

Ab Initio Calculations on Potential Intermediates in Metal Reductions of Carbonyl Compounds. Stereochemical Considerations

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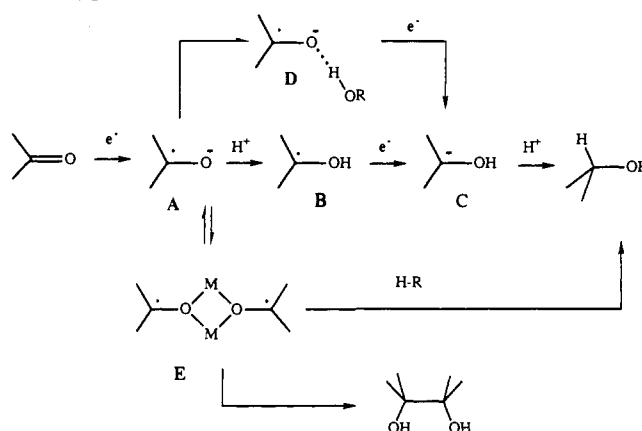
Abstract: Conformational preferences of ketyls, hydroxyalkyl radicals, and hydroxyalkyl carbanions derived from propionaldehyde and cyclohexanone have been studied with ab initio molecular orbital calculations. Each species is significantly pyramidalized toward a tetrahedral geometry, and there is staggering about the single bonds to the pyramidal center. For the 1-hydroxypropyl radical, there is little conformational preference about the C₁-C₂ bond. For both propionaldehyde ketyl and the 1-hydroxypropyl anion, the conformations with the methyl group situated gauche to the C-O bond and anti to the nonbonding orbital (*anti* conformation) are considerably less stable than the conformations with the methyl group gauche to both the C-O bond and the nonbonding orbital (*inside* conformation). The third conformations with the methyl group anti to the C-O bond are least stable (*outside* conformation). Cyclohexanone ketyl, the 1-hydroxycyclohexyl radical, and the 1-hydroxycyclohexyl anion in equatorial conformations are 2.4, 0.8, and 3.9 kcal/mol respectively, more stable than in axial conformations at the MP2/6-31+G* level. The high equatorial preferences of the cyclic species dramatically contrast with the conformational preferences of the acyclic species. The mechanism and stereochemistry of metal reductions are also discussed.

Introduction

Dissolving metal reductions of ketones have been studied extensively in order to understand their detailed mechanism and stereochemical control.¹⁻⁴ Most of the mechanistic discussions are based on the House reaction scheme² as shown in Scheme I. Electron transfer from the dissolving metal to the ketone generates a radical anion intermediate, the ketyl, A. In good proton donor solvents, A accepts a proton to form a hydroxyalkyl radical, B, which leads to a hydroxyalkyl anion, C, upon acceptance of a second electron. Protonation of the carbanion intermediate completes the reaction. However, the detailed mechanism and the stage where product stereochemistry is determined are still controversial. Many believe that the hydroxyalkyl radical (B) conformational equilibrium is where reaction stereoselectivity is determined.² However, Yamamoto et al. recently rationalized the stereoselectivity of dissolving metal reductions of several chiral acyclic ketones using the relative stabilities of hydroxyalkyl anion conformers, C.⁵ Pradhan⁴ suggested that free hydroxyalkyl radicals may not even form in such reactions, since ketyls are weaker bases than alkoxide ions.⁶ He proposed that the hydroxyalkyl anion is formed by simultaneous electron transfer and proton transfer to the hydrogen-bonded ketyl, D.⁴ He suggested that the cyclohexanone ketyl exists in a single form which has the radical orbital extended in the axial direction, and the stereoselectivity is determined by the degree of this radical orbital extension (pyramidalization). Rautenstrauch suggested that the stereoselectivity is likely determined by the relative rates of proton transfer to the two forms of the hydroxyalkyl anion.⁷ When the solvent is not a good proton donor, the ketyl radical anion exists as a dimer, E, and the stereoselectivity is suggested to be determined by hydrogen atom abstraction by the ketyl.^{3,8}

Because of these contrasting mechanistic hypotheses, we undertook a theoretical study of the conformations of these inter-

Scheme I



mediates. We have carried out calculations on the ketyls, hydroxyalkyl radicals, and hydroxyalkyl anions derived from propionaldehyde and from cyclohexanone. Metal counterions were not included at this stage of our work, since it is known that they have little influence on the stereoselectivity when the reaction occurs in good proton donor solvents.⁹ These calculations reveal some interesting conformational features, and provide some clues for the understanding of the detailed mechanism and stereochemical control of the dissolving metal reductions.

Results and Discussion

The calculations were carried out with Pople's GAUSSIAN 88 program.¹⁰ For the ketyl and radical species, calculations were performed with the unrestricted Hartree-Fock (UHF) method, while the restricted Hartree-Fock (RHF) method was used for the anions. Geometry optimizations were generally performed with the 3-21G and 6-31G* basis sets, and the anionic species were also optimized with the 6-31+G and 6-31+G* basis sets.¹¹ The energies were further evaluated with MP2/6-31+G* calculations. Selected geometrical parameters and Mulliken atomic charges are given in Tables I and II, and calculated total energies

(9) A good summary can be found in ref 7.

(10) GAUSSIAN 88: Frisch, M. J.; Head-Gordon, M.; Schlegel, H. B.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R.; Kahn, L. R.; Stewart, J. J. P.; Fluder, E. M.; Topiol, S.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1988.

(11) The calculated relative energies (MP2/6-31+G*) of the anion species are about the same with the 6-31G* and 6-31+G* geometries. The 6-31+G* optimizations were not performed for the ketyl species because similar results are expected.

- (1) Barton, D. H. R.; Robinson, C. H. *J. Chem. Soc.* **1954**, 3045.
 (2) House, H. O. In *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972.
 (3) Huffman, J. W. *Acc. Chem. Res.* **1983**, *16*, 399.
 (4) Pradhan, S. K. *Tetrahedron* **1986**, *42*, 6351.
 (5) Yamamoto, Y.; Matsuoka, K.; Nemoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 4475.
 (6) Neta, P. *Adv. Phys. Org. Chem.* **1976**, *12*, 221.
 (7) Rautenstrauch, V. *J. Chem. Soc., Chem. Commun.* **1986**, 1558.
 (8) (a) Huffman, J. W.; Wallace, R. H. *J. Am. Chem. Soc.* **1989**, *111*, 8691. (b) Rautenstrauch, V. *Tetrahedron* **1988**, *44*, 1613. (c) Huffman, J. W.; Liao, W.-P.; Wallace, R. H. *Tetrahedron Lett.* **1987**, *28*, 3315. (d) Pradhan, S. K.; Thakker, K. R.; McPhail, A. L. *Ibid.* **1987**, *28*, 1813. (e) Rautenstrauch, V.; Willhalm, B.; Thommen, W.; Burger, U. *Helv. Chim. Acta* **1981**, *64*, 2109. (f) Pradhan, S. K.; Sohani, S. V. *Tetrahedron Lett.* **1981**, *22*, 4133. (g) Huffman, J. W.; Alabran, D. M.; Bethea, T. A.; Ruggles, A. C. *J. Org. Chem.* **1964**, *29*, 2963.

Table I. Selected Geometrical Parameters (6-31G* Unless Noted) and Mulliken Atomic Charges (H's Are Summed into Heavy Atoms) of Minimum Energy Conformations of Ketyl, Hydroxyalkyl Radical, and Hydroxyalkyl Anion Derived from Propionaldehyde

| struct | distance ^c | | | $\angle\text{HC}_1\text{C}_2^d$ | D^d | D_{in}^d | D_{anti}^d | D_{out}^d | Q_O | Q_{C_1} | Q_{C_2} | Q_{C_3} |
|----------------|-----------------------|-------------------------------|-------------------------------|---------------------------------|-------|------------|--------------|-------------|--------|-----------|-----------|-----------|
| | OC ₁ | C ₁ C ₂ | C ₂ C ₃ | | | | | | | | | |
| 1 | 1.285 | 1.530 | 1.531 | 111.0 | 32.8 | 53.6 | -66.7 | 175.8 | -0.785 | 0.035 | -0.154 | -0.096 |
| 2 | 1.286 | 1.530 | 1.538 | 110.6 | 34.2 | 60.5 | -59.4 | 177.8 | -0.784 | 0.031 | -0.142 | -0.105 |
| 3 | 1.283 | 1.529 | 1.532 | 110.5 | 32.6 | 47.8 | -67.8 | 169.1 | -0.788 | 0.038 | -0.120 | -0.130 |
| 4 | 1.367 | 1.497 | 1.531 | 119.0 | 34.5 | 58.5 | -63.7 | -179.4 | -0.253 | 0.247 | -0.011 | 0.017 |
| 5 | 1.367 | 1.496 | 1.536 | 119.0 | 35.0 | 53.7 | -68.1 | 169.6 | -0.251 | 0.246 | -0.005 | 0.010 |
| 6 | 1.365 | 1.496 | 1.529 | 119.0 | 34.5 | 51.5 | -64.0 | 173.6 | -0.257 | 0.255 | 0.007 | -0.004 |
| 7 | 1.504 | 1.530 | 1.534 | 104.4 | 67.6 | 74.9 | -47.6 | -165.5 | -0.469 | -0.266 | -0.127 | -0.138 |
| 8 | 1.506 | 1.533 | 1.543 | 104.4 | 67.4 | 69.3 | -53.6 | -176.2 | -0.469 | -0.264 | -0.130 | -0.137 |
| 9 | 1.500 | 1.532 | 1.532 | 104.2 | 67.6 | 66.9 | -50.7 | -173.8 | -0.472 | -0.263 | -0.123 | -0.142 |
| 7 ^a | 1.536 | 1.527 | 1.534 | 107.6 | 66.0 | 77.0 | -45.6 | -162.4 | -0.354 | -0.526 | -0.145 | 0.025 |
| 8 ^a | 1.539 | 1.530 | 1.546 | 107.9 | 65.7 | 67.3 | -55.6 | -177.8 | -0.408 | -0.528 | 0.120 | -0.184 |
| 9 ^a | 1.533 | 1.531 | 1.535 | 107.4 | 66.3 | 66.4 | -50.8 | -173.0 | -0.374 | -0.588 | 0.249 | -0.287 |
| 7 ^b | 1.487 | 1.523 | 1.533 | 105.9 | 64.8 | 76.8 | -45.8 | -162.7 | -0.325 | -0.594 | -0.120 | -0.039 |
| 8 ^b | 1.490 | 1.527 | 1.544 | 106.2 | 64.6 | 68.0 | -55.0 | -177.0 | -0.379 | -0.565 | 0.138 | -0.195 |
| 9 ^b | 1.485 | 1.527 | 1.531 | 105.8 | 65.3 | 65.8 | -51.4 | -173.6 | -0.342 | -0.665 | 0.273 | -0.267 |

^aThe 6-31+G basis set. ^bThe 6-31+G* basis set. ^cIn Å. ^dIn deg.**Table II.** Selected Geometrical Parameters (6-31G* Unless Noted) and Mulliken Atomic Charges (H's Are Summed into Heavy Atoms) of Minimum Energy Conformations of Ketyl, Hydroxyalkyl Radical, and Hydroxyalkyl Anion Derived from Cyclohexanone

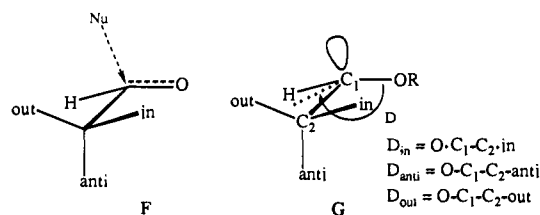
| struct | distance ^b | | | $\angle\text{C}_2\text{C}_1\text{C}_6^c$ | D^c | D_{in}^c | D_{anti}^c | D_{out}^c | Q_O | Q_{C_1} | Q_{C_2} | Q_{C_3} |
|-----------------|-----------------------|-------------------------------|-------------------------------|--|-------|------------|--------------|-------------|--------|-----------|-----------|-----------|
| | OC ₁ | C ₁ C ₂ | C ₂ C ₃ | | | | | | | | | |
| 10 | 1.284 | 1.529 | 1.534 | 112.1 | 32.5 | 44.0 | -72.0 | 166.4 | -0.821 | 0.308 | -0.136 | -0.076 |
| 11 | 1.291 | 1.537 | 1.539 | 109.5 | 40.7 | 46.7 | -73.6 | 165.4 | -0.815 | 0.273 | -0.141 | -0.048 |
| 12 | 1.380 | 1.503 | 1.535 | 118.6 | 35.2 | 51.6 | -64.0 | 174.9 | -0.303 | 0.319 | -0.008 | -0.001 |
| 13 | 1.385 | 1.505 | 1.541 | 115.3 | 40.0 | 42.2 | -79.9 | 160.3 | -0.297 | 0.299 | -0.014 | 0.014 |
| 14 | 1.487 | 1.526 | 1.535 | 106.9 | 64.2 | 65.3 | -52.8 | -174.1 | -0.469 | -0.032 | -0.132 | -0.080 |
| 15 | 1.507 | 1.537 | 1.544 | 107.2 | 66.0 | 64.4 | -58.8 | -179.6 | -0.468 | -0.046 | -0.131 | -0.068 |
| 14 ^a | 1.519 | 1.527 | 1.537 | 108.2 | 63.8 | 65.3 | -52.2 | -173.0 | -0.333 | -0.537 | 0.119 | -0.159 |
| 15 ^a | 1.545 | 1.538 | 1.545 | 108.8 | 65.6 | 63.2 | -60.2 | 178.5 | -0.390 | -0.304 | -0.009 | -0.102 |

^aThe 6-31+G basis set. ^bIn Å. ^cIn deg.**Table III.** Total Energies (-au) and Relative Energies (in Parentheses, kcal/mol) of Minimum Energy Conformations of Ketyl, Hydroxyalkyl Radical, and Hydroxyalkyl Anion Derived from Propionaldehyde

| | ketyl | 1, inside | 2, anti | 3, outside |
|----------------------|---------|------------------|-------------------|-------------------|
| 3-21G/3-21G | | 190.787 55 (0.0) | 190.786 72 (0.5) | 190.784 82 (1.7) |
| 6-31G*/6-31G* | | 191.865 48 (0.0) | 191.865 21 (0.2) | 191.864 15 (0.8) |
| 6-31+G**/6-31G* | | 191.891 24 (0.0) | 191.890 54 (0.4) | 191.890 35 (0.6) |
| MP2/6-31+G**/6-31G* | | 192.472 71 (0.0) | 192.471 75 (0.6) | 192.470 28 (1.5) |
| | radical | 4, inside | 5, anti | 6, outside |
| 3-21G/3-21G | | 191.420 57 (0.0) | 191.420 77 (-0.1) | 191.419 91 (0.4) |
| 6-31G*/6-31G* | | 192.486 44 (0.0) | 192.486 64 (-0.1) | 192.486 58 (-0.1) |
| 6-31+G**/6-31G* | | 192.492 91 (0.0) | 192.492 95 (0.0) | 192.493 16 (-0.1) |
| MP2/6-31+G**/6-31G* | | 193.047 98 (0.0) | 193.048 03 (0.0) | 193.047 54 (0.3) |
| | anion | 7, inside | 8, anti | 9, outside |
| 3-21G/3-21G | | 191.334 82 (0.0) | 191.335 12 (-0.2) | 191.332 94 (1.2) |
| 6-31+G**/6-31+G* | | 192.359 78 (0.0) | 192.358 22 (1.0) | 192.357 97 (1.1) |
| 6-31G*/6-31G* | | 192.401 10 (0.0) | 192.399 70 (0.9) | 192.399 63 (0.9) |
| 6-31+G**/6-31G* | | 192.430 51 (0.0) | 192.428 59 (1.2) | 192.428 95 (1.0) |
| 6-31+G**/6-31+G* | | 192.431 24 (0.0) | 192.429 14 (1.3) | 192.429 55 (1.1) |
| MP2/6-31+G**/6-31G* | | 193.029 65 (0.0) | 193.027 16 (1.6) | 193.026 67 (1.9) |
| MP2/6-31+G**/6-31+G* | | 193.029 92 (0.0) | 193.027 25 (1.7) | 193.026 72 (2.0) |

and relative energies of the species are collected in Tables III and IV.

The *inside*, *anti*, and *outside* conformations of each of the intermediates derived from propionaldehyde are shown in Figure 1. These conformations are assigned in analogy to the nomenclature established for transition states of nucleophilic addition reactions, F. Here, *anti* refers to the position of the methyl group



most distant from the nucleophile, while *inside* and *outside* refer to near or far from the CO bond. There is significant pyramidalization at the C₂ position in each of the structures. This is indicated by the angle D in Table I, which describes the out-of-plane bending of the C-O bond about the H-C₂-C₃ plane. The extent of pyramidalization is about the same for the ketyl and for the radical (33–35°), but it is significantly larger for the anion (65–67°). The orientation of the methyl group has little influence on the degree of pyramidalization.

The nature of pyramidalization of ketyl radical anions and hydroxy radicals has been debated.¹² For comparison, we also

(12) Fukui, K. In *Theory of Orientation and Stereoselection*; Springer-Verlag: West Berlin, 1975; Chapter 7. Dewar, M. J. S. *J. Am. Chem. Soc.* 1984, 106, 669. Kawamura, T.; Koyama, T.; Yonezawa, T. *J. Am. Chem. Soc.* 1973, 95, 3220.

Table IV. Total Energies (–au) and Relative Energies (in Parentheses, kcal/mol) of Equatorial and Axial Conformations of Ketyl, Hydroxyalkyl Radical, and Hydroxyalkyl Anion Derived from Cyclohexanone

| ketyl | 10, equatorial | 11, axial |
|----------------------|------------------|-------------------|
| 3-21G//3-21G | 306.100 40 (0.0) | 306.100 20 (0.1) |
| 6-21G**//6-31G* | 307.819 53 (0.0) | 307.817 67 (1.2) |
| 6-31+G**//6-31G* | 307.844 96 (0.0) | 307.841 08 (2.4) |
| MP2/6-31+G**//6-31G* | 308.820 0 (0.0) | 308.815 41 (2.4) |
| radical | 12, equatorial | 13, axial |
| 3-21G//3-21G | 306.727 99 (0.0) | 306.728 05 (0.0) |
| 6-31G**//6-31G* | 308.434 59 (0.0) | 308.432 29 (1.4) |
| 6-31+G**//6-31G* | 308.442 13 (0.0) | 308.439 38 (1.7) |
| MP2/6-31+G**//6-31G* | 309.386 31 (0.0) | 309.384 97 (0.8) |
| anion | 14, equatorial | 15, axial |
| 3-21G//3-21G | 306.650 15 (0.0) | 306.651 02 (–0.5) |
| 6-31+G**//6-31+G | 308.263 10 (0.0) | 308.259 72 (2.1) |
| 6-31G**//6-31G* | 308.355 89 (0.0) | 308.352 69 (2.0) |
| 6-31+G**//6-31+G | 308.382 81 (0.0) | 308.377 78 (3.2) |
| 6-31+G**//6-31G* | 308.383 67 (0.0) | 308.378 91 (3.0) |
| MP2/6-31+G**//6-31+G | 309.378 16 (0.0) | 309.371 92 (3.9) |

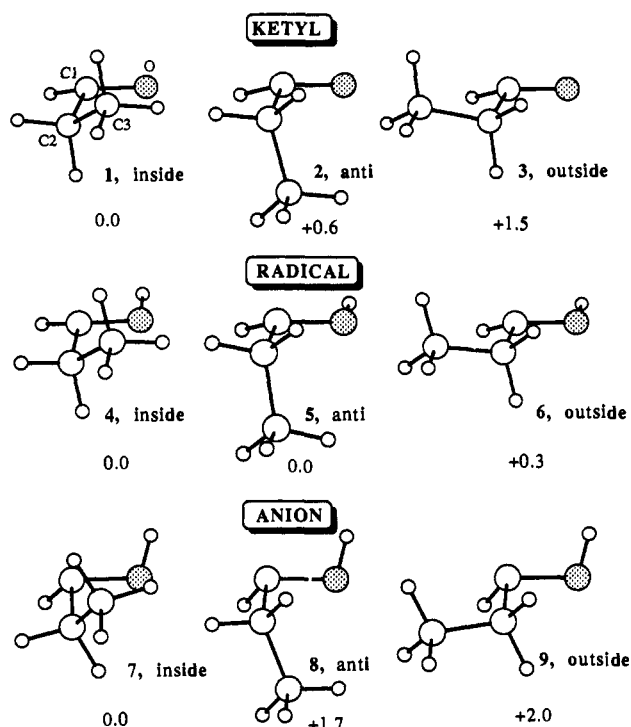


Figure 1. Structures (6-31G* for ketyl and radical, 6-31+G* for anion) of the ketyl, hydroxyalkyl radical, and hydroxyalkyl anion derived from propionaldehyde. The relative energies of the structures calculated by MP2/6-31+G* are also shown.

calculated the intermediates derived from formaldehyde.¹³ MP2/6-31+G* geometrical optimizations indicate formaldehyde ketyl to be planar; i.e., there is no pyramidalization at carbon. The hydroxymethyl radical and the hydroxymethyl anion have similar pyramidalization as in the corresponding structures, 1–9. It is known that methyl radical is planar.¹⁴ The hydroxy substituent and other electronegative substituents promote radical pyramidalization.¹⁵ We also evaluated the barrier to inversion at the carbon center of these species. The inversion barrier is very low for the hydroxymethyl radical (0.7 kcal/mol, MP4/6-31+G*), but it is about 12 kcal/mol (MP4/6-31+G*) for the hydroxy-

methyl anion. This latter barrier is considerably higher than that for methyl anion, which was reported by Schleyer et al. to be 2.8 kcal/mol.¹⁶

The C–O bond lengths are quite different in the different species (Table I). Ketyls have C–O bond lengths intermediate between the values of normal C–O double and single bonds and give considerable double bond character. The C–O bonds of hydroxypropyl radicals (3–6) are only slightly shorter than a normal C–O single bond. This results from a small stabilizing interaction between the radical singly-occupied orbital and the oxygen lone-pair.¹⁷ The hydroxy OH bond is nearly perpendicular to the radical orbital in each structure. This conformation maximizes this interaction. The C–O bonds in the anion species (7–9) are longer than normal C–O single bonds by about 0.1 Å. This reduces repulsive interactions between the anion and oxygen lone-pair orbitals.

Structures 1–9 are staggered about the C₁–C₂ bond. This is better indicated by the dihedral angles between the allylic bonds and the C₁–O bond, collected in Table I. The values of D_{in} , D_{anti} , and D_{out} are the dihedral angles between the C₁–O bond and the *inside*, *anti*, and *outside* allylic bonds, respectively, as defined in structure G.

The *inside* and *anti* methyl conformers of the hydroxypropyl radical both have *gauche* O–C–C arrangements and have similar energies. Thus, there is no orientation preference for the methyl group with respect to the singly occupied radical orbital. Schlegel et al. found that the C–O bond vicinal to a radical orbital also has no special orientational preference.¹⁸ The *outside* conformation of the hydroxypropyl radical is less stable by 0.3 kcal/mol. This is similar to the situation of propanol and methyl propyl ether where *gauche* conformations are more stable than the *anti* conformation by about 0.4 kcal/mol.^{19,20} These calculations suggest that the radical orbital extension effect suggested by Pradhan⁴ is unimportant in determining the conformational preference of cyclic hydroxyalkyl radical species.¹² The CO bond prefers to be *gauche* to a methyl because of stabilization arising from polarization of the alkyl group by the oxygen, as will be discussed later.

The *inside* conformation of the propionaldehyde ketyl is most stable. The *anti* and *outside* conformers are higher in energy by 0.6 and 1.5 kcal/mol, respectively, at MP2/6-31+G*. This indicates that *anti*-periplanar arrangement of the methyl group with respect to the partially-filled orbital on carbon is destabilizing. The methyl group is an electron-donor (with respect to H), and the negative charge of the radical anion is partially situated at C₁. This causes the *anti* conformer to be destabilized by closed-shell repulsions. The *outside* conformer is least stable, because the *inside* and *anti* conformers benefit from electrostatic stabilizing interactions between the methyl and negatively charged O atom.

The order of conformer energies for the hydroxypropyl anion is the same as that of the ketyl, but the energy differences are larger. The *anti* and *outside* conformers are less stable than the *inside* by 1.7 and 2.0 kcal/mol, respectively. It is likely that the *anti* methyl conformer is significantly destabilized because part of the negative charge of the anion is situated at the C₁ center, as indicated by Mulliken atomic charges given in Table I. This destabilization is also indicated by the long C₁–O and C₁–C₂ bond lengths in the *anti* conformer. It should be noted that the large basis set dependence of the conformational preference (the 3-21G basis set gives a preference for the *anti* conformer) is as expected for an effect which is mainly electrostatic in nature. The methyl group incorrectly behaves as an acceptor with a poor basis set

(16) Spitznagel, G. W.; Clark, T.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Comp. Chem.* **1982**, *3*, 363. Clark, T.; Korner, H.; Schleyer, P. v. R. *Tetrahedron Lett.* **1980**, *21*, 743. Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J. *J. Org. Chem.* **1981**, *46*, 4108.

(17) Clark, T.; Nelsen, S. F. *J. Am. Chem. Soc.* **1988**, *110*, 868 and references therein.

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(14) Symons, C. R. *Nature (London)* **1969**, *724*, 686.

(15) Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 5046. Pacansky, J.; Dupuis, M. J. *J. Chem. Phys.* **1978**, *68*, 4276; **1979**, *71*, 2095; **1980**, *73*, 1867. Pacansky, J.; Confel, H. *Ibid.* **1980**, *72*, 5285. Yoshimine, M.; Pacansky, J. *Ibid.* **1981**, *74*, 5468.

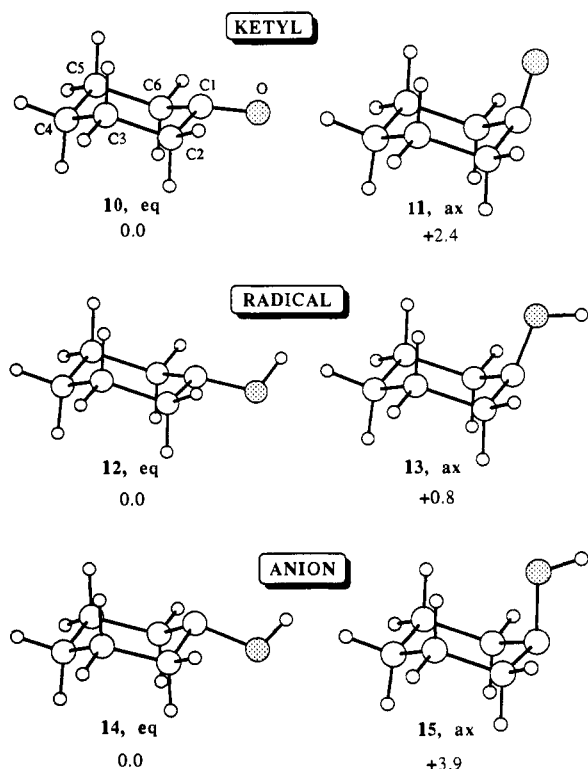


Figure 2. Structures (6-31G* for ketyl and radical, 6-31+G for anion) of ketyl, hydroxyalkyl radical, and hydroxyalkyl anion derived from cyclohexanone. The relative energies (kcal/mol) of the structures by MP2/6-31+G* calculations are shown.

(3-21G). This phenomenon has been noticed in the case of crotyl anion.²¹

Figure 2 shows the structures of equatorial and axial conformations of the intermediates derived from cyclohexanone. Only chair conformations of the six-membered rings were studied. For the optimization of the hydroxycyclohexyl radical, the OH bond was restricted to be eclipsed with the radical orbital in C_s symmetry. Although the OH is not in the best orientation, this is not likely to influence the calculated relative stabilities of the two conformers significantly.

The calculations indicate that the equatorial conformations are more stable than the axial conformations for all species (Table IV). Considering that the A -value of OH is only 0.5–0.8 kcal/mol,²² the equatorial preference is very large for the ketyl and anion species.

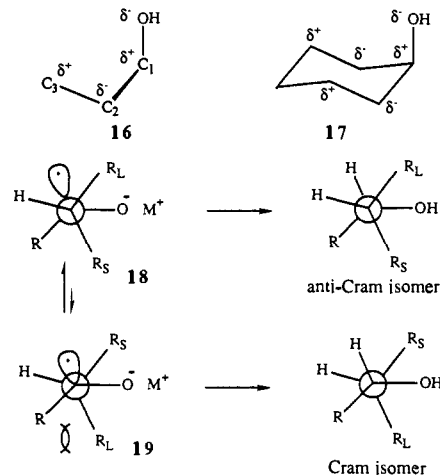
The 1-hydroxycyclohexyl radical has been studied with ESR spectroscopy.^{23–24} While Lloyd et al. reported a 1.8-kcal/mol preference for equatorial conformation in the 4-methyl-1-hydroxycyclohexyl radical,²³ Micheau et al. reported that the equatorial conformation is only slightly more stable than the axial conformation.²⁴ A previous calculation by Lloyd with the STO-3G basis set gave a 0.3-kcal/mol preference for the axial conformation;²⁵ this value is similar to our 3-21G result. However, with a good basis set and inclusion of electron correlation energy, a 0.8-kcal/mol preference for the equatorial conformation of the 1-hydroxycyclohexyl radical is calculated. This is similar to the A -value of the OH group.²²

In the equatorial conformations, there are two “outside” C–C

bonds, and in the axial conformations there are two “anti” C–C bonds. If the conformational preferences for the cyclic systems were the same as for the acyclic systems, the equatorial conformations would be less stable than the axial conformations by 1.8, 0.6, and 0.6 kcal/mol, respectively, for the cyclohexanone ketyl, 1-hydroxycyclohexyl radical, and 1-hydroxycyclohexyl anion. These expectations are dramatically different from the calculations, since the equatorial conformations are more stable than the axial conformations by 2.4, 0.8, and 3.9 kcal/mol, respectively, for these three species.

Why is there such a large discrepancy between acyclic and cyclic systems? First of all, such a discrepancy exists even in hydroxycyclohexane. The equatorial conformation of hydroxycyclohexane is more stable than the axial conformation by 0.5–0.8 kcal/mol, while the gauche C–C–O conformation of propanol is more stable than the anti conformation by 0.3 kcal/mol regardless of whether the C–C–O–H is gauche or anti.²⁰ Thus, even here there is a more than 1-kcal/mol discrepancy between the acyclic and cyclic systems. A detailed analysis of this and related phenomena will be described in another paper.²⁰ For the present cases, besides the often suggested steric interactions in the axial conformations,²⁶ three additional reasons are given to explain this phenomenon.

(1) Induced Dipole Interactions. In the acyclic species, the *outside* conformations are less stable than the *inside* and *anti* conformations. That is, the C₂–C₃ bond prefers to be gauche to the O–C₁ bond. This is caused by electrostatic interactions. The O–C₁ bond polarizes the gauche C₂–C₃ bond (see Table I for atomic charges) as shown in 16, and this induced dipole interacts in a stabilizing fashion with the C–O dipole. This interaction is absent if the C₂–C₃ bond is anti to the O–C₁ bond. This rationalization of the gauche preference is similar to the explanation of the conformational preference of propionaldehyde offered by Wiberg et al.²⁷



In the axial conformations of cyclic species, there are two such stabilizing interactions, as shown in 17. However, the induced C₂–C₃ and C₆–C₅ dipoles are parallel, and these destabilize each other. As a result, the gauche preference of the O–C–C–C unit is partially canceled out in the axial conformation of cyclic systems.

(2) Torsional Strain. Figure 3 shows views of *anti* and axial conformers of the intermediates derived from propionaldehyde and cyclohexanone, sighting down the C₁–O bonds. As can be seen, the C₂–C₃ and C₅–C₆ bonds in each cyclic structure must be nearly parallel. However, the C₂–C₃ bonds in the acyclic structures point outward. Therefore, in order to achieve the conformation in cyclic structures, rotation about the C₁–C₂ bond is necessary. This is indicated by the deviations of the D_{anti} dihedral angles in the cyclic structures from the values of the corresponding acyclic structures: 14°, 12°, and 5° respectively for the ketyl, hydroxyalkyl radical, and hydroxyalkyl anion species. Therefore, the C₂–C₃ and C₅–C₆ bonds in the axial conformers cannot adopt

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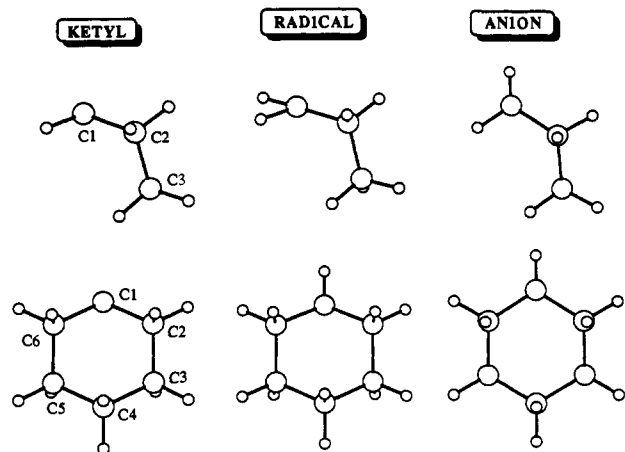


Figure 3. Views of *anti* and axial conformations of the ketyls, hydroxyalkyl radicals, and hydroxyalkyl anions derived from propionaldehyde (top line) and cyclohexanone (bottom line). The view is sighting directly from C_1 towards O; the O atoms are hidden behind the carbons.

the optimal conformation present in the acyclic molecules. The axial conformers are destabilized relative to the acyclic analogues. The C_2-C_3 bonds in the *outside* conformers of the acyclic intermediates are nearly parallel to the C_1-O bonds. Almost no geometrical distortion is necessary for the C_2-C_3 bonds to adopt the conformations in the equatorial conformers of cyclic structures. This is indicated by small differences in D_{out} of the cyclic and acyclic structures. Thus, the equatorial conformers are not destabilized relative to the acyclic analogues. The overall result is the destabilization of the axial conformers with respect to the equatorial conformers. The above analysis can be described in another way. The ring of cyclohexanone is somewhat flattened to reduce ring strain.^{28c} Upon the formation of the intermediates, pyramidalization at C_1 and staggering about the C_1-C_2 and C_1-C_6 bonds are necessary. Pyramidalization in the axial direction (to form equatorial conformer) is more favorable, because staggered conformations can be formed without introducing ring strain. Pyramidalization in the equatorial direction is less favorable, because ring strain is introduced in order to form the ideal staggered arrangement. We have used a similar argument to explain the stereoselectivities of nucleophilic additions to cyclohexanones.²⁸

(3) Destabilization by Electron-Donation. In the cases of ketyls and hydroxyalkyl anions, we pointed out earlier that a C-C bond *anti* to the anion orbital causes destabilization by electron-donation. In the axial conformations of the cyclohexanone ketyl and hydroxycyclohexyl anion, there are two C-C bonds *anti* to the carbanion orbital. This results in a destabilization larger than the sum of the two individual interactions in the acyclic species. Such destabilization is apparent from the bond lengths involving C_1 . The O- C_1 and C_1-C_2 in **11** are longer than the corresponding bonds in **10** by 0.007 and 0.008 Å, respectively. The two differences increase to 0.020 and 0.011 Å in the hydroxycyclohexyl anions (**15** versus **14**). These bond length differences are larger than those in the corresponding acyclic structures. This electrostatic destabilizing effect does not exist in the hydroxy radical cases.

Stereochemical Considerations. It has been suggested that the 7-norbornyl anion inversion is slower than proton abstraction in protic solvents.²⁹ Hydroxy or alkoxy substituents significantly increase the anion inversion barrier,³⁰ as supported by the cal-

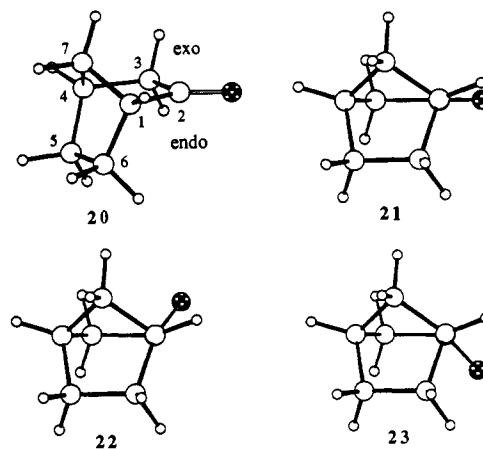


Figure 4. MM2 structure of bicyclo[2.2.1]hepta-2-one, **20**, and its Newman projection view sighting down the C_1-C_2 bond, **21**. Exo and endo ketyls are shown by **22** and **23**, respectively. The structure **22** is less stable because of partial eclipsing.

culations. Thus, the reaction of lithiated chiral alkoxy anions with a variety of electrophiles occurs with retention of configuration at low temperatures.^{30,31} Besides, the calculated high equatorial preference of the hydroxycyclohexyl anion is too large to account for the observed stereoselectivity.³² Therefore, the arguments that the stereoselectivity of dissolving metal reductions of saturated ketones is determined by the intermediate anion equilibrium or the rate of proton abstraction by the anion can be ruled out. Instead, rapid equilibrium of the ketyl or the hydroxyalkyl radical occurs, but once the carbanion is formed, it is likely to be protonated before inversion occurs.

Thus, the stereoselectivities of dissolving metal reductions are determined either by the ketyl or by the hydroxyalkyl radical equilibria; both have low inversion barriers. The calculations suggest that the equatorial preference of the cyclohexanone ketyl is about the same as the equatorial preference found experimentally in dissolving metal reductions.³² The calculated equatorial preference for the hydroxycyclohexyl radical is too low to account for the observed stereoselectivities. The calculations support Pradhan's proposal—that is, free hydroxyalkyl radical intermediates are not formed during reductions in protic solvents.⁴ The stereoselectivity is determined by the alkyl ketyl equilibrium.³³ This explanation of stereoselectivity can be extended to the cases where the major products are thermally less stable.^{3,4,7,8,34} For example, reductions of bicyclo[2.2.1]heptan-2-ones always lead to the formation of *endo*-hydroxy products regardless of whether they are thermally more stable or not.^{3,4,7} House suggested that the torsional strain of these bicyclo systems favors the radical intermediate with the radical orbital in the *endo* direction.² Our explanation is the same, except the ketyl species are considered. Structure **22** is the Newman projection of bicyclo[2.2.1]heptan-2-one, **21**. There is partial staggering about the C_1-C_2 bond. Upon the formation of ketyl, pyramidalization is easier in the *exo* direction, **23**, than the *endo* direction, **22**, resulting in the favorable formation of *endo* alcohol product.

Yamamoto et al. observed that the reductions of a variety of chiral ketones by dissolving metals and by SmI_2 lead to anti-Cram stereoselectivity. The stereoselectivity is very similar in both protic and aprotic solvents.^{5,35} We suggest that the stereoselectivity is determined by the relative stabilities of ketyl conformers **18** and

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19.³⁶ The conformations with one alkyl group *outside* are expected to be higher in energy. Structure 18 is more stable than 19, because the *inside* position is less crowded sterically than the *anti* position. This leads to the observed anti-Cram stereoselectivity.^{28,37} These results also support the notion that in protic

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solvents, the conformational preferences of the ketyl dictate the stereochemistry of dissolving metal reduction.

Acknowledgment. We are grateful to Sir Derek H. R. Barton (Texas A&M University) for directing our attention to this interesting problem, to Dean Peter Rabideau (Louisiana State University) and Professor Paul von Rague Schleyer (University of Erlangen-Nurnberg) for helpful advice and extensive discussions, and to the National Institutes of Health for financial support of this research. We also thank the IBM Corp. for a grant of computer time on the IBM 3090/600J Supercomputer administered through the Office of Academic Computing at UCLA.

Layer-by-Layer Etching of Two-Dimensional Metal Chalcogenides with the Atomic Force Microscope

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Abstract: The atomic force microscope (AFM) is used to etch off individual layers from the surface of two-dimensional metal dichalcogenide crystals, extending our earlier work on this phenomena with the scanning tunneling microscope (*J. Am. Chem. Soc.* 1990, 112, 7498). The etching proceeds via a nucleation and growth of holes, where the nucleation sites are provided by missing chalcogenide atoms from the surface of the crystal. Some substrates, such as $NbSe_2$, show faceted triangular etch pits which are observed to be rotated 180° on alternate layers, indicative of the polytype of the material. Counting nucleation sites over a given area provides a new method for determining extremely small deviations from stoichiometry in layered materials. The rate of the etching process was proportional to the force applied to the AFM tip. The mechanism for etching appears to be related to direct bonding interactions between tip atoms and substrate atoms with dangling bonds. The etching process could be simulated with a computer model relating the probability of removal of a given atom with its nearest neighbor environment. The implications of the strong interactions between AFM and STM tips and substrates probed in air are discussed. The nanofabrication of several small device-like structures is demonstrated.

Introduction

The scanning tunneling and atomic force microscopes have evolved into useful tools for the characterization and manipulation of matter on an extremely small scale. Probing surfaces in air with these techniques sets them apart from many other surface characterization techniques which require high vacuum conditions. Surfaces exposed to ambient conditions are always covered by adsorbed layers of water and hydrocarbon contaminants which can wet either an STM or AFM tip and, due to capillary forces, have a significant effect on the interaction between the tip and the substrate. Herein we extend our earlier work¹ on the layer-by-layer STM etching of 2D substrates, such as $SnSe_2$ and $NbSe_2$, to the AFM. The AFM has the advantage of allowing measurement and some control of the force applied to the tip facilitating the investigation of the role of the tip-substrate interaction in the etching process. Similar etching patterns and rates are obtained with the AFM, suggesting that the mechanism for removal of material is the same for both the STM and AFM. Our results perhaps shed some light on the controversy about the magnitude of tip interactions with the substrate during STM experiments performed in air.

Results

Figure 1 shows a series of AFM images taken by continuously scanning a $0.5 \times 0.5 \mu m$ area of a $SnSe_2$ crystal with the AFM

tip. The figure shows the nucleation and growth of rounded holes in the top layer of material resulting in the nearly complete removal of this layer and subsequent nucleation of the second layer. Continued scanning would result in the removal of many additional layers. The process is completely analogous to that observed on the same substrate with an STM tip.^{1a} $NbSe_2$ ^{1a} and MoS_2 ^{1b} when etched with the STM, produced triangular nucleation sites which continued to grow as triangular features and showed rotation of the triangle upon etching of the second layer. Figure 2 shows an analogous behavior with the AFM for $NbSe_2$. Note the 180° rotation of the triangles in the second layer due to the 2H polytype of the $NbSe_2$ where alternate layers are rotated 180° with respect to each other. The etched structures are completely stable over periods of several days exposure to laboratory air if they are not scanned by the AFM tip. Other layered structure dichalcogenides were also observed to etch in the AFM including TaS_2 , SnS_2 , $ZrSe_2$, $MoSe_2$, $HfSe_2$, and $TiSe_2$. $MoTe_2$, WSe_2 , WTe_2 , $ReSe_2$, and WS_2 crystals, grown in our lab, were not observed to etch. Graphite was also not observed to etch, but high forces did produce wrinkling of the graphite surface.

Variation of the force applied to the cantilever, via the piezoelectric elements of the AFM, resulted in the observation that the rate of removal of material was directly related to the applied force. Cratering, or buildup of material on the sides of the etched areas, was only observed at very high applied forces (>150 nN)

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