$$RBCl_2 + O(C_2H_5)_2 \rightleftharpoons RB^-Cl_2{:}O^+(C_2H_5)_2 \quad (8)$$

At 0°, the uptake of 90% of 1 mol of oxygen by a solution of *n*-hexyldichloroborane required only 9 min. Analysis revealed the presence of 85% peroxide. At −18°, the uptake of oxygen was essentially quantitative and analysis revealed a 94% yield of peroxide. The presence of 5 mol % of iodine also inhibited the uptake of oxygen for long periods of time.

The product of this reaction is presumably the alkylperoxydichloroborane, RO_2BCl_2, possibly existing as the etherate. Indeed, hydrolysis of the reaction product provides the alkyl hydroperoxide in yields in the neighborhood of 90% or better. Consequently, the reaction of oxygen with the alkyldichloroborane provides the simple new route to the alkyl hydroperoxides for which we had been searching. We applied the reaction to a series of alkyldichloroboranes (Table I).

Table I. Oxidation of Alkyldichloroboranes for the Formation of Hydroperoxides

$RBCl_2$,[a] R =	Time,[b] min	% Yield,[c] ROOH
1-Hexyl	20	94
3-Hexyl	5	93
2-Methyl-1-pentyl	5	84
Cyclopentyl	30	91
Cyclohexyl	4	93
Norbornyl	5	91

[a] 5 mmol in 10 ml of ether at −18°. [b] Time for absorption of 5 mmol of oxygen. [c] By iodometric titration.

The following procedure for the preparation of cyclohexyl hydroperoxide is representative. A dry 200-ml flask equipped with a magnetic stirring bar with Teflon collar and septum inlet was flushed with nitrogen. The flask was cooled to −18° (ice–salt bath) and charged with 100 ml of dry ether and 8.75 g, 50 mmol, of cyclohexyldichloroborane. The flask was attached to an automatic gas generator previously flushed with oxygen (inject 15 ml of 30% hydrogen peroxide into the generator with an empty 100-ml flask in place of the reaction flask). The remaining nitrogen above the solution was removed by injecting 3 ml of 30% hydrogen peroxide into the generator. The system was brought to atmospheric pressure by withdrawing a small amount of oxygen and the reaction initiated by rapid stirring. The reaction was monitored by following the buret filled with 3% hydrogen peroxide. After completion of the absorption of oxygen, the solution was hydrolyzed with 20 ml of water. The solution was saturated with potassium carbonate and the organic phase separated. The organic phase was dried (potassium carbonate) and distilled to give 5.2 g, 89%, of cyclohexyl hydroperoxide, bp 40–41° (0.1 mm), $n^{20}D$ 1.4650 (lit.[13] bp 42–43° (0.1 mm), $n^{20}D$ 1.4645).

This procedure provides an efficient method for the conversion of boranes into the corresponding alkyl hydroperoxides. It is applicable to a wide variety of alkyl groups which may not be accommodated by other methods. Furthermore, the reaction suggests that the alkyldichloroboranes may undergo other free-radical reactions. We are continuing to investigate these possibilities.

(13) C. Walling and S. A. Buckler, *J. Amer. Chem. Soc.*, 77, 6032 (1955).

(14) National Science Foundation Predoctoral Fellow, 1970–1972.

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A Criticism of the Use of Certain Bridged Bicyclic Hydroxycarboxylic Acids as Model Compounds for the Concept of Orbital Steering

Sir:

Understanding of enzymatic catalysis on a molecular level in terms of relatively simple models has been one of the fundamental aims of physical organic chemistry.[1-4] Storm and Koshland[5] have emphasized the prime role of optimal juxtapositioning of reacting groups between the enzyme and substrate. This orientational factor is basically an entropic contribution to enzymatic catalysis and is thought to depend upon the "steering" of relevant atoms in order to achieve the best orbital overlap for reactions. Undoubtedly this phenomenon, along with many other factors,[6-8] plays some role in enzymatic catalysis, but a central question concerns the magnitude of orbital steering effects. In order to assess quantitatively the effect of such optimal orbital orientation upon reaction rate, Koshland, *et al.*,[9-12] have used as model compounds bridged bicyclic hydroxycarboxylic acids. In these systems the hydroxyl group and carboxyl group are held fixed in space. Intramolecular lactonization obviously is facilitated by this propitious arrangement relative to the bimolecular esterification reaction between an alcohol and acid molecule. The kinetic effects are impressive; for example, intramolecular lactonization can be as much as 10^4 times faster even after correction for proximity and torsional effects.

The concept of orbital steering has been rather strongly criticized on the basis of the theoretical interpretation of the kinetic results.[13-15] A more fundamental criticism which is the subject of this communication is that the theory rests in part on incorrect structures.

(1) M. L. Bender, "Mechanisms of Homogeneous Catalysis from Protons to Proteins," Wiley-Interscience, New York, N. Y., 1971, Chapter 19.
(2) T. C. Bruice and S. J. Benkovic in "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin, New York, N. Y., 1966, Chapter 1.
(3) F. H. Westheimer, *Advan. Enzymol. Relat. Subj. Biochem.*, 24, 441 (1962).
(4) W. P. Jencks in "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969.
(5) D. R. Storm and D. E. Koshland, Jr., *Proc. Nat. Acad. Sci. U. S.*, 66, 445 (1970).
(6) S. Milstein and L. A. Cohen, *J. Amer. Chem. Soc.*, 94, 9158 (1972).
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(8) R. T. Borchardt and L. A. Cohen, *ibid.*, 94, 9175 (1972).
(9) G. A. Dafforn and D. E. Koshland, Jr., *Proc. Nat. Acad. Sci. U. S.*, 68, 2463 (1971).
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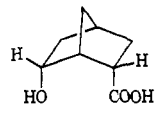
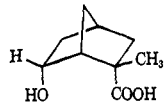
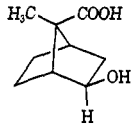
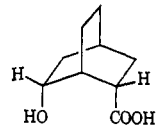
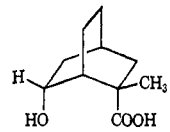
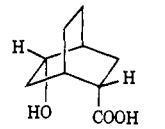
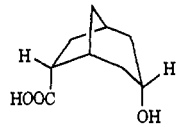
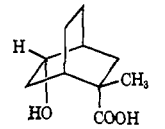
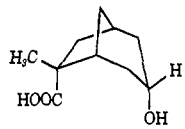
(11) D. R. Storm and D. E. Koshland, Jr., *J. Amer. Chem. Soc.*, 94, 5805 (1972).
(12) D. R. Storm and D. E. Koshland, Jr., *ibid.*, 94, 5815 (1972).
(13) T. C. Bruice, A. Brown, and D. O. Harris, *Proc. Nat. Acad. Sci. U. S.*, 68, 658 (1971).
(14) M. I. Page and W. P. Jencks, *ibid.*, 68, 1678 (1971).
(15) T. C. Bruice and A. Turner, *J. Amer. Chem. Soc.*, 92, 3422 (1970); B. Capon, *J. Chem. Soc. B*, 1207 (1971).

Table I. Rates of Lactonization for Various Bridged Bicyclic Hydroxycarboxylic Acids[a]

Compound	Correct structure	K^{H^+}, M^{-1} min^{-1}
 1		1120
 2	 3	0.30
 4		0.950
 5		107
 6	 7	10.0
 8	 9	522

[a] Taken from ref 12.

Inspection of the rate data in Table I immediately reveals a striking inconsistency. Methyl group substitution in the 2-exo position (compound **2** compared to **1**) *decreases* the rate of lactonization by 3740 while the analogous change in **4** compared to **5** *increases* the rate by a factor of 100. These data led us to suspect an incorrect structure as is in fact the case. Compound **2** is in reality the rearranged hydroxycarboxylic acid **3**. These compounds were originally confused by Meek and Trapp[16] but corrected as early as 1961 by Beckmann and Geiger,[17] and their work has also been confirmed by us.[18]

Hydroxy acids **4**[19] and **5**[20] are correct as drawn and the rate enhancement of 100 is real and also expected. It probably stems from a compression effect of the type originally suggested by Bunnett and Hauser[21] and discussed by Cohen[6-8] in which the methyl group acts to decrease the rotational possibilities for the carboxyl group, leading to an energetically more favorable orientation for lactonization. The rate decrease of 3740 between **1** and **3** is probably due largely to a distance factor[22,23] although other important parameters such as torsional strain, solvation, and angle strain must certainly play a role.

Structures **6** *vs.* **7** and **8** *vs.* **9** are more complicated and could only be sorted out on the basis of complete chemical degradations to known compounds.[20]

It is worth noting that the kinetic effect of methylation in going from **7** to **9** is as expected based upon compression. In a corollary sense one can argue that a favorable orientation of atomic orbitals results from this structural modification. In this sense the present work does not call into question the validity of the *concept* of orbital steering, but rather questions some of the *premises* which derive from incorrect models.

Acknowledgment. The authors wish to thank Professor C. W. Jefford, University of Geneva, for helpful discussions.

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(17) S. Beckmann and H. Geiger, *Chem. Ber.*, **94**, 48 (1961).

(18) We have repeated the work of Beckmann and Geiger,[17] using different oxidizing conditions, namely, oxidation of **3** with RuO_4 in base to 2-keto-7-*anti*-methylbicyclo[2.2.1]heptane-7-*syn*-carboxylic acid, mp 206–208° (lit.[17] 206–208°) (ir 1735 cm^{-1}), followed by Wolff–Kishner reduction to 7-methylbicyclo[2.2.1]heptanecarboxylic acid, mp 194–195° (lit.[17] 194–195°). 6-*endo*-Hydroxy-2-*exo*-methylbicyclo[2.2.1]-heptane-2-*endo*-carboxylic acid γ-lactone has mp 65–66°. 2-*exo*-Hydroxy-7-*anti*-methylbicyclo[2.2.1]heptane-7-*syn*-carboxylic acid γ-lactone has mp 125–126°. Storm and Koshland[12] used the material of mp 125–126° as the source of **2**.

(19) H. W. Whitlock, *J. Amer. Chem. Soc.*, **87**, 2214 (1965).

(20) Structures **5**, **7**, and **9** are established by work reported in the following communication.

(21) J. F. Bunnett and C. F. Hauser, *J. Amer. Chem. Soc.*, **87**, 2214 (1965).

(22) Inspection of Dreiding models of **3** reveals around a 0.7 Å greater distance between the hydroxyl group and carboxyl carbonyl group relative to **1**. There also exists qualitative information about the difficulty of bridging between the C_2–C_7 positions. Isoborneol does not undergo intramolecular oxidative cyclization between the C_2 hydroxyl and C_7 methyl group upon reaction with lead tetraacetate.[23] Also acidification of a basic solution of the lactone related to **3** does not cause spontaneous lactonization as does occur with 2,6 substituted compounds such as **1** and **4**.

(23) R. E. Partch, *J. Org. Chem.*, **28**, 276 (1963).

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Acid-Catalyzed Lactonization of *exo*- and *endo*-Bicyclo[2.2.2]oct-5-enecarboxylic Acids. Structural Clarifications

Sir:

Considerable confusion exists in the literature regarding the structure of the δ-lactone obtained in the intramolecular lactonization of *exo*- and *endo*-bicyclo-[2.2.2]oct-5-enecarboxylic acids, **1** and **2**, respectively. For example, the lactone thought to be **5** has been used as a model compound in the development of the concept of orbital steering,[1] when in fact, the correct structure of the δ-lactone from the acid-catalyzed cyclization of **1** or **2** is **4**, *vide infra*. Similarly, iodo-δ-lactone (**6**) has been claimed,[2] but attempts to repeat this synthesis by us and others[3] has failed to produce any lactone other than the expected 2,6-γ-lactone (Scheme I).

(1) D. R. Storm and D. E. Koshland, Jr., *J. Amer. Chem. Soc.*, **94**, 5815 (1972).

(2) W. R. Boehme, E. Schipper, W. G. Scharpf, and J. Nichols, *ibid.*, **80**, 5488 (1958).

(3) H. W. Whitlock, *ibid.*, **84**, 3412 (1962).