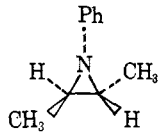
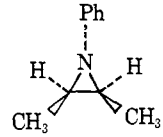
−80°. At this temperature, the phenyl group is frozen into one conformer rather than rapidly equilibrating. Thus the trans isomer shows two absorptions (2 m, δ 1.79 and 2.09) for the ring protons, and two broadened doublets (δ 0.85 and 1.26) for the methyl groups. This strongly suggests that hydrogen and methyl exist both syn and anti to the phenyl (conformer **1**). In accordance with expectations, the cis



1



2

isomer showed only one absorption (multiplet, δ 2.07) for the ring protons and one absorption (d, δ 1.24) for the methyl group (conformer **2**) at −80°. This stereochemical assignment is in accordance with prediction and with similar reactions of this type.[6,8]

This procedure provides for the first time a convenient synthesis of ring substituted *N*-phenyl- and *N*-alkylaziridines in which the stereochemistry of the ring substituents may be easily defined. Furthermore, based on previous work, the N-alkyl groups must retain the original stereochemistry of the group attached to boron.[5] Consequently, the present procedure is exceptionally promising for providing a relatively simple, direct route to aziridines with well defined stereochemistry.

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Alan B. Levy,[9] Herbert C. Brown*
Richard B. Wetherill Laboratory, Purdue University
West Lafayette, Indiana 47907
Received March 17, 1973

Controlled Reaction of Oxygen with Alkyldichloroborane Etherates. A Convenient Synthesis of Alkyl Hydroperoxides in High Yield

Sir:

Alkyldichloroboranes in inert solvents react remarkably rapidly with 0.5 molar equiv of oxygen, either at 0 or −78°. The reaction is strongly inhibited by iodine and must involve a free-radical chain process, yet the product contains little peroxide. In diethyl ether the reaction proceeds readily with the uptake of 1 molar equiv of oxygen. The product is readily hydrolyzed to the corresponding alkyl hydroperoxide. This procedure provides a convenient new route to the alkyl hydroperoxide in excellent yield.

Trialkylboranes undergo a facile free-radical chain autoxidation[1] which may be stoichiometrically controlled to give essentially quantitative conversions into alcohols.[2] At low temperature the initially formed peroxide (eq 1) reacts with a second mole of oxygen to

$$R_3B + O_2 \longrightarrow RO_2BR_2 \quad (1)$$

produce a diperoxide (eq 2). The hydroperoxide can

$$RO_2BR_2 + O_2 \longrightarrow (RO_2)_2BR \quad (2)$$

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(2) H. C. Brown, M. M. Midland, and G. W. Kabalka, *J. Amer. Chem. Soc.*, **93**, 1024 (1971).

be liberated by the addition of 30% hydrogen peroxide (eq 3).[3] This process provides a valuable route to

$$(RO_2)_2BR + H_2O_2 + 2H_2O \longrightarrow ROH + 2RO_2H + B(OH)_3 \quad (3)$$

alkyl hydroperoxides. It is limited in that only two of the alkyl groups on boron are converted to the desired peroxide. It would be highly desirable to have a borane in which the alkyl group is converted entirely to the hydroperoxide.

Accordingly, the autoxidation of a number of *B*-alkylborane derivatives was examined in the automatic gasimeter[4] adapted for oxidation as previously described.[2,3] *B*-Alkyl-9-borabicyclo[3.3.1]nonane[5] undergoes rapid oxidation. Unfortunately, the cyclooctyl–boron bonds are preferentially oxidized. *B*-Alkyl-3,5-dimethylborinanes have been used successfully to transform the *B*-alkyl group selectively in free-radical reactions.[6] However, selective oxidation of the *B*-alkyl group failed. Dimethyl alkylboronic esters failed to oxidize. The *B*-alkyl catecholborane esters[7] reacted only sluggishly with oxygen.

However, the uptake of oxygen by *n*-butyldichloroborane[8,9] in toluene or hexane was exceptionally fast, the reaction being complete in less than 2 min at 0° or even at −78°. This reaction was strongly inhibited by iodine,[10] the presence of 5 mol % causing no oxygen to be absorbed in over 96 hr.[11] Consequently, the reaction must involve a free-radical chain process. Yet the product contained only traces of peroxide.

It appears, therefore, that the reaction must proceed through the formation of the alkylperoxydichloroborane (eq 4–6) but the latter must be lost in a rapid

$$RBCl_2 + O_2 \longrightarrow R\cdot + \cdot O_2BCl_2 \quad (4)$$

$$R\cdot + O_2 \longrightarrow RO_2\cdot \quad (5)$$

$$RO_2\cdot + RBCl_2 \longrightarrow RO_2BCl_2 + R\cdot \quad (6)$$

subsequent reaction (eq 7). This proposed mechanism

$$RO_2BCl_2 + RBCl_2 \longrightarrow 2ROBCl_2 \quad (7)$$

also accounts for the stoichiometry observed, an uptake of 0.5 mol of oxygen/mol of borane.

We discovered that the presence of ether greatly decreased the rate of the intermolecular oxidation (eq 7) without seriously affecting the rate of autoxidation at 0°. This is evidently a consequence of the coordination of alkyldichloroboranes with ethyl ether (eq 8).[8,12]

(3) H. C. Brown and M. M. Midland, *ibid.*, **93**, 4078 (1971).
(4) C. A. Brown and H. C. Brown, *ibid.*, **84**, 2829 (1962); *J. Org. Chem.*, **31**, 3989 (1966).
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(7) H. C. Brown and S. K. Gupta, *ibid.*, **93**, 1816 (1971).
(8) The alkyldichloroboranes are reported to be spontaneously flammable in air: P. A. McCusker, E. C. Ashby, and H. S. Makowski, *ibid.*, **79**, 5182 (1957).
(9) H. C. Brown and A. B. Levy, *J. Organometal. Chem.*, **44**, 233 (1972); H. C. Brown and N. Ravindran, *J. Amer. Chem. Soc.*, **95**, 2396 (1973).
(10) M. M. Midland and H. C. Brown, *ibid.*, **93**, 1506 (1971).
(11) This extremely long induction period (tri-*n*-butylborane oxidation is inhibited for 12.5 min by 5 mol % of iodine) suggests a very inefficient initiation step. This is evidently due to the electronic effect of the two chlorines on the boron.
(12) At −78° the rate of autoxidation becomes negligible, presumably because dissociation of the complex is too small to permit the chain reaction to proceed. The presence of 1.2 mol of tetrahydrofuran, a stronger complexing agent, greatly reduces the rate of oxidation and leads to lower yields of peroxide.

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

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.

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M. Mark Midland,[14] Herbert C. Brown*
Richard B. Wetherill Laboratory, Purdue University
West Lafayette, Indiana 47907
Received March 30, 1973

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.

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