delta T$ = +0.39 to −2.8 × 10^{-3} Hz/K). Thus, the silyl ethers have a great preference for the CO eclipsed form while the methyl ethers have a small preference for the CH eclipsed form.

The four-bond coupling constants $^4J_{13}$ are small for both the silyl and the methyl ethers, Table 3. However, the $^4J_{13}$ of the silyl ethers are slightly greater than that of the methyl ethers. More importantly, the $\Delta J/\Delta T$ for the four-bond coupling have negative signs for the silyl ethers (**3a–d**) and positive signs for the methyl ethers (**6a–d**) indicating a reversal in stability of the rotational isomers. It is known that ^4J is the smallest in magnitude when the CH bond is eclipsed with the C=C bond.[12] Thus, the information obtained from the four-bond coupling constants ^4J corroborates the conclusion drawn from the ^3J, i.e., the silyl ethers have a predominant C–O eclipsed form and the methyl ethers have a more stable C–H eclipsed form.

2. Chiral α,β-Unsaturated Aldehydes Prefer the s-trans Isomer. As the data in Table 1 shows, although the $\Delta J/\Delta T$ for $^3J_{12}$ and $^4J_{13}$ have opposite signs for the silyl ethers (**3a–d**) and the methyl ethers (**6a–d**), there is one trend common to all compounds. The three-bond couplings $^3J_{34}$ between the aldehydic proton H_4 and the vinylic proton H_3 become greater at lower temperatures for both series of structures. This indicates a shift of population toward the s-trans isomer, which has a torsional angle ($\tau_{H_3C\text{-}CH_4}$) of 180°. According to Boltzman distribution law, the more stable isomer should become more populated at lower temperatures. Therefore, qualitatively it is shown by the data in Table 1 that the s-trans isomer is more stable for all eight α,β-unsaturated aldehydes. Quantitatively, it is possible to calculate the energy difference by the following equations.

$$\ln K_{eq} = -\Delta H/RT + \Delta S/R \quad (2)$$

$$K_{eq} = (1 - pa)/pa \quad (3)$$

$$J_{obsd} = paJ_t + (1 - pa)J_c \quad (4)$$

$$(1 - pa)/pa = (J_{obsd} - J_c)/(J_t - J_{obsd}) \quad (5)$$

Equation 2 is the standard van't Hoff analysis, which allows one to obtain the thermodynamic parameters ΔH and ΔS by measuring the equilibrium constant K_{eq} at various temperatures. In eq 3, pa is the fractional population of the s-trans isomer and 1-pa is the population s-cis isomer. The J_{obsd} in eq 4 is the observed coupling constant, and J_t and J_c are the coupling constants characteristic of the s-trans and the s-cis isomers, respectively. Solving pa from eq 4, one can obtain the equilibrium constant, K_{eq}, by using eqs 3 and 5.[13] Thus, the enthalpic and entropic differences between the two isomers can be obtained by using eqs 2–5 and the VT-NMR data in Table 1.

However, the choice of J_t and J_c makes a difference in the calculated values of K_{eq}. Consequently, the calculated values of ΔH and ΔS also depend on the choice of J_t and J_c. Bothner-By used a least-square analysis program to search for the best J_t and J_g values in his study of simple allylic compounds.[13a] However, as Knowles has pointed out, such analysis can give multiple answers.[13b] Therefore Knowles has used known coupling constants from similar compounds in the literature as standards. We have combined these two approaches, i.e., first, reasonable values of J_t and J_c are found based on known compounds which have similar structure to the individual conformers, and then a least-square analysis is performed to find the J_t and J_c with the smallest error.

The J_t value of 9.5–10.5 Hz was chosen based on the experimental coupling constant of 3-methyl-2-butenal.[14] The methyl group at C_3 destabilizes the s-cis conformation and the coupling constant of 10.0 Hz reflects the anti orientations of protons H_a and H_b. The value of J_c (2.5

(12) (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.

(13) For examples of the application of the *J*-averaging method, see: (a) Bothner-By, A. A.; Castellano, S.; Ebersole, S. J.; Gunther, H. *J. Am. Chem. Soc.* **1966**, *88*, 2466. (b) Copley, S. D.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 5008.

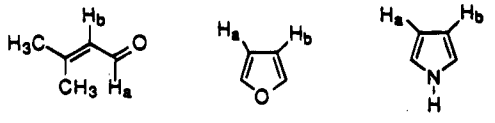
(14) Cardillo, G.; Orena, M.; Sandri, S. *Tetrahedron* **1976**, *32*, 107.

Table 4. Selected Coupling Constants J_t and J_c and the Corresponding Calculated Energy Differences ($\Delta H°$, cal/mol) between the s-trans and the s-cis Isomers

4-(TBDMSO)-2-Pentenal (**3a**): $\Delta H = 450 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	745	580	454	695	529	404	639	474	348
σ	18	14	11	15	13	14	17	17	21
4-(TBDMSO)-2-Hexenal (**3b**): $\Delta H = 460 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	749	583	456	699	533	406	643	477	351
σ	15	12	9	13	11	13	16	17	21
5-Methyl-4-(TBDMSO)-2-Hexenal (**3c**): $\Delta H = 450 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	746	580	454	696	530	404	640	475	349
σ	26	17	13	19	15	15	22	19	22
5,5-Dimethyl-4-(TBDMSO)-2-hexenal (**3d**): $\Delta H = 450 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	737	574	449	687	523	398	631	467	342
σ	8	7	7	9	10	14	16	18	23
4-Methoxy-2-pentenal (**6a**): $\Delta H = 400 \pm 100$									
J_t(Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	669	519	402	617	467	351	559	410	293
σ	20	14	10	14	11	12	14	15	20
4-Methoxy-2-hexenal (**6b**): $\Delta H = 410 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	685	532	413	633	480	362	576	423	304
σ	6	4	7	7	10	15	16	19	25
4-Methoxy-5-methyl-2-hexenal (**6c**): $\Delta H = 420 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	695	540	420	644	489	369	587	432	312
σ^a	18	13	10	14	12	13	15	17	21
4-Methoxy-5,5-dimethyl-2-hexenal (**6d**): $\Delta H = 420 \pm 100$									
J_t (Hz)	9.5	10	10.5	9.5	10	10.5	9.5	10	10.5
J_c (Hz)	2.5	2.5	2.5	3.0	3.0	3.0	3.5	3.5	3.5
$\Delta H°$	699	543	423	647	492	372	591	435	315
σ	36	27	20	31	23	18	27	22	21

[a] Standard deviation of ΔH over six experiments at different temperatures.

to 3.5 Hz) was chosen based on the coupling constants of furan and pyrole.[15] Although these two compounds are



Compound:	3-methyl-2-butenal	furan	pyrole
Jab:	10.0 Hz	3.1-3.8 Hz	3-4 Hz

not the same as the s-cis isomer of an α,β-unsaturated aldehyde, the J_c values so chosen are the best solutions (smallest standard deviations) for eq 2 when $J_t = 10.5$ Hz. Since the carbonyl function is an electron-withdrawing group, it is expected that the J_c in an α,β-unsaturated aldehyde should be smaller than the J_{ab}'s in furan and pyrole.[16]

Using the carefully chosen values of J_t and J_c and the data from Table 3, eq 2 gives good straight line fit with ΔS in the range of 0.1−0.5 eu. Bothner-By had assumed $\Delta S = 0$ in his studies of simple alkenes.[12a] In the current case, it is reasonable to expect a very small difference in entropy between the s-cis and the s-trans conformers. Therefore, to avoid overinterpretation of the VT-NMR data, we have also assumed $\Delta S = 0$. The calculated $\Delta H°$s based on each set of J_t and J_c are listed in Table 4. It can be seen that when $J_t = 10.5$ Hz and $J_c = 2.5$ Hz, the smallest standard deviation is obtained for most of the aldehydes. Thus, the energy differences in chloroform between the s-trans and the s-cis conformations of the aldehydes **3** and **6** are in the range of 400 to 500 cal/mol. These values are smaller than those reported for acrolein in the gas phase.[3] However, solvents are known to reduce or even reverse conformational energy differences.[17]

Conclusion

Both the results from the VT-NMR studies and from the MP2/6-31G* ab initio calculations indicate that the s-trans forms of α,β-unsturated aldehydes are more

(15) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 5th ed., John Wiley & Sons: New York, 1991.

(16) For studies on the relationship between substituent electronegativity and the magnitude of coupling constant, see: Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783, and references cited therein.

(17) Abraham, R. J.; Bretschneider, E. In *Internal Rotation in Molecules*; Orville-Thomas, W. J., Ed.; John Wiley & Sons: London, 1974; Chapter 13.

stable than the s-cis isomers. The energy difference obtained from the VT-NMR experiments (~500 cal/mol) is about one-half that from the ab initio calculations. This discrepancy could be due to the solvent effect.[17] Both theory and experiments predict that the C—O eclipsed form is the global minimum except when the allylic hydroxy group is protected with a methyl group. Thus, the ground state conformational stability of a chiral alkene can be controlled by using a desired protective group. When the C—O eclipsed form is desired, a silyl ether group should be employed, while when the C—H eclipsed form is desired, an alkyl ether group should be employed.

Acknowledgment. This research is supported in part by grants from the National Institutes of Health (GM44260 and GM49745). Acknowledgment is made to the donors of the Petroleum Research Fund (PRF No. 26684-AC4), administered by the American Chemical Society, for the partial support of this research. We thank 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. We are grateful for the computing resources provided by the Ohio Supercomputer Center and the Miami University Academic Computing Service.

Supplementary Material Available: The *Z*-matrix for conformations of **A**—**R** (6-31G*) (6 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.