J. Phys. Chem. A **2001,** *105,* 10123−10132

An ab Initio Theory and Density Functional Theory (DFT) Study of Conformers of Tetrahydro-2*H*-pyran

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Received: June 19, 2001

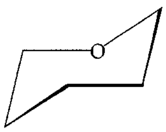
Ab initio theory with the 3-21G, 6-31G(d), 6-31G(d,p), 6-311G(d,p), 6-31+G(d), and 6-311+G(d,p) basis sets and density functional theory (SVWN, pBP, BLYP), including the hybrid density functional methods B3LYP, B3PW91, and B3P86, have been used to calculate the energies of the chair, half-chair, sofa, twist, and boat conformers of tetrahydro-2*H*-pyran (oxacyclohexane, oxane, pentamethylene oxide, tetrahydropyran, THP). The enthalpies ($\Delta H°$), entropies ($\Delta S°$), and free energies ($\Delta G°$) of the conformers were also determined. The energy difference (ΔE, kcal/mol) between the chair and the 2,5-twist conformer is 5.92 to 6.10 (HF), 5.78 to 6.10 (MP2), 6.71 to 6.82 (SVWN), 6.04 to 6.12 (pBP), and 5.84 to 5.95 (BLYP, B3LYP, B3PW91, B3P86). The energy difference (ΔE, kcal/mol) between the chair and the 1,4-boat conformer is 6.72 to 7.05 (HF), 6.76 to 7.16 (MP2), 6.97 to 7.20 (SVWN), 6.26 to 6.36 (pBP), and 6.23 to 6.46 (BLYP, B3LYP, B3PW91, B3P86). The transition state between the chair conformation and the 2,5-twist conformation is 11 kcal/mol higher in energy than the chair conformer.

Introduction

One of the most important recent development in computational chemistry is the rise in the use of density functional theory (DFT).[1−23] The introduction of gradient-corrected (nonlocal) functionals and hybrid approaches has quickly led to the development of new mathematical expressions for exchange and correlation terms, which are useful in calculating geometries, energies, vibrational frequencies, NMR chemical shifts, and other important molecular properties. It appears that new DFT methods may give equal to or greater accuracy and efficiency for medium-sized or larger molecular systems at lower computational costs than ab initio methods.[22,23]

The existence of naturally occurring heterocyclic compounds such as alkaloids and carbohydrates has motivated the conformational study of carbocycles and heterocycles.[24−28] Substituted tetrahydro-2*H*-pyrans (oxacyclohexane, oxane, pentamethylene oxide, tetrahydropyran, THP) have been investigated in only a few computational studies.[29−33] The goals of those studies included ring-substituent interactions and stereoelectronic effects (anomeric effect, hyperconjugative orbital interactions). On the other hand, the various conformers of the parent tetrahydro-2*H*-pyran have not been systematically studied computationally.[28−30]

Owing to need for additional comparison studies among modern ab initio theory and density functional theory and to an absence of detailed and systematic computational reports on the conformers of tetrahydro-2*H*-pyran, this study was undertaken in order to help elucidate the influences of replacing a methylene group in cyclohexane with an oxygen atom (to give tetrahydro-2*H*-pyran) by using ab initio theory with the 3-21G, 6-31G(d), 6-31G(d,p), 6-311G(d,p), 6-31+G(d), and 6-311+G(d,p) basis sets and density functional theory (SVWN, pBP, BLYP) including the hybrid density functional methods B3LYP, B3PW91, and B3P86. The conformers of tetrahydro-2*H*-pyran which have been studied include the chair (**1**), half chairs (**2a**, **2b**, **2c**), sofas (**3a**, **3b**, **3c**, **3d**), 2,5-twist (**4a**), 1,4-twist (**4b**), 1,4-boat (**5a**), and 2,5-boat (**5b**).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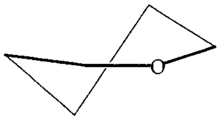
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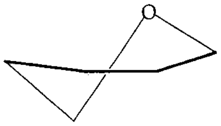
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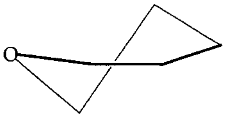
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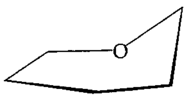
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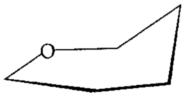
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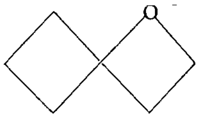
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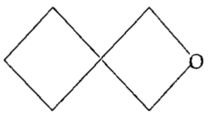
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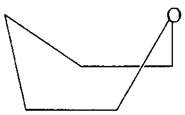
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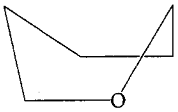
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10.1021/jp012342c CCC: $20.00

Computational Methods

Many different functionals have been proposed as suitable for use in density functional calculations on atoms and molecules. They are generally distinguished by the way that they treat the exchange and correlation components. The simplest models, i.e., SVWN, are called local spin density or local density models [Local Density Approximation, (LDA); Local Spin Density Approximation (LSDA)] and involve only the values of the electron spin densities.[5,6] Despite the simplicity of the fundamental assumptions, LSDA methods are often found to provide results with an accuracy similar to that obtained by HF methods.[23]

Gradient Corrected or Generalized Gradient Approximation (GGA) functionals (nonlocal methods) involve both the values of the electron spin densities and their gradients (B or B88,[7] LYP,[11] PW86,[14−16] PW91 or P91 or PW92,[18] B95[10]). The Becke[7] gradient corrected exchange functional (B or B88) is often combined with the gradient corrected correlation functional LYP.[11] The perturbative DFT model (pBP)[20,21] is based on the nonlocal corrections to the local density model proposed by Becke[7−9] and Perdew.[15,17] The SVWN and pBP models are combined with the DN* and DN** numerical basis sets. DN* is a representation in which the valence shell of all atoms is split into inner and outer parts, and polarization functions have been added to all atoms except hydrogen. DN** is identical to DN*, except that polarization functions are also placed on hydrogen atoms.[20,21]

There are several hybrid functionals, such as the Adiabatic Connection Model (ACM) and the Becke three parameter functional (B3), that define the exchange functional as a linear combination of Hartree−Fock, local, and gradient corrected exchange terms. This exchange functional is then combined with the local and/or gradient-corrected correlation functional. Examples of DFT hybrid functionals are B3LYP,[10−12] B3PW91,[10,11,14−16] and B3P86.[8,12,15]

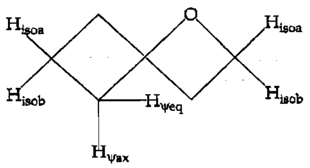
The calculations were carried out using the MacSpartan Pro,[34] the Spartan[34] and the Gaussian 94[35]and 98[36] computational programs. The HF/6-31G(d) geometry optimized structures were used as starting points for the other calculations and the MP2 single point energies were calculated on the respective HF geometry optimized structures. For consistency, the 6-31G(d) basis set was chosen for the BLYP, B3LYP, B3P86, and B3PW91 calculations. For brevity, the MP2/6-31G(d)//HF/6-31G(d) calculation will be shown as MP2//6-31G(d) and others will be handled analogously. Frequency calculations were computed on the HF/6-31G(d), BLYP, B3LYP, B3P86, and B3PW91 geometry optimized structures. Although some zero point energies (ZPE) were scaled [0.9135, HF/6-31G(d), 1.0119, BLYP, 0.9804, B3LYP] for thermochemical calculations,[22] the zero point energies for B3P86 and B3PW91 were not scaled. The frequencies were not scaled.

Finding one imaginary frequency (saddle point) does not guarantee that one has found a transition structure which is involved in the ring reversal mechanism. Although saddle points always connect two minima on the potential energy surface, these minima may not be the structures of interest. An intrinsic reaction coordinate (IRC) calculation examines the reaction path leading down from a transition structure on a potential energy surface. The calculation starts at the saddle point and follows the reaction in both directions from the transition state. Thus, the IRC calculation definitively connects two minima on the potential energy surface by a path which passes through the transition state between them.[22] In this study, IRC calculations in the forward and reverse directions were performed on the transition state optimized structures.

Torsional angles (τ) were constrained in the half-chair (**2a** C2−O1−C6−C5 = 0° and C2−C3−C4−C5 = 64.2°; **2b** C2−C3−C4−C5 = 0° and C2−O1−C5−C6 = 74.5°; **2c** O1−C2−C3−C4 = 0° and O1−C6−C5−C4 = 67.4°), sofa (**3a** C3−C2−O1−C6−C5 are coplanar; **3b** C2−C3−C4−C5−C6 are coplanar; **3c** O1−C2−C3−C4−C5 are coplanar; **3d** C2−O1−C6−C5−C4 are coplanar), and boat (**5a** O1−C2−C3−C4 and O1−C2−C3−C4 = 0°) (**5b** C2−C3−C4−C5 and C2−O1−C6−C5) structures for partial optimizations.

Accurate geometries generally refer to bond lengths that are within about 0.01 to 0.02 Å of experiment and bond and dihedral angles that are within 1° to 2° of the experimentally measured value.[22] It should also be noted that the calculational methods give some approximation to the equilibrium bond lengths (r_e), whereas the experimental values cited in the references from electron diffraction (r_g) and microwave (r_s) spectroscopic studies give vibrationally averaged values. These numbers are different physical quantities and have different numerical values. Thus, although the differences are usually small, r_e needs to be converted to r_g and to r_s in order to make more accurate comparisons.[37] The van der Waals radii of C = 1.70 Å, H = 1.20 Å, and O = 1.50 Å are used in the discussion.[38−47] Nonbonded distances less than the sum of the van der Waals radii of the atoms are considered to be repulsive steric interactions.

In contrast to the chair conformation of tetrahydro-2*H*-pyran (**1**), with only the axial and equatorial positions available for substituents, the twist conformation has three positions. These are the pseudoaxial (ψ_{ax}), pseudoequatorial (ψ_{eq}), and isoclinal (iso). By analogy with cyclohexane, there are two isoclinal positions (C2, C5) in the 2,5-twist structure **4a** and one (C4) in the 1,4-twist form **4b**. For clarity in the discussion, the isoclinal hydrogens have been designated H_{isoa} and H_{isob} (**4a′**, **4b′**).



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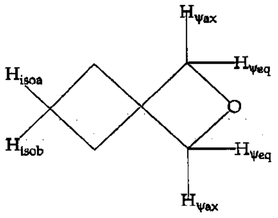

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Results and Discussion

HF/6-31G(d) frequency calculations showed that the chair (**1**), 2,5-twist (**4a**), and 1,4-twist (**4b**) structures of tetrahydro-2*H*-pyran have real vibrational frequencies and that each of the half chair (**2a** −254.6 cm^{-1}, **2b** −230.8 cm^{-1}, **2c** −226.2 cm^{-1}), the sofa (**3a** −258.6 cm^{-1}, **3b** −239.2 cm^{-1}, **3c** −246.2 cm^{-1}, **3d** −265.3 cm^{-1}), the 1,4-boat (**5a** −101.0 cm^{-1}), and the 2,5-boat (**5b** −104.5 cm^{-1}) conformers has one imaginary vibrational frequency. The hypothetical planar structure (HF/6-31G(d) $E = -269.977\,177$ H) has three imaginary vibrational frequencies (−377.29, −277.98, −259.10 cm^{-1}).

The calculated geometrical parameters, including repulsive nonbonded interactions, for the most stable conformers of tetrahydro-2*H*-pyran (**1**, **4a**, **5a**) are shown in Tables 1−12 and in the Supporting Material (**4b**).

TABLE 1: Torsional Angles (*τ*, °) in the Chair Conformer (1) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP
$\mathrm{H_{ax}}$−C2−C3−$\mathrm{H_{ax}}$	175.4	173.0	172.6	175.3	175.7	174.0	173.3	173.4
$\mathrm{H_{eq}}$−C2−C3−$\mathrm{H_{eq}}$	63.6	63.7	63.9	62.2	61.0	62.8	63.4	63.2
$\mathrm{H_{ax}}$−C3−C4−$\mathrm{H_{eq}}$	56.9	54.3	53.8	56.0	56.6	54.7	54.5	54.7
$\mathrm{H_{eq}}$−C3−C4−$\mathrm{H_{ax}}$	55.9	53.2	52.6	54.6	55.0	53.4	53.2	53.4
C6−O1−C2−$\mathrm{H_{ax}}$	61.1	61.7	62.1	61.1	60.1	61.0	61.7	61.7
C6−O1−C2−$\mathrm{H_{eq}}$	178.1	178.1	178.5	176.6	176.4	177.1	177.9	177.9
C2−C3−C4−C5	54.4	51.4	51.1	52.4	52.3	51.5	51.3	51.4
O1−C2−C3−C4	56.5	55.2	54.8	57.2	56.9	56.3	55.9	55.8
C2−O1−C6−C5	60.2	60.4	60.0	61.9	61.2	61.0	60.5	60.4

TABLE 2: Bond Angles (°) in the Chair Conformer (1) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP
O1−C2−$\mathrm{H_{ax}}$	109.9	109.7	109.5	109.7	109.3	109.4	109.8	109.8
O1−C2−$\mathrm{H_{eq}}$	106.1	106.4	106.5	105.8	106.4	105.8	105.6	106.0
O1−C2−C3	110.6	111.4	111.5	111.3	111.8	111.8	111.9	111.8
C2−O1−C6	113.2	113.6	113.7	110.9	111.1	111.2	111.5	112.0
C2−C3−C4	109.9	110.2	110.3	110.0	109.8	111.8	110.3	110.2
C3−C4−C5	109.6	109.9	110.0	109.9	109.9	110.2	110.2	110.1

TABLE 3: Bond Lengths (Å) in the Chair Conformer (1) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C2	1.440	1.401	1.401	1.427	1.407	1.434	1.440	1.423	1.416
C2−C3	1.533	1.525	1.524	1.523	1.509	1.531	1.543	1.531	1.524
C3−C4	1.542	1.531	1.531	1.529	1.515	1.539	1.548	1.537	1.531
C2−$\mathrm{H_{ax}}$	1.087	1.091	1.092	1.103	1.115	1.119	1.113	1.105	1.106
C2−$\mathrm{H_{eq}}$	1.080	1.082	1.083	1.094	1.101	1.107	1.102	1.095	1.095
C3−$\mathrm{H_{ax}}$	1.084	1.087	1.088	1.096	1.105	1.111	1.105	1.098	1.099
C3−$\mathrm{H_{eq}}$	1.085	1.087	1.087	1.097	1.103	1.109	1.105	1.098	1.098
C4−$\mathrm{H_{ax}}$	1.087	1.089	1.090	1.097	1.107	1.113	1.108	1.100	1.100
C4−$\mathrm{H_{eq}}$	1.084	1.087	1.086	1.099	1.103	1.108	1.104	1.097	1.097

TABLE 4: Nonbonded Distances (Å) in the Chair Conformer (1) of Tetrahydro-2*H*-pyran

	HF/3-21G(d)	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C3	2.445	2.418	2.419	2.436	2.415	2.457	2.472	2.447	2.438
C2−C4	2.517	2.507	2.508	2.499	2.474	2.520	2.537	2.517	2.506
C2−C6	2.405	2.345	2.346	2.350	2.320	2.370	2.381	2.360	2.344
C3−C5	2.520	2.507	2.508	2.503	2.481	2.522	2.541	2.520	2.509

TABLE 5: Torsional Angles (*τ*, °) in the 2,5-Twist Conformer (4a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6−311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
$\mathrm{H_{isoa}}$−C2−C3−$\mathrm{H}_{\psi\mathrm{ax}}$	145.9	148.2	149.1	148.2	147.5	147.8	146.7	147.0	147.8
$\mathrm{H_{isob}}$−C2−C3−$\mathrm{H}_{\psi\mathrm{eq}}$	93.5	88.3	87.2	89.4	89.3	88.6	89.8	89.4	88.5
$\mathrm{H_{isoa}}$−C5−C6−$\mathrm{H}_{\psi\mathrm{ax}}$	139.4	146.2	147.2	147.2	149.2	147.2	144.7	145.5	146.2
$\mathrm{H_{isob}}$−C5−C6−$\mathrm{H}_{\psi\mathrm{eq}}$	99.9	90.4	89.2	90.7	87.8	89.7	92.1	91.1	90.4
$\mathrm{H}_{\psi\mathrm{ax}}$−C3−C4−$\mathrm{H}_{\psi\mathrm{ax}}$	175.5	179.9	179.4	177.1	177.8	179.9	179.8	179.8	179.4
$\mathrm{H}_{\psi\mathrm{eq}}$−C3−C4−$\mathrm{H}_{\psi\mathrm{eq}}$	52.9	55.1	55.5	52.7	52.8	54.3	54.9	54.8	54.2
$\mathrm{H}_{\psi\mathrm{ax}}$−C4−C5−$\mathrm{H_{isoa}}$	42.9	33.9	32.7	36.7	35.7	34.2	35.5	35.1	35.0
$\mathrm{H}_{\psi\mathrm{eq}}$−C4−C5−$\mathrm{H_{isob}}$	42.7	34.2	32.9	36.6	36.0	34.6	35.7	34.9	35.2
C6−O1−C2−$\mathrm{H_{isoa}}$	163.2	159.1	157.7	161.5	160.8	159.6	160.8	160.3	160.8
C6−O1−C2−$\mathrm{H_{isob}}$	79.7	84.9	86.3	82.5	83.2	84.8	83.3	84.0	83.2
C2−C3−C4−C5	64.8	61.1	60.6	63.5	63.8	61.5	63.9	61.0	63.8
O1−C2−C3−C4	22.3	26.1	27.3	25.0	25.9	25.6	26.0	24.6	25.9
C2−O1−C6−C5	68.6	69.8	69.4	72.5	72.1	70.3	72.2	70.0	72.1

Tetrahydro-2*H*-pyran has a chair structure (**1**, C_s point group) similar to cyclohexane, and other six-membered heterocyclohexanes, although it is somewhat more puckered than cyclohexane in order to accommodate the bond angles and bond lengths characteristic of oxygen.[24−33] There are a number of repulsive nonbonded hydrogen−hydrogen distances in tetrahydro-2*H*-pyran that are less than or near to the sum (2.40 Å) of the van der Waals radius for hydrogen.[38−47]

The BLYP calculations generally gave longer bond lengths for all conformers than the other methods. The HF/3-21G calculations generally gave longer C−O and C−C bond lengths than the other basis sets. The SVWN calculated C2−C3 bond lengths are consistently shorter than those calculated by the other DFT methods. Although the HF/3-21G calculation gave a C−O bond length of 1.440 Å for the chair conformer (**1**), the other five basis sets at the HF level and the SVWN calculations gave values from 1.400 to 1.407 Å. It is known that owing largely to the restriction to single-determinant wave functions, the 6-31G(d) basis set underestimates single bond lengths involving electronegative first-row atoms.[48] The MP2/6-31G(d) calculated C−O bond length for the chair conformer (**1**) was 1.427 Å. The hybrid density functional methods B3LYP, B3P86, and B3PW91 gave C−O bond length values from 1.414 to 1.423 Å for the chair conformer **1**. The BLYP calculations gave a C−O bond length of 1.440 Å for **1**, whereas the pBP calculations gave a value of 1.434 Å. Similar trends are seen in the calculated C−O bond lengths in the twist (**4a**, **4b**) and boat (**5a**) conformers. Many of the calculated C−O bonds lengths for **1**

TABLE 6: Bond Angles (°) in the 2,5-Twist Conformer (4a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C2−H$_{isoa}$	105.3	105.7	105.7	104.9	105.4	104.9	105.8	106.0	106.0
O1−C2−H$_{isob}$	109.8	109.8	109.7	109.7	109.8	109.7	110.0	109.9	110.0
O1−C6−H$_{\psi ax}$	109.8	109.8	109.7	109.8	109.5	109.8	109.9	109.9	110.0
O1−C6−H$_{\psi eq}$	106.2	106.7	106.8	106.2	106.9	106.1	104.6	106.0	106.0
O1−C2−C3	110.3	112.2	112.3	110.1	112.2	112.7	111.1	112.7	112.6
O1−C6−C5	111.3	110.7	110.8	112.1	110.6	110.9	112.9	112.6	112.6
C2−O1−C6	112.9	113.6	113.9	110.4	110.6	111.3	111.6	115.0	115.1
C2−C3−C4	108.5	109.4	109.6	109.4	108.8	109.6	110.1	110.6	110.6
C3−C4−C5	109.3	109.8	109.9	109.3	109.1	109.9	111.0	110.8	110.6
C4−C5−C6	109.5	110.0	110.2	108.8	109.2	110.0	109.7	110.6	110.5

TABLE 7: Bond Lengths (Å) in the 2,5-Twist Conformer (4a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C2	1.443	1.405	1.405	1.431	1.413	1.440	1.445	1.427	1.420
C2−C3	1.549	1.538	1.536	1.537	1.524	1.547	1.558	1.545	1.540
C3−C4	1.538	1.529	1.529	1.527	1.513	1.536	1.545	1.534	1.529
C4−C5	1.545	1.539	1.539	1.536	1.523	1.548	1.557	1.545	1.539
C5−C6	1.551	1.537	1.537	1.536	1.523	1.546	1.558	1.545	1.540
C6−O1	1.440	1.400	1.399	1.426	1.408	1.434	1.439	1.422	1.415
C2−H$_{isoa}$	1.080	1.082	1.084	1.093	1.102	1.108	1.102	1.094	1.094
C2−H$_{isob}$	1.085	1.089	1.090	1.101	1.111	1.117	1.111	1.103	1.104
C3−H$_{\psi ax}$	1.085	1.087	1.088	1.097	1.105	1.110	1.104	1.096	1.096
C3−H$_{\psi eq}$	1.084	1.085	1.086	1.095	1.102	1.108	1.106	1.098	1.098
C4−H$_{\psi ax}$	1.083	1.086	1.086	1.095	1.104	1.109	1.104	1.097	1.097
C4−H$_{\psi eq}$	1.083	1.086	1.086	1.095	1.101	1.107	1.103	1.096	1.096
C5−H$_{isoa}$	1.083	1.086	1.086	1.095	1.102	1.108	1.104	1.096	1.096
C5−H$_{isob}$	1.085	1.087	1.088	1.097	1.105	1.110	1.106	1.098	1.098
C6−H$_{\psi ax}$	1.086	1.089	1.090	1.101	1.111	1.117	1.112	1.103	1.104
C6−H$_{\psi eq}$	1.079	1.083	1.082	1.094	1.102	1.107	1.103	1.095	1.096

TABLE 8: Nonbonded Distances (Å) in the 2,5-Twist Conformer (4a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C3	2.471	2.444	2.444	2.463	2.439	2.487	2.472	2.445	2.465
O1−C5	2.455	2.417	2.417	2.429	2.410	2.455	2.503	2.475	2.435
C2−C4	2.507	2.502	2.504	2.491	2.469	2.518	2.552	2.531	2.503
C2−C6	2.403	2.347	2.350	2.346	2.319	2.373	2.385	2.362	2.346
C3−C5	2.515	2.509	2.511	2.498	2.473	2.524	2.541	2.521	2.508
C4−C6	2.528	2.520	2.521	2.507	2.483	2.534	2.995	2.515	2.518

TABLE 9: Torsional Angles (τ, °) in the 1,4-Boat Conformer (5a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
H$_{ax}$−C2−C3−H$_{ax}$	2.8	0.8	0.4	0.4	1.1	1.4	0.4	0.1	0.1
H$_{eq}$−C2−C3−H$_{eq}$	5.0	2.9	2.5	2.1	0.9	1.0	2.0	2.1	2.0
H$_{ax}$−C5−C6−H$_{ax}$	2.8	0.8	0.4	0.4	1.1	1.4	0.4	0.1	0.1
H$_{eq}$−C5−C6−H$_{eq}$	5.0	2.9	2.5	2.1	0.9	1.0	2.0	2.1	2.0
H$_{ax}$−C3−C4−H$_{eq}$	56.7	52.7	52.2	54.3	55.2	53.7	52.9	52.9	53.4
H$_{eq}$−C3−C4−H$_{ax}$	57.6	64.1	53.0	55.3	55.9	54.3	53.4	53.6	54.2
H$_{ax}$−C4−C5−H$_{eq}$	57.6	64.1	52.9	55.3	55.9	54.3	53.4	53.6	54.2
H$_{eq}$−C4−C5−H$_{ax}$	56.7	52.7	52.2	54.3	55.1	53.7	52.9	52.9	53.4
C6−O1−C2−H$_{ax}$	63.9	64.0	64.0	61.9	60.5	61.4	63.5	63.5	63.1
C6−O1−C2−H$_{eq}$	179.3	179.6	179.6	177.5	176.1	176.9	178.9	178.9	178.4
C2−C3−C4−C5	56.2	51.9	51.4	53.3	53.5	52.4	51.7	51.8	52.2
O1−C2−C3−C4	0.6	1.2	1.4	2.5	2.8	3.1	2.5	2.2	2.2
C2−O1−C6−C5	58.8	59.2	59.1	61.3	62.0	61.5	59.8	59.8	60.2

are in excellent agreement with the experimentally determined values for substituted tetrahydro-2*H*-pyrans.[49−53] The average of 22 experimentally determined C−O bond lengths for substituted tetrahydro-2*H*-pyrans is 1.441 Å.[49]

The molecular structure of tetrahydro-2*H*-pyran has been studied by microwave spectroscopy (MW)[50−52] and electron diffraction (ED).[53] The electron diffraction C−O bond length for the chair conformer (**1**) is 1.420 Å, which is in excellent agreement with the MP2/6-31G(d) and B3LYP calculations. The gas-phase ED studies of oxacyclopentane (tetrahydrofuran) gave the average C−O bond length of 1.428 Å[54,55] and the MW spectrum of strained oxacyclobutane (trimethylene oxide) gave a C−O bond length of 1.449 Å.[56] Electron diffraction (ED) studies showed that the six-membered diheterocyclohexane 1,4-dioxane, which contains two ether groups in the ring, has a C−O bond length of 1.423 Å.[57]

All levels of theory showed that the C2−C3 bond lengths in the chair conformer (**1**) and the 1,4-twist conformer (**4b**) are shorter than their respective C3−C4 bond lengths. The C2−C3 bond length increases in going from the chair conformer (**1**) to the 2,5-twist form (**4a**) to the 1,4-boat structure (**5a**). At the HF/3-21G, pBP, and B3LYP theoretical levels, the C2−C3 bond lengths in the chair conformer (**1**) are 1.533, 1.531, and 1.531 Å, respectively, whereas the corresponding C3−C4 bond lengths are 1.542, 1.539, and 1.537 Å. The electron diffraction (ED) C−C bond lengths in tetrahydro-2*H*-pyran,[53] oxacyclopentane,[54,55] and 1,4-dioxane[57] are 1.531, 1.537, and 1.523 Å, respectively.

TABLE 10: Bond Angles (°) in the 1,4-Boat Conformer (5a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C2−H$_{\mathrm{ax}}$	109.7	109.5	109.4	109.3	108.9	109.5	109.5	109.5	109.5
O1−C2−H$_{\mathrm{eq}}$	105.4	105.7	105.9	105.0	105.8	105.1	104.8	105.2	105.3
O1−C6−H$_{\mathrm{ax}}$	109.7	109.5	109.4	109.3	108.9	109.5	109.5	109.5	109.5
O1−C6−H$_{\mathrm{eq}}$	105.4	105.7	105.9	105.0	105.8	105.1	104.8	105.2	105.3
O1−C2−C3	111.2	111.9	112.0	111.8	111.8	112.2	112.3	112.3	112.2
O1−C6−C5	111.2	111.9	112.0	111.8	111.8	112.2	112.3	112.2	112.2
C2−O1−C6	113.1	113.6	113.7	110.3	110.2	111.1	111.4	111.9	111.5
C2−C3−C4	109.3	110.1	110.2	109.6	109.3	109.9	110.1	110.0	109.8
C3−C4−C5	109.2	109.8	110.0	109.6	109.6	110.1	110.3	110.2	110.0
C4−C5−C6	109.3	110.1	110.2	109.6	109.3	109.9	110.1	110.0	109.8

TABLE 11: Bond Lengths (Å) in the 1,4-Boat Conformer (5a) of Tetrahydro-2*H*-pyran

	HF/3-21G	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C2	1.440	1.400	1.400	1.426	1.407	1.434	1.440	1.422	1.416
C2−C3	1.556	1.547	1.547	1.546	1.535	1.559	1.568	1.555	1.550
C3−C4	1.537	1.530	1.530	1.528	1.515	1.538	1.548	1.536	1.530
C2−H$_{\mathrm{ax}}$	1.085	1.089	1.090	1.101	1.113	1.117	1.112	1.103	1.104
C2−H$_{\mathrm{eq}}$	1.079	1.081	1.082	1.093	1.100	1.106	1.101	1.094	1.094
C3−H$_{\mathrm{ax}}$	1.085	1.087	1.088	1.097	1.104	1.110	1.105	1.098	1.098
C3−H$_{\mathrm{eq}}$	1.083	1.085	1.086	1.095	1.102	1.108	1.104	1.096	1.096
C4−H$_{\mathrm{ax}}$	1.082	1.085	1.086	1.095	1.103	1.108	1.103	1.096	1.096
C4−H$_{\mathrm{eq}}$	1.084	1.086	1.086	1.094	1.102	1.107	1.104	1.096	1.096

TABLE 12: Nonbonded Distances (Å) in the 1,4-Boat Conformer (5a) of Tetrahydro-2*H*-pyran

	HF/3-21Gd	HF/6-31G(d)	HF/6-311+G(d,p)	MP2/6-31G(d)	SVWN/DN**	pBP/DN**	BLYP	B3LYP	B3PW91
O1−C3	2.473	2.444	2.444	2.463	2.436	2.484	2.499	2.472	2.462
C2−C4	2.525	2.522	2.524	2.512	2.487	2.535	2.553	2.532	2.519
C2−C6	2.403	2.343	2.343	2.342	2.308	2.365	2.379	2.356	2.341
C3−C5	2.510	2.04	2.507	2.498	2.475	2.521	2.541	2.519	2.507

The shorter C2−C3 bond lengths may arise from the electronegative effect.[58] The electronegative effect is an inductive effect which occurs when atoms of different electronegativities are bonded together. If an electronegative atom is attached to a carbon−carbon bond, the electronegative atoms preferentially pulls the more polarizable p electrons toward it, leading to a bond dipole. This puts more p character in the bond toward the electronegative atom and leaves more s character in the remaining bonds which leads to shorter bond lengths and larger bond angles. The atom losing electron density has its effective nuclear charge increased and its occupied orbitals contracted. This results in additional bond shortening because the bond length of the attached bonds will get shorter as the size of the bonding orbitals decrease. In addition, the van der Waals radius of the atom will be decreased. However, because the electronegative atom or group being attached may also simultaneously exert steric and/or electrostatic interactions on the remainder of the molecule, the total net change of any particular angle or bond may be large or small or may in fact be in a direction opposite to that required by the electronegative effect.[58]

Although the MP2/6-31G(d) calculated carbon−hydrogen bond lengths are longer than those calculated at the HF levels, all calculations showed that the C2−H$_{\mathrm{ax}}$ bond lengths are longer than the C2−H$_{\mathrm{eq}}$ bond lengths in the four structures **1**, **4a**, (C2−H$_{\mathrm{isoa}}$ > C2−H$_{\mathrm{isob}}$), **4b**, (C2−H$_{\psi\mathrm{ax}}$ > C2−H$_{\psi\mathrm{eq}}$), and **5a**. In contrast, the C3−H$_{\mathrm{ax}}$ and C3−H$_{\mathrm{eq}}$ (**1**), C3−H$_{\psi\mathrm{ax}}$ and C3−H$_{\psi\mathrm{eq}}$ (**4a**), and C3−H$_{\psi\mathrm{ax}}$ and C3−H$_{\psi\mathrm{eq}}$ (**4b**) bond lengths are essentially the same (Tables 3, 7, 11). The DFT calculated values of the C2−H$_{\mathrm{ax}}$ bond length in the chair conformer (**1**) were closest to the ED determined C−H bond length in tetrahydro-2*H*-pyran (1.116 Å).[53] An explanation for the longer C2−H$_{\mathrm{ax}}$ bond lengths vs the C2−H$_{\mathrm{eq}}$ bond lengths in the unconstrained conformers (**1**, **4a**, **4b**) includes the involvement of one or more stereoelectronic interactions (anomeric effect,[24,59−62] Bohlmann effect,[63,64] hyperconjugative orbital interactions,[62,66−68] Perlin effect,[69,70] trans lone pair effect).[71]

A lone pair of electrons on oxygen, when properly aligned (antiperiplanar) with the C2−H$_{\mathrm{ax}}$ bond, can donate electron density from the lone pair orbital to the antibonding (σ*) C2−H$_{\mathrm{ax}}$ orbital (anomeric effect). The Perlin effect[69,70] has been ascribed to a stereoelectronic *n*-σ* interaction between the axially directed nonbonding electron pair on the oxygen and the antiperiplanar axial C−H bond. This lengthens and weakens the C−H bond which attenuate the Fermi coupling. The result is that the one-bond NMR coupling constants $^1J_{\mathrm{C-H}}$ are greater for the equatorial hydrogens than for the axial hydrogens (ca. 170 and 160 Hz, respectively).[61,68−70] Amines which have a hydrogen on the carbon attached to nitrogen so that the carbon−hydrogen σ* bond is antiperiplanar to the lone pair axis show abnormally low stretching frequencies (Bohlmann Bands) for those C−H bonds. Thus, the anomeric effect, the Bohlmann effect, hyperconjugative orbital interactions, and the Perlin effect have been described as different manifestations of the same phenomenon, the trans lone pair effect.[71] Any of these stereoelectronic interactions in tetrahydro-2*H*-pyran would be expected to lengthen (weaken) the C2−H$_{\mathrm{ax}}$ bond.

HF gave a C2−O1−C6 bond angle of 113.7°, MP2 110.9°, SVWN and pBP 111.1°, BLYP 111.5°, and the hybrid density functional methods (B3LYP, B3PW91, B3P86) 111.7° for the chair conformer (**1**). Electron diffraction (ED) gave a C2−O1−C6 bond angle of 111.5° for **1**.[53] The electron diffraction C−O−C bond angles for 1,4-dioxane[57] and dimethyl ether[72] are 112.4° and 111.4°, respectively. The microwave (MW) C−O−C bond angle for dimethyl ether is 111.4°.[73,74] The calculated values of the C2−O1−C6 bond angle for the 1,4-boat conformer **5a** were similar to those obtained for the chair structure (**1**). Although the HF, SVWN, pBP, and BLYP levels of theory gave C−O−C bond angle values for the 2,5-twist **4a** which were similar to the values for **1** and **5a**, the hybrid

TABLE 13: HF Total Energies (H), Relative Energies (Δ*E*, kcal/mol), and Dipole Moments (*μ*, D) of the Chair (1), Half-Chair (2), and Sofa (3) Conformers of Tetrahydro-2*H*-pyran

	6-31G(d)	6-31G(d,p)	6-311G(d,p)	6-31+G(d)	6-311+G(d,p)
1	−270.017 907 $\Delta E = 0.0$ $\mu = 1.57$	−270.033 126 $\Delta E = 0.0$ $\mu = 1.57$	−270.085 020 $\Delta E = 0.0$ $\mu = 1.56$	−270.022 920 $\Delta E = 0.0$ $\mu = 1.69$	−270.088 592 $\Delta E = 0.0$ $\mu = 1.69$
2a	−270.002 132 $\Delta E = 9.90$ $\mu = 1.77$	−270.017 321 $\Delta E = 9.90$ $\mu = 1.76$	−270.069 297 $\Delta E = 9.87$ $\mu = 1.76$	−270.007 350 $\Delta E = 9.77$ $\mu = 1.88$	−270.072 828 $\Delta E = 9.89$ $\mu = 1.87$
2b	−270.001 709 $\Delta E = 10.2$ $\mu = 1.56$	−270.016 876 $\Delta E = 10.20$ $\mu = 1.56$	−270.068 723 $\Delta E = 10.2$ $\mu = 1.53$	−270.006 868 $\Delta E = 10.1$ $\mu = 1.67$	−270.072 392 $\Delta E = 10.2$ $\mu = 1.66$
2c	−270.000 290 $\Delta E = 11.1$ $\mu = 1.59$	−270.015 446 $\Delta E = 11.1$ $\mu = 1.59$	−270.067 235 $\Delta E = 11.2$ $\mu = 1.56$	−270.005 344 $\Delta E = 11.0$ $\mu = 1.70$	−270.070 829 $\Delta E = 11.1$ $\mu = 1.69$
3a	−270.001 828 $\Delta E = 10.1$ $\mu = 1.76$	−270.017 016 $\Delta E = 10.1$ $\mu = 1.76$	−270.068 976 $\Delta E = 10.1$ $\mu = 1.75$	−270.007 033 $\Delta E = 9.97$ $\mu = 1.88$	−270.072 493 $\Delta E = 9.91$ $\mu = 1.87$
3b	−270.000 669 $\Delta E = 10.8$ $\mu = 1.55$	−270.015 838 $\Delta E = 10.8$ $\mu = 1.55$	−270.067 699 $\Delta E = 10.9$ $\mu = 1.51$	−270.005 880 $\Delta E = 10.7$ $\mu = 1.66$	−270.071 417 $\Delta E = 10.8$ $\mu = 1.65$
3c	−270.000 234 $\Delta E = 11.1$ $\mu = 1.62$	−270.015 394 $\Delta E = 11.1$ $\mu = 1.62$	−270.067 211 $\Delta E = 11.2$ $\mu = 1.59$	−270.005 297 $\Delta E = 11.2$ $\mu = 1.73$	−270.070 792 $\Delta E = 11.2$ $\mu = 1.72$
3d	−269.999 805 $\Delta E = 11.4$ $\mu = 1.76$	−270.014 981 $\Delta E = 11.4$ $\mu = 1.76$	−270.066 919 $\Delta E = 11.4$ $\mu = 1.74$	−270.004 997 $\Delta E = 11.2$ $\mu = 1.88$	−270.070 498 $\Delta E = 11.4$ $\mu = 1.87$

TABLE 14: MP2 Single Point Total Energies (H) and Relative Energies (Δ*E*, Kcal/Mol) of the Chair (1), Half-Chair (2), and Sofa (3) Conformers of Tetrahydro-2*H*-pyran

	MP2//6-31G(d)	MP2//6-31G(d,p)	MP2//6-311G(d,p)	MP2//6-31+G(d)	MP2//6-311+G(d,p)
1 $\Delta E = 0.0$	−270.842 417 $\Delta E = 0.0$	−270.923 686 $\Delta E = 0.0$	−271.024 522 $\Delta E = 0.0$	−270.857 075 $\Delta E = 0.0$	−271.032 827
2a $\Delta E = 11.1$	−270.824 719 $\Delta E = 11.0$	−270.906 227 $\Delta E = 11.2$	−271.006 713 $\Delta E = 10.9$	−270.839 701 $\Delta E = 10.9$	−271.015 404
2b $\Delta E = 11.0$	−270.824 936 $\Delta E = 10.9$	−270.906 332 $\Delta E = 10.6$	−271.007 690 $\Delta E = 10.9$	−270.839 756 $\Delta E = 10.4$	−271.016 179
2c $\Delta E = 12.0$	−270.823 356 $\Delta E = 11.9$	−270.904 713 $\Delta E = 11.6$	−271.006 080 $\Delta E = 11.9$	−270.838 174 $\Delta E = 11.4$	−271.014 603
3a $\Delta E = 11.3$	−270.824 390 $\Delta E = 11.2$	−270.905 891 $\Delta E = 11.4$	−271.006 338 $\Delta E = 11.1$	−270.839 329 $\Delta E = 11.2$	−271.015 007
3b $\Delta E = 11.7$	−270.823 811 $\Delta E = 11.6$	−270.905 260 $\Delta E = 11.2$	−271.006 334 $\Delta E = 11.5$	−270.838 673 $\Delta E = 11.1$	−271.015 214
3c $\Delta E = 12.2$	−270.823 008 $\Delta E = 12.1$	−270.904 354 $\Delta E = 11.9$	−271.005 580 $\Delta E = 12.1$	−270.837 856 $\Delta E = 11.8$	−271.014 055
3d $\Delta E = 12.7$	−270.822 199 $\Delta E = 12.6$	−270.903 656 $\Delta E = 12.6$	−271.004 462 $\Delta E = 12.5$	−270.837 230 $\Delta E = 12.3$	−271.013 233 1

density functional methods (B3LYP, B3PW91, B3P86) gave larger values (115.1°). All levels of calculation gave a larger C2−O1−C6 bond angle (113.8° to 117.0°) for **4b** than for **1**, **4a**, and **5a**.

The electron diffraction O−C−C bond angle for **1** is 111.8°.[53] With the exception of the HF/3-21G (110.6°) value, all levels of theory gave a O1−C2−C3 bond angle in the narrow range 111.4° to 111.8° for the chair conformer (**1**). Slightly larger values were calculated for the O1−C2−C3 bond angles in **4a**, **4b**, and **5a**. Although it has been suggested that in saturated oxanes the C−O−C bond angle is expected to be larger than the O−C−C bond angle, this not consistent with the ED data for **1**.[75−78] However, the ab initio calculations on **1**, the ED studies on oxacyclopentane [54,55] and 1,4-dioxane,[57] and the X-ray diffraction (XD) studies on polyether compounds[78] are in accord with this expectation. This seems reasonable if one takes into account the repulsive nonbonded interactions, including those between the axial hydrogens on C2 and C6 across the C−O−C angle, that are absent for the O−C−C bond angle.

Although the DFT methods gave slightly larger values, similar C−C−C bond angles for the chair conformer (**1**) were calculated by all theoretical methods. The electron diffraction C−C−C bond angle for **1** is 108.3° and the torsional angles (τ) are C−C−C−C (52.5°), C−O−C−C (59.9°), and O−C−C−C (56.9°).[53] All levels of theory, except HF/3-21G, calculated the C−C−C−C torsional angle (τ) in the chair conformer (**1**) to be in the range from 51.1° to 52.4° (Table 1). The calculated C−C−C−C torsional angle (τ) in the 1,4-boat structure (**5a**, Table 9) was similar to that in the chair conformer (**1**), the largest C−C−C−C torsional angle ($\tau = 60.9°$ to $64.8°$) was calculated for the 2,5-twist form (**4a**, Table 5), and the smallest (($\tau = 28.1°$ to 29.5°) for the 1,4-twist conformer (**4b**). At all levels of theory, the C−O−C−C torsional angle ($\tau = 60.0°$ to $61.8°$) in the chair conformer (**1**) is close to the ED value. Similarly, the calculated O−C−C−C torsional angle (τ) in the chair conformer (**1**) was also close to the electron diffraction (ED) value.

The ab inito calculated dipole moment (1.6 to 1.7 D) for the chair conformer (**1**) of tetrahydro-2*H*-pyran was close to the experimentally determined value of 1.74 D.[50−52,78,79] The DFT methods gave dipole moment values smaller than the experimental value. The dipole moment of the cyclic monoether oxacyclopentane was determined from the Stark effect in the pure rotational spectrum and was found to vary from 1.52 to 1.76 D depending on the pseudorotational state.[80]

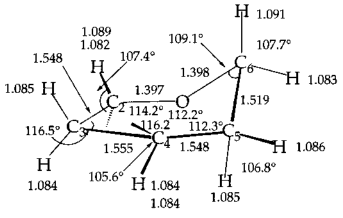
As in cyclohexane, the boat conformers (**5**) of tetrahydro-2*H*-pyran are flexible and twisting of one of the bonds relative

TABLE 15: DFT Total Energies (H), Relative Energies (Δ*E*, kcal/mol), and Dipole Moments (*μ*, D) of the Chair (1), Half-Chair (2), and Sofa (3) Conformers of Tetrahydro-*2H*-pyran

	SVWN/DN*	SVWN/DN**	pBP/DN*	pBP/DN**
1	−269.485 469	−269.504 002	−271.847 751	−271.868 666
	$\Delta E = 0.0$	$\Delta E = 0.0$	$\Delta E = 0.0$	$\Delta E = 0.0$
	$\mu = 1.51$	$\mu = 1.48$	$\mu = 1.59$	$\mu = 1.55$
2a	−269.468 192	−269.487 140	−271.832 336	−271.853 547
	$\Delta E = 10.8$	$\Delta E = 10.6$	$\Delta E = 9.67$	$\Delta E = 9.49$
	$\mu = 1.78$	$\mu = 1.74$	$\mu = 1.84$	$\mu = 1.80$
2b	−269.467 925	−269.487 458	−271.832 467	−271.853 815
	$\Delta E = 11.0$	$\Delta E = 10.4$	$\Delta E = 9.60$	$\Delta E = 9.32$
	$\mu = 1.52$	$\mu = 1.48$	$\mu = 1.59$	$\mu = 1.56$
2c	−269.465 893	−269.485 053	−271.830 880	−271.852 257
	$\Delta E = 12.3$	$\Delta E = 11.9$	$\Delta E = 10.6$	$\Delta E = 10.3$
	$\mu = 1.56$	$\mu = 1.52$	$\mu = 1.62$	$\mu = 1.58$
3a	−269.467 792	−269.486 296	−271.831 589	−271.852 686
	$\Delta E = 11.1$	$\Delta E = 11.1$	$\Delta E = 10.1$	$\Delta E = 10.0$
	$\mu = 1.77$	$\mu = 1.73$	$\mu = 1.83$	$\mu = 1.79$
3b	−269.467 469	−269.486 649	−271.831 995	−271.853 775
	$\Delta E = 11.3$	$\Delta E = 10.9$	$\Delta E = 9.89$	$\Delta E = 9.34$
	$\mu = 1.50$	$\mu = 1.47$	$\mu = 1.56$	$\mu = 1.53$
3c	−269.465 977	−269.485 192	−271.831 091	−271.852 496
	$\Delta E = 12.2$	$\Delta E = 11.8$	$\Delta E = 10.5$	$\Delta E = 10.1$
	$\mu = 1.60$	$\mu = 1.56$	$\mu = 1.67$	$\mu = 1.63$
3d	−269.465 444	−269.484 501	−271.829 959	−271.851 280
	$\Delta E = 12.6$	$\Delta E = 12.2$	$\Delta E = 11.2$	$\Delta E = 10.9$
	$\mu = 1.75$	$\mu = 1.71$	$\mu = 1.82$	$\mu = 1.78$

to another leads to slightly more stable twist conformations. The 2,5-twist (**4a**) and 1,4-twist (**4b**) structures are close in energy (Tables 16-18). All levels of theory, except SVWN ($\Delta E = 6.71$ and 6.82 kcal/mol), gave an energy difference (ΔE) between the chair conformer **1** and the 2,5-twist conformer **4a** in the range of 5.78 to 6.12 kcal/mol. The HF ($\Delta E = 6.76$ to 7.16 kcal/mol) and SVWN ($\Delta E = 6.97$ and 7.20 kcal/mol) methods gave the largest energy difference between the chair conformer (**1**) and the 1,4-boat conformer (**5a**). The pBP, BLYP, and hybrid density functional methods (B3LYP, B3PW91, B3P86) gave energy differences (ΔE) between **1** and **5a** in the range 6.23 to 6.46 kcal/mol. The 1,4-boat conformer **5a** is less stable than the chair form (**1**) in part because of the eclipsing interactions of the hydrogens on C2 and C3 and those on C5 and C6. The repulsive flagpole nonbonded hydrogen−hydrogen interaction in the 2,5-boat structure **5b** contributes to its higher energy relative to **5a**. The O1 to C4−H nonbonded distance in **5a** is 2.612 Å, and the C3−H to C6−H nonbonded distance in **5b** is 2.353 Å.

The constraints were removed from the constrained structures that gave one imaginary frequency during partial optimizations. These unconstrained structures and the 1,4-boat structure (**5a**) were subjected to transition state optimizations, followed by frequency calculations. To ascertain whether the resulting transition structures were involved in the ring reversal mechanism of the chair conformer (**1**), these transition structures were subjected to intrinsic reaction coordinate (IRC) calculations in the forward and reverse directions. The transition structure (**2cc**) from the half-chairs **2b** and **2c** and from sofas **3b** and **3c** is the transition state between the chair conformer **1** and the 2,5-twist conformer (**4a**). The boat structures **5a** and **5b** did not change significantly during transition state optimizations and IRC calculations.



τ O1-C2-C3-C4 = 6.6°
τ C2-C3-C4-C5 = 12.9°
τ C2-O1-C6-C5 = 75.5°

2cc

To compare the calculated energy differences (ΔE) between the conformers of tetrahydro-2*H*-pyran to the experimentally determined barrier to ring reversal, ΔE must be corrected for the difference in zero-point energies (ZPE) between the conformers, the change in $\Delta H°$ on going from 0 to 298.15 K must be computed, and $\Delta H°$ must then be converted to $\Delta G°$ using the calculated energy difference (Tables 19, 20).[81,82] The HF conformational free energy ($\Delta G° = 10.5 \pm 0.1$ kcal/mol at 298 K) for the chair conformer going to transition state **2cc** via the half-chair (**2b**, **2c**) and sofa (**3b**, **3c**) structures is in excellent agreement with the experimentally determined ring reversal barrier for tetrahydro-2*H*-pyran ($\Delta G^{\ddagger} = 10.3$ kcal/mol at 212 K).[83,84] The barriers to ring reversal for 1,3-dioxane ($\Delta G^{\ddagger} = 9.9 \pm 0.2$ kcal/mol at 203 K),[85]1,4-dioxane ($\Delta G^{\ddagger} = 9.97$ kcal/mol),[86−88] and cyclohexane ($\Delta G^{\ddagger} = 10.2$ to 10.5 kcal/mol at 223 K) are similar to the value for the chair conformer (**1**) of tetrahydro-2*H*-pyran.[24,89,90] As with cyclohexane, the transition state **2cc** can undergo pseudorotation to the 2,5-twist structure (**4a**). With one exception, all levels of theory calculated the energy difference (ΔE) between the chair (**1**) and the 2,5-twist (**4a**) conformer of tetrahydro-2*H*-pyran to be in the narrow range of 5.78 to 6.10 kcal/mol (Table 20).

Conclusions

The geometry optimized structure of the chair conformer (**1**) of tetrahydro-2*H*-pyran is consistent with the ED and MW

TABLE 16: Total Energies (H), Relative Energies (Δ*E*, Kcal/Mol), and Dipole Moments (*μ*, D) of the Chair (1), Twist (4), and Boat (5) Conformers of Tetrahydro-*2H*-pyran

	HF/6-31G(d)	HF/6-31G(d,p)	HF/6-311G(d,p)	HF/6-31+G(d)	HF/6-311+G(d,p)
	−270.017 907	−270.033 126	−270.085 020	−270.022 920	−270.088 592
1	$\Delta E = 0.0$	$\Delta E = 0.0$	$\Delta E = 0.0$	$\Delta E = 0.0$	$\Delta E = 0.0$
	$\mu = 1.57$	$\mu = 1.57$	$\mu = 1.56$	$\mu = 1.69$	$\mu = 1.69$
	−270.008 476	−270.023 659	−270.075 440	−270.013 346	−270.078 874
4a	$\Delta E = 5.92$	$\Delta E = 5.94$	$\Delta E = 6.01$	$\Delta E = 6.01$	$\Delta E = 6.10$
	$\mu = 1.58$	$\mu = 1.58$	$\mu = 1.56$	$\mu = 1.58$	$\mu = 1.69$
	−270.006 842	−270.022 056	−270.074 097	−270.011 978	−270.077 617
4b	$\Delta E = 6.94$	$\Delta E = 6.95$	$\Delta E = 6.85$	$\Delta E = 6.87$	$\Delta E = 6.89$
	$\mu = 1.78$	$\mu = 1.78$	$\mu = 1.75$	$\mu = 1.90$	$\mu = 1.89$
	−270.007 203	−270.022 233 1	−270.074 077	−270.011 957	−270.077 352
5a	$\Delta E = 6.72$	$\Delta E = 6.84$	$\Delta E = 6.87$	$\Delta E = 6.88$	$\Delta E = 7.05$
	$\mu = 1.48$	$\mu = 1.48$	$\mu = 1.56$	$\mu = 1.59$	$\mu = 1.58$
	−270.006 137	−270.021 348	−270.073 326	−270.011 229	−270.076 828
5b	$\Delta E = 7.39$	$\Delta E = 7.39$	$\Delta E = 7.34$	$\Delta E = 7.34$	$\Delta E = 7.38$
	$\mu = 1.76$	$\mu = 1.76$	$\mu = 1.74$	$\mu = 1.88$	$\mu = 1.87$

TABLE 17: MP2 Single Point Total Energies (H) and Relative Energies (Δ*E*, Kcal/Mol) of the Chair (1), Twist (4), and Boat (5) Conformers of Tetrahydro-2*H*-pyran

	MP2//6-31G(d)	MP2//6-31G(d,p)	MP2//6-311G(d,p)	MP2//6-31+G(d)	MP2//6-311+G(d,p)
1	−270.842 417 $\Delta E = 0.0$	−270.923 686 $\Delta E = 0.0$	−271.024 522 $\Delta E = 0.0$	−270.857 075 $\Delta E = 0.0$	−271.032 827 $\Delta E = 0.0$
4a	−270.832 829 $\Delta E = 6.02$	−270.914 163 $\Delta E = 5.98$	−271.015 314 $\Delta E = 5.78$	−270.847 361 $\Delta E = 6.10$	−271.023 468 $\Delta E = 5.88$
4b	−270.830 677 $\Delta E = 7.37$	−270.911 988 $\Delta E = 7.34$	−271.013 194 $\Delta E = 7.11$	−270.845 700 $\Delta E = 7.14$	−271.021 691 $\Delta E = 6.99$
5a	−270.831 266 $\Delta E = 7.00$	−270.912 519 $\Delta E = 7.01$	−271.013 746 $\Delta E = 6.76$	−270.845 667 $\Delta E = 7.16$	−271.021 794 $\Delta E = 6.92$
5b	−270.829 565 $\Delta E = 8.06$	−270.910 929 $\Delta E = 8.01$	−271.012 029 $\Delta E = 7.84$	−270.844 323 $\Delta E = 8.00$	−271.020 584 $\Delta E = 7.68$

TABLE 18: Density Functional Theory Total Energies (H), Relative Energies (Δ*E*, Kcal/Mol), and Dipole Moments (*μ*, D) of the Chair (1), Twist (4), and Boat (5) Conformers of Tetrahydro-2*H*-pyran

	SVWN/DN*	SVWN/DN**	pBP/DN*	pBP/DN**	BLYP	B3LYP	B3PW91	B3P86
1	−269.485 469 $\Delta E = 0.0$ $\mu = 1.51$	−269.504 002 $\Delta E = 0.0$ $\mu = 1.48$	−271.847 751 $\Delta E = 0.0$ $\mu = 1.59$	−271.868 666 $\Delta E = 0.0$ $\mu = 1.55$	−271.626 003 $\Delta E = 0.0$ $\mu = 1.35$	−271.770 638 $\Delta E = 0.0$ $\mu = 1.41$	−271.673 380 $\Delta E = 0.0$ $\mu = 1.42$	−272.644 597 $\Delta E = 0.0$ $\mu = 1.42$
4a	−269.474 603 $\Delta E = 6.82$ $\mu = 1.54$	−269.493 313 $\Delta E = 6.71$ $\mu = 1.50$	−271.837 995 $\Delta E = 6.12$ $\mu = 1.83$	−271.859 038 $\Delta E = 6.04$ $\mu = 1.58$	−271.616 587 $\Delta E = 5.91$ $\mu = 1.36$	−271.761 161 $\Delta E = 5.95$ $\mu = 1.43$	−271.664 068 $\Delta E = 5.84$ $\mu = 1.43$	−272.635 165 $\Delta E = 5.92$ $\mu = 1.43$
4b	−269.473 103 $\Delta E = 7.76$ $\mu = 1.75$	−269.491 791 $\Delta E = 7.66$ $\mu = 1.71$	−271.836 295 $\Delta E = 7.19$ $\mu = 1.83$	−271.857 849 $\Delta E = 6.79$ $\mu = 1.79$	−271.614 887 $\Delta E = 6.98$ $\mu = 1.59$	−271.759 526 $\Delta E = 6.97$ $\mu = 1.64$	−271.662 357 $\Delta E = 6.92$ $\mu = 1.65$	−272.633 438 $\Delta E = 7.00$ $\mu = 1.66$
5a	−269.474 002 $\Delta E = 7.20$ $\mu = 1.40$	−269.492 902 $\Delta E = 6.97$ $\mu = 1.36$	−271.837 620 $\Delta E = 6.36$ $\mu = 1.50$	−271.858 691 $\Delta E = 6.26$ $\mu = 1.43$	−271.616 075 $\Delta E = 6.23$ $\mu = 1.26$	−271.7604 20 $\Delta E = 6.41$ $\mu = 1.33$	−271.663 232 $\Delta E = 6.37$ $\mu = 1.33$	−272.634 302 $\Delta E = 6.46$ $\mu = 1.33$
5b	−269.472 826 $\Delta E = 7.93$ $\mu = 1.75$	−269.491 811 $\Delta E = 7.65$ $\mu = 1.71$	−271.836 705 $\Delta E = 6.93$ $\mu = 1.81$	−271.857 837 $\Delta E = 6.80$ $\mu = 1.78$				

TABLE 19: Thermochemistry for Conformers of Tetrahydro-2*H*-pyran

level	conformer	ZPE, kcal/mol	*E* (Thermal), kcal/mol	entropy (S°), cal/mol-K
HF/6-31G(d)	**1**	98.920	102.144	72.595
BLYP/6-31G(d)		89.549	93.060	74.161
B3LYP/6-31G(d)		92.376	95.791	73.615
B3PW91/6-31G(d)		92.587	95.996	73.564
B3P86/6-31G(d)		92.684	96.088	73.524
HF/6-31G(d)	**2a**	98.565	102.646	72.510
HF/6-31G(d)	**2b**	98.858	101.898	72.264
HF/6-31G(d)	**2c**	98.729	101.864	73.720
HF/6-31G(d)	**3a**	98.548	101.638	72.618
HF/6-31G(d)	**3b**	98.888	101.991	73.708
HF/6-31G(d)	**3c**	98.668	101.800	73.452
HF/6-31G(d)	**3d**	98.479	101.707	74.505
HF/6-31G(d)	**4a**	98.851	102.245	74.215
BLYP/6-31G(d)		89.369	93.094	76.555
B3LYP/6-31G(d)		92.237	95.852	75.735
B3PW91/6-31G(d)		92.489	96.085	75.515
B3P86/6-31G(d)		92.585	96.176	75.486
HF/6-31G(d)	**4b**	98.706	102.156	74.752
BLYP/6-31G(d)		89.253	93.026	75.004
B3LYP/6-31G(d)		92.105	95.774	74.938
B3PW91/6-31G(d)		92.346	95.999	74.712
B3P86/6-31G(d)		92.442	96.092	74.680
HF/6-31G(d)	**5a**	98.787	101.731	71.108
BLYP/6-31G(d)		89.336	92.562	72.621
B3LYP/6-31G(d)		92.184	95.317	72.105
B3PW91/6-31G(d)		92.418	95.765	72.034
B3P86/6-31G(d)		92.513	95.633	72.000
HF/6-31G(d)	**5b**	98.668	101.644	71.283

TABLE 20: Conformational Enthalpies (Δ*H*°, Kcal/Mol) and Free Energies (Δ*G*°, Kcal/Mol) between Conformers of Tetrahydro-2*H*-pyran

	Δ*E*	Δ*H*° 0 K	Δ*H*° 212 K	Δ*G*° 212 K	Δ*H*° 298 K	Δ*G*° 298 K
	chair (**1**) and transition state **2cc**					
HF/6-31G(d)	11.0	10.9	10.8	10.5	10.8	10.5
HF/6-31G(d,p)	11.2	11.0	10.8	10.6	10.9	10.6
HF/6-311G(d,p)	11.2	11.0	10.9	10.6	10.9	10.6
HF/6-31+G(d)	11.0	10.9	10.8	10.5	10.8	10.4
HF/6-311+G(d,p)	11.1	11.0	10.9	10.6	10.9	10.5
MP2//6-31G(d)	12.0	11.8	11.7	11.4	11.7	11.4
MP2//6-31G(d,p)	11.9	11.7	11.6	11.4	11.6	11.3
MP2//6-311G(d,p)	11.6	11.4	11.3	11.1	11.3	11.0
MP2//6-31+G(d)	11.9	11.7	11.6	11.3	11.6	11.3
MP2//6-311+G(d,p)	11.4	11.3	11.2	10.9	11.7	10.8
	chair (**1**) and 2,5-twist (**4a**)					
HF/6-31G(d)	5.92	5.86	5.88	5.47	6.03	5.54
HF/6-31G(d,p)	5.94	5.88	5.90	5.50	6.05	5.57
HF/6-311G(d,p)	6.01	5.95	5.98	5.57	6.12	5.64
HF/6-31+G(d)	6.01	5.95	5.97	5.62	6.12	5.64
HF/6-311+G(d,p)	6.10	6.04	6.06	5.65	6.21	5.72
MP2//6-31G(d)	6.02	5.95	5.98	5.57	6.12	5.64
MP2//6-31G(d,p)	5.98	5.91	5.94	5.53	6.08	5.60
MP2//6-311G(d,p)	5.78	5.72	5.74	5.33	5.89	5.40
MP2//6-31+G(d)	6.10	6.03	6.06	5.65	6.20	5.72
MP2//6-311+G(d,p)	6.87	5.80	5.84	5.43	5.97	5.49
BLYP/6-31G(d)	5.91	5.73	5.87	5.46	5.94	5.23
B3LYP/6-31G(d)	5.95	5.81	5.91	5.50	6.01	5.38
B3PW91/6-31G(d)	5.84	5.75	5.81	5.40	5.93	5.35
B3P86/6-31G(d)	5.92	5.82	5.88	5.47	6.01	5.42

experimental data. Several levels of theory calculated values for the carbon−oxygen bond length in the chair conformer (**1**) which are consistent with the experimentally measured C−O bond length. The MP2/6-31G(d) geometry optimized structure of **1** has a longer C−O bond length than the HF calculated values with the 6-31G(d), 6-31G(d,p), and 6-311G(d,p) basis sets. Among the DFT methods, the pBP and B3LYP calculated C−O bond lengths came closest to the experimental values (1.422 Å to 1.440 Å), whereas the SVWN values were more consistent with the HF 6-31G(d), 6-31G(d,p), and 6-311G(d,p) results. The C2−C3 bond lengths are shorter than the C3−C4 bond lengths. This difference may arise from the electronegative effect. The C2−H_{ax} bond lengths are longer than the C2−H_{eq}

bond lengths in **1**, **2cc**, **4a**, and **4b**, whereas the $C3-H_{ax}$ and $C3-H_{eq}$ and the $C4-H_{ax}$ and $C4-H_{eq}$ bond lengths are essentially the same. The longer $C2-H_{ax}$ bond lengths are probably due to hyperconjugative stereoelectronic interactions.

The mechanism for ring reversal of the chair conformer (**1**) of tetrahydro-2*H*-pyran probably involves a fluxional transition state with several virtually isoenergetic conformations which could serve as transition states for ring reversal. Intrinsic reaction coordinate (IRC) calculations showed that the transition state structures from half-chairs **2b** and **2c** and sofas **3b** and **3c** were precursors to the transition state (**2cc**) between the chair (**1**) and the 2,5-twist conformer (**4a**). The HF calculated barrier to ring reversal for the chair conformer (**1**) of tetrahydro-2*H*-pyran ($\Delta G^\circ = 10.3$ to 10.5 kcal/mol) is in excellent agreement with the experimentally determined value. The calculated energy difference (ΔE) between the chair (**1**) and the 2,5-twist (**4a**) conformers of tetrahydro-2*H*-pyran is in the narrow range of 5.78 to 6.10 kcal/mol.

Acknowledgment. We thank Ms. Monet H. Nguyen and Ms. Nhu N. T. Nguyen for expert assistance and acknowledge the National Science Foundation (Grant Nos. NSF CHE-9015849 and CHE-9311713) for partial support of this work.

Supporting Information Available: Torsional angles, bond angles, bond lengths, and nonbonded distances in the 1-4-twist boat conformer (**4b**) of tetrahydro-2H-pyran. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Hohenberg, P.; Kohn, W. *Phys. Rev.* **1964**, *136*, B864.

(2) Kohn, W.; Sham, L. *J. Phys. Rev.* **1965**, *140*, A1133.

(3) Kohn, W. *J. Comput. Chem.* **1999**, *20*, 1.

(4) Frenking, G. *J. Comput. Chem.* **1999**, *20*, v.

(5) Slater, J. C. *Quantum Theory of Molecular and Vol. 4: The Self-Consistent Field for Molecular Solids*; McGraw-Hill: New York, 1974.

(6) Vosko, H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200.

(7) Becke, A. D. *Phys. Rev.* **1988**, *A38*, 3098.

(8) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(9) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372.

(10) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040.

(11) Becke, A. D. *J. Chem. Phys.* **1997**, *107*, 8554.

(12) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B41*, 785.

(13) Parr, R. G.; Yang, W. *Density-functional Theory of Atoms and Molecules*; Oxford University Press: Oxford, 1989.

(14) Perdew, J. D.; Wang, Y. *Phys. Rev. B* **1986**, *33*, 8800.

(15) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 5048, 8822.

(16) Perdew, J. P. *Phys. Rev. B* **1986**, *34*, 7406.

(17) Perdew, P.; Wang, Y. *Phys. Rev. B* **1992**, *45*, 13 244.

(18) Perdew, J. P.; Chevary, S. H.; Vosko, K. A.; Jackson, M. R.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, *46*, 6671.

(19) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11 623.

(20) Hehre, W. J.; Lou, L. *A Guide to Density Functional Calculations in Spartan*; Wavefunction, Inc.: Irvine, CA, 1997.

(21) Hehre, W. J.; Yu, J.; Klunzinger, P. E.; Lou, L.; *A Brief Guide to Molecular Mechanics and Quantum Chemical Calculations*; 1998, Wavefunction, Inc.: Irvine, CA, 1998. See also the compilations therein.

(22) Foresman, J. B.; Frisch, A. *Exploring Chemistry with Electronic Structure Methods*; Gaussian, Inc.: Pittsburgh, 1996.

(23) Jensen, F. *Introduction to Computational Chemistry*; Wiley: New York, 1999.

(24) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; Chapter 11.

(25) *Conformational Behavior of Six-Membered Rings*; Juaristi, E., Ed.; VCH Publishers: New York, 1995.

(26) Ridell, F. G. *The Conformational Analysis of Heterocyclic Compounds*; Academic Press: New York, 1980.

(27) Lambert, J. B.; Featherman, S. I. *Chem. Rev.* **1975**, *75*, 611.

(28) Cremer, D.; Szabo, K. J. In *Conformational Behavior of Six-Membered Rings*; Juaristi, E., Ed.; VCH Publishers: New York, 1995; Chapter 3.

(29) Freeman, F.; Kasner, M. L.; Hehre, W. J. *J. Mol. Struct. (Theochem)* **1999**, *487*, 87.

(30) Freeman, F.; Kasner, J. A.; Kasner, M. L.; Hehre, W. J. *J. Mol. Struct. (Theochem.)* **2000**, *496*, 19.

(31) Wiberg, K. B.; Murcko, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 4821.

(32) Zheng, Y.-J.; Le Grand, S. M.; Merz, K. M., Jr. *J. Comput. Chem.* **1992**, *13*, 772.

(33) Senderowitz, H.; Aped, P.; Fuchs, B. *Tetrahedron* **1993**, *49*, 3879.

(34) MacSpartan Pro and Spartan are available from Wavefunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612.

(35) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94*, revision B.2; Gaussian, Inc.: Pittsburgh, PA, 1995.

(36) 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.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.

(37) Ma, B.; Lii, J.-H.; Schaeffer, H. F., III; Allinger, N. L. *J. Am. Chem. Soc.* **1996**, *100*, 8763, and references therein.

(38) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

(39) Pauling, L. *Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960; pp 260−261.

(40) Proserpio, D. M.; Hoffmann, R.; Levine, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 3217.

(41) Chauvin, R. *J. Phys. Chem.* **1992**, *96*, 9194.

(42) O'Keeffe, M.; Brese, N. E. *J. Am. Chem. Soc.* **1991**, *113*, 3226.

(43) Halgren, T. *J. Am. Chem. Soc.* **1992**, *114*, 7827.

(44) Allinger, N. L.; Zhou, X.; Bergsma, J. *J. Mol. Struct. (Theochem)* **1994**, *312*, 69.

(45) Carroll, F. A. *Perspectives on Structure and Mechanism in Organic Chemistry*; Brooks/Cole: New York, 1998; pp 5−8.

(46) Wiberg, K. B.; Murcko, M. A. *J. Comput. Chem.* **1987**, *8*, 1124.

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

(48) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(49) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G. *J. Chem. Soc. Perkin Trans. 2* **1987**, S1.

(50) Rao, V. M.; Kewley, R. *Can. J. Chem.* **1969**, *47*, 1289.

(51) Lowe, R. S.; Kewley, R. *J. Mol. Struct.* **1976**, *60*, 312.

(52) Lopez, J. C.; Alonso, J. L.; Villamana, R. M. *J. Mol. Struct.* **1986**, *147*, 67.

(53) Breed, H. E.; Gundersen, G.; Seip, R. *Acta Chem. Scand. A* **1979**, *33*, 225.

(54) Geise, H. J.; Adams, W. J.; Bartell, L. S. *Tetrahedron* **1969**, *25*, 3045.

(55) Almenningen, A.; Seip, H. M.; Willadsen, T. *Acta Chem. Scand.* **1969**, *23*, 2748.

(56) Oyanagi, K.; Fukuyama, T.; Kuchitsu, K.; Bohn, R. K.; Li, S. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 751.

(57) Davis, M.; Hassel, O. *Acta Chem. Scand.* **1963**, *17*, 1181.

(58) Bent, H. A. *Chem. Rev.* **1961**, *61*, 275.

(59) *59. The Anomeric Effect and Associated Stereoelectronic Effects*; Thatcher, G., Ed.; American Chemical Society Symposium Series 539. American Chemical Society: Washington, DC, 1993.

(60) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects of Oxygen*; Springer: Berlin, 1983.

(61) Juaristi, E.; Cuevas, G.; Vela, A. *J. Am. Chem. Soc.* **1994**, *116*, 5796 and references therein.

(62) Juaristi, E.; Cuevas, G. *Tetrahedron* **1992**, *48*, 5019, and references therein.

(63) Bohlmann, F. *Angew. Chem.* **1957**, *69*, 641.

(64) Bohlmann, F. *Chem. Ber.* **1958**, *91*, 2157.

(65) Freeman, F.; Po, H. N.; Hehre, W. J. *J. Comput. Chem.* **1993**, *14*, 1376.

(66) Freeman, F.; Po, H. N.; Hehre, W. J. *J. Comput. Chem.* **1997**, *18*, 1392.

(67) Freeman, F.; Po, H. N.; Hehre, W. J. *J. Mol. Struct. (Theochem)*, **2000**, *503*, 145.

(68) Anet, F. A. L.; Kopelevich, M. *J. Am. Chem. Soc.* **1986**, *108*, 2109.

(69) Perlin, A. S.; Casu, B. *Tetrahedron Lett*. **1969**, 2921.

(70) Wolfe, S.; Pinto, B. M.; Varma, V.; Leung, R. Y. N. *Can. J. Chem*. **1990**, *68*, 1051.

(71) Thomas, H. D.; Chen, K.; Allinger, N. L. *J. Am. Chem. Soc*. **1994**, *116*, 5887.

(72) Kimura, K.; Kubo, M. *J. Chem. Phys*. **1959**, *30*, 151.

(73) Kasai, P. H.; Myers, R. J. *J. Chem. Phys*. **1959**, *30*, 1096.

(74) Bukis, U.; Kasai, P. H.; Myers, R. J. *J. Chem. Phys*. **1963**, *38*, 2753.

(75) Pickett, H. M.; Strauss, H. L. *J. Chem. Phys*. **1970**, *53*, 376.

(76) Astrup, E. E. *Acta Chem. Scand*. **1973**, *27*, 1345.

(77) Busetti, V.; Del Pra, A.; Mammi, M. *Acta Crystallogr*. **1969**, *B25*, 1191.

(78) Krajewski, J. W.; Gluzinski, P.; Andrianov, V. M.; Zhbankov, R. G. *Bull. Pol. Acad. Sci., Chem*. **1989**, *37*, 353; *Chem. Abstr*. 1**991**, *114*, 80 747.

(79) No, K. T.; Grant, J. A.; Scherega, H. A. *J. Phys. Chem*. **1990**, *94*, 4732.

(80) Engerholm, G. G.; Luntz, A. C.; Gwinn, W. D.; Harris, D. O. *J. Chem. Phys*. **1969**, *50*, 2446.

(81) Wiberg, K. B.; Hammer, J. D.; Castejon, H.; Bailey, W. F.; DeLeon, E. L.; Jarret, R. M. *J. Org. Chem*. **1999**, *64*, 2085.

(82) Wiberg, K. B.; Castejon, H.; Bailey, W. F.; Ochterski, J. *J. Org. Chem*. **2000**, *65*, 1181.

(83) Lambert, J. B.; Keske, R. G.; Weary, D. K. *J. Am. Chem. Soc*. **1967**, *89*, 5921.

(84) Lambert, J. B.; Mixan, C. E.; Johnson, D. H. *J. Am. Chem. Soc*. **1973**, *95*, 4634.

(85) Friebolin, H.; Schmid, H. G.; Kabuss, S.; Faisst, W. *Org. Magn. Reson*. **1969**, *1*, 67.

(86) Jensen, F. R.; Neese, R. A. *J. Am. Chem. Soc*. 1**971**, *93*, 6329.

(87) Anet, F. A. L.; Sandstrom, J. *J. Chem. Soc., Chem. Comm*. 1**971**, 1558.

(88) Chapman, D. M.; Hester, R. E. *J. Phys. Chem. A* **1997**, *101*, 3382.

(89) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 686−690 and references therein.

(90) Bushweller, C. H. In *Conformational Behavior of Six-Membered Rings*; Juaristi, E., Ed.; VCH Publishers: New York, 1995; Chapter 2.