

Conformational Effects on Optical Rotation. 3-Substituted 1-Butenes

Kenneth B. Wiberg,* Patrick H. Vaccaro,* and James R. Cheeseman

Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06752-8107, and Gaussian, Inc., 140 Washington Avenue, North Haven, Connecticut 06473

Received September 17, 2002; E-mail: kenneth.wiberg@yale.edu

Abstract: A calculation of the optical rotation of (R)-(-)-3-chloro-1-butene found a remarkably large dependence on the C=C—C—C torsional angle. At $\tau = 0^\circ$, $[\alpha]_D = +244^\circ$, whereas at $\tau = 180^\circ$, $[\alpha]_D = -526^\circ$. The effect of conformation on the optical rotation was confirmed by a study of the temperature dependence of the rotation. An analysis of the data gave the difference in free energy between the low- and high-energy conformers as 1315 cal/mol and gave the optical rotation of the low-energy conformer and the average of the rotations of the higher energy forms. Although a large effect was found, the observed rotations are a factor of 2.6 smaller than the calculated values, independent of both conformation and wavelength from 589 to 365 nm. The effect of replacing Cl with F, CN, and CCH was examined theoretically. The effects of substituents are remarkably small despite large changes in the calculated electronic transition energies.

1. Introduction

The optical activity of chiral organic molecules was discovered nearly 200 years ago,¹ and the phenomenon receives wide use in characterizing these compounds. A number of attempts have been made to gain an understanding of the phenomenon. Some have made use of empirical models such as Brewster's rules² and the quadrant and octant rules.³ Others have made use of theoretical methods. Early studies⁴ have been followed by increasingly more sophisticated procedures that now usually give fairly satisfactory approximations to the optical rotation at the sodium D line.^{5–9} However, few of these studies have addressed the question of exactly how structural changes affect the optical rotation.

Our interest in the phenomenon has led us to examine several aspects of the overall problem. The theoretical calculations

usually refer to the gas phase, and we have developed a method for the accurate measurement of optical rotations in the gas phase.¹⁰ This allows a better comparison of theory and experiment and also provides a reference point for studies of solvent effects on optical rotation.¹¹ We have studied the effect of conformational changes on the rotation, and this is the subject of the present paper. We also are studying the tensor components of the optical rotation since they are more closely related to the physical process that results in the rotation. The observed rotation is derived from the trace of the 3×3 tensor, which frequently has elements with opposite signs so that the trace is much smaller than the tensor components. This is one reason it is difficult to accurately calculate the optical rotation.

2. 3-Chloro-1-butene (1)

1 is one of the simplest molecules that is chiral. It has conformational flexibility in that the C=C—C—C torsional angle (τ) can take any value from 0 to 360°. The potential energy curve calculated at the B3LYP/6-311+G* level is shown in Figure 1. Here, for each torsional angle all of the other structural parameters were relaxed. The low-energy conformers are shown in Figure 2. Earlier ab initio calculations found the same conformers.^{12,13} The lowest energy form has the hydrogen at the chiral center eclipsed with the double bond, and the other two rotamers have significantly higher energies. It has been studied both by infrared spectroscopy and electron diffraction.

- (1) Biot, J. B. *Mem. Acad. Sci.* **1817**, 2, 114.
- (2) Brewster, J. H. *Tetrahedron* **1961**, 13, 106.
- (3) Cf. Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; p 1022 ff.
- (4) Cf. Caldwell, D. J.; Eyring, H. *The Theory of Optical Rotation*; Wiley-Interscience: New York, 1971.
- (5) Polavarapu, P. L. *Mol. Phys.* **1997**, 91, 551. Polavarapu, P. L.; Zhao, C. *Chem. Phys. Lett.* **1998**, 296, 105. Polavarapu, P. L.; Chakraborty, D. K.; Ruud, K. *Chem. Phys. Lett.* **2000**, 319, 595. Polavarapu, P. L. *Chirality* **2002**, 14, 768.
- (6) Kondru, R. K.; Wipf, P.; Beratan, D. N. *J. Am. Chem. Soc.* **1998**, 120, 2204. Kondru, R. K.; Wipf, P.; Beratan, D. N. *Science* **1998**, 282, 2247. Kondru, R. K.; Wipf, P.; Beratan, D. N. *J. Phys. Chem. A* **1999**, 103, 6603.
- (7) Cheeseman, J. R.; Frisch, M. J.; Devlin, F. J.; Stephens, P. J. *J. Phys. Chem. A* **2000**, 104, 1039. Devlin, F. J.; Cheeseman, J. R.; Frisch, M. J. *J. Phys. Chem. A* **2001**, 105, 5356. Mennucci, B.; Tomasi, J.; Cammi, R.; Cheeseman, J. R.; Frisch, M. J.; Devlin, F. J.; Stephens, P. J. *J. Phys. Chem. A* **2002**, 106, 6102.
- (8) Helgaker, T.; Ruud, K.; Bak, K. L.; Jorgensen, P.; Olsend, J. *Faraday Discuss.* **1994**, 99, 165. Ruud, K.; Helgaker, T. *Chem. Phys. Lett.* **2002**, 352, 533. Ruud, K.; Taylor, P. R.; Astrand, P.-O. *Chem. Phys. Lett.* **2001**, 337, 215.
- (9) Grimme, S. *Chem. Phys. Lett.* **2001**, 352, 533.

- (10) Müller, T.; Wiberg, K. B.; Vaccaro, P. H. *J. Phys. Chem. A* **2000**, 104, 5959. Müller, T.; Wiberg, K. B.; Vaccaro, P. H.; Cheeseman, J. R.; Frisch, M. J. *J. Opt. Soc. Am. B* **2002**, 19, 125.
- (11) Kumata et al. found a remarkable range of optical rotations for propylene oxide as the solvent was varied: Kumata, Y.; Furukawa, I.; Fuene, T. *Bull. Chem. Soc. Jpn.* **1970**, 43, 3920.
- (12) Stavenbrekk, P. J.; Stølevik, R. *J. Mol. Struct.* **1987**, 159, 153.
- (13) Schei, S. H. *J. Mol. Struct.* **1984**, 118, 319.

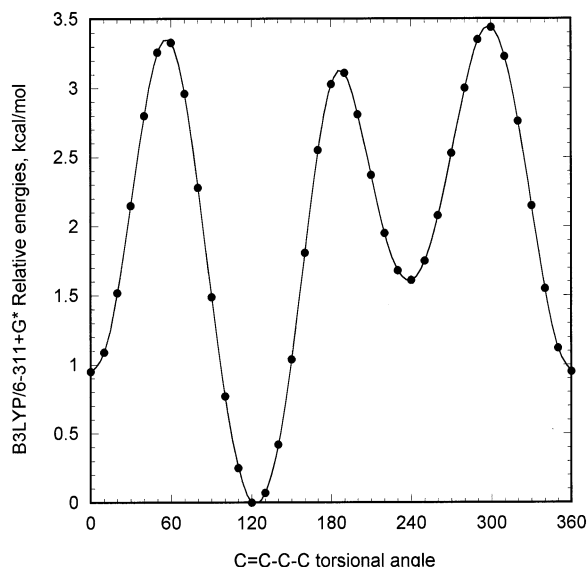


Figure 1. Effect of C=C-C-C torsional angle on the relative energies of 3-chloro-1-butene rotamers calculated at the B3LYP/6-311+G* level.

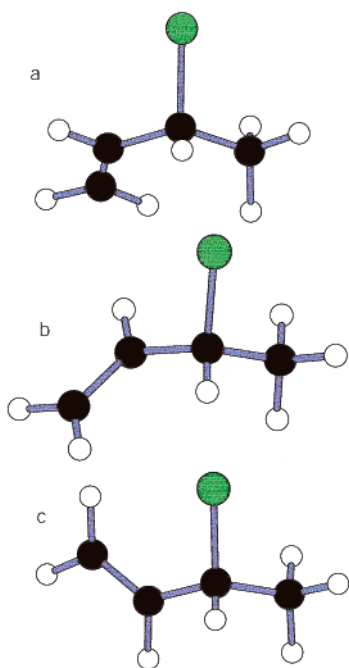


Figure 2. Structures of minimum energy conformers of 3-chloro-1-butene: (a) $\tau = 0^\circ$, methyl eclipsed with the double bond; (b) $\tau = 120^\circ$, hydrogen eclipsed with the double bonds; (c) $\tau = 240^\circ$, chlorine eclipsed with the double bond.

An early IR study showed that it exists in at least two forms,¹⁴ and the ED study found three conformers, with the major form being $76\% \pm 10\%$ at 20°C , with the proportion of this form decreasing to $62\% \pm 10\%$ at 180°C .¹³ As part of a more recent vibrational spectroscopic study,¹⁵ the MP2/6-311++G**₀-calculated energy differences for the conformers were obtained, and are in agreement with other calculated relative energies (see below). However, this study also reported variable-temperature infrared studies using xenon solutions of **1**. The ΔH values thus obtained are markedly different from any of the calculated

Table 1. Calculated Relative Energies for 3-Chloro-1-butene Conformers, 298 K

level	t	rel ΔH	rel ΔG
B3LYP/6-311+G* (opt)	0	1.10	1.30
	120	0.00	0.00
	240	1.59	1.68
MP2/6-311+G* (opt) ^{a,b}	0	1.26	1.46
	120	0.00	0.00
	240	1.43	1.52
CCD/6-311++G** (opt) ^b	2.3	1.19	1.39
	121.9	0.00	0.00
	240.2	1.45	1.54
CCSD(T)/6-311++G(2df,2pd) ^b	2.3	0.76	0.96
	121.9	0.00	0.00
	240.2	0.95	1.04
G2	2.0	0.88	1.05
	119.6	0.00	0.00
	240.9	1.02	1.10

^a These data were taken from ref 15. ^b The zero-point and thermal corrections used the B3LYP/6-311+G* frequencies.

values, and in view of the results presented below, they are probably incorrect.

To obtain more accurate relative energies, the three low-energy forms were studied via G2¹⁶ calculations. Although this generally gives quite good calculated energies, it seemed possible that it might not be equally successful for relative conformational energies. The geometries of the forms may change a little from one theoretical level to another, and the use of MP2/6-31G* for the geometry calculation and HF/6-31G* for the vibrational frequency calculation might not be completely satisfactory. Therefore, additional calculations were carried out using B3LYP/6-311+G* for the frequency calculations, CCD/6-311++G(2df,2pd) for the geometry optimization,¹⁷ and CCSD(T)/6-311++G(2df,2pd) for the final energy calculation. The results of the calculations at several theoretical levels are shown in Table 1. It can be seen that the G2 and CCSD(T) calculations are in very good agreement, but give relative energies that are significantly different from those found at lower theoretical levels, and are quite different from the reported experimental energy differences.

The optical rotation for (*R*)-(–)-**1** was calculated at 20° intervals of the torsional angle (Figure 1) at the B3LYP/6-311++G** level, giving the result shown in Figure 3. The calculated change in specific rotation at 589 nm with torsional angle is remarkable, going from -526° at $\tau = 180^\circ$ to $+367^\circ$ at $\tau = 320^\circ$. The rotations calculated for other wavelengths are given in the Supporting Information. Using the G2 relative free energies given in Table 1, and the calculated rotations for the three low-energy forms, the mixture of rotamers at 20°C should have $[\alpha]_D = -112^\circ$. It may be noted that the maximum rotation is found when the C=C-C-C torsional angle is close to 0° , and the minimum rotation is found when this torsional angle is close to 180° .

The optical rotation also was calculated using larger basis sets to see whether this might lead to a significant effect on the calculated values. The result is shown in Table 2. The basis set effect is relatively small.

(16) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221.

(17) CCSD gradients are not implemented in the programs available to us, and therefore, the geometry optimization was carried out using CCD. This is similar to the use of MP2/6-31G* geometries along with QCISD(T) energy calculations in the G2 model chemistry.

(14) Schei, S. H.; Klæboe, P. *Acta Chem. Scand.*, **A 1983**, *37*, 315.

(15) Lee, M. J.; Fusheng, F.; Hur, S. W.; Liu, J.; Gounev, T. K.; Durig, J. R. *J. Raman Spectrosc.* **2000**, *31*, 157.

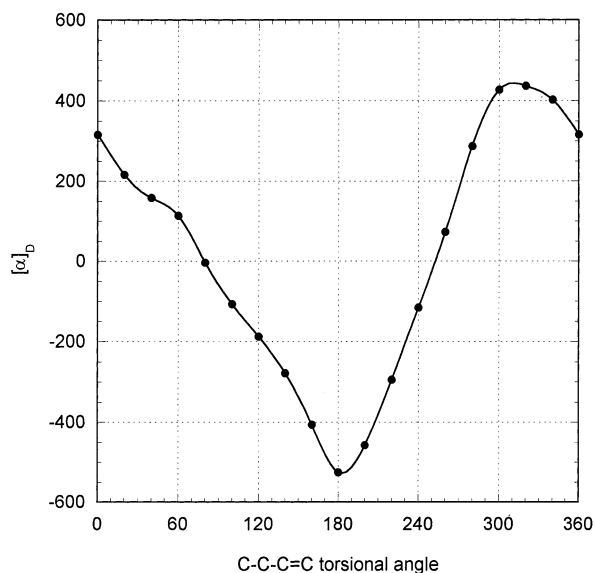


Figure 3. Calculated optical rotation of 3-chloro-1-butene, B3LYP/6-311++G**.

Table 2. Effect of Basis Set on the Calculated B3LYP Specific Rotations of 3-Chloro-1-butene

tors angle (deg)	wavelength (nm)	6-311++G**	6-311++G(2d,2p)	aug-cc-pVDZ	aug-cc-pVTZ
0	633	265.9	273.6	273.1	276.5
	589.3	316.4	325.6	324.6	328.7
	578	332.2	341.5	340.4	344.6
	546	383.2	399.4	392.3	397.4
	436	707.3	727.2	719.2	729.5
	365	1242.9	1277.5	1254.9	1274.5
120	355	1370.4	1408.1	1381.9	1404.0
	633	-157.5	-153.7	-150.1	-149.5
	589.3	-188.1	-183.6	-179.3	-178.8
	578	-197.6	-192.9	-188.3	-187.8
	546	-228.9	-223.2	-218.2	-217.8
	436	-430.7	-422.6	-410.8	-411.6
240	365	-774.5	-765.4	-739.6	-744.2
	355	-857.8	-850.1	-819.4	-825.0
	633	-98.5	-99.6	-99.9	-98.9
	589.3	-116.0	-117.4	-114.3	-116.7
	578	-121.4	-122.9	-119.6	-122.0
	546	-138.8	-141.3	-136.9	-139.6
	436	-242.8	-247.6	-240.6	-245.0
	365	-397.6	-405.9	-395.9	-402.5
	355	-432.0	-426.8	-430.6	-437.5

The rotation of **1** has been estimated to be $[\alpha]_D = 61^\circ$.¹⁸ It was possible to separate the two enantiomers of **1** using a chiral analytical GC column. A sample of (*R*)-**1** with $\alpha_D^{25} = -36.02^\circ$ ($l = 1$, neat) was found to have an excess of the *R* form of 69.94%, whereas a sample of (*S*)-**1** with $\alpha_D^{25} = 24.34^\circ$ ($l = 1$, neat) was found to have an excess of the *S* form of 47.12%. This corresponds to -51.5° and $+51.7^\circ$, respectively, as the maximum rotations. Using $d = 0.900$ g/mL, $[\alpha]_D^{25} = \pm 57.3^\circ$. This is smaller than the computational estimate by a factor of 2.

In view of the remarkably large calculated changes in optical rotation with torsional angle, it seemed appropriate to try to obtain experimental data related to the rotation. Since there is a significant difference in energy among the rotamers, with one of the high-energy forms of (*R*)-**1** having a large positive rotation and the low-energy form having a negative rotation, one would

Table 3. Observed Optical Rotation of 3-Chloro-1-butene as a Function of Temperature^a

T ($^\circ\text{C}$)	α (deg) at various wavelengths, nm				
	589.3	578	546	436	365
0.0	-4.339	-4.550	-5.265	-9.837	-17.368
10.0	-4.253	-4.461	-5.159	-9.628	-16.986
20.0	-4.163	-4.365	-5.048	-9.413	-16.590
30.0	-4.077	-4.274	-4.943	-9.211	-16.222
40.0	-3.982	-4.176	-4.830	-8.998	-15.841
50.0	-3.897	-4.086	-4.725	-8.801	-15.491
60.0	-3.815	-4.000	-4.626	-8.613	-15.153
70.0	-3.728	-3.909	-4.522	-8.414	-14.799

^a The rotations are reproducible to $\sim 0.002^\circ$. $c = 0.10864$ g/mL in methylcyclohexane, $l = 1$ dm, 0.699 ee.

expect the rotation to become less negative as the temperature is raised and the mole fraction of the higher energy form increases. The optical rotation was studied from 0 to 70 $^\circ\text{C}$ in methylcyclohexane solution. This solvent was chosen since it might be expected to give a relatively small solvent effect and would accommodate the temperature range. The data are given in Table 3. The solvent expands with increasing temperature, and 10.00 mL of methylcyclohexane at 0 $^\circ\text{C}$ becomes 10.93 mL at 80 $^\circ\text{C}$. The observed rotations were corrected accordingly so that they are referred to the concentration at 20 $^\circ\text{C}$.

The G2 and CCSD(T) calculations indicate that the higher energy conformations have essentially the same relative energy. Thus, in analyzing the temperature dependence, it was assumed that their concentrations would be equal. The rotation at any temperature is given by

$$\alpha_{\text{obsd}} = \alpha_A X_A + \alpha_B X_B + \alpha_C X_C$$

where X_A is the mole fraction of the low-energy form, X_B and X_C are the mole fractions of the higher energy forms, and α_A , α_B , and α_C are the corresponding optical rotations, which are presumably temperature independent. Then the assumption of equal energies for the two higher energy conformations requires

$$X_B = X_C = X_A \exp(-\Delta G/RT)$$

which leads to

$$\alpha_{\text{obsd}} = (\alpha_A + 2\alpha' \exp(-\Delta G/RT))/(1 + 2 \exp(-\Delta G/RT))$$

The equation has as unknowns α_A , $\alpha' = (\alpha_B + \alpha_C)/2$, and ΔG . The values of these quantities could be obtained by a nonlinear least-squares fit to the experimental data using the same ΔG for all wavelengths (Figure 4), which gives the results shown in Table 4. Here, the α values have been converted to specific rotations, $[\alpha]$, using the concentration of **1** in the solution. The ΔG was 1315 ± 25 cal/mol (1σ). Since this is somewhat larger than the value calculated at the G2 or CCSD(T) level, the expected changes in rotation for $\Delta G = 1000$ and 1200 cal/mol were examined. The curvatures of the experimental data and the calculated values for $\Delta G = 1315$ cal/mol were small, but they were significantly larger using the other energies. Thus, 1315 cal/mol is clearly a better fit to the experimental data. Although this is somewhat larger than the calculated relative energy, it would not be surprising if the conformational energies were somewhat different in solution than in the gas phase (corresponding to the calculations). This has been found in other cases such as butane.¹⁹

(18) Young, W. G.; Caserio, F. F., Jr. *J. Org. Chem.* **1961**, *26*, 245.

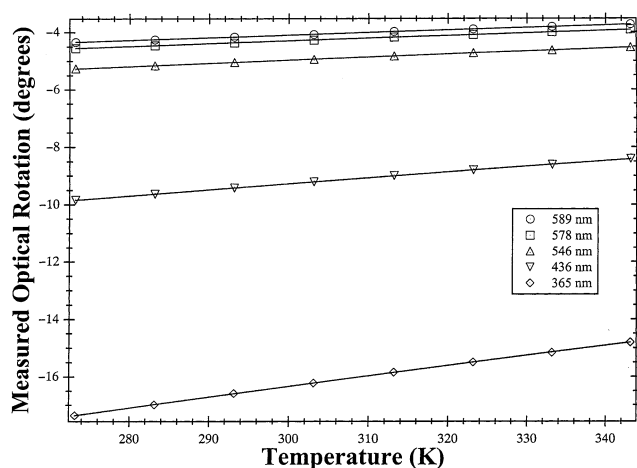


Figure 4. Nonlinear least-squares fit of the temperature dependence of the optical rotation of 3-chloro-1-butene.

Table 4. Quantities Derived from the Temperature Dependence of the Rotation

wavelength (nm)	ΔG	$[\alpha]_{\lambda}$ (deg)		$[\alpha]_{(B+C)/2}$ (deg)	
		obsd	calcd ^a	obsd	calcd ^b
589	1315 ± 25	-73.5 ± 0.6	-188.1	34.7 ± 1.5	104.1
578	1315 ± 25	-77.1 ± 0.6	-197.6	36.5 ± 1.5	109.3
546	1315 ± 25	-89.2 ± 0.7	-228.1	43.3 ± 1.3	129.1
436	1315 ± 25	-167.3 ± 1.3	-430.7	86.6 ± 2.2	239.8
365	1315 ± 25	-296.9 ± 2.2	-774.5	156.1 ± 5.3	435.8
ratio ^c		2.57 ± 0.01		2.9 ± 0.1	

^a B3LYP/6-311++G** -calculated optical rotation of the lower energy conformer. ^b Average of the calculated rotations of the two higher energy conformers. ^c Ratio of calculated to observed rotations.

In addition, if one makes the reasonable assumption that the calculated rotations will be in approximately constant ratio to the correct rotations for the rotamers of a given compound, then the agreement between the ratio of α_A to α' for $\Delta G = 1315$ cal/mol is much better than for $\Delta G = 1000$ or 1200 cal/mol. The ratio of α_A to α' at 589 nm from the calculated rotations is -1.81 , and the 1315 cal/mol data give -2.12 , whereas using 1200 cal/mol it would be -2.57 and using 1000 cal/mol it would be -3.41 .

Table 4 includes the calculated rotations. For the low-energy conformers, the ratios of the observed rotations to the calculated values are $\sim 1:2.57$, and appear to be independent of wavelength.²⁰ Similarly, the ratio of the average of the observed rotations of the higher energy conformers to the observed values is 2.9 ± 0.1 . This indicates that the calculated optical rotations at 589 and 365 nm should be related linearly, and this is the case (Figure 5). However, a comparison of the calculated values at 589 and 250 nm began to show significant scatter.

The fairly large deviation between the calculated and observed specific rotations led us to examine whether molecular vibrations

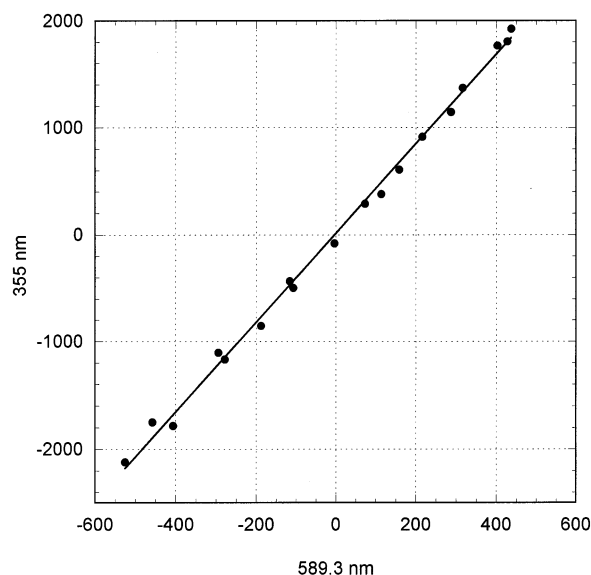


Figure 5. Comparison of the calculated optical rotations of **1** as a function of the torsional angle at 589 and 365 nm.

could lead to large changes in optical rotation. It is difficult to average the specific rotation over all of the vibrational modes for a molecule with 30 normal modes.²¹ Therefore, each vibrational mode was examined separately to see whether it might strongly affect the calculated rotation. This approach also allows one to determine which modes have a large effect on the optical rotation.

The root-mean-square amplitude for normal mode displacement at temperature T , Δx (Å), is given by²²

$$\Delta x = \pm((16.8576/\nu) \times \coth(0.719384\nu/T))^{1/2}$$

where ν is the calculated vibrational frequency (cm^{-1}). The hyperbolic cotangent embodies contributions from higher lying vibrational levels and, in the case of room temperature ensembles ($T = 300$ K), rapidly approaches unity for vibrational frequencies in excess of ~ 1100 cm^{-1} .

The optimized coordinates for the 120° conformer were modified by the product of Δx and the Cartesian displacement coordinates for a given mode. The specific rotation was calculated using both $+\Delta x$ and $-\Delta x$ for each of the normal modes, giving the result shown in Table 5. Some of the modes give large changes in calculated specific rotations, but in each case the average of the rotation calculated from positive and negative displacements of the coordinates is close to that for the equilibrium ground-state structure. Thus, the vibrational modes are expected to have little net effect on the calculated rotation.

Vibrational modes 8 (C=C stretch) and 30 (C-C-C=C torsion) lead to unusually large changes in calculated energies. These modes correspond to large-amplitude motions that are not well described using rectilinear displacement coordinates, and as a result lead to artificial distortions of other internal coordinates. This is especially the case with mode 30 for which Δx is very large. This is the C-C-C=C torsional mode, and Figure 3 shows that the change in rotation with torsional angle

(19) Herrebout, W. A.; van der Veken, B. J.; Wang, A.; Durig, J. R. *J. Phys. Chem.* **1995**, *99*, 578. Pratt, L. R.; Hsu, C. S.; Chandler, D. *J. Chem. Phys.* **1978**, *68*, 4202.

(20) A reviewer suggested that the discrepancy between experiment and theory might not exist in HF predictions. This seemed unlikely in view of the published work on calculations of optical rotation (cf. ref 7), but calculations were carried out at the HF/6-311++G** level, giving specific rotations (589 nm) of 263.4° , -178.7° , and -77.5° at torsional angles of 0° , 120° , and 240° , respectively. These may be compared with the corresponding B3LYP/6-311++G** predictions of 316.4° , -188.1° , and -116.0° . The values at a 120° torsional angle, where the experimental value is best determined, are essentially the same.

(21) Ruud, K.; Taylor, P. R.; Astrand, P. O. *Chem. Phys. Lett.* **2001**, *337*, 217.

(22) Cyvin, S. J. *Molecular Vibrations and Mean Square Amplitudes*; Universitets Forlaget: Oslo, Norway, 1968.

Table 5. Effect of Vibrational Modes on the Calculated Optical Rotation of 3-Chloro-1-butene

mode	freq	Δx	E_{rel}^a		$[\alpha]_{\text{D}}^b$ (deg)		av $[\alpha]_{\text{D}}$ (deg)	correction ^c
			positive	negative	positive	negative		
gs			0.00	0.00	-201.3	-201.3	-201.3	
1	3216	0.0724	2.66	2.48	-212.7	-190.4	-201.6	-0.25
2	3147	0.0732	2.19	2.72	-185.5	-216.6	-201.1	0.25
3	3131	0.0739	2.53	2.72	-195.5	-207.4	-201.5	-0.15
4	3123	0.0735	2.38	2.52	-183.1	-219.5	-201.3	0.00
5	3107	0.0737	2.49	2.36	-196.7	-203.8	-200.3	1.05
6	3096	0.0738	2.55	2.29	-193.8	-211.0	-202.4	-1.10
7	3037	0.0745	2.07	2.45	-199.5	-195.8	-197.7	3.65
8	1704	0.0995	4.85	5.97	-244.7	-164.3	-204.5	-3.20
9	1509	0.1058	1.14	1.16	-194.0	-200.9	-197.5	3.85
10	1502	0.1060	1.10	1.12	-198.0	-202.8	-200.4	0.90
11	1466	0.1073	1.34	1.16	-220.1	-184.0	-202.1	-0.75
12	1424	0.1089	1.35	1.10	-206.0	-191.5	-198.8	2.55
13	1342	0.1123	1.27	1.26	-191.5	-212.0	-201.8	-0.45
14	1326	0.1129	1.21	1.19	-206.9	-194.8	-200.9	0.45
15	1274	0.1153	1.06	1.10	-218.0	-184.3	-201.2	0.15
16	1200	0.1189	1.75	1.71	-223.8	-173.7	-198.8	2.55
17	1110	0.1238	1.81	1.68	-232.3	-167.9	-200.1	1.20
18	1046	0.1278	1.19	1.17	-180.4	-221.3	-200.9	0.45
19	1023	0.1293	0.86	0.85	-432.4	29.2	-201.6	-0.30
20	987	0.1318	0.93	0.92	-265.6	-141.8	-203.7	-2.40
21	951	0.1345	1.01	1.00	-238.7	-163.2	-201.0	0.35
22	871	0.1412	1.34	1.23	-218.4	-189.7	-204.1	-2.75
23	715	0.1585	1.05	1.12	-323.8	-80.8	-202.3	-1.00
24	618	0.1738	1.38	1.21	-229.6	-176.7	-203.2	-1.85
25	454	0.2158	1.48	1.64	-211.4	-188.9	-200.2	1.15
26	322	0.2832	0.85	0.81	-194.7	-205.7	-200.2	1.10
27	304	0.2977	1.04	0.94	-199.7	-209.3	-204.5	-3.20
28	280	0.3193	0.83	0.97	-235.0	-159.1	-197.1	4.25
29	252	0.3510	0.85	0.61	-203.1	-196.6	-199.9	1.45
30	104	0.8157	3.61	3.61	[-134.2] ^d	[-356.6]	[-245.4]	[-44.1] ^d
sum								7.95 ^e

^a Relative energies (kcal/mol) calculated at the B3LYP/76-311++G** level. Positive and negative refer to the sense of Δx used in the calculations. ^b Calculated specific rotations for the deformed molecules obtained at the B3LYP/6-311++G** level. ^c Calculated correction to the optical rotation for the given mode (see the text). ^d These values are not reliable since this is a torsional mode that is poorly described using rectilinear coordinates. The use of curvilinear coordinates (Figure 2) would lead to a small correction for this mode. ^e Net correction to the specific rotation.

around 120° using curvilinear coordinates will average to $\sim -200^\circ$.

The large effects on the optical rotation found with modes 8, 19, 20, and 23 are interesting and will receive further attention. A description of the normal modes has been published,¹⁵ and the changes in internal coordinates for the distorted structures may be found in the Supporting Information.

To estimate the magnitude of vibrational corrections, the optical rotation can be cast as a function of nuclear coordinates, $\alpha(\mathbf{Q})$, where \mathbf{Q} denotes the set of $3N - 6$ displacement coordinates describing canonical normal modes of vibration, $\mathbf{Q} \equiv \{Q_1, Q_2, Q_3, \dots, Q_{3N-6}\}$. By performing a Taylor series expansion of $\alpha(\mathbf{Q})$ about the equilibrium configuration ($\mathbf{Q} = \mathbf{0} \equiv \{0, 0, 0, \dots, 0\}$), one finds

$$\alpha(\mathbf{Q}) = \alpha(\mathbf{0}) + \sum_{i=1}^{3N-6} \left(\frac{\partial \alpha(\mathbf{Q})}{\partial Q_i} \right)_0 Q_i + \frac{1}{2} \sum_{i=1}^{3N-6} \sum_{j=1}^{3N-6} \left(\frac{\partial^2 \alpha(\mathbf{Q})}{\partial Q_i \partial Q_j} \right)_0 Q_i Q_j + \dots$$

$$\approx \alpha(\mathbf{0}) + \sum_{i=1}^{3N-6} \alpha_i^{(1)}(\mathbf{0}) Q_i + \frac{1}{2} \sum_{i=1}^{3N-6} \sum_{j=1}^{3N-6} \alpha_{ij}^{(2)}(\mathbf{0}) Q_i Q_j$$

where the latter expression results from truncating the expansion at second order and introducing a shorthand notation for the partial derivatives. For a vibrational state specified by

$|\mathbf{v}\rangle \equiv |v_1, v_2, v_3, \dots, v_{3N-6}\rangle$, the expectation value of optical rotation, $\langle \alpha \rangle_{\mathbf{v}} = \langle \mathbf{v} | \alpha(\mathbf{Q}) | \mathbf{v} \rangle$, now can be evaluated as

$$\langle \alpha \rangle_{\mathbf{v}} = \langle \alpha(\mathbf{0}) \rangle_{\mathbf{v}} + \sum_{i=1}^{3N-6} \alpha_i^{(1)}(\mathbf{0}) \langle Q_i \rangle_{\mathbf{v}} + \frac{1}{2} \sum_{i=1}^{3N-6} \sum_{j=1}^{3N-6} \alpha_{ij}^{(2)}(\mathbf{0}) \langle Q_i Q_j \rangle_{\mathbf{v}} = \alpha(\mathbf{0}) + \frac{1}{2} \sum_{i=1}^{3N-6} \alpha_{ii}^{(2)}(\mathbf{0}) \langle Q_i^2 \rangle_{\mathbf{v}}$$

where the final equality follows from the fact that $\langle Q_i \rangle_{\mathbf{v}} = 0$ and $\langle Q_i Q_j \rangle_{\mathbf{v}} = \langle Q_i^2 \rangle_{\mathbf{v}} \delta_{ij}$ within the harmonic oscillator limit. Finally, this expression can be averaged over a thermal distribution of molecules to obtain

$$\bar{\alpha} = \sum_{\mathbf{v}} P_{\mathbf{v}}(T) \langle \alpha \rangle_{\mathbf{v}} = \alpha(\mathbf{0}) + \frac{1}{2} \sum_{i=1}^{3N-6} \alpha_{ii}^{(2)}(\mathbf{0}) (\Delta x_i)^2$$

where $P_{\mathbf{v}}(T)$ represents the normalized population of quantum state $|\mathbf{v}\rangle$ at absolute temperature T (essentially the Boltzmann probability distribution) and Δx_i is equal to the previously mentioned thermal displacement of normal coordinate Q_i :

$$(\Delta x_i)^2 = \sum_{\mathbf{v}} P_{\mathbf{v}}(T) (\langle Q_i^2 \rangle_{\mathbf{v}} - \langle Q_i \rangle_{\mathbf{v}}^2) = \sum_{\mathbf{v}} P_{\mathbf{v}}(T) \langle Q_i^2 \rangle_{\mathbf{v}}$$

Building upon the already tabulated values of $\alpha(\mathbf{0})$ and $\alpha(\mathbf{0} \pm \Delta x_i)$, the second-order derivative required for the calcula-

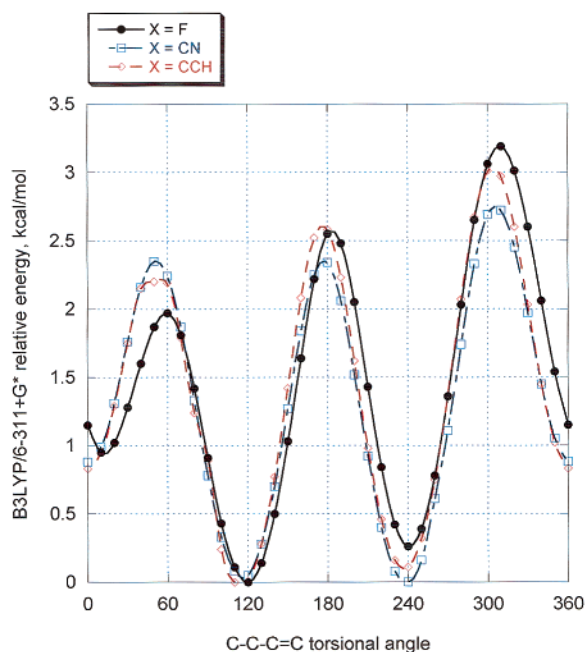


Figure 6. Effect of C–C=C torsional angle on the relative energies of 3-fluoro-1-butene (closed circles), 3-cyano-1-butene (open squares), and 3-ethynyl-1-butene (open tilted squares), calculated at the B3LYP/6-311+G* level.

tion of $\langle\alpha\rangle_v$ and $\bar{\alpha}$ can be estimated numerically through use of the standard three-point formula

$$\alpha_{ii}^{(2)}(\mathbf{0}) \approx \frac{\alpha(\mathbf{0}+\Delta x_i) - 2\alpha(\mathbf{0}) + \alpha(\mathbf{0}-\Delta x_i)}{(\Delta x_i)^2}$$

Table 5 contains a compilation of the second-order corrections to optical activity determined for each vibrational mode of **1** by means of the above formulation. Excluding the influence of mode 30 owing to its previously mentioned anomalous behavior, the total vibrational correction at room temperature is found to be only +7.95°. Although more sophisticated analyses which incorporate the influence of mechanical anharmonicity might increase this value,²³ it is highly unlikely that such treatments will be able to account for the factor of 2–3 discrepancy that we have uncovered between theoretically predicted and experimentally measured optical rotation parameters.

3. 3-Fluoro-1-butene (2)

We are interested in examining the effect of substituents on optical rotation, and therefore, **2** was studied to see the effect of replacing Cl by F. The potential energy curve calculated at the B3LYP/6-311+G* theoretical level is shown in Figure 6. The three low-energy forms are the same as found with **1**, but the relative energies are different. Qualitatively, one might say that the steric effects of chlorine and methyl are similar so that the 120° and 240° rotamers of **1** have approximately the same energy. Fluorine is smaller, and so the form with the fluorine eclipsed with the double bond has a lower relative energy than found with the chloride. The relative energies of the conformers also were calculated at the G2 level (Table 6). The conformations of **2** have been studied experimentally via IR spectroscopy,

(23) Ruud, K.; Åstrand, P.-O.; Taylor, P. R. *J. Chem. Phys.* **2000**, *112*, 2668.

Table 6. Calculated Relative Energies, 298 K^a

compound	B3LYP/6-311+G*			G2		
	tors ^a	H _{rel}	G _{rel}	tors	H _{rel}	G _{rel}
3-chloro-1-butene	0.33	1.10	1.30	2.00	0.87	1.05
	56.55*	2.27	3.74	54.99	2.16	3.27
	123.09	0.00	0.00	119.57	0.00	0.00
	188.64*	2.47	3.48	183.61	2.22	3.30
	238.85	1.59	1.68	240.91	1.01	1.10
3-fluoro-1-butene	298.19*	2.87	3.89	302.97	2.31	3.40
	12.86	1.01	1.12	16.92	0.90	1.01
	59.21*	1.27	2.30	59.42	1.07	2.17
	119.77	0.00	0.00	115.62	0.00	0.00
	183.65*	1.91	2.94	179.22	1.87	2.97
3-cyano-1-butene	240.49	0.24	0.40	242.72	0.19	0.38
	308.84*	2.64	3.68	313.83	2.27	3.41
	1.31	0.99	1.13	0.68	1.10	1.19
	51.44*	1.73	2.70	51.23	1.86	2.87
	115.88	0.05	-0.06	115.30	0.42	0.29
3-ethynyl-1-butene	177.13*	1.71	2.67	176.94	1.87	2.86
	238.44	0.00	0.00	242.26	0.00	0.00
	306.16*	2.21	3.17	309.62	2.10	3.09
	1.14	0.96	1.23	0.96	0.71	0.92
	50.70*	1.73	2.82	50.88	1.51	2.64
	114.54	0.00	0.00	113.80	0.00	0.00
	176.39*	1.96	3.01	175.72	1.73	2.82
	236.64	0.13	0.29	239.96	-0.17	-0.03
	304.12*	2.49	3.54	307.87	1.98	3.09

^a Transition states are indicated by an asterisk.

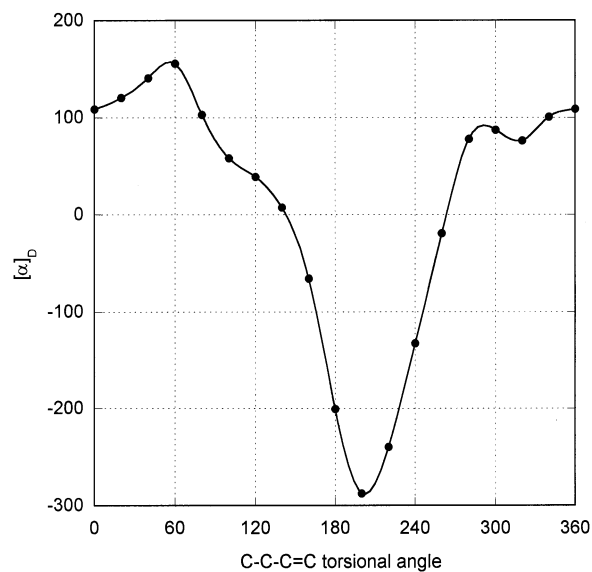


Figure 7. Calculated optical rotation of 3-fluoro-1-butene, B3LYP/6-311++G**.

copy,²⁴ and our G2-calculated results are in very good agreement with the experimental observations.²⁵

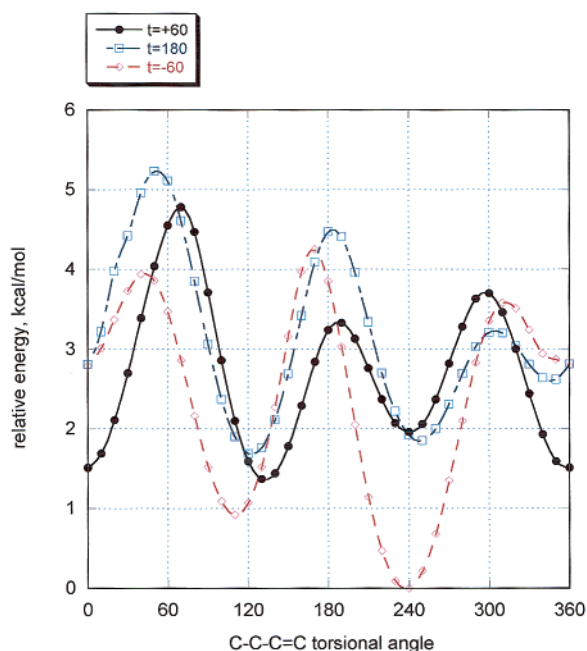
The specific rotation of (*R*)-(-)-**2** as a function of the C=C–C–C torsional angle was calculated at the B3LYP/6-311+G* level, and the 589 nm data are shown in Figure 7. Data for other wavelengths may be found in the Supporting Information. The plot is remarkably similar to that for **1**, in both shape and magnitude. It appears that the replacement of Cl by F does not have an important effect on the optical rotation despite the difference in the calculated electronic transition energies for **1** and **2** (Table 7).

(24) Durig, J. R.; Hur, S. W.; Gounev, T. K.; Feng, F.; Guirgis, G. A. *J. Phys. Chem. A* **2001**, *105*, 4216.

(25) A comparison may be found in the Supporting Information.

Table 7. B3LYP/6-311++G** TDDFT Calculated Transition Energies

state	3-chloro-1-butene			3-fluoro-1-butene			3-cyano-1-butene			3-ethynyl-1-butene		
	eV	nm	f	eV	nm	f	eV	nm	f	eV	nm	f
1	6.12	202.7	0.059	6.82	181.9	0.045	6.72	184.5	0.034	6.17	201.0	0.005
2	6.18	200.7	0.013	7.13	173.9	0.101	7.00	177.1	0.278	6.28	195.7	0.050
3	6.58	188.5	0.050	7.17	173.0	0.224	7.15	173.4	0.031	6.36	194.9	0.019
4	6.75	183.6	0.211	7.28	170.3	0.004	7.25	171.1	0.012	6.58	188.5	0.062
5	6.99	177.3	0.004	7.36	168.4	0.027	7.29	170.1	0.009	6.66	186.1	0.006

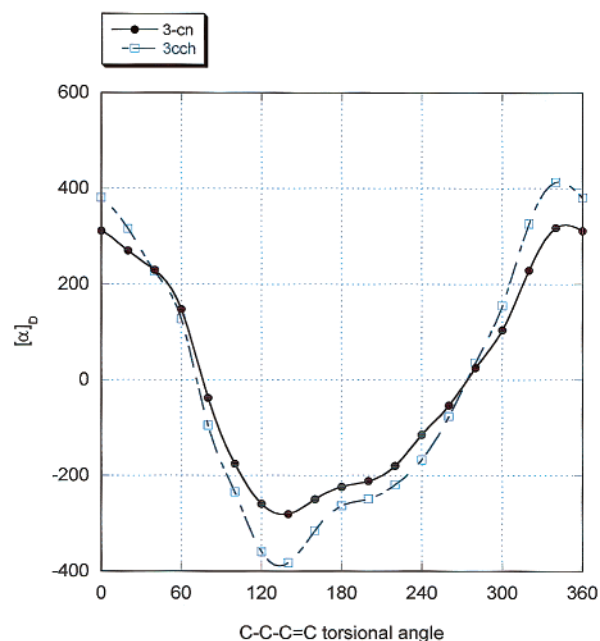
**Figure 8.** Effect of the C–C–C=C torsional angle on the relative energies of 3-butene-2-ol rotamers calculated at the B3LYP/6-311+G* level.

It would be interesting to examine the temperature dependence of the optical rotation of **2**, but this is not practical in solution because of its high vapor pressure. It may prove possible to carry out this study in the gas phase.¹⁰ In addition, **2** has not as yet been prepared in optically active form, and studies of this problem are in progress. The calculated optical rotation for the equilibrium mixture of conformers at 25 °C is -6.4° .

As was found with **1**, the calculated optical rotations at 589 and 365 nm are linearly related. A comparison of 589 and 250 nm showed considerably less scatter than was found with **1**. This probably results from the higher electronic transition energies of **2** as compared to **1** (Table 7).

4. 3-Butene-2-ol (**3**)

It would be interesting to compare OH with F as the substituent, and therefore, the energies of the conformers of **3** were studied at the B3LYP/6-311+G* level (Figure 8). Here, there are two variable torsional angles: C=C–C–C and C–C–O–H. In the calculations, the latter was made approximately trans, +gauche, or –gauche, and the energies were obtained by scanning the C–C=C=C torsional angle with complete geometry optimization, except for the fixed torsional angle, at each point. The complexity of the potential energy curves, with many minima having similar energies with probably different optical rotations, made it impractical to further study the molecule. As a result, we have restricted our investigation to compounds where the substituent does not add conformational complexity.

**Figure 9.** Calculated optical rotations of 3-cyano- and 3-ethynyl-1-butene, B3LYP/6-311+G*.

5. 3-Cyano-1-butene (**4**)

A cyano group provides a different kind of substituent in that it is an unsaturated system, and might lead to significant changes in the optical rotation. The cyano group is sterically small, and if the conformational preference were largely due to a steric effect, **4** should be similar to **2**. The potential energy curve for rotation about the C=C–C–C torsional angle was calculated at the B3LYP/6-311+G* level, giving the data shown in Figure 6. The rotamer in which the methyl group eclipses the double bond has the highest energy, and the ones in which a hydrogen or the cyano group eclipses the double bond have essentially the same energy. There is little difference in the potential energy curves for **2** and **4**.

The specific rotation of (*R*)-(–)-**4** was calculated at 20° intervals at the B3LYP/6-311++G** level, giving the $[\alpha]_D$ values summarized in Figure 9. Data for other wavelengths may be found in the Supporting Information. Although there is a change in the shape of the curve as compared to those of **1** and **2**, the large positive rotations are again found near 0°, and the large negative rotations are again in the vicinity of 180°. The range of optical rotation is about 60% that of **1**.

The enantiomers of **4** have not as yet been reported. The rotation calculated using the relative energies in Table 6 and the data in Figure 9 is $[\alpha]_D = -133^\circ$. We are currently studying the preparation of a single enantiomer of **4**.

6. 3-Ethynyl-1-butene (5)

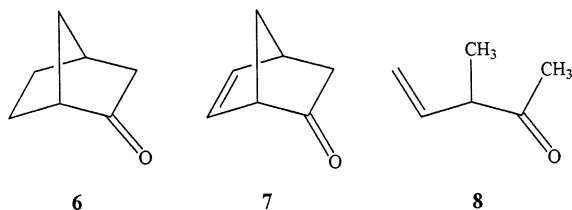
An ethynyl group is more similar to a carbon–carbon double bond than is a cyano group. Therefore, its effect on optical rotation was calculated. The effect of the C=C–C–C torsional angle on the energy, calculated at the B3LYP/6-311+G* level, is shown in Figure 6. The relative energies are close to those for F or CN as the substituent, confirming that the energies are largely determined by steric effects.

The specific rotations of (*R*)-(-)-**5** at 589 nm calculated at 20° intervals at the B3LYP/6-311++G** level are included in Figure 9. Data for other wavelengths may be found in the Supporting Information. The curves for **4** and **5** are remarkably similar, despite the difference between CN and C≡CH as substituents. For example, the carbon in the CN group has a large positive charge, whereas this is not the case with the ethynyl group. The calculated specific rotation of (*R*)-(-)-**5** based on the calculated rotations and the G2 relative energies is $[\alpha]_D = -201^\circ$. Chiral forms of **5** have not been reported, and we are currently studying their preparation.

The optical rotation arises from electric and magnetic transition dipole terms between the ground state and the excited states of a molecule.²⁶ To gain some information concerning the excited states of **4** and **5**, TDDFT/6-311++G** calculations were carried out for the first five singlet states of each. The transition energies are summarized in Table 6. It can be seen that they differ by ~0.6 eV, which makes the similarity of the optical rotation/torsional angle curves that much more remarkable.

7. 2-Norbornanone (6) and 2-Norbornenone (7)

Whereas **6** has $[\alpha]_D = -17^\circ$,²⁷ **7** has $[\alpha]_D = -1160^\circ$.²⁸ The B3LYP/6-311+G*-calculated specific rotations using the above configurations are -13° and -1230° , respectively. In view of the large effect of conformation on the optical rotation of 3-chloro-1-butene, it seemed possible that the greatly enhanced rotation of **7** was the result of having a torsional angle that would lead to a large rotation. As a model system, the remote bridgehead carbon of **7** was deleted and replaced by hydrogens (**8**). To reduce the H···H nonbonded repulsion, the bond angles



at the chiral carbon were set to 109.5° (C–C–C) or 120° (C=C=C). The specific rotation was calculated at the B3LYP/6-311+G* level, and the effect of changing the torsional angle was examined using rigid rotations. The result is shown in Figure 10. The (O=C)–C–C=C torsional angle of **10** which corresponds to **7** is 291°, which would lead to a predicted rotation of -1700° . Considering the crude model, this is in satisfactory agreement with the calculated value for **7** itself,

(26) Condon, E. U. *Rev. Mod. Phys.* **1937**, *9*, 432.

(27) Berson, J. A.; Walia, J. S.; Remanick, A.; Suzuki, S.; Reynolds-Warnhoff, P.; Willner, D. *J. Am. Chem. Soc.* **1961**, *83*, 3986.

(28) Sandman, J.; Mislow, K. *J. Org. Chem.* **1968**, *33*, 2924. Mislow, K.; Berger, J. G. *J. Am. Chem. Soc.* **1956**, *84*, 1956.

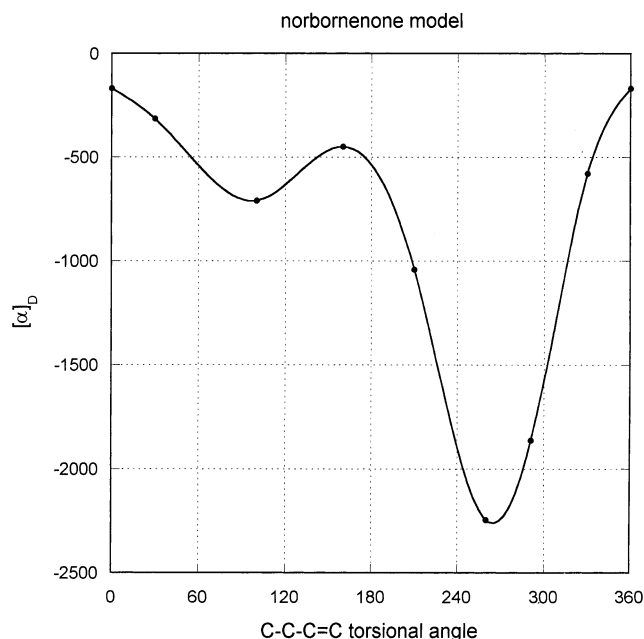
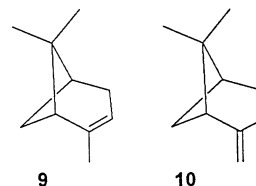


Figure 10. Effect of the (O=C)–C–C=C torsional angle on the calculated optical rotation of the norbornenone model **8**.

-1200° . The orientation of the double bond with respect to the rest of the molecule is a major factor in determining the optical rotation.

8. α - and β -Pinenes

The pinenes present another example of the importance of the orientation of a double bond on the optical rotation. (1*S*,5*S*)-(-)- α -Pinene (**9**) and (1*S*,5*S*)-(-)- β -pinene (**10**) are



known to be related since both on hydrogenation give the same pinane.²⁹ Although both have a negative sign of rotation at 589 nm and the rotation of **9** becomes more negative at 355 nm both in the gas phase and in solution, the rotation of **10** changes sign as the wavelength is reduced, and is positive at 355 nm both in the gas phase and in solution. Ab initio calculations for **9** agree with the direction of the change in optical rotation with wavelength, but with **10**, the calculations incorrectly predict a positive sign of rotation at 589 nm (Table 8).³⁰ However, the rotation of **10** is small, and the error is within the error bar of the optical rotation calculations ($\pm 30^\circ$).⁷

Although it is not apparent at 589 nm, the shorter wavelength data clearly show that the change in orientation of the double bond between **9** and **10** results in a reversal of the sign of the optical rotation.

9. Summary

The potential energy curves for the 3-substituted 2-butenes are determined by steric factors. The conformers of **1** where

(29) Lipp. *Justus Liebigs Ann. Chem.* **1930**, *63*, 412.

(30) In our previous paper (ref 10), the signs of the calculated rotations of β -pinene were inadvertently reversed.

Table 8. Specific Rotation of the Pinenes

compound	phase	specific rotation (deg) at various wavelengths (nm)	
		355	633
(-)- α -pinene	gas	-189	-48
	soln ^a	-165	-46
	calcd ^b	-89	-34
(-)- β -pinene	gas	71	-12
	soln ^a	22	-17
	calcd ^b	254	21

^a Cyclohexane solution, $c = \sim 0.1$ g/mL. ^b B3LYP/6-311++G(2d,2p)//B3LYP/TZ2p.

methyl or chlorine eclipses the double bond have equal higher energies, with the hydrogen-eclipsed structure having the lowest energy. With **2–4**, the substituent has little steric interaction with the double bond, and only the methyl-eclipsed structure has a higher energy.

The calculated optical rotations of **1–4** as a function of the C=C–C–C torsional angles are similar with large positive rotations around 0° and large negative rotations around 180°. The large effect of the torsional angle on the rotation was confirmed by a measurement of the temperature dependence of the rotation of **1** and a determination of the maximum rotation of **1**. It was found that the calculated rotations were too large by a factor of 2.6, which was independent of wavelength. The difference in energy between the low- and high-energy conformers was found to be 1.3 kcal/mol in methylcyclohexane solution as compared to the calculated 1.1 kcal/mol in the gas phase.

The effect of replacing Cl by F, CN, or CCH is relatively small, whereas the calculated transition energies are quite different. The optical rotations of these compounds have not as yet been determined experimentally.

It has been found that modern theoretical methods are usually capable of predicting the sign and approximate magnitude of the optical rotation at the sodium D line.^{5–9} However, there are some aspects of the calculations that are not well understood. The origin of the exaggerated calculated rotation of 3-chloro-1-butene is not understood. The origin of the very strong dependence of the optical rotation on the orientation of the double bonds in **1–4** as well as **8–10** also is not understood.

The results of this investigation help to define the problem of accounting for structural effects on optical rotation. It seems unlikely that further studies of the optical rotation itself will cast much additional light on the problem. It is more likely that an examination of the tensor components would be useful. They are more directly related to the physical process, and it should be possible to analyze them on a state by state fashion to determine which MOs are primarily responsible for the effects that have been observed. This currently is being explored.

9. Experimental Section

3-Butene-2-ol (**3**) was resolved as its acid phthalate using brucine.³¹ It was converted to the chloride **1** with hexachloroacetone and triphenylphosphine.³² The chloride thus formed contains about 5% of

(31) Constantin, G.; Ville, G. *Bull. Soc. Chim. Fr.* **1971**, 2974.

the achiral isomer crotyl chloride. The percent of the chiral form vs the racemic form and the achiral impurity could be determined using an analytical chiral GC column. Racemic **1** gave equal areas for the two enantiomers. A sample of **3** with $\alpha_D^{25} = +21.7^\circ$ ($l = 1$, neat) gave **1** having $\alpha_D^{25} = -36.02^\circ$ ($l = 1$, neat). It contained a 69.94% excess of (-)-**1**, making the maximum rotation +51.5°. A sample of **3** with $\alpha_D^{25} = -14.9^\circ$ ($l = 1$, neat) gave **1** having $\alpha_D^{25} = +24.34^\circ$. It contained a 47.12% excess of (+)-**1**, making the maximum rotation -51.7°. Thus, the maximum rotation is taken as $\alpha_D^{25} = \pm 51.6^\circ$ ($l = 1$, neat) and $[\alpha]_D^{25} = \pm 57.3^\circ$ ($d = 0.900$ g/mL).

The temperature dependence of the optical rotation of **1** was determined in an approximately 10% solution of **1** in methylcyclohexane. A jacketed cell with $l = 1$ dm and a volume of 6 mL was used. An ethylene glycol/water mixture from an external thermostat was circulated through the jacket of the cell. The temperature at the cell was taken as that of the circulating bath liquid at the exit of the polarimeter cell. The temperatures could be determined with an uncertainty of less than 0.1 C using a set of ASTM precision thermometers which were marked at 0.1 intervals. The optical rotations were measured with a reproducibility of $\sim 0.002^\circ$. One filling hole of the cell was fitted with a short syringe with a loose stopper that allowed the solution to change its volume with changing temperature.

The volume expansion of methylcyclohexane on heating was determined by filling a 10 mL volumetric flask to the mark at 80 °C, and then cooling it to 0 °C. The amount of methylcyclohexane required to bring it to the mark was determined both gravimetrically and volumetrically, and both methods found that 0.85 mL was required. The measured optical rotations were scaled accordingly.

10. Calculations

The ab initio calculations were carried out using Gaussian-99.³³ The calculations of the optical activity made use of the B3LYP density functional model, and the transition energies were calculated using time-dependent density functional theory at the same level that was used for the optical activity calculations.

Acknowledgment. The studies at Yale were carried out with the aid of grants from the National Science Foundation. We thank Prof. William Bailey and Mr. Matthew R. Luderer (University of Connecticut) for determining the % ee of the samples of **1**.

Supporting Information Available: Tables of calculated energies and calculated optical rotations at different wavelengths, a table of internal coordinates for vibrationally distorted 3-chloro-1-butenes, and a comparison of experimental and calculated rotational barriers for 3-fluoro-1-butene (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA0211914

- (32) Magid, R. M.; Fuchey, O. S.; Johnson, L. L.; Allen, T. G. *J. Org. Chem.* **1979**, *446*, 359.
- (33) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Baboul, A. G.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T. A.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 99*, development version (rev. B); Gaussian, Inc.: Pittsburgh, PA, 1998.