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From Cyclohexane to 2-Hydroxy-3-oxanone: A Conformation Study

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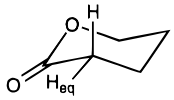
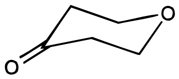
Density functional calculations are reported on all stable chair and twist-boat conformations of cyclohexane, cyclohexanol, oxane, cyclohexanone, 3-oxanone, 2-oxanol, 2-hydroxycyclohexanone, and 2-hydroxy-3-oxanone. With just one exception, the chair conformation is predicted to lie lower in energy than the twist-boat conformations. Either individually replacing a hydroxyl for hydrogen, introducing an oxygen into the ring, or incorporating a carbonyl group into cyclohexane reduces the energy difference between chair and twist-boat. In cyclohexanol the equatorial chair lies lower in energy than the axial chair. The axial chair anomers of 2-oxanol, 2-hydroxycyclohexanone, and 2-hydroxy-3-oxanone lie lower in energy than the equatorial chair anomers. In 2-hydroxy-3-oxanone the equatorial chair lies higher in energy than one of the twist-boat conformations. Stereoselective reduction of 2-hydroxy-3-oxanones is shown to result from sterically controlled attack.

Introduction

It has long been established that the chair conformation is the most stable conformation of cyclohexane. The same is also true for the pyranose ring of carbohydrates. The *δ*-lactones (**I**), however, have conformations that are somewhat distorted away from the chair.[1] It is argued[1] this distortion is in response to steric interactions between the carbonyl group and the equatorial C−H bond on the adjacent carbon atom. The rings of 4-oxanones (**II**) are also rather flat and the calculated ring-inversion barrier is small.[2] The shorter lengths of the bonds to the ring oxygen atom (1.45 Å) compared to the C−C bond lengths (1.55 Å) may contribute to ring flattening.[2] However, 1,4-dioxane with two ring-oxygen atoms has a chair conformation that is slightly more puckered than cyclohexane.[3]



I



II

The conformation of the ring in cyclic-ketone systems plays an important role in determining the stereoselectivity of nucleophilic addition to the carbonyl. It is observed that the more flattened the ring, the more axial the attack.[4] There are many hypotheses that offer explanations for the preferred direction of attack. In flattened ring systems axial delivery enables the nucleophile to adopt an optimal antiperiplanar arrangement with vicinal C−H bonds in the transition state.[5] Alternatively, puckered rings may experience less *torsional strain* if attack by the nucleophile occurs equatorially.[6] Also, steric effects may prevent axial attack by bulky nucleophiles when the ring is more puckered and are likely to be a dominant influence on the outcome.[2] Inherently, conformational preferences will play an important role in discriminating the direction of attack.

Presented here are the results of calculations on the chair and twist-boat conformations of a variety of six-membered-ring systems which include cyclohexane, cyclohexanol, oxane (tetrahydropyran), cyclohexanone, 2-oxanol, 3-oxanone, 2-hydroxycyclohexanone, and 2-hydroxy-3-oxanone. The effect of replacing atoms in cyclohexane with oxygen on the relative energies and structures of the various conformations is examined.

Methods

Standard ab initio molecular orbital[7] calculations were performed using the GAUSSIAN 94 program.[8] Geometries were optimized at the HF/6-31G(d) level. Frequencies at this level, scaled by 0.8929, were used to obtain zero-point vibrational corrections[9] and enthalpy temperature corrections.[10]

Density functional theory (DFT) calculations were performed using the DGauss program.[11] Calculations were carried out using the gradient-corrected exchange and correlation functionals due to Becke (B)[12] and Lee, Yang, and Parr(LYP).[13] Geometries were optimized using the DZVP(A1)[14] basis, and single-point energies evaluated using the TZVP(A2)[14] basis. Calculated energies and corrections are presented in Table 1. Unless otherwise noted, energies quoted are enthalpies at 298 K and geometrical parameters those optimized at the B-LYP/DZVP-(A1) level. Optimized geometries (Cartesian coordinates) at this level are presented as Supporting Information.

Results and Discussion

On the potential energy surface of cyclohexane there are only two types of minima, the chair (**1**) and twist-boat (**3**), and two (first-order) transition states, the half-chair (**2**) and boat (**4**). The half-chair and twist-boat are calculated to lie 36.0 ($\Delta G^{\ddagger}_{298}$) and 23.5 ($\Delta G_{298}$) kJ mol^{-1} above the chair, respectively.[15] The boat lies 4.8 ($\Delta G^{\ddagger}_{298}$) kJ mol^{-1} above the twist-boat.[15] The barrier to conversion in the chair is known from experiment[16] to be 43.5 kJ mol^{-1}, in good agreement with the calculated value. The free energy of activation of the twist-boat to chair transformation is 22.2 kJ mol^{-1} in an argon matrix,[17] significantly larger than the calculated barrier of 12.5 kJ mol^{-1}. The

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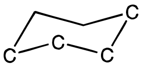
TABLE 1: Calculated Energies (hartrees), Energy Corrections (millihartrees), and Relative Energies (kJ mol^{-1}) of Various Conformations of Ring Systems

		B-LYP/ TZVP(A2)	ZPVE	ΔH_{298-0}	H_{298}	ΔH_{298}
cyclohexane						
1	C	−235.802 20	162.90	6.88	−235.632 42	0.0
2	H	−235.787 41	162.71	6.68	−235.618 02	37.8
3	S	−235.792 66	162.85	7.14	−235.622 67	25.6
4	B	−235.791 55	162.73	6.41	−235.622 41	26.3
cyclohexanol						
5	C	−311.043 93	167.49	8.05	−310.868 39	0.0
6	C	−311.042 56	167.70	7.99	−310.866 87	4.0
7	S	−311.034 56	167.60	8.18	−310.858 78	25.2
8	S	−311.034 39	167.48	8.29	−310.858 62	25.7
9	S	−311.033 92	167.66	8.19	−310.858 07	27.1
oxane						
10	${}^{4}C_{1}$, ${}^{1}C_{4}$	−271.731 13	140.76	6.58	−271.583 79	0.0
11	${}^{3}S_{1}$, ${}^{1}S_{3}$	−271.722 30	140.65	6.83	−271.574 82	23.6
12	${}^{5}S_{1}$, ${}^{1}S_{5}$	−271.721 30	140.45	6.92	−271.573 93	25.9
cyclohexanone						
13	C	−309.853 49	144.92	7.62	−309.700 95	0.0
14	S	−309.847 89	144.66	7.81	−309.695 42	14.4
3-oxanone						
15	C	−345.777 35	122.43	7.38	−345.647 54	0.0
16	${}^{1}S_{3}$, ${}^{3}S_{1}$	−345.774 77	122.35	7.50	−345.644 92	6.9
2-oxanol						
17	${}^{1}C_{4}{}^{\alpha}$, ${}^{4}C_{1}{}^{\beta}$	−346.982 74	145.85	7.57	−346.829 32	0.0
18	${}^{4}C_{1}{}^{\alpha}$, ${}^{1}C_{4}{}^{\beta}$	−346.981 32	145.31	7.70	−346.828 31	2.7
19	${}^{2}S_{0}{}^{\alpha}$, ${}^{0}S_{2}{}^{\beta}$	−346.977 40	145.67	7.77	−346.823 96	14.1
20	${}^{1}S_{5}{}^{\alpha}$, ${}^{5}S_{1}{}^{\beta}$	−346.975 46	145.53	7.84	−346.822 09	19.0
21	${}^{1}S_{3}{}^{\alpha}$, ${}^{3}S_{1}{}^{\beta}$	−346.975 43	145.74	7.78	−346.821 82	19.7
22	${}^{0}S_{2}{}^{\alpha}$, ${}^{2}S_{0}{}^{\beta}$	−346.972 80	145.26	7.94	−346.819 60	25.5
23	${}^{3}S_{1}{}^{\alpha}$, ${}^{1}S_{3}{}^{\beta}$	−346.972 45	145.27	7.91	−346.819 27	26.4
24	${}^{5}S_{1}{}^{\alpha}$, ${}^{1}S_{5}{}^{\beta}$	−346.972 59	145.67	7.77	−346.819 15	26.7
2-hydroxycyclohexanone						
25	C	−385.088 36	149.59	8.82	−384.929 95	0.0
26	C	−385.086 92	149.38	8.82	−384.928 72	3.2
27	S	−385.081 95	149.38	8.99	−384.923 58	16.7
28	S	−385.080 77	149.12	9.09	−384.922 56	19.4
29	S	−385.080 70	149.20	9.12	−384.922 38	19.9
30	S	−385.080 33	149.12	9.05	−384.922 16	20.4
31	S	−385.079 72	149.19	9.17	−384.921 36	22.6
32	S	−385.079 27	149.29	9.04	−384.920 94	23.7
2-hydroxy-3-oxanone						
33	${}^{1}C_{4}{}^{\alpha}$, ${}^{4}C_{1}{}^{\beta}$	−421.026 10	127.56	8.40	−420.890 14	0.0
34	${}^{1}S_{3}{}^{\alpha}$, ${}^{3}S_{1}{}^{\beta}$	−421.021 68	127.30	8.57	−420.885 81	11.4
35	${}^{4}C_{1}{}^{\alpha}$, ${}^{1}C_{4}{}^{\beta}$	−421.019 00	126.97	8.50	−420.883 53	17.4
36	${}^{0}S_{2}{}^{\alpha}$, ${}^{2}S_{0}{}^{\beta}$	−421.018 87	127.30	8.57	−420.883 00	18.7
37	${}^{2}S_{0}{}^{\alpha}$, ${}^{0}S_{2}{}^{\beta}$	−421.015 51	126.96	8.75	−420.879 80	27.1
38	${}^{3}S_{1}{}^{\alpha}$, ${}^{1}S_{3}{}^{\beta}$	−421.015 34	126.87	8.69	−420.879 78	27.2

cryogenic matrix may contribute to the disagreement . The energy difference between chair and twist-boat conformations is in good agreement with the previous theoretical study by Dixon and Komornicki ($\Delta H_{298} = 28.9$ kJ mol^{-1} compared with 25.6 kJ mol^{-1} calculated here).[18] There is, however, quite a large difference in the relative energy of the half-chair and boat transition-state conformations ($\Delta H_{298} = 50.2$ and 33.1 kJ mol^{-1}, respectively, compared with 37.8 and 26.3 kJ mol^{-1} calculated here). The C−C bond length in the chair conformer is found to be 1.551 Å, and the CCC angle calculated here, 111.8°, is very similar to the value found by electron diffraction measurements,[3] 111.6°. There are two types of carbon atom in the twist-boat conformation, either apical (C_a) or lateral (C_l). Dihedral angles in the twist-boat are either staggered ($C_lC_aC_aC_l$, 60.0°) or partially eclipsed ($C_lC_lC_aC_a$, 29.1°), whereas in the chair they are all roughly staggered, 53.9°. Bonds between apical carbons (C_a-C_a, 1.548 Å) are 0.015 Å shorter than those between apical and lateral atoms (C_a-C_l, 1.563 Å), resulting from the staggered arrangement about the C_a-C_a bond. The angles $C_aC_lC_a$ (113.3°) are slightly larger than the $C_aC_aC_l$ angles (112.0°), and both are larger than the CCC angles in the chair conformation, indicating a ring that is slightly flatter than the chair. These features are present in the study by Dixon and Komornicki.[18]



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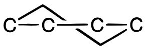

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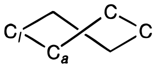

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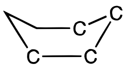
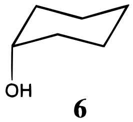


4

There are two chair conformations of cyclohexanol, with the hydroxyl group either equatorial (**5**) or axial (**6**). The equatorial conformer lies 4.0 kJ mol^{-1} below the axial. The twist-boat conformers **7** and **8**, with the hydroxyl group in the isoclinal and equatorial positions, respectively, lie 25.2 and 25.7 kJ mol^{-1} above **5**. Lying 27.1 kJ mol^{-1} higher than **5** is the twist boat **9**, in which the hydroxyl group is in the axial position. Bulky substituents tend, in general, to assume equatorial or isoclinal rather than axial positions. The difference in energy for the twist-boat conformers of cyclohexanol is, however, only 1.4 kJ mol^{-1}. Replacing a hydrogen atom with a hydroxyl group in cyclohexane, therefore, has very little effect upon the energy difference between chair and twist-boat and produces only small changes on the geometry of cyclohexane.

5



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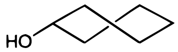

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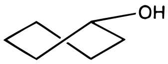

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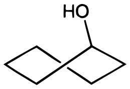
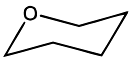


9

In oxane there are three minima, one chair (**10**) and two twist-boat conformations (**11**, **12**), which are calculated to lie 23.6 and 25.9 kJ mol^{-1} above the chair, respectively. Introduction of an oxygen atom into the ring of cyclohexane thus also has little effect upon the energy difference between the twist-boat and chair conformations. The C−C bonds are similar to those found in cyclohexane. Concordantly, the C−O bonds in **10** and the O−C$_a$ bond in **11** (1.448 Å) are shorter than the C−O bonds between apical and lateral atoms in **11** and **12** (1.456 Å). Also, the COC angle in **12** in the lateral position (115.0°) is larger than in either **10** (111.3°) or **11** (112.0°). For comparison, the COC angle in dioxane from electron diffraction experiments[3] is 112.5°. In dimethyl ether, the C−O bond and COC angle are calculated to be 1.436 Å and 111.9°, respectively.



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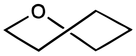

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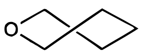
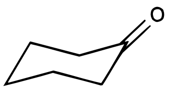


12

Only two minima could be located for cyclohexanone, the chair (**13**) and one twist-boat (**14**). The twist-boat is distorted toward the boat conformation. The calculated energy difference between these two conformations is 14.4 kJ mol^{-1}. Therefore, the energy difference between chair and twist-boat conformations of cyclohexane is almost halved by the introduction of a carbonyl group. The CC(═O)C angle in **13** and **14** is 115.9° and 115.3°, respectively. The C−C bonds adjacent to the carbonyl bond are significantly shorter (1.532−1.540 Å) than the other ring C−C bonds (1.548−1.569 Å). In **14** the bonds between apical atoms (1.548, 1.554 Å) are smaller than the bonds between apical and lateral atoms (1.556, 1.569 Å); however, the distinction is considerably smaller than that observed in cyclohexane as a result of the distortion toward the boat conformation. The calculated C−C bond and CCC angle in acetone are 1.533 Å and 116.6°, respectively.



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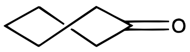
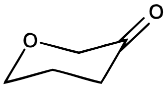


14

No stable minima with either $^{2}S_{0}$ or $^{5}S_{1}$ conformations of 3-oxanone could be found, while the twist-boat **16** is distorted toward the $^{3,0}B$ conformation (as was found in cyclohexanone). The energy difference between the chair (**15**) and twist-boat (**16**) conformations is just 6.9 kJ mol^{-1}. The effect of introducing a carbonyl group or a ring oxygen into cyclohexane reduces the energy of the twist-boat relative to the chair by 11.2 and 2.0 kJ mol^{-1}, respectively. The combined effect of these changes yields a predicted difference between chair and twist-boat for 3-oxanone of 12.4 kJ mol^{-1}. This is larger than the observed difference of 6.9 kJ mol^{-1}, suggesting a modest cooperative effect of 5.5 kJ mol^{-1} from the two oxygen atoms. The geometrical features are similar to those in cyclohexanone and oxane. Derivatives of 3-oxanone have been observed to adopt twist-boat,[19] chair,[20] and $^{3,0}B$ boat[21] conformations.



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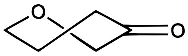
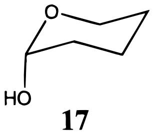


16

There exist two possible anomers of 2-oxanol and therefore eight possible minima conformations (**17**−**24**). For the chair conformations, the hydroxyl group in the equatorial position (**18**) is 2.7 kJ mol^{-1} higher than in the axial position (**17**). The twist-boat conformations **19**−**24** lie between 14.1 and 26.7 kJ mol^{-1} above **17**. It is generally expected that bulky substituents on the oxane ring will prefer equatorial positions to ensure minimal steric interaction. However, conformations **20** and **21**, which have the hydroxyl group in the axial position, are lower in energy than **24** and **23**, in which it is equatorial. Both **17** and **21** have a lone-pair of electrons on the ring oxygen antiperiplanar to the O(H)−C bond (the O(H)−C−O−C dihedral angle is approximately 60°). As a result of hyperconjugation in **17**, the C(OH)−O (1.441 Å) bond is 0.011 Å shorter and the O−C(H$_2$) (1.463 Å) bond 0.011 Å longer than in **18**, where the O(H)−C bond is trans to the O−C(H$_2$) bond. In **21** the C(OH)−O bond, between two apical atoms, is shorter, 1.433 Å, while the C−O bond is longer, 1.473 Å, than in **17**. In the twist-boat conformations **19** and **20** the C(OH)−C bond is not quite antiperiplanar with the ring-oxygen lone-pair electrons (O(H)−C−O−C ≅ 90°). Hyperconjugation in **19** reduces the C(OH)−O bond (involving the lateral carbon, 1.450 Å) such that it is slightly shorter than the O−C(H$_2$) bond (involving both apical atoms, 1.457 Å), while in **20**, the C(OH)−C and O−C(H$_2$) bonds are 1.442 and 1.466 Å, respectively, similar to those lengths found in the axial chair **17**. The C−O(H) bond in **18** is 0.038 Å shorter than in the equatorial chair of cyclohexanol, **5**. The C−O(H) bonds in **17**, **19**-**21** are roughly 0.025 Å longer than in the other conformations as a result of hyperconjugation.



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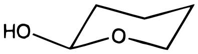

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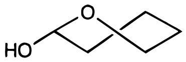

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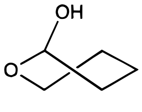

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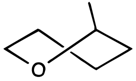

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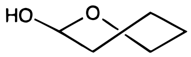

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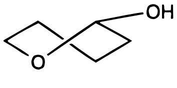

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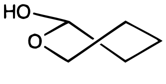


24

In cyclohexanol the equatorial chair lies 4.0 kJ mol^{-1} lower than the axial chair, while in 2-oxanol the equatorial chair lies 2.7 kJ mol^{-1} higher than the axial chair, indicating an anomeric effect in 2-oxanol of 6.7 kJ mol^{-1}. The anomeric difference in

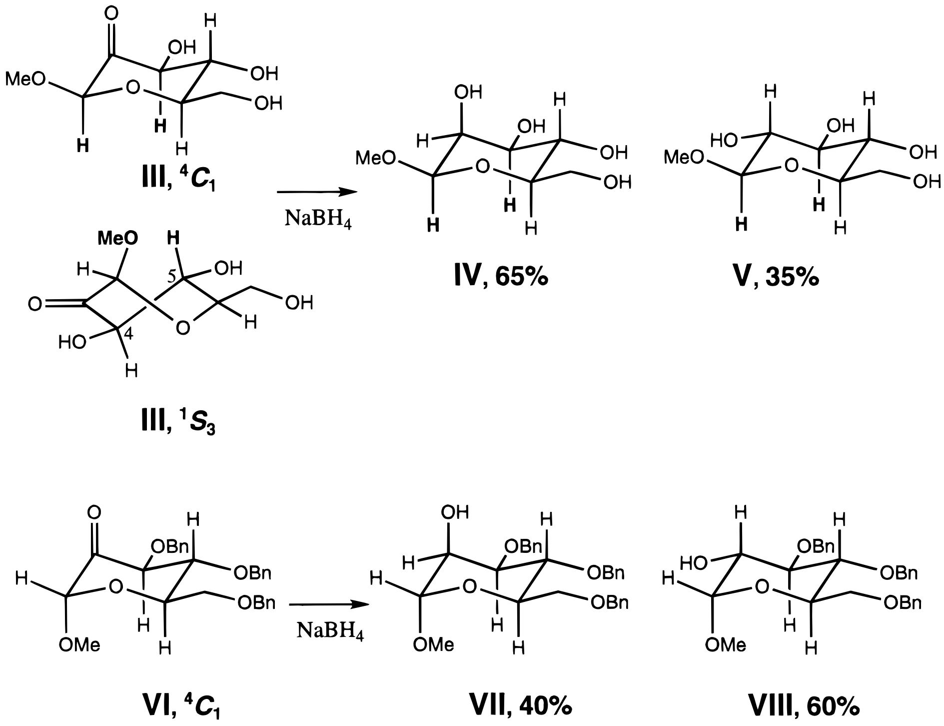
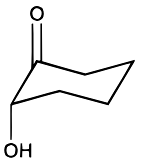


Figure 1.

the twist-boat conformations is slightly larger, 8.1−11.4 kJ mol^{-1}. So for example, where **8** lies 1.4 kJ mol^{-1} lower in energy than **9**, **24** lies 7.7 kJ mol^{-1} higher than **20**, a difference of 9.1 kJ mol^{-1}. The twist-boats **19**−**21** all have energies relative to **17** that are less than the sum of the differences calculated in oxane and cyclohexanol (−5.1, −4.4, and −1.4 kJ mol^{-1}, respectively), whereas **22**−**24** have relative energies that are greater (6.3, 6.7, and 4.7 kJ mol^{-1}, respectively). So for example, replacement of a hydrogen in cyclohexane by a hydroxyl on an apical carbon in an equatorial position (**8**) reduces the energy difference between the (axial) chair and twist-boat by 4.4 kJ mol^{-1}, and introduction of an oxygen into the ring in the apical position reduces the energy difference between chair and twist-boat by 2.0 kJ mol^{-1}; the combined effect, a predicted energy difference between **17** and **19**, of 19.2 kJ mol^{-1}, is 5.1 kJ mol^{-1} greater than the calculated energy difference of 14.1 kJ mol^{-1}.

For 2-hydroxycyclohexanone, the axial chair conformation (**25**) is of lowest energy, with the equatorial chair lying 3.2 kJ mol^{-1} higher in energy. The twist-boat conformations (**27**−**32**) lie 16.7−23.7 kJ mol^{-1} above **25**. It would appear that the effects of the hydroxyl and carbonyl groups are not cooperative; all twist-boats (**27**−**32**) lie higher in energy (above the chair) than does the twist-boat of cyclohexanone **16** lie above the chair **15**.

Introduction of the carbonyl group adjacent to the hydroxyl group of 2-oxanol has a dramatic effect upon the relative energies of the different conformations. The lowest energy conformation of 2-hydroxy-3-oxanone is the chair (**33**) with the hydroxy group in the axial position (α-anomer). The equatorial chair (**35**, β-anomer) lies 17.4 kJ mol^{-1} higher than the axial conformer. This difference is considerably larger than found in either 2-oxanol (**17**, **18**) or 2-hydroxycyclohexanone (**25**, **26**). Of the four twist-boat conformers located, one in the $^1S_3$ conformation (**34**) lies 6 kJ mol^{-1} lower than the equatorial chair and 11.4 kJ mol^{-1} higher than the axial chair. In comparison, the energy difference between the $^1C_4$ and $^1S_3$ conformations of 2-hydroxycyclohexanone (**29**, **25**) and 2-oxanol (**21**, **17**) is 19.9 and 19.7 kJ mol^{-1}, respectively, while for 3-oxanone (**16**, **15**) the difference is 6.9 kJ mol^{-1}. This difference in 2-hydroxy-3-oxanone is therefore intermediate between these related systems. Conversely, the energy of **37** (relative to the chair) is larger than the relative energies of either of the closely related structures **23** or **30**.



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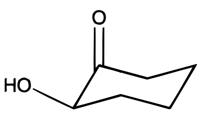

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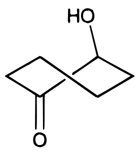

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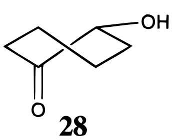

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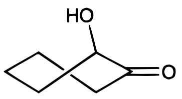

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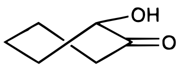

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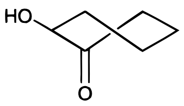

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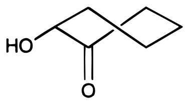

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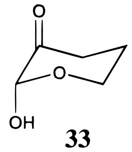
The two lowest energy conformations, **33** and **34**, have the O(H)−C bond antiperiplanar to a lone-pair of electrons on the ring oxygen. The C(OH)−O bond (between apical atoms, 1.427 Å) and O−C bond (between apical and lateral atoms, 1.471 Å) in **34** are shorter and longer, respectively, than those in **33** (1.437 and 1.465 Å). The C−C(OH) bond adjacent to the carbonyl group is roughly 0.025 Å longer than the other C−C bond adjacent to the carbonyl in **33**, **34**, **35**, and **38**, and 0.038 Å longer in **36** and **37**, where the atoms in the C−C bond are both apical. There are many examples of derivatives of

2-hydroxy-3-oxanone that adopt the axial chair conformation[22] and at least one example where the $^5S_1$ conformation is adopted.[23] The $^5S_1$ conformation of 2-hydroxy-3-oxanone collapses to the $^1S_3$ conformation.



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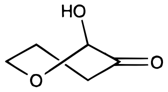

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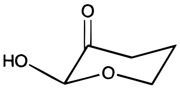

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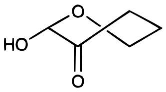

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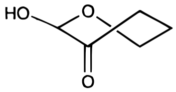

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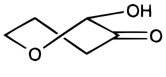

38

Borohydride reduction of **III** yields **IV** in significantly larger amounts than **V**.[24] (See Figure 1.) In the chair conformation, axial attack is hindered by steric interactions between the one axial nonvicinal C_5-H hydrogen atom, whereas stereoelectronic effects including torsional repulsion between the bonds of the two vicinal C−H bonds (C_2-H and C_4-H) and the bond forming between the hydride and the carbon of the carbonyl group will restrict equatorial attack. According to the Cieplak model,[25] the vicinal C−H bonds favor axial attack. It would appear, then, that π-facial selectivity in **III** is not sterically controlled. The calculations here suggest, however, that the conformation of **III** is most likely twist-boat, $^1S_3$. Attack leading to axial addition is hindered by the methoxy group and the C_5-H hydrogen. The C_4-H bond should offer little torsional repulsion to hinder equatorial attack and is the only vicinal bond in an antiperiplanar arrangement capable of fulfilling the Cieplak criteria for directed axial attack. Preferential formation of **IV** therefore would appear to be sterically controlled, in direct contrast to predictions from the chair conformation. The axial chair derivative **VI** yields **VIII** in higher yield than **VII**, as expected for sterically controlled attack.[26] There are in fact many examples that show reduction of the carbonyl of the β-anomer of derivatives of 2-hydroxy-3-oxanone occurs with stereoselective (sometimes total) control, preferentially forming the axial adduct.[27] In contrast, reduction of the α-anomer generally forms the equatorial adduct, although the reaction may be less stereospecific.[28] Conformational flexibility has also been attributed to the unexpected diastereofacial selectivity observed for 4-tetrahydropyrans.[2]

Summary

The energy difference between chair and twist-boat conformations in cyclohexane is 25.6 kJ mol^{-1}. Replacement of a hydrogen in cyclohexane with a hydroxyl (cyclohexanol) has little effect on the energy difference. Similarly, introduction of an oxygen into the ring (oxane) affects the energy difference by no more than 2 kJ mol^{-1}. Incorporation of a carbonyl group (cyclohexanone) almost halves the energy difference. The reduction in the energy difference caused by the hydroxy and carbonyl groups in 3-oxanone is larger than predicted from the reductions observed in cyclohexanol and cyclohexanone, indicating a small cooperative effect. The juxtaposition of the hydroxyl and ring oxygen in 2-oxanol introduces hyperconjugative interactions that lower the energy of conformations in which the C−O(H) bond is antiperiplanar or nearly antiperiplanar with a lone-pair of electrons on the ring oxygen. The equatorial chair in 2-oxanol and 2-hydroxycyclohexanone lies 2.7 and 3.2 kJ mol^{-1} higher, respectively, than the axial chair conformations. Similarly, the lowest energy conformation of 2-hydroxy-3-oxanone is the axial chair. The next lowest energy conformation, lying 11.4 kJ mol^{-1} higher than the axial chair, is a twist-boat. The equatorial chair lies a further 6.0 kJ mol^{-1} higher in energy. The relative energies of the various conformations of 2-hydroxy-3-oxanone cannot be predicted from the calculated relative energies of the related systems. The α-anomers of 2-hydroxy-3-oxanones are predicted to adopt twist-boat conformations. Stereoselective reduction, which favors axial attack, is therefore sterically controlled.

Supporting Information Available: Optimized geometries at the B-LYP/DZVP(A1) level (7 pages). Ordering information is given on any current masthead page.

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