

# Conformational Analysis of Chiral Alkenes and Oxonium Ions: Ab Initio Molecular Orbital Calculations and an Improved MM2 Force Field

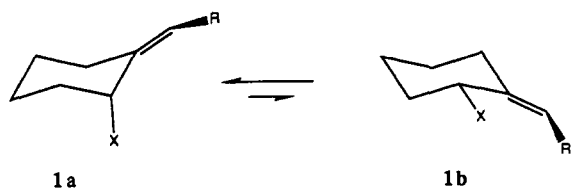
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Contribution from the Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California 90024, and Fachbereich Chemie der Philipps-Universität,<sup>†</sup> Hans-Meerwein-Strasse, D-3550, Marburg, Germany. Received June 11, 1990

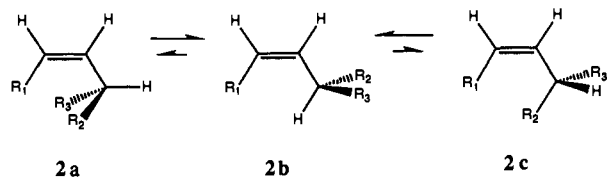
**Abstract:** Calculations on the conformations of isopropylbenzene, 3-methyl-1-butene, 4-methyl-*cis*-2-pentene, and 2,3-dimethyl-1-butene, were performed at the MP2/6-31G\*//3-21G level. Calculations on the O-alkylated aldehyde cations, *O*-isopropylacetaldehyde (36), *cis*-*O*-isopropylaldehyde (37), *O*-methylformaldehyde (38), *cis*- and *trans*-protonated acetaldehyde (39), *cis*- and *trans*-*O*-methylacetaldehyde (40), and *O*-ethylformaldehyde (41) as well as *cis*- and *trans*-protonated propionaldehyde (42), were performed at the MP2/6-31G\*//6-31G\* level. 3-Methyl-1-butene has little 1,3-allylic strain in any conformation; consequently, the two conformational minima, the double-skew and skew-eclipsed conformers, differ in energy by only 0.7 kcal/mol, with the skew-eclipsed conformer being the global minimum. The oxonium ion, *O*-isopropylacetaldehyde, 36, exhibited increased 1,3-strain in the crowded configurations so that the double-skew conformer is 1.2 kcal/mol more stable than the skew-eclipsed conformer. Both 4-methyl-*cis*-2-pentene and *cis*-*O*-isopropylacetaldehyde, 37, which have methyl groups *cis* to isopropyl groups, have a 3.2–3.5 kcal/mol preference for the skew conformer due to strong 1,3-allylic strain in the crowded conformations. That 1,2-allylic strain is small relative to 1,3-allylic strain in alkenes is demonstrated by 2,3-dimethyl-1-butene, which has a methyl group geminal to an isopropyl group on one terminus of the double bond and a double-skew conformer which is only 0.5 kcal/mol lower in energy than the skew-eclipsed conformer. The normal MM2 parameters for alkenes were found to give conformational energies for 3-methyl-1-butene, 4-methyl-*cis*-2-pentene, and 3,3-dimethyl-1-butene which were inconsistent with the ab initio results. New MM2 parameters were developed for alkenes and oxonium salts. MM2 calculations, using these new parameters, for rotation about the allylic bond of a series of alkenes were consistent with the same potential energy surfaces determined by ab initio calculations. Allinger's new force field, MM3, also improves the results for alkenes to some extent. The new force fields plus the existing MM2 force field for aromatic hydrocarbons were used to calculate the conformations of relatively large chiral molecules for aromatic, olefinic, and oxonium ion systems. The selectivities of these compounds with electrophilic and nucleophilic reagents are related to the conformational equilibria of the ground-state molecules.

## Introduction

Allylic 1,3-strain influences the conformational preferences of allylic systems. The scope of this phenomenon was recognized by Johnson,<sup>1</sup> who demonstrated it in alkylidenecyclohexanes. A substituent X in **1** prefers the axial position. Conformation **1b** is destabilized, since X and the vinylic substituent R are in close proximity. This phenomenon also influences the conformations

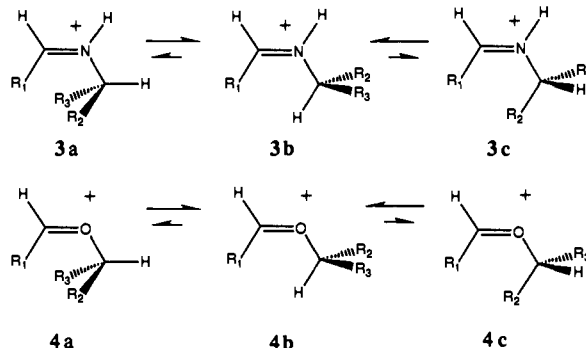


of open chain allylic systems **2** with *cis* substituents.<sup>2,3</sup> In the



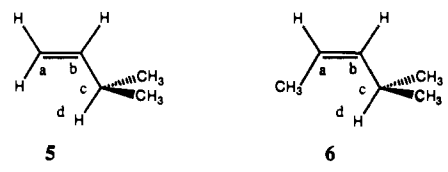
most stable conformer, **2b**, the substituents  $R_2$  and  $R_3$  are disposed such that they may differentiate the diastereotopic faces of the double bond. This has been the key to high asymmetric induction in the addition reactions at the double bond realized in the pioneering studies by Kishi<sup>4-6</sup> and Evans,<sup>7,8</sup> among others as well as in work in our laboratories.<sup>9</sup> Hoffmann has recently reviewed the use of 1,3-allylic strain as a controlling factor in stereoselective transformations of alkenes and heteroatomic double bonds.<sup>10</sup>

Indeed the conformational preferences of allylic systems such as **2** have become one of the most reliable controlling elements in asymmetric synthesis. However, quantitative information on the energetics of conformational equilibria of such molecules is still lacking. In general, a substituent at the *Z*-position appears to be essential in order to bias the conformational equilibrium in favor of **2b**.<sup>10</sup> The equilibrium of **2** ( $R_1 = \text{Me}$ ) should lie heavily in favor of **2b**, because of the presence of the *cis*-methyl group. If the methyl substituent is lacking as in **2** ( $R_1 = \text{H}$ ), then the conformational preference should be only weak. However, in



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<sup>‡</sup> University of California.

**Table I.** Ab Initio Energies of Compounds 5 and 6 and as a Function of  $\phi_{abcd}$ <sup>a</sup>


$\phi = \langle abcd \rangle$

$\phi$ , deg	energy, hartrees (kcal/mol)		
	3-21G// 3-21G	6-31G*// 3-21G	MP2/6-31G*// 3-21G
Compound 5			
0	-194.064 55 (0.00)	-195.140 86 (0.00)	-195.788 06 (0.0)
70	-194.059 87 (2.94)	-195.136 42 (2.78)	-195.783 92 (2.60)
120	-194.062 66 (1.19)	-195.139 34 (0.95)	-195.786 89 (0.73)
180	-194.060 05 (2.82)	-195.136 05 (3.02)	-195.784 10 (2.48)
Compound 6			
0	-232.884 21 (0.0)	-234.176 71 (0.0)	-234.955 82 (0.0)
100	-232.874 83 (5.89)	-234.168 18 (5.35)	-234.948 07 (4.86)
180	-232.877 31 (4.33)	-234.170 33 (4.01)	-234.950 34 (3.44)

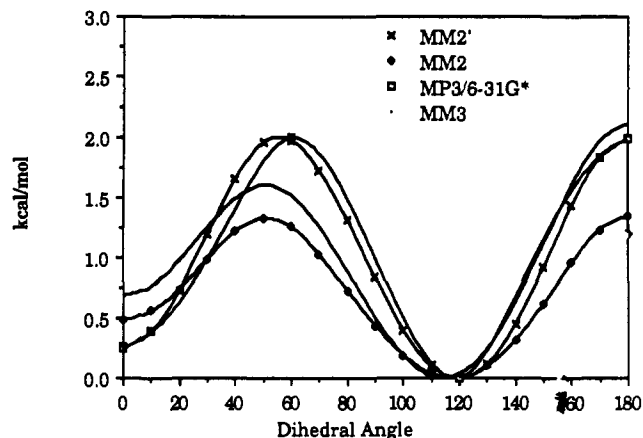
<sup>a</sup>Geometries are fully optimized at conformational minima; otherwise, geometries are fully optimized except for  $\phi_{abcd}$ .

heterosubstituted allylic systems such as 3 or 4, experimental asymmetric induction<sup>11-23</sup> and spectroscopic<sup>24,25</sup> measurements suggest that conformer b is markedly favored over conformers a or c even when  $R_1 = H$ . In the case of 3 ( $R_1 = H$ ) this is in line with MMP2 calculations, which show a 2-kcal preference for 3b over 3a or 3c.<sup>26</sup> Recent ab initio calculations on 3 ( $R_1 = R_2 = R_3 = H$ ) have determined the barrier for rotation about the C-N single bond to be 1.3 kcal/mol at the 6-31G\* level.<sup>27</sup> We report here on the energetics of the conformational equilibria of 2 as it pertains to alkene and aromatic systems, and on the oxonia system, 4.

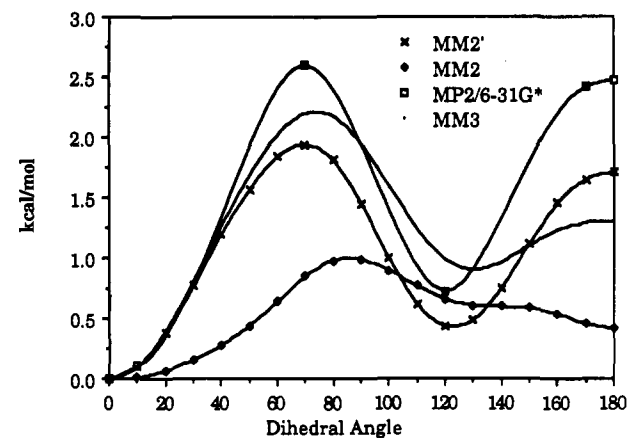
### Computational Methods

Ab initio calculations were performed with the GAUSSIAN82 or GAUSSIAN86 program packages.<sup>28</sup> Molecular mechanics calculations were run with the MM2(82) program<sup>29</sup> modified to include equivalency of

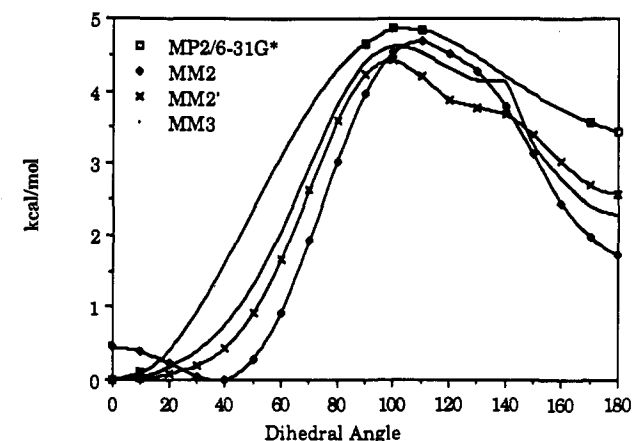
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**Figure 1.** MM2, MM2', MM3, and ab initio torsional energies for 1-butene, 8. Dihedral angle is  $\angle C_1C_2C_3C_4$ .



**Figure 2.** MM2, MM2', MM3, and ab initio torsional energies for 3-methyl-1-butene, 5. Dihedral angle is  $\angle C_1C_2C_3H$ .



**Figure 3.** MM2, MM2', MM3, and ab initio torsional energies for *cis*-4-methyl-2-pentene, 6. Dihedral angle is  $\angle C_2C_3C_4H$ .

certain atom types.<sup>30</sup> The standard MM2(82) parameters used in this work are unchanged in the MM2(85) force field. The new or modified parameters developed in this work are given in Table XXIII.

- (28) (a) Binkley, J. S.; Frisch, M. J.; Defrees, D. J.; Raghavachari, K.; Whiteside, R. A.; Schlegel, H. B.; Fleuder, E. M.; Pople, J. A. GAUSSIAN 82; Carnegie-Mellon University: Pittsburgh, PA. (b) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fleuder, E. M.; Pople, J. A. GAUSSIAN 86; Carnegie-Mellon Quantum Mechanical Publishing Unit: Pittsburgh, PA.  
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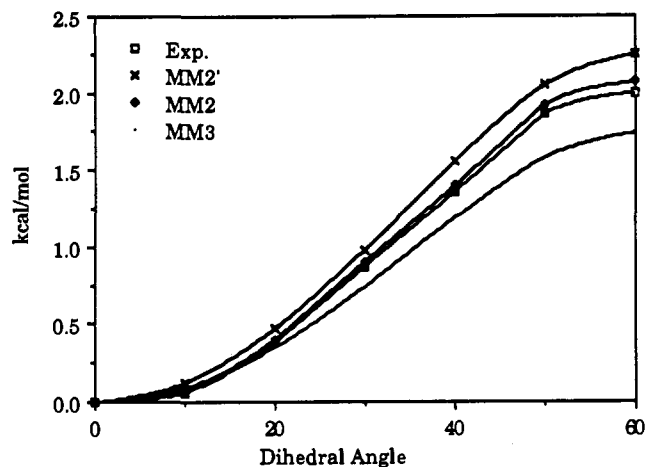
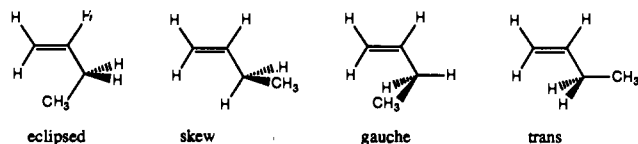


Figure 4. MM2, MM2', MM3, and ab initio torsional energies for propene, 7. Dihedral angle is  $\angle\text{CCCH}$ .

### Results and Discussion

**Alkenes.** Wiberg and co-workers have performed MP3/6-31G\*\*//3-21G level calculations for rotation about the allyl C-C bond of 1-butene.<sup>31a</sup> The results are summarized in Figure 1 (the MM2 and MM2' curves will be defined later). Two minima were found: the eclipsed conformation and the skew conformation with the skew being more stable by 0.25 kcal/mol. Two energy maxima were found for this rotation: the gauche and trans configurations which were 2.0 kcal/mol higher in energy than the skew conformer. Thus, the barrier to rotation of 1-butene is the same as that of propene.<sup>31b</sup>



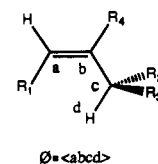
We performed similar calculations of 3-methyl-1-butene, 5, and *cis*-4-methyl-2-pentene, 6. Optimization of the geometry of 5 as a function of the torsional angle,  $\phi_{abcd}$ , was carried out at the 3-21G level. The geometries were fully optimized at the energy minima. For other conformers, the  $\phi_{abcd}$  torsional angle was incremented from 10–30°, and all other variables were optimized. The results (Table I) show that the 3-21G level predicts the double-skew ( $\phi = 0^\circ$ ) and the skew-eclipsed ( $\phi = 122^\circ$ ) conformations to be minima, while the trans-gauche ( $\phi = 70^\circ$ ) and double-gauche ( $\phi = 180^\circ$ ) configurations are energy maxima. MP2/6-31G\*\*//3-21G single point calculations at these extrema showed a 0.7 kcal/mol stabilization of the double-skew conformer over the skew-eclipsed conformer with energy barriers to rotation of 2.6 ( $\phi = 70^\circ$ ) and 2.5 ( $\phi = 180^\circ$ ) kcal/mol (see Figure 2).

Optimization of the geometry of 6 as a function of the  $\phi_{abcd}$  dihedral angle was carried out at the 3-21G level in the manner described for 5 above. The global and local minima occur at the double-skew ( $\phi = 0^\circ$ ) and the double-gauche ( $\phi = 180^\circ$ ) conformations, respectively, while the energy maximum occurs at  $\phi$

(30) Our version of MM2 was modified by David C. Spellmeyer to include an atom type equivalency property which allows a user to equivalence two atom types. This enables one to redefine one or two parameters of an atom type without having to duplicate numerous definition cards. The redefined parameters are simply read in along with the two atom types that are to be made equivalent. The equivalence mechanism set the parameters for the new atom type equal to the parameters for the other atom type (which are defined internal to the program) and then redefines the parameters that are read in.

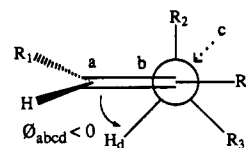
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Table II. Conformational Minima of Alkenes 9–27 as Calculated by MM2'

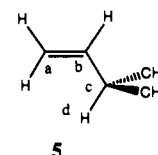


compd	R1	R2	R3	R4	conformer $\phi$ , ° deg	relative energy, kcal/mol
9	Me	Me	tBu	H	10	0.0
					-150	3.5
10	Me	Me	iPr	H	0	0.0
					180	2.7
11	Me	Ph	Me	H	-40	0.0
					-170	1.5
					130	3.5
12	Me	tBu	tBu	H	0	0.0
					180	7.2
13	H	Me	tBu	H	5	0.0
					-140	0.9
14	H	Me	iPr	H	0	0.0
					-130	1.1
					150	1.6
15	H	Ph	Me	H	-10	0.1
					-90	1.0
					120	0.0
16	H	iPr	iPr	H	-5	0.0
					145	1.5
17	H	iPr	tBu	H	-10	0.0
					-160	2.5
18	H	tBu	tBu	H	0	0.0
					170	3.4
19	OMe	Me	Me	H	0	0.0
					125	1.4
					175	1.7
20	OMe	Me	tBu	H	10	0.0
					-140	1.6
23	Me	Me	Me	Me	1	0.0
					180	2.3
24	Me	Me	tBu	Me	10	0.0
					-160	2.6
25	Me	tBu	tBu	Me	5	0.0
					180	2.5
26	H	Me	tBu	Me	5	0.0
					-160	0.3
27	H	tBu	tBu	Me	0	0.5
					175	0.0

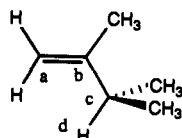
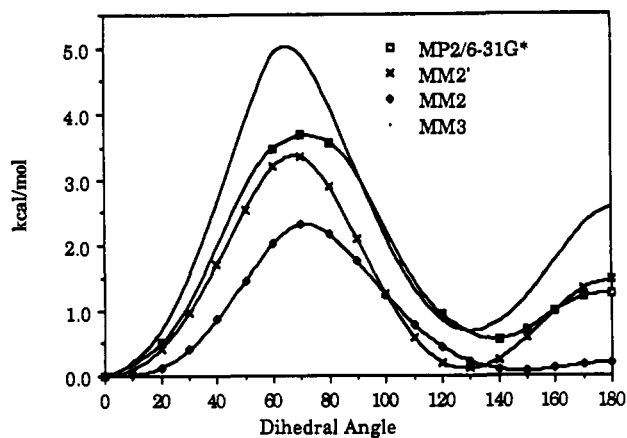
<sup>a</sup> Sign of the angle  $\phi$ : when looking through atom b toward atom c, if atom d is counterclockwise from atom a, then the sign is negative, as shown below. Note also that  $\phi_{abcR_2} = \phi_{abcd} + 120^\circ$  and  $\phi_{abcR_3} = \phi_{abcd} - 120^\circ$ .



$= 100^\circ$  (see Table I). MP2/6-31G\*\*//3-21G single point calculations showed that the double-skew conformer is 3.4 kcal/mol



more stable than the double-gauche conformer. There is an energy barrier of 4.7 kcal/mol ( $\phi = 100^\circ$ ) for rotation between the conformers (see Figure 3). The energy maximum at  $\phi = 100^\circ$  may be surprising in light of the calculations on 5 which showed an energy minimum at  $\phi = 122^\circ$ . However, this eclipsed conformation in 6 has severe steric repulsion between two methyl

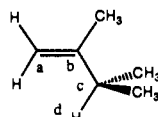


22

 $\phi = \langle abcd \rangle$ 

Figure 5. MM2, MM2', MM3, and ab initio torsional energies for 2,3-dimethyl-1-butene, 22. Dihedral angle is  $\angle C_1C_2C_3H$ .

Table III. Ab Initio Energies of Compound 22 and as a Function of  $\phi_{abcd}$ <sup>a</sup>



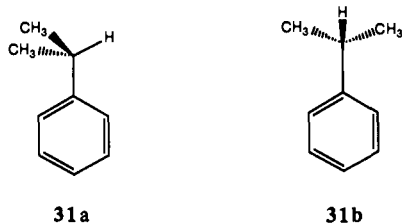
22

 $\phi = \langle abcd \rangle$ 

$\phi$ , deg	energy, au (kcal/mol)		
	3-21G//3-21G	6-31G*//3-21G	MP2/6-31G*//3-21G
0	-232.88470 (0.00)	-234.17667 (0.00)	-234.95811 (0.00)
70	-232.87826 (4.04)	-234.17034 (3.97)	-234.95225 (3.68)
142	-232.88391 (0.50)	-234.17567 (0.63)	-234.95722 (0.56)
180	-232.88271 (1.25)	-234.17470 (1.24)	-234.95611 (1.26)

<sup>a</sup>Geometries are fully optimized at conformational minima; otherwise, geometries are fully optimized except for  $\phi_{abcd}$ .

Table IV. Ab Initio Energies of Compound 31<sup>a</sup>



31a

31b

configuration	energy, hartrees (kcal/mol)		
	3-21G//3-21G	6-31G*//3-21G	MP2/6-31G*//3-21G
31a	-345.8794772 (0.00)	-347.807781 (0.00)	-348.96089 (0.00)
31b	-345.8739074 (3.49)	-347.8026657 (3.21)	-348.956315 (2.87)

<sup>a</sup>The geometries of 31a and 31b were constrained to  $C_1$  symmetry in the optimization.

Table V. Relative MM2 Energies of the Conformers of Aromatic Compounds 32-35

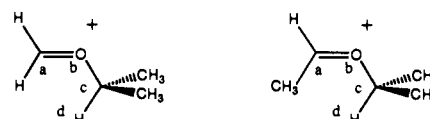
compd	relative energy, kcal/mol $E(b) - E(a)$	compd	relative energy, kcal/mol $E(b) - E(a)$
32	1.5	34	1.0
33	1.3	35	0.3

Table VI. Ratio of Stereoisomers for the Complexation of  $Cr(CO)_6$  with Compounds 32-35

reactant	exptl <sup>a</sup> ratio c/d	exptl <sup>a</sup> $\Delta G(d - c)$ , kcal/mol	MM2 $\Delta E(b - a)$ , kcal/mol
32	85:15	1.4	1.5
33	89:11	1.7	1.3
34	76:24	1.0	1.0
35	69:31	0.7	0.3

<sup>a</sup>Temperature = 413 K.

Table VII. Ab Initio Energies of Compounds 36 and 37 as a Function of  $\phi_{abcd}$ <sup>a</sup>



36

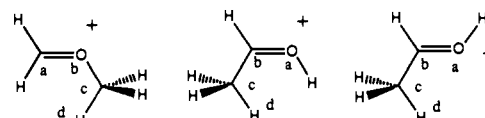
37

 $\phi = \langle abcd \rangle$ 

$\phi$ , deg	energy, hartrees (kcal/mol)	
	6-31G*//6-31G*	MP2/6-31G*//6-31G*
Compound 36		
0	-231.29529 (0.0)	-231.97436 (0.0)
80	-231.29237 (1.83)	-231.97149 (1.80)
120	-231.29310 (1.38)	-231.97245 (1.20)
180	-231.29235 (1.85)	-231.97113 (2.03)
Compound 37		
0	-270.352676 (0.22)	-271.162869 (0.16)
30	-270.35302 (0.00)	-271.16313 (0.00)
120	-270.34404 (5.64)	-271.15369 (5.92)
180	-270.34784 (3.25)	-271.15792 (3.27)

<sup>a</sup>Geometries were fully optimized at the conformational minima for 36 and 37. The geometries were fully optimized at the other conformations of 36 except for the  $\phi_{abcd}$  angle.

Table VIII. Ab Initio Energies of Compounds 38 and 39 as a Function of  $\phi_{abcd}$ <sup>a</sup>



38

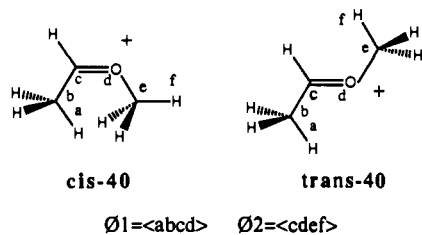
cis-39

trans-39

 $\phi = \langle abcd \rangle$ 

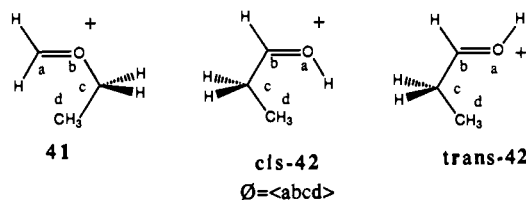
$\phi$ , deg	energy, au (kcal/mol)		
	3-21G//3-21G	6-31G*//6-31G*	MP2/6-31G*//MP2/6-31G*
Compound 38			
0	-152.35091 (0.0)	-153.20403 (0.0)	-153.63272 (0.0)
60	-152.34940 (0.95)	-153.20274 (0.80)	-153.63099 (1.09)
Compound cis-39			
0		-153.22540 (0.0)	-153.65621 (0.0)
60		-153.22371 (1.06)	-153.65413 (1.30)
Compound trans-39			
0		-153.22611 (0.0)	-153.65691 (0.0)
60		-153.22464 (0.92)	-153.65501 (1.20)

<sup>a</sup>See footnote for Table VII.

**Table IX.** Ab Initio Energies of Compounds *trans*- and *cis*-40 as a Function of  $\phi_{abcd}$  and  $\phi_{cdef}$ 

		energy, hartrees (kcal/mol)	
$\phi_1$ , deg	$\phi_2$ , deg	6-31G*//6-31G*	MP2/6-31G*//6-31G*
<i>trans</i> -40			
0	0	-192.269 20 (0.0)	-192.814 45 (0.00)
0	60	-192.268 12 (0.68)	-192.812 969 (0.93)
60	0	-192.267 66 (0.96)	-192.812 591 6 (1.16)
<i>cis</i> -40			
0	60	-192.265 25 (0.0)	-192.810 665 (0.00)
60	0	-192.264 01 (0.77)	-192.809 578 (0.68)
0	0	-192.263 92 (0.83)	-192.809 453 (0.76)

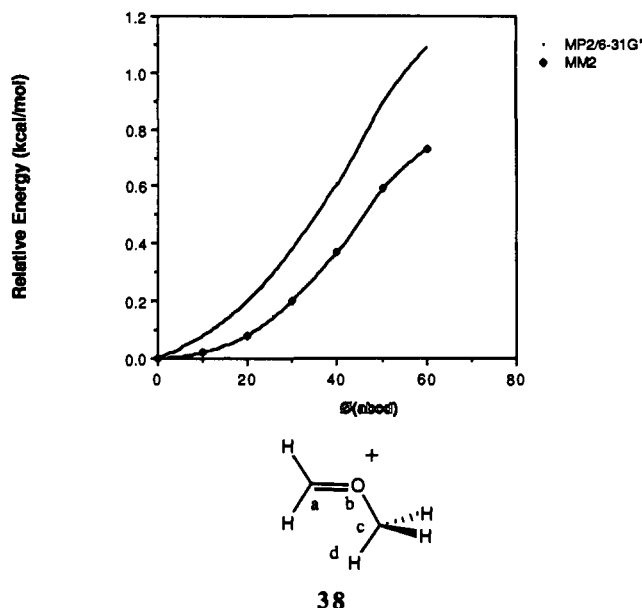
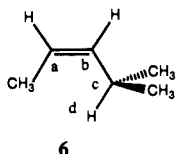
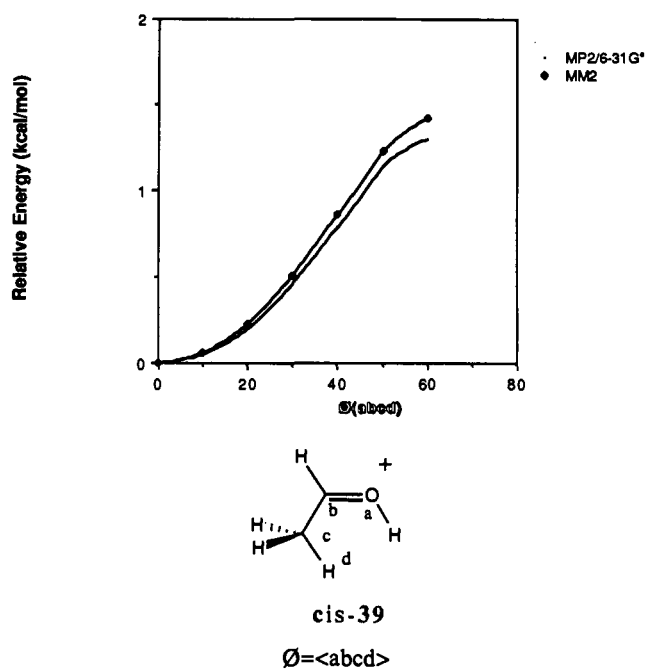
<sup>a</sup>Geometries were fully optimized at the conformational minima and were fully optimized at the other configurations except for the  $\phi_{abcd}$  and  $\phi_{cdef}$  angles.

**Table X.** Ab Initio Energies of Compounds 41 and *trans*- and *cis*-42 as a Function of  $\phi_{abcd}$ 

		energy, au (kcal/mol)	
$\phi$ , deg		6-31G*//6-31G*	MP2/6-31G*//6-31G*
Compound 41			
0		-192.248 43 (1.20)	-192.794 82 (0.81)
45		-192.247 67 (1.68)	-192.793 52 (1.62)
120		-192.250 34 (0.0)	-192.796 11 (0.0)
180		-192.249 18 (0.73)	-192.794 42 (1.06)
<i>trans</i> -42			
0		-192.265 79 (0.0)	-192.813 17 (0.0)
60		-192.263 27 (1.58)	-192.810 11 (1.92)
120		-192.265 08 (0.45)	-192.812 11 (0.66)
180		-192.263 54 (1.41)	-192.809 69 (2.18)
<i>cis</i> -42			
0		-192.266 11 (0.0)	-192.813 93 (0.0)
60		-192.262 36 (2.35)	-192.809 27 (2.92)
120		-192.264 80 (0.83)	-192.811 80 (1.34)
180		-192.263 13 (2.35)	-192.809 35 (2.87)

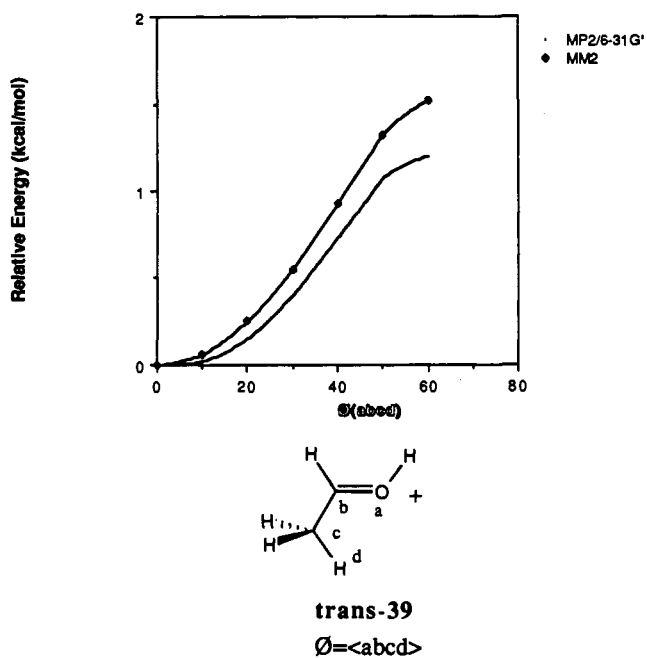
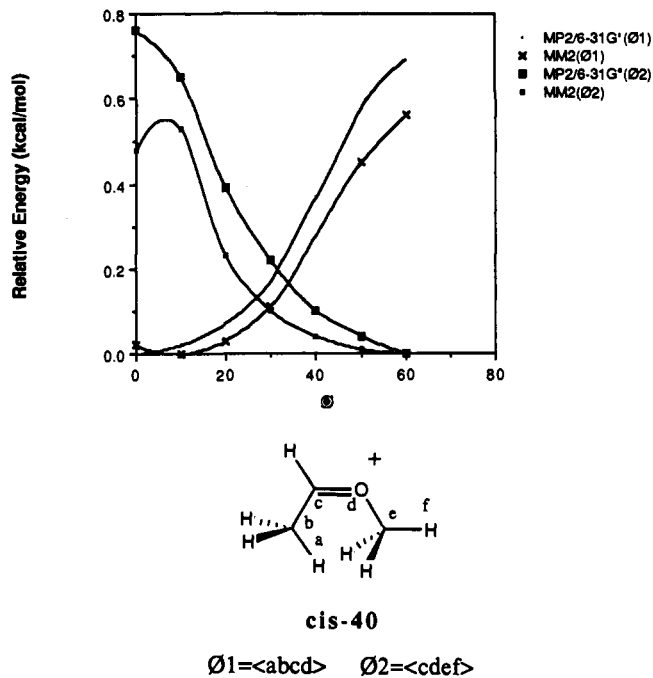
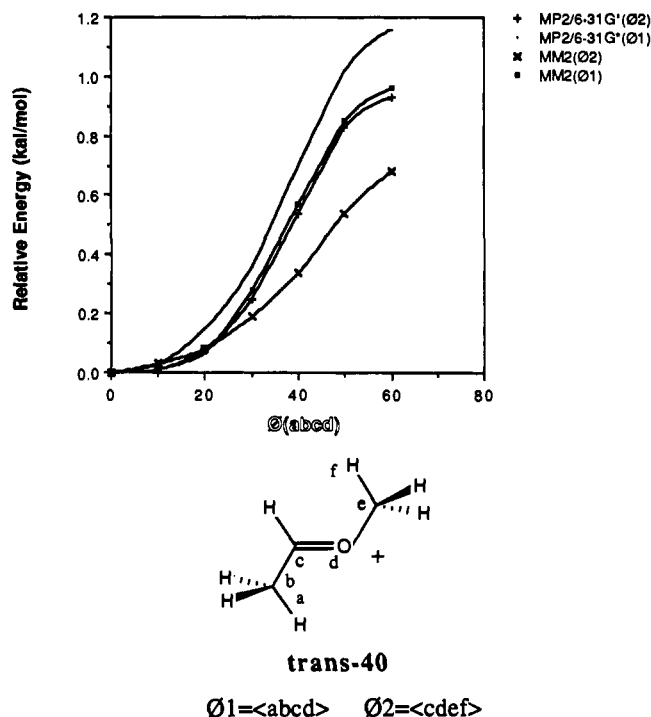
<sup>a</sup>Geometries were fully optimized at the conformational minima and were fully optimized at the other configurations except for the  $\phi_{abcd}$  angle.

groups which destabilizes this configuration. This preference for a double-gauche conformation over an eclipsed conformation for 6 was first predicted by Karabatsos and Fenoglio in their review on rotational isomerism about carbon-carbon single bonds.<sup>32</sup>

**Figure 6.** MM2 and ab initio torsional energies for 38.**Figure 7.** MM2 and ab initio torsional energies for *cis*-39.

The ab initio calculations on 5 and 6 are consistent with experimental data on the selectivity of stereofacial attack of nucleophiles and electrophiles on the double bond of the alkene. Alkene 6 models olefins like 2 ( $R_1 = \text{Me}$ ) with *cis*-methyl groups. The calculations on 6 show that 2 ( $R_1 = \text{Me}$ ) should have a 3–4 kcal/mol preference for conformer 2b over 2a or 2c, so that only 2b is significantly populated. This “conformational lock” in the ground state of the alkenes should allow the substituents  $R_2$  and  $R_3$  to differentiate the diastereotopic faces of the double bond in the transition states of the reactions of the alkenes with nucleophiles or electrophiles. This results in high asymmetric induction in addition reactions at the double bond for compounds like 2.<sup>10</sup> We do not mean to imply by conformational lock that the barrier for internal rotation is necessarily large compared to the energy barrier of the reaction. On the contrary, since the barriers to rotation about the allylic bonds in 5 and 6 are 2.5 and 4.7

(32) Karabatsos, G. J.; Fenoglio, D. J. *Topics in Stereochemistry* 1970, 5, 167.

Figure 8. MM2 and ab initio torsional energies for *trans*-39.Figure 10. MM2 and ab initio torsional energies for *cis*-40.Figure 9. MM2 and ab initio torsional energies for *trans*-40.

kcal/mol, respectively, most addition reactions will have an energy barrier larger than this. Thus, according to the Curtin-Hammett principle, the relative energies of the transition states of these reactions will control the stereoselectivities. Nevertheless, the factors which influence the reactant conformational energies of alkenes (e.g., 1,3-strain) will also influence the transition state conformational energies so that differences in energies of the conformers of the reactants should model the differences in the corresponding configurations of the transition states.<sup>33</sup> When we describe the conformational lock we imply that the 3–4-

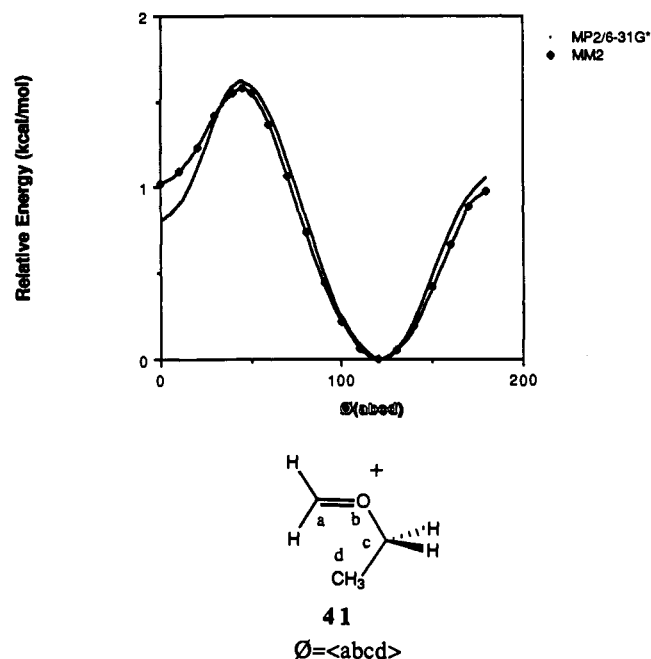


Figure 11. MM2 and ab initio torsional energies for 41.

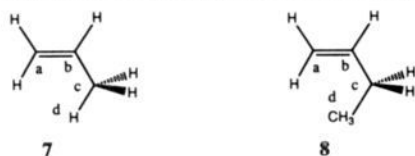
kcal/mol preference for **2b** over **2a** and **2c** will translate into approximately a 3–4 kcal/mol-preference for the corresponding transition state of **2b**, so that only one stereoisomer will be observed in the product of the reaction.

Calculations on alkene **5** show that compounds like **2** ( $R_1 = H$ ) will have approximately a 0.7-kcal/mol preference for conformer **2b** over **2a** or **2c**. According to this hypothesis, this should translate into only a small preference for the transition state of **2b** over the transition states of **2a** or **2c** and hence a considerable loss of asymmetric induction of **2** ( $R_1 = H$ ) compared to **2** ( $R_1 = Me$ ). This should result in a loss of the ability of  $R_2$  and  $R_3$  to differentiate the faces of the double bond. Experimental data bear this out, since generally poor asymmetric induction in addition reactions to **2** ( $R_1 = H$ ) is observed.<sup>10</sup>

Since the ab initio calculations on **5** and **6** only model the equilibria of chiral compounds **2**, it was desirable to calculate the potential surfaces of **2** directly. Calculations at the ab initio level

(33) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108. For examples where the most stable ground-state and transition-state conformers are different from each other for alkenes of this type, see: ref 9.

on **2** were not feasible, so MM2 force field calculations were employed. To determine the reliability of the force field, the potential surfaces of isopropylethylene (**5**), 4-methyl-*cis*-2-pentene (**6**), propene (**7**), and 1-butene (**8**) were calculated as a function

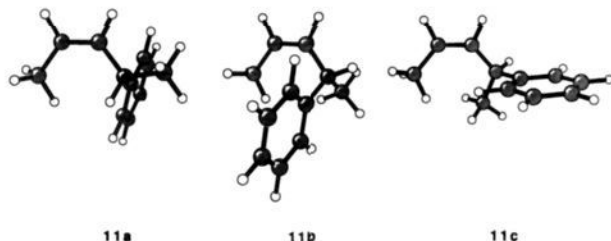


of  $\phi_{abcd}$  by MM2 and compared to ab initio or experimental data. The results (Figures 1–4) show at least qualitative agreement between the ab initio or experimental data and the MM2 calculations for the minima of **6–8**, but the rotational barrier for **8** as calculated by MM2 differs significantly from the ab initio results. Furthermore, the MP2/6-31G\*//6-31G\* level calculations and the MM2 calculations on **5** are in serious disagreement. Not only do the MM2 calculations give poor energy barriers, but the force field misses the  $\pm 120^\circ$  minima predicted by the ab initio calculations.

To correct for this inadequacy, the MM2 force field was modified so that the potential surface of 1-butene matched the MP3/6-31G\*//3-21G potential surface calculated by Wiberg.<sup>31a</sup> This is shown in Figure 1. There are experimental data on 1-butene as well.<sup>34–36</sup> The C=C–C–H and C=C–C–C torsional parameters were changed from ( $V_1 = 0.0$ ,  $V_2 = 0.0$ ,  $V_3 = -0.24$ ) and ( $V_1 = -0.44$ ,  $V_2 = 0.24$ ,  $V_3 = 0.06$ ), respectively, to ( $V_1 = 0.0$ ,  $V_2 = 0.0$ ,  $V_3 = -0.30$ ) and ( $V_1 = -0.54$ ,  $V_2 = 0.44$ ,  $V_3 = -0.60$ ), respectively. This new MM2 force field, hereafter referred to as MM2', was tested by recalculating the potential surfaces of **5–7** as a function  $\phi_{abcd}$  by using the new parameters. As is shown in Figures 2–4, the MM2' calculations are in good agreement with the ab initio results at all points on the potential surfaces, even for compound **5**.

The rotational surfaces of **9–20** were calculated as a function of  $\phi_{abcd}$ , with the MM2' force field. The minima and their relative energies are summarized in Table II. Compounds **9–12** are derivatives of compound **2** ( $R_1 = \text{Me}$ ) where  $R_2$  and  $R_3$  are combinations of Me, *i*-Pr, Ph, and *t*-Bu groups. The conformational energies of **9–12** are similar to those of compound **6**. The double-skew conformer ( $\phi \sim 0^\circ$ ) is the global minimum in each case, and other conformers are at least 1.5 kcal/mol higher in energy. Thus high asymmetric induction, due to differentiation of the faces of the double bond by  $R_2$  and  $R_3$ , is possible.

Interestingly, MM2' calculations on **11** with  $R_2 = \text{Me}$  and  $R_3 = \text{Ph}$  showed only a 1.5-kcal/mol preference for the double-skew conformer, **11a**, over the double-gauche conformer, **11b**. For



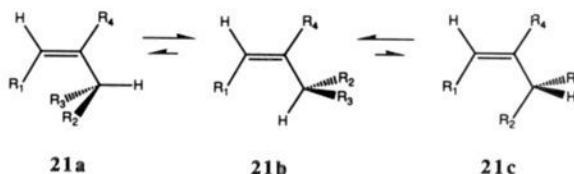
comparison, compound **6** shows a preference greater than 2.5 kcal/mol. In conformer **11b** the plane of the phenyl ring is orthogonal to the *cis*-methyl group. In this conformation the phenyl ring is less sterically demanding than the methyl group. Thus the phenyl group is less effective than a methyl group toward providing a conformational lock. This is in accord with NMR

spectroscopy studies on 1-methyl-1-phenylcyclohexane which showed that the methyl group prefers the equatorial position by 0.3 kcal/mol.<sup>37</sup> Compound **11** should then be less effective toward inducing asymmetric induction in addition reactions than **9**, **10**, or **12**.

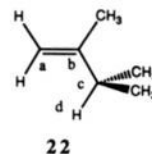
Compounds **13–15** are derivatives of **2** ( $R_1 = \text{H}$ ), where  $R_2$  and  $R_3$  equal Me, Ph, *i*-Pr, and *t*-Bu groups. MM2' calculations were performed on these compounds to determine if bulky substituents at  $R_2$  and/or  $R_3$  could effectively lock the conformation of **2** ( $R_1 = \text{H}$ ) into the double-skew ( $\phi = 0^\circ$ ) conformer. The results show that  $R_2$  and  $R_3$  both need to be equal to or larger than an isopropyl group (compounds **16–18**) to have greater than a 1.5-kcal/mol preference for the double-skew conformation. When either of the  $R_2$  or  $R_3$  groups is smaller than the isopropyl group (compounds **13–15**), then the conformational equilibria are similar to that of model compound **5**, where the double-skew and skew-eclipsed conformers are relatively close in energy.

To model 1,3-strain in the reaction of ester enolates, the potential surfaces of compounds **19** and **20** were calculated by MM2' as a function of  $\phi_{abcd}$ . The calculations show that although the OMe substituent at  $R_1$  is a better conformational lock than a hydrogen (e.g., compound **5**), it is not as effective as a methyl group. In **19** and **20**, 90% would exist as the double-skew conformer ( $\phi = 0^\circ$ ) at  $25^\circ$ , while in **9**, **10**, and **12** >99% would exist in the double-skew conformation. These results are in accord with the stereoselectivity observed in the alkylation and protonation of ester enolates in which the additions to the enolate have been shown to take place with 90–99% diastereoselectivity.<sup>10</sup>

1,2-Allylic strain, defined as the geminal interaction between the chiral moiety and the methyl group in compound **21**, may also



play an important role in influencing the conformational equilibria of alkenes. The steric interaction between  $R_2$  or  $R_3$  and the methyl group of **21** should destabilize conformers **b** relative to conformers **a** or **c**. To quantitate the energetics of this interaction, 3-21G ab initio calculations were performed on 2,3-dimethyl-1-butene, **22**. The results are listed in Table III and shown in Figure 5. Two



minima were found at the 3-21G level: the double-skew and the eclipsed-skew. MP2/6-31G\* single point calculations at these minima showed the double-skew ( $\phi = 0^\circ$ ) conformers is 0.6 kcal/mol lower in energy than the eclipsed ( $\phi = 142^\circ$ ) conformation. The barriers to rotation between the conformers were calculated to be 3.7 ( $\phi = 160^\circ$ ) and 1.3 ( $\phi = 180^\circ$ ) kcal/mol (see Figure 5). The eclipsed-skew conformation ( $\phi = 142^\circ$ ) is rotated considerably from the angle of  $\phi$  in the eclipsed-skew conformer of **5** ( $\phi = 122^\circ$ ). The interaction between the geminal-methyl group and the isopropyl group (1,2-strain) for the two conformers of **22** is very small compared to the interaction between the *cis*-methyl group and the isopropyl group (1,3-strain) in the conformers of **6**. This shows that 1,3-allylic strain is a much larger factor in determining the conformations of alkenes than 1,2-strain, as has been suggested by Johnson.<sup>1</sup>

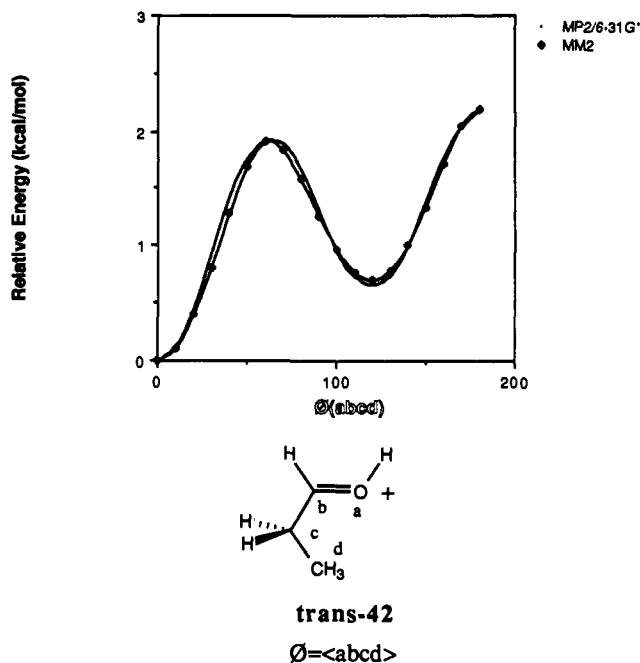
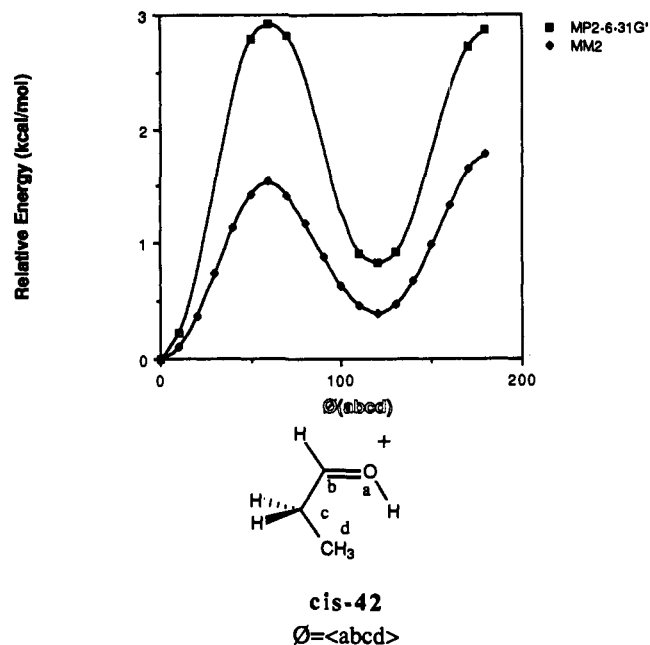
MM2 and MM2' calculations were carried out on **22** to test the accuracy of the two force fields in calculating 1,2-allylic strain. As shown in Figure 5, the potential surface of **22** as a function

(34) Kondo, S.; Hirota, E.; Morino, Y. *J. Mol. Spectrosc.* **1968**, *28*, 471. Harmony, M. D.; Laurie, V. W.; Kuchowski, R. L.; Schwendeman, R. H.; Ramsey, D. A.; Lovas, F. J.; Lafferty, W. J.; Maki, A. G. *J. Phys. Chem. Ref. Data* **1979**, *8*, 619.

(35) Durig, J. R.; Compton, D. A. C. *J. Phys. Chem.* **1980**, *84*, 773.

(36) Experimental results in refs 34 and 35 are different, so that the new MM2 parameters were deduced by fitting to the MP3/6-31G\*//3-21G level ab initio calculations.

(37) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959. DeBeule, H.; Tavernier, D.; Anteunis, M. *Tetrahedron* **1974**, *30*, 3573.

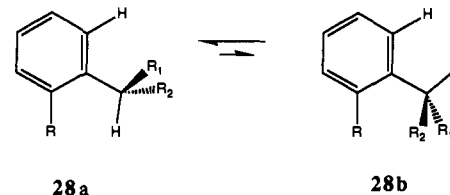
Figure 12. MM2 and ab initio torsional energies for *trans*-42.Figure 13. MM2 and ab initio torsional energies for *cis*-42.

of  $\phi_{abcd}$  as calculated by MM2' is in good agreement with the 3-21G ab initio calculations, while the MM2 potential surface is clearly in error. The MM2' force field was used to calculate the potential surfaces of chiral alkenes like **21**. The results of the MM2' calculations are shown in Table II (compounds **23**–**27**). The compounds with a methyl group at  $R_1$  (**23**–**25**) still have a large preference ( $>2.3$  kcal/mol) for the double-skew ( $\phi = 0^\circ$ ) conformer over the double-gauche ( $\phi = 180^\circ$ ) conformers, while compounds with a hydrogen at  $R_1$  (**26** and **27**) still show little difference in energy between double-skew and eclipsed ( $\phi = 120^\circ$ ) conformers. Thus the MM2' calculations also suggest that the 1,2-strain is small relative to the 1,3-allylic strain.

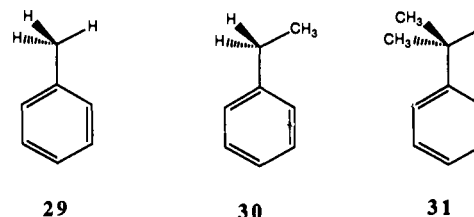
During the course this research, MM3, Allinger's new force field for hydrocarbons, was published.<sup>38</sup> We carried out calcu-

lations on compounds **5**, **6**, **7**, **8**, and **22**, and the MM3 results are included in the figures already presented for these molecules. MM3 is a considerable improvement over MM2 and gives results more like MM2'. However, there still are considerable quantitative differences between MM2' and MM3.

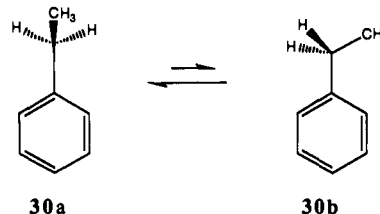
**Aromatics.** 1,3-Benzylic strain may also play an important role in the conformational equilibria of aromatic compounds. Steric interactions between  $R$ ,  $R_1$ , and  $R_2$  in **28b** should force the equilibrium toward conformer **28a**. If these interactions are large



enough, the configuration will be "locked" into conformer **28a**. This conformational lock would then allow  $R_1$  and  $R_2$  to differentiate the diastereotopic faces of the aromatic ring. In order to test the accuracy of the MM2 force field for these systems, the barriers for rotation about the  $C_{\text{aryl}}-C_{\text{alkyl}}$  bond for compounds **29**–**31** were calculated and compared to experimental data.



The MM2 rotational barrier for **29** was calculated to be 0.0 kcal/mol. This is consistent with experimental data which show the energy to be essentially rotationally invariant with respect to this C–C bond.<sup>39</sup> The calculated barrier for rotation about the  $C_{\text{aryl}}-C_{\text{alkyl}}$  bond in ethyl benzene is 1.0 kcal/mol, consistent with the experimental barrier<sup>40</sup> of 1.2 kcal/mol. The energy minimum and maximum for this rotation are shown in configurations **30a** and **30b**, respectively. The energies of these same extrema have also been calculated by using ab initio calculations at the 6-31G\*//6-31G\* level;<sup>41</sup> conformer **30a** was predicted to be 1.4 kcal/mol more stable than **30b**.



The experimental barrier for rotation of the  $C_{\text{aryl}}-C_{\text{alkyl}}$  in isopropylbenzene is controversial. This barrier for 3,5-(di-bromoisopropyl)benzene has been determined to be 2.0 kcal/mol by nuclear magnetic resonance spectroscopy,<sup>42a</sup> while microwave spectroscopy indicated that the barrier in isopropylbenzene is only 0.2 kcal/mol.<sup>42b</sup> Seeman et al. observed by laser jet spectroscopy that the lowest energy conformation of **31** is the eclipsed conformer **31a**.<sup>43</sup> The MM2 calculations on isopropylbenzene showed a

(39) Kreiner, W. A.; Rudolph, H. D.; Tan, B. T. *J. Mol. Spectrosc.* **1973**, *48*, 86. Pang, F.; Boggs, J. E.; Pulay, P.; Fogaraski, G. *J. Mol. Struct.* **1980**, *66*, 281.

(40) Parr, W. J. E.; Schaefer, T. *Acc. Chem. Res.* **1980**, *13*, 400. Miller, A.; Scott, D. W. *J. Chem. Phys.* **1978**, *68*, 1317.

(41) Schaefer, T.; Penner, G. H.; Sebastian, R. *Can. J. Chem.* **1987**, *65*, 873.

(42) (a) Schaefer, T.; Parr, W. J. E.; Danchura, W. *J. Magn. Reson.* **1977**, *25*, 167. (b) True, N. S.; Farag, M. S.; Bohn, R. K.; MacGregor, M. A.; Radhakrishnan, J. *J. Phys. Chem.* **1983**, *87*, 4622.

(43) Seeman, J. I.; Secor, H. V.; Breen, P. J.; Grassian, V. H.; Bernstein, E. R. *J. Am. Chem. Soc.* **1989**, *111*, 3140.

(38) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551. Allinger, N. L.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8566. Allinger, N. L.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8576.



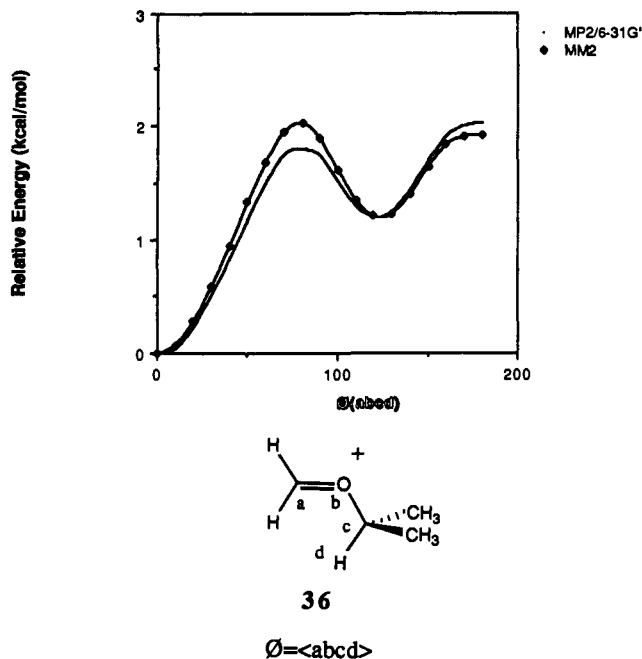


Figure 14. MM2 and ab initio torsional energies for 36.

barrier of 2.5 kcal/mol with the energy minima and energy maxima corresponding to **31a** and **31b**, respectively. MP2/6-

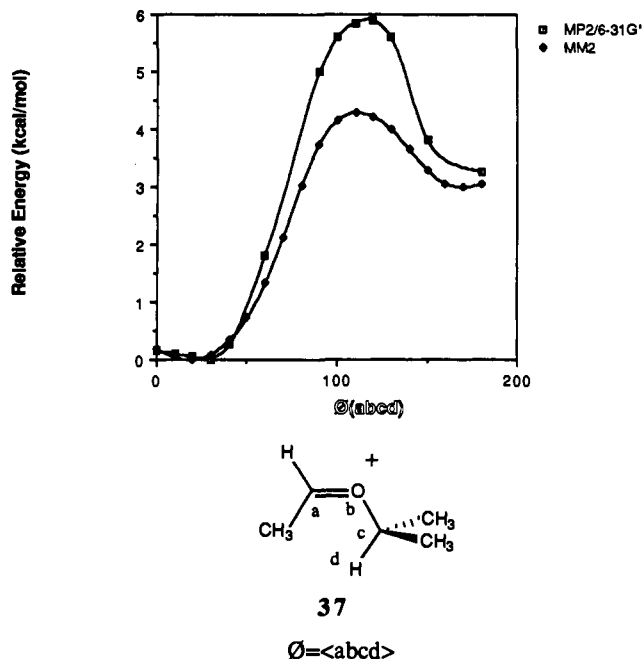
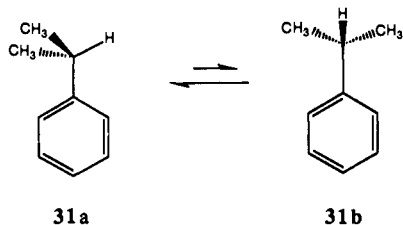
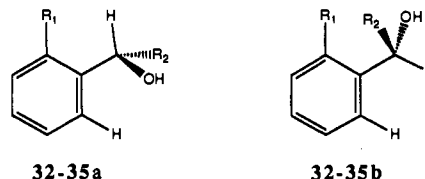


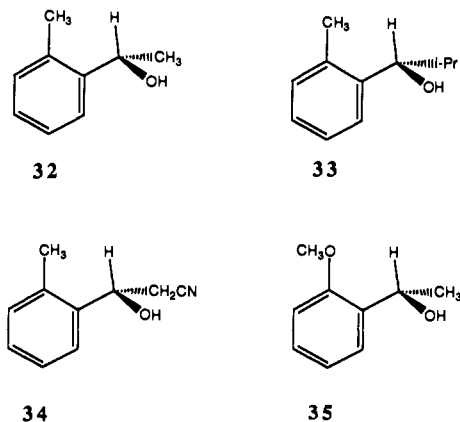
Figure 15. MM2 and ab initio torsional energies for 37.

provide only a modest conformational lock, since conformer **a** is favored over **b** by 1.0–1.5 kcal/mol. Thus only modest stereoselectivity should be obtained upon electrophilic or nucleophilic



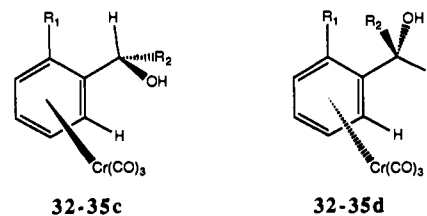
31G\* ab initio calculations on configurations **31a** and **31b** with 3-21G geometries showed a 2.9 kcal/mol stabilization of **31a** over **31b** (Table IV). Thus the calculational methods support the larger experimental barrier of 2.0 kcal/mol determined by NMR spectroscopy. The microwave spectroscopy study may be measuring a rapid intramolecular vibrational redistribution, which is known to occur at energies as low as 0.25 kcal/mol.<sup>44</sup>

Since the MM2 force field gives reasonable rotational barriers for aromatic systems, calculations were performed on the chiral compounds **32–35** shown below. All rotational isomers were



considered. Two minima were found for these compounds, conformers **a** and **b**, shown below. Their relative energies are listed in Table V. The MM2 calculations predict that **32–34** would

attack. The calculations also predict that almost no stereoselectivity would be obtained with compound **35**, since only a 0.3 kcal/mol difference in energy was calculated between **35a** and **35b**. Brocard and co-workers<sup>45</sup> have determined the stereoselectivity of the reactions of **32–35** with  $\text{Cr}(\text{CO})_6$  to form the  $\text{Cr}(\text{CO})_3$  complex. The authors suggest that the hydroxy group in **32–35** directs the attack of the  $\text{Cr}(\text{CO})_6$ , such that the reactions of **a** and **b** with  $\text{Cr}(\text{CO})_6$  would lead to complexes **c** and **d**. Thus

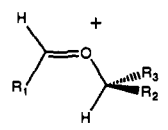


the ratio of **c:d** can be used to gauge the accuracy of the stereoselectivity predicted by the MM2 calculations. Table VI lists the ratio of adducts obtained from the reactions of **32–35** with  $\text{Cr}(\text{CO})_6$ . The observed stereoselectivity compares fairly well to the ratio of isomers predicted by the MM2. This demonstrates that the MM2 force field can be used to calculate 1,3-benzylic strain in aromatic compounds and to predict stereoselectivity for the reactions of these systems with nucleophiles or electrophiles.

**Oxonium Ions.** The geometry of compound **36** was optimized for various fixed values of the  $\phi_{abcd}$  torsional angle at the 6-31G\* level. The geometries were fully optimized at the energy minima. The results (Table VII) show that the 6-31G\* level predicts the double-skew ( $\phi = 0^\circ$ ) and the skew-eclipsed ( $\phi = 120^\circ$ ) conformations to be minima and the trans-gauche ( $\phi = 80^\circ$ ) and

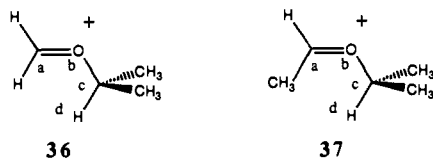
(44) True, N. S. *Chem. Phys. Lett.* **1983**, *101*, 326.

(45) Brocard, J.; Pelinski, L.; Lebibi, J.; Mahmoudi, M.; Maciejewski, L. *Tetrahedron* **1989**, *45*, 709.

**Table XI.** Conformational Minima of Oxonium ions **43** and **44** as Calculated by MM2


compd	R1	R2	R3	conformer $\phi$ , deg	relative energy, kcal/mol
<b>43</b>	H	Me	Ph	-40	0.0
				180	1.1
				120	1.0
<b>44</b>	Me	Me	iPr	-10	0.0
				165	3.0

double-gauche ( $\phi = 180^\circ$ ) configurations to be the energy maxima on this potential surface. MP2/6-31G\*\*//6-31G\* single point calculations indicated the double-skew conformer is 1.2 kcal/mol more stable than the skew-eclipsed conformer with energy barriers of 1.8 ( $\phi = 80^\circ$ ) and 2.0 ( $\phi = 180^\circ$ ) kcal/mol for rotation between the conformers. The calculated 1.2-kcal/mol difference between the conformers is almost twice that of alkene analogue **5** (0.7 kcal/mol).

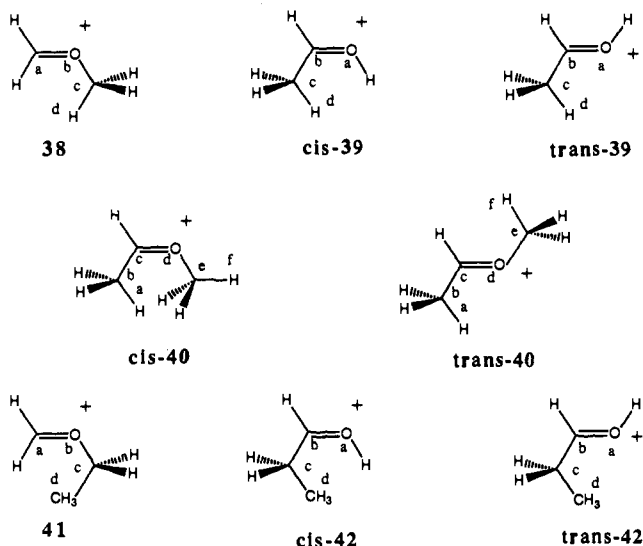


This large difference in energy between conformers in **36** relative to **5** can be ascribed to increased steric interaction between the isopropyl group and the cis hydrogen. The shorter C=O double bond (1.21 Å) relative to the C=C bond (1.32 Å) causes the isopropyl hydrogens to be 0.1–0.2 Å closer to the cis hydrogen than these are in compound **5**. As a consequence, the skew-eclipsed conformer in **36** is much less than the skew-eclipsed conformer of **5**. This is manifested in a 0.01-Å increase in the bc bond length and a 3.5° increase in the abc angle in **36**, going from the double-skew conformer to the skew-eclipsed conformer. In contrast, the bc bond length and abc angle in **5** are increased by only 0.005 Å and 1.8°, respectively, going from the double-skew to the skew-eclipsed conformers. It should be noted that the barriers for rotation at 80° and 180° for **36** (1.8 and 2.0 kcal/mol, respectively) are lower than the barriers at 70° and 180° for **5** (2.6 and 2.5 kcal/mol, respectively). This is due to less 1,2-strain in the conformational maxima for **36** than in **5**. The lone pair on the oxygen atom in **36** is less sterically demanding than the hydrogen atom at carbon b in **5**. As a result, the conformations at 80 and 180° in **36** in which a methyl substituent and H<sub>d</sub> from the isopropyl group nearly eclipse this lone pair are less destabilized than the 70 and 180° conformations in **5** in which the methyl and H<sub>d</sub> eclipse the hydrogen atom at carbon b. The 1.2-kcal/mol energy difference between the conformers in **36** is consistent with experimental data on the selectivity of stereofacial attack of nucleophiles on the double bond on the chiral oxonium salts.<sup>10</sup> Calculations on **36** model the equilibria of molecules such as **4** (R<sub>1</sub> = H) with a chiral moiety cis to a hydrogen atom. In such molecules, **4b** should be at least 1.2 kcal/mol more stable than **4a** or **4c**. This significant preference for conformer **4b** allows for modest-to-good asymmetric induction when nucleophiles are added to oxonium ion **4** (R<sub>1</sub> = H).

Optimization of the geometry of compound **37** as a function of  $\phi_{abcd}$  was carried out at the 6-31G\* level. The geometries of the energy minima were fully optimized. For other values of  $\phi$ , only the dihedral angles of the methyl hydrogens were optimized. The results are given in Table VII. The double-skew ( $\phi = 30^\circ$ ) and the double-gauche ( $\phi = 180^\circ$ ) conformations are the global and local minima, respectively. The eclipsed-skew ( $\phi = 120^\circ$ ) conformation is the energy maximum for rotation between the conformers. MP2/6-31G\*\*//6-31G\* single point calculations on the energy extrema showed a 3.3-kcal/mol stabilization of the

double-skew conformer over the double-gauche with an energy barrier for rotation between the conformers of 5.9 kcal/mol. The difference in energy in **37** between the double-skew ( $\phi = 0^\circ$ ) minimum and the skew-eclipsed ( $\phi = 120^\circ$ ) maximum (5.9 kcal/mol) is larger than the difference in energy between these conformations in **6** (4.9 kcal/mol). This is caused by an increase in 1,3-strain, due to the shortening of the bond length going from the C=C to C=O bond. The bc bond length and the abc bond angle are increased more for **37** than **6** by 0.011 Å and 6°, respectively, going from the double-skew to the skew-eclipsed configurations. The energy difference between the two minima in **37** is slightly lower than the difference in energy between these two minima in **6**. The minimum at  $\phi = 180^\circ$  in **6** is 3.4 kcal/mol higher in energy than the double-skew minimum, while the minimum at 180° in **37** is 3.3 kcal/mol higher in energy than the double-skew conformer. Once again, there is less 1,2-strain in the anti conformer (180°) of **37** than in **6** because of the decrease in steric demand with a lone pair compared to a hydrogen atom. The double-skew conformer in **37** is in a broad potential minimum compared to **6** as is shown in Figure 3 and later in Figure 15. The increased 1,3-strain between the hydrogen atom of the isopropyl group and the cis-methyl group in **37** is relieved somewhat by rotation of the  $\phi_{abcd}$  angle to 30° so that the well of this minimum ranges from -30 to 30°. The energy difference between the minima is consistent with experimental data on **4** (R = Me). Such compounds show excellent asymmetric induction upon attack of nucleophiles on the oxonium ion double bond. From the model studies on **37**, these derivatives should be essentially locked into the double-skew conformer, which would allow R<sub>2</sub> and R<sub>3</sub> to effectively differentiate the faces of the double bond in these oxonium ions.

A force field for oxonium ions was developed so that the equilibria of the chiral compounds could be calculated directly. The parameters for the oxonium ion functionality were developed by fitting to ab initio calculations on compounds **38–42**. The ab initio energies were obtained at the MP2/6-31G\*\*//6-31G\*\* level. The results are shown in Tables VIII–X. The force field pa-



rameters (KS, L[0]) for bonds adjacent to and including the C=O<sup>+</sup> bond were chosen so that these bond lengths for compounds **38** and **39**, as determined by the MM2 force field, were within 0.02 Å of the same bond lengths calculated with the MP2/6-31G\*\*//3-21G basis set. Similarly the bending parameters (KS,  $\phi[0]$ ) for angles involving the C=O<sup>+</sup> bond were chosen so that these angles in compounds **38** and **39**, as calculated by the force field, were within 2° of these same angles calculated at the MP2/6-31G\*\*//3-21G level. These parameters are listed in Table XXIII.

Table XXIII. Torsional, Stretching, Bending, and van der Waals Parameters

A. Alkenes													
Additional Torsional Parameters													
atom type				V1	V2	V3	atom type				V1	V2	V3
2	2	1	1	-0.54	0.44	-0.60	2	2	1	5	0.0	0.0	-0.30
B. Phenyl <sup>a</sup>													
Additional Torsional Parameters													
atom type				V1	V2	V3	atom type				V1	V2	V3
1	27	27	1	0.0	9.2	0.0 <sup>b</sup>	5	27	27	5	0.0	9.2	0.0 <sup>b</sup>
1	27	27	5	0.0	9.2	0.0 <sup>b</sup>	5	27	27	27	0.0	9.2	0.0 <sup>b</sup>
1	27	27	27	0.0	9.2	0.0 <sup>b</sup>	27	27	27	27	0.0	9.2	0.0 <sup>b</sup>
Additional Stretching Parameters <sup>b</sup>													
atom type				KS	L(0)	atom type				KS	L(0)		
27	27			8.0667	1.390	27	5			4.6	1.101		
27		1		4.4	1.497								
Additional Bending Parameters <sup>b</sup>													
atom type				KS	$\phi(0)$	atom type				KS	$\phi(0)$		
27	27	27		0.43	120.0	27	27	5		0.36	120.0		
27		27	1	0.45	120.0								
C. Oxonium Ions													
Additional Torsional Parameters													
atom type				V1	V2	V3	atom type				V1	V2	V3
5	29	30	21	0.0	6.57	0.0	30	29	1	5	0.0	0.0	-0.03
5	29	30	1	0.0	6.57	0.0	30	29	1	1	-1.04	0.64	-0.60
5	29	30	28	0.0	6.57	0.0	29	30	1	5	0.0	0.0	0.10
1	29	30	21	0.0	6.57	0.0	29	30	1	1	-0.15	0.30	-0.80
1	29	30	1	0.0	6.57	0.0	28	30	1	1	0.0	0.0	0.01
1	29	30	28	0.0	6.57	0.0	28	30	1	5	0.0	0.0	0.52
Additional Stretching Parameters													
atom type				KS	L(0)	atom type				KS	L(0)		
29	30			10.8	1.245	30	28			4.6	0.60		
30		1		5.36	1.487	30	21			4.6	0.999		
29		1		5.36	1.445								
Additional van der Waals Parameter													
atom type				E <sub>p</sub>				R					
28				0.016				1.20					
Additional Bending Parameters													
atom type				KS	$\phi(0)$	atom type				KS	$\phi(0)$		
5	29	30		0.37	119.5	1	30	28		0.35	122.2		
1	29	30		0.46	126.0	21	30	28		0.25	122.0		
29	30	1		0.55	117.5	5	29	5		0.32	125.0		
29	30	28		0.35	122.0	1	29	5		0.36	128.0		
29	30	21		0.36	111.2	1	29	1		0.45	128.0		

<sup>a</sup> Equivalency: atom type 27 set equal to atom type 2. <sup>b</sup> Beckhaus parameters.<sup>48</sup> <sup>c</sup> Equivalency: atom types 29 and 30 were set equal to type 2, and atom type 28 was set equal to type 20.

The torsional parameters for rotation about the C=O bond were optimized so that the barrier for rotation about this bond in **38** fits the 26.3 kcal/mol barrier calculated by Cremer<sup>46</sup> for **38** at the MP2/6-31G\* level. A small V<sub>1</sub> barrier was added for the C—C—O—C and the C—C—O—H torsional angles so that the global minima of the cis isomers, **39** and **40**, were 0.3 and 2.0 kcal/mol less stable than the trans isomers **39** and **40**, respectively, as was determined by the ab initio studies. The torsional parameters for the C—O—C—H and H—C—C—O dihedrals were chosen such that the MM2 calculations for rotation about the  $\phi_{abcd}$  torsional angle best fit the MP2/6-31G\* calculations for compounds **38–40**. A comparison of the MM2 and ab initio results for rotation about these dihedral angles is shown in Figures 6–10. The figures show that the potential surfaces about these dihedral angles as calculated by MM2 for compounds **38–40** are reasonable as compared to the ab initio results. The worst fit was

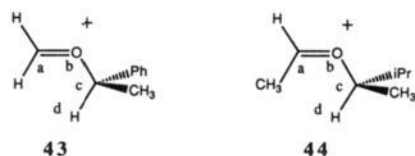
the potential surface for compounds **38** (Figure 6) and *trans*-**39** (Figure 8), where the C—O—C—H and O=C—C—H rotational barriers were calculated to be 0.7 and 1.5 kcal/mol, respectively, by MM2, while the ab initio calculations determined these barriers to be 1.1 and 1.2 kcal/mol, respectively.

The C—O—C—C and C—C—C=O torsional parameters were obtained by fitting the MM2 calculations on compounds **41** and *trans*-**42** to match the MP2/6-31G\* calculations. A comparison of the MM2 and ab initio results are shown in Figures 11 and 12. Ab initio calculations were also performed on *cis*-**42**, and a comparison of the MP2/6-31G\* and the MM2 calculations is shown in Figure 13. The MM2 calculations for *cis*-**42** predict potential maxima that are much lower in energy than those predicted by the MP2/6-31G\* calculations. Presumably there is an electronic or electrostatic phenomenon in *cis*-**42** that the MM2 force field calculations omit. Since the object of the force

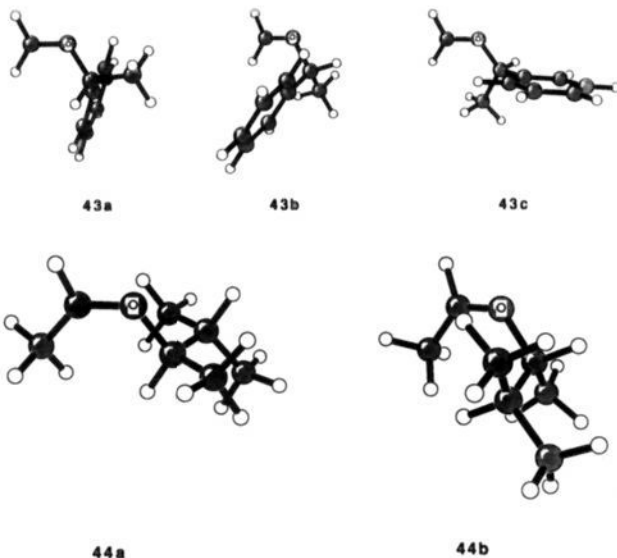
field was to model the configurations of oxonium ions, not protonated aldehydes, this shortcoming is deemed to be minor, but care should be taken if this force field is to be used for the conformational analysis of protonated aldehydes.

The ab initio calculations on **36** and **37** provided an opportunity to test this new force field. The MM2 and ab initio calculations on **36** and **37** are compared in Figures 14 and 15. Figure 14 shows that the MM2 results are in good agreement with the MP2/6-31G\* calculations for the conformational minima and for the barriers for rotation between the conformers for **36**. Likewise Figure 15 and Table VII show that the MM2 and the 6-31G\* or MP2/6-31G\* calculations are in good agreement at the conformational minima (i.e.,  $\phi = 30^\circ$  and  $\phi = 180^\circ$ ) for **37**. The barrier for rotation ( $\phi \sim 120^\circ$ ) between minima, however, is calculated to be 1.7 kcal/mol higher at the MP2/6-31G\* level than when using MM2. Both the MP2/6-31G\* and MM2 calculations showed that the double-skew conformer ( $\phi = 30^\circ$ ) resides in a broad potential well (see Figure 15).

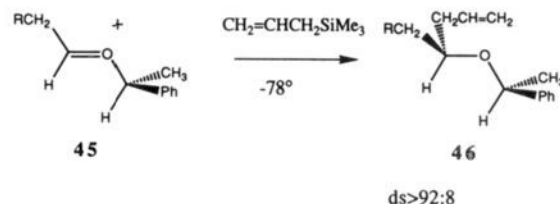
Since the MM2 force field for oxonium salts gives reasonable energies and geometries, the potential surfaces of chiral compounds **43** and **44** were calculated as a function of the  $\phi_{abcd}$  torsional angle using the new force field. The results are shown in Table XI.



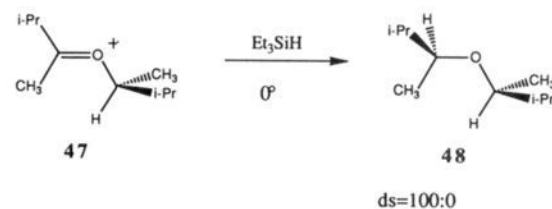
According to the MM2 calculations, **43** should principally exist as conformer **43a**, with  $\phi = -40^\circ$ , although conformers **43b** and **43c**, with  $\phi = 180^\circ$  and  $120^\circ$ , should be significantly populated since they are only about 1 kcal/mol higher in energy. Thus the MM2 calculations would predict that nucleophilic attack on the



double bond on the oxonium salt **43** could occur with at least respectable stereofacial selectivity. In fact it has been observed experimentally that **45** is converted to products with a 92/8 diastereomer ratio favoring **46**.<sup>16</sup> This 92/8 ratio translates into a 1.4 kcal/mol preference for attack on one face of the oxonium ion double bond.



The MM2 calculations on compound **44** predict that essentially one conformer should be significantly populated (**44a**,  $\phi = -10^\circ$ ), since the other conformational minimum (**44b**,  $\phi = 165^\circ$ ) is about 3 kcal/mol higher in energy. In fact **47** is converted to **48** with 100% stereofacial selectivity.<sup>47</sup>



## Conclusion

Ab initio calculations show that 1,3-strain plays an important role in the conformations of alkenes and oxonium ions. Compounds with a methyl group cis to the isopropyl group on the double bond (**6** and **33**) are effectively locked into a single conformation, while compounds in which a hydrogen is cis to the isopropyl group (**5** and **36**) show significant population of several conformers. New force fields developed for the alkenes and oxonium ions and the existing force field for aromatic compounds give reasonable conformational energetics and allow for the calculation of the equilibria of the conformers in large chiral derivatives. A comparison of these calculated equilibria with the stereoselectivity of the addition of electrophiles or nucleophiles to the double bond show that factors which control the equilibria (including 1,3-strain) in the ground state are related to factors influencing the relative activation energies for additions to these molecules. When steric interactions between the reagent and the alkene substituent are relatively small, attack occurs on the less-hindered side of the double bond, whereas large interactions between the reagent and the substituents may cause the reaction to occur in a geometry more closely resembling a high-energy conformer.<sup>9</sup>

**Acknowledgment.** We are grateful to the National Institutes of Health for financial support of this research and to Alfred Finocchio for performing the MM3 calculations.

**Supplementary Material Available:** Tables XII–XV of 3-21G geometries of the conformational minima of **5**, **6**, **22**, and **31a,b**, respectively, Tables XVI, XVII, and XX–XXII of 6-31G\* geometries of the conformational minima of **36**, **37**, *trans*- and *cis*-**40**, **41**, and *trans*- and *cis*-**42**, respectively, Table XVIII of the geometry of **38**, and Table XIX of MP2/6-31G\* geometries of *cis*- and *trans*-**39** (20 pages). Ordering information is given on any current masthead page.

(47) Sassaman, M. B.; Kotian, K. D.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **1987**, *52*, 4314.

(48) Beckhaus, H.-D. *Chem. Phys. Ber.* **1983**, *116*, 86.