Table VI. The Shortest Intermolecular Distances (in Å)

O–C(5)	4	$0\bar{1}1$	3.270	C(2)–H(7A)	2	012	2.97
N(1)–N(6)	2	112	3.390	C(2)–H(7B)	2	112	2.98
C(2)–N(4)	3	010	3.292	C(2)–H(13A)	3	010	2.81
C(2)–N(9)	4	102	3.350	N(3)–H(7A)	2	012	2.99
N(3)–N(9)	2	112	3.396	N(3)–H(2)	3	$01\bar{1}$	3.37
N(4)–C(2)	3	$01\bar{1}$	3.292	N(4)–H(2)	3	$01\bar{1}$	2.87
N(4)–C(7)	4	001	3.162	N(4)–H(7A)	4	001	2.60
C(11)–C(11)	2	112	3.374	N(4)–H(7B)	4	001	2.93
O–H(5)	4	$0\bar{1}1$	2.35	C(5)–C(7)	4	001	3.27
O–H(13B)	1	$0\bar{1}0$	2.82	C(8)–H(13A)	2	112	2.98
O–H(13A)	2	112	2.88	C(8)–H(7B)	3	000	2.95
O–H(13B)	2	012	2.83	N(9)–N(3)	2	112	3.40
N(1)–H(7A)	2	012	3.03	N(9)–H(13A)	2	112	2.94
N(1)–H(13A)	3	010	2.71	N(9)–H(7B)	3	000	2.47
N(1)–H(13C)	4	$1\bar{1}2$	2.80	N(9)–H(2)	4	$1\bar{1}2$	2.46

modified version of the Gaentzel, Sparks, and Trueblood ACA Old Program #317), a general program for Fourier summation by Dr. S. T. Rao, the Sayres relation by Dr. R. E. Long (ACA(New) #2). We are grateful to the following agencies for financial assistance: National Institutes of Health, Grants No. GM-15787 and AM-3942, and the National Science Foundation, Grant No. GB-8690.

Radical Cyclization during Autoxidation of 5-Hexenylmagnesium Bromide[1]

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Abstract: No cyclization to cyclopentylmethanol occurs in the reaction of 5-hexenylmagnesium bromide with *t*-BuOOMgCl. The amount of cyclization observed during the autoxidation of 5-hexenylmagnesium bromide increases markedly as the O_2 concentration in the solution is decreased. These observations are consistent with a radical chain mechanism in which cyclization of 5-hexenyl radicals competes with their reaction with oxygen but appears to rule out any simple bimolecular reaction between Grignard reagent and oxygen.

The autoxidation of Grignard reagents to magnesium salts of alcohols is generally considered

$$2RMgX + O_2 \longrightarrow 2ROMgX \tag{1}$$

$$RMgX + O_2 \longrightarrow ROOMgX \tag{2}$$

$$ROOMgX + RMgX \longrightarrow 2ROMgX \tag{3}$$

to follow the two-step path originally proposed by Porter and Steele,[3] since the intermediate hydroperoxides may be obtained in good yield (30–90% for aliphatic Grignard reagents) if the Grignard reagent is added slowly to oxygen-saturated solvents at −78°.[4] The second step, reaction 3, apparently involves a simple nucleophilic attack on oxygen (perhaps *via* the rearrangement of an intermediate complex in which oxygen is coordinated with the magnesium) and is observed in the reaction of organometallics with a variety of peroxide derivatives.[4]

The first step, reaction 2, can either be formulated as a simple insertion or a radical chain. In their initial study, Walling and Buckler could find no evidence for a chain process, since diphenylamine, a good autoxidation inhibitor, did not decrease hydroperoxide yields, and butyraldehyde, which is readily autoxidized, did not interfere with the reaction or undergo cooxidation. Subsequently, however, rearrangements typical of radical processes have been observed to accompany autoxidations of certain Grignard reagents and have been taken as evidence for the radical chain path. Thus 3,3-diphenylallylcarbinylmagnesium bromide yields appreciable amounts of cyclopropyldiphenylmethanol on autoxidation, but only open-chain products on carbonation.[5] Similarly 3,5-hexadienylmagnesium bromide gives some 1- and 3-cyclopropylallyl alcohol on autoxidation, but no cyclized products on carbonation.[5] Finally, 5-hexenylmagnesium bromide on autoxidation gives approximately 25% cyclopentylmenthanol but little or no cyclization in other reactions.[6] The cyclization is evidently not reversible, since autoxidation of

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[1] Taken from the Ph.D. Thesis of A. Cioffari, Columbia University, 1970. Support of this work by a grant from the National Science Foundation and a Fellowship to A. Cioffari from the National Institutes of Health is gratefully acknowledged.

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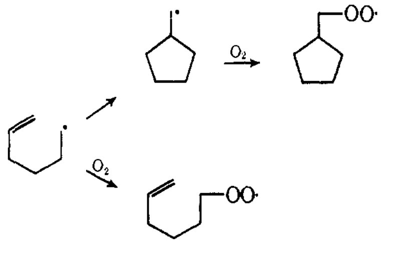
[3] C. W. Porter and C. S. Steele, *J. Amer. Chem. Soc.*, **42**, 2650 (1920).

[4] C. Walling and S. A. Buckler, *ibid.*, 77, 6032 (1955).

[5] M. E. H. Howden, J. Burdon, and J. D. Roberts, *ibid.*, **88**, 1732 (1966).

cyclopentylmagnesium bromide gives no open-chain alcohol.[6]

All of these results are consistent with free-radical processes, and those with 5-hexenylmagnesium bromide are particularly interesting since cyclization of the 5-hexenyl radical to the cyclopentylmethyl radical (a rather unexpected result) has been demonstrated in several other systems.[7] However while they are suggestive of a radical chain involving as one step the competition they do not really eliminate two alternatives: cyclization during eq 3, the RMgX-ROOMgX reaction, or cyclization during a bimolecular RMgX-O_2 reaction, and, in fact, cyclizations involving both 4,5- and 5,6-double bonds have been observed in other Grignard systems.[8]



(4)

To eliminate these possibilities, we have now examined the RMgX-ROOMgX reaction of 5-hexenylmagnesium bromide, and also the dependence of cyclization on oxygen concentration during autoxidation, since sequence 4 clearly predicts increased cyclization with increased lifetime of the 5-hexenyl radical. On the other hand, it is difficult to see how any simple bimolecular process would show an amount of cyclization dependent on oxygen concentration. Our results, carried out in duplicate on two lots of 5-hexenylmagnesium bromide, are summarized in Table I.

Table I. Autoxidation of 5-Hexenylmagnesium Bromide

Expt	Conditions	[RMgX], *M*	Products, %[c] Open chain	Cyclized
A	RMgX hydrolyzed	1.19[a]	95.2	4.8
		1.11[b]	93.5	6.5
B	RMgX + *t*-BuOOMgCl, room temp	1.19[a]	93.8	6.2
		1.11[b]	92.9	6.1
C	Inverse autoxidation at −78°	0.595[a]	90.2	9.8
		1.19[a]	94.3	5.7
		0.555[b]	88.2	11.8
		1.11[b]	92.3	7.7
D	Rapid autoxidation with O_2 at 0°	1.19[a]	78.9	21.1
		1.11[b]	73.8	26.2
E	Slow autoxidation – air at room temp	1.19[a]	65.5	34.5
		1.11[b]	59.2	40.8

[a] Lot 1 of RMgX prepared from 1,2,6-tribromohexane. [b] Lot 2 prepared from 6-bromo-1-hexene. [c] Relative yields of alcohols except in A where products are 1-hexene and methylcyclopentane. Actual yields 70–85% except in C.

In experiment A, each lot was hydrolyzed and shown to yield 1-hexene as expected plus about 5% methylcyclopentane. Apparently this arises from a small amount of cyclopentylmethylmagnesium bromide produced during formation of the reagent, and has been noted previously.[6] In B the Grignard reagents were treated with 1 equiv of *t*-BuOOMgX (prepared by autoxidation of *t*-butylmagnesium chloride). Since no additional cyclization was observed in the resulting alcohols, plainly no cyclization accompanies reaction 3.

In C the Grignard reagent was added to O_2-saturated solvent at −78°. The resulting peroxide was then reduced with KI and alcohols were determined. Yields were relatively low (30–44%), as has been noted with other RMgBr compounds, presumably because of some oxidation of bromide ion to bromine.[4] These conditions should ensure rapid reaction with oxygen and minimize radical lifetimes, and not more than 5% additional cyclization is observed.

In D the Grignard reagent was autoxidized by bubbling a rapid stream of oxygen through the solution at 0°, and in E a slow stream of dry air was passed over the stirred reagent at room temperature for several hours. These conditions should give increasingly long lifetimes to any intermediate 5-hexenyl radicals and lead to increasing amounts of cyclization as observed.[9] In fact, in E, since half of the alcohol is produced *via* reaction 3, up to 80% cyclization of the intermediate hydroperoxide must have taken place.

While we believe that these experiments rule out any simple bimolecular process for eq 2 and support a radical-chain mechanism for the cyclization involving eq 4, we must point out that the details of the chain are still in doubt. Since autoxidation occurs rapidly at −78°, some sort of redox initiation is indicated, *e.g.*

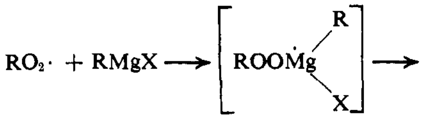
$$RMgX + O_2 \longrightarrow R\cdot + MgX^+ + O_2\cdot^- \qquad (5)$$

Propagation *via* a redox chain was initially proposed by Russell[10] but more recently a displacement chain

$$R\cdot + O_2 \longrightarrow RO_2\cdot \qquad (6)$$

$$RO_2\cdot + R^- \longrightarrow RO_2^- + R\cdot \qquad (7)$$

has been suggested[11] substituting eq 8 for 7. Formulation 8 is similar to that proposed for the autoxidation of trialkylboranes[12] and has a number of analogies in other radical reactions of electron-deficient compounds.[11,12] Considering that Grignard reagents are essentially covalent compounds which in ether solvents are at best only slightly dissociated into ion pairs,



$$RO_2\cdot + RMgX \longrightarrow \left[ROO\overset{R}{\underset{X}{Mg}} \right] \longrightarrow ROOMgX + R\cdot \qquad (8)$$

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(6) R. C. Lamb, P. W. Ayers, M. K. Toney, and J. F. Garst, *J. Amer. Chem. Soc.*, **88**, 4261 (1966).

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(8) E. A. Hill, H. G. Richey, Jr., and T. C. Rees, *J. Org. Chem.*, **28**, 2161 (1963); H. G. Richey, Jr., and T. C. Rees, *Tetrahedron Lett.*, 4297 (1966); H. G. Richey, Jr., and A. M. Rothman, *ibid.*, 1457 (1967).

(9) Temperatures also increase from run C to E, and increased temperature should also favor cyclization which has an appreciable activation energy while carbon radical reactions with O_2 are close to diffusion controlled. Thus a portion of the effect may be due to temperature rather than oxygen concentration.

(10) G. A. Russell, *J. Amer. Chem. Soc.*, **76**, 1595 (1954).

(11) C. Walling, *Advan. Chem. Ser.*, **No. 75**, 166 (1968).

(12) E. C. Coffee and A. G. Davies, *J. Chem. Soc. C*, 1493 (1966); A. G. Davies and B. P. Roberts, *ibid.*, *B*, 1074 (1968). These authors have observed that autoxidation of organozinc, -cadmium, and -boron compounds are subject to typical chain initiation and inhibition although the effect could not be observed with Grignard reagents or organolithium compounds.

and that the resulting ROOMgX, which is highly soluble in nonpolar solvents, is also presumably nonionic, eq 8 seems to us a more plausible reaction path in this sort of system, although simple electron transfer between radicals and anions may well occur in more highly ionized systems.

Experimental Section

Reagents. Ether solutions of 5-hexenylmagnesium bromide were prepared either from 6-bromo-1-hexene or from the more available 1,2,6-tribromohexane[13] and, as seen in Table I, gave equivalent results. While both lots showed about 5% cyclization during formation, as noted, there was no evidence for further change on storage under N_2. Solutions of *t*-BuOOMgCl were prepared by inverse addition of *t*-BuMgCl to oxygen-saturated ether at −78°. The best yields (89%) were obtained using dilute (0.55 *M*) solutions and slow addition.

Experimental runs were carried out as indicated in Table I. After reaction they were hydrolyzed with aqueous NH_4Cl, reduced with KI and acetic acid when necessary (run C) with quantitative titration of a sample for peroxide, dried, and analyzed by gas–liquid chromatography (glc) using internal standards and prior calibration with authentic samples. Hexene and methylcyclopentane were analyzed on a didecyl phthalate column at 70° using pentane as standard and the alcohols were analyzed on 20% Carbowax 20M at 140° using cyclohexanol as standard.

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The Mechanism of Reduction of Alkylmercuric Halides by Metal Hydrides[1]

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Abstract: Reductive demercuration of representative alkylmercuric bromides by metal hydrides has been shown to involve generation of intermediate alkyl radicals by comparison of the product distributions obtained on demercuration with those observed on reduction of the corresponding alkyl chlorides by tri-*n*-butyltin hydride under free-radical conditions. Reductions of neophylmercuric bromide (**1**) and 1,7,7-trimethylbicyclo[2.2.1]heptyl-2-mercuric bromide (**2**) using sodium borodeuteride, diethylaluminum deuteride, deuterio(tri-*n*-butylphosphine)-copper(I), and tri-*n*-butyltin deuteride occur without the rearrangements characteristic of intermediate carbonium ions. Reductions of *exo*- and *endo*-norbornyl-2-mercuric bromides (**3** and **4**) with the same reducing agents yield ∼90:10 mixtures of *exo*- and *endo*-norbornane-2-d_1. Reductions of *exo*- and *endo*-2-chloronorbornane with tri-*n*-butyltin deuteride yield an 84:16 mixture of these norbornane-d_1 epimers. The relative yields of 3-acetoxynortricyclene (**13**), *anti*-7-acetoxynorborn-5-ene (**16**), and *exo*-2-acetoxynorborn-5-ene (**17**) obtained on reduction of *cis*-*exo*-2-acetoxynorborn-5-ene-3-mercuric bromide (**5**) and *exo*,*exo*-3-acetoxynortricyclyl-5-mercuric bromide (**6**) with metal deuterides compare closely with those obtained on reduction of *endo*-2-chloro-*exo*-3-acetoxynorborn-5-ene (**8**) and *exo*-3-chloro-*exo*-5-acetoxynortricyclene (**12**) with tri-*n*-butyltin hydride. For comparison, *exo*-2-chloro-*endo*-3-acetoxynorborn-5-ene (**7**), *endo*-2-chloro-*endo*-3-acetoxynorborn-5-ene (**9**), and *exo*-3-chloro-*endo*-5-acetoxynortricyclene (**11**) have also been reduced with tri-*n*-butyltin hydride. The products from reductions of these alkyl chlorides provide evidence that norborn-5-en-3-yl radicals substituted at the 2 and 7 positions interconvert rapidly through appropriate nortricyclyl radicals (*e.g.*, **18** ⇄ **19** ⇄ **20** and **21** ⇄ **22** ⇄ **23**). Reductive demercuration of the alkylmercuric chlorides is proposed to involve intermediate alkylmercuric hydrides.

The development of promising procedures for the Markovnikov conversion of olefins to alcohols, ethers, and amides based on the generation of alkylmercury compounds by solvomercuration followed by demercuration using sodium borohydride has renewed interest in organomercurials as synthetic intermediates.[3,4] The mechanism of the solvomercuration steps in these procedures is well understood;[5,6] the mechanism of reductive demercuration using metal hydrides is less clear.[7]

The major fraction of the evidence pertinent to the mechanism of reaction of sodium borohydride and alkylmercurials is stereochemical in nature. Reductions of methyl 2-acetoxymercuri-2-deoxy-2,3,4,6-tetra-O-acetyl-*β*-D-mannopyranoside and related compounds,[8] *cis*-2-acetoxybicyclo[2.1.1]hexane-3-mercuric acetate,[9] *cis*-*exo*-2-hydroxybicyclo[2.2.1]heptane-3-mercuric chloride,[10] and *trans*-1-hydroxycyclopentyl-2-mercuric acetate[11] are reported to proceed with predominant or exclusive retention of configuration at the carbon atom originally bonded to mercury, while reductions of *eryth-*

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[1] Supported by tha National Science Foundation, Grant No. GP-14247, and the National Institutes of Health, Grant No. GM-16020.

[2] National Institutes of Health Predoctoral Fellow, 1966–1970.

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