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 (29) The often reported "errors" from regression analysis are not realistic and give only the reproducibility of the data.

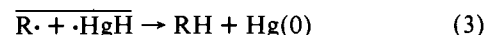
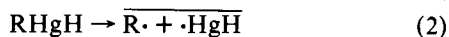
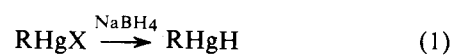
Reductive Demercuration of Hex-5-enyl-1-mercuric Bromide by Metal Hydrides. Rearrangement, Isotope Effects, and Mechanism

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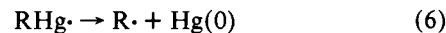
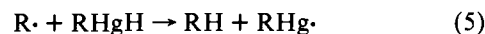
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Abstract: The use of the rearrangement of hex-5-enyl radical intermediates as a mechanistic probe has been examined in the reductive demercurations of hex-5-enyl-1-mercuric bromide (**1**). Methylcyclopentane and 1-hexene are the major products from reductions of **1** by sodium borohydride, lithium aluminum hydride, and tri-*n*-butyltin hydride. The formation of methylcyclopentane and the absence of cyclohexane are consistent with a noncage, free-radical chain mechanism for these reductions. The sodium amalgam reduction of **1** produces only 1-hexene. Hex-5-en-1-ol and a peroxide are formed from sodium borohydride reductions of **1** in the presence of molecular oxygen. Isotope effects for transfer of hydrogen to the intermediate hex-5-enyl radicals have been determined from the 1-hexene/methylcyclopentane product ratio, since rearrangement of the 5-hexenyl radical competes with hydrogen abstraction. The magnitude of these isotope effects (1.8 ± 0.2) is the same for reductive demercurations of **1** by sodium borohydride, lithium aluminum hydride, and tri-*n*-butyltin hydride; these results provide evidence for a common hydrogen-transfer agent, such as hex-5-enyl-1-mercuric hydride, for all of these metal-hydride reductions. The validity of the competing rearrangement method of determining hydrogen isotope effects has been demonstrated by determining the isotope effect for the tri-*n*-butyltin hydride reduction of 6-bromo-1-hexene (2.8 ± 0.2) at 40 °C.

Versatile synthetic procedures for the Markownikoff conversion of alkenes,² allenes,³ and cyclopropanes⁴ to alcohols, ethers, amides, amines, peroxides, and azides have been developed using the mercuriation-reductive demercuration sequence.⁵ Since metal hydrides, particularly sodium borohydride, have generally been used to effect the reductive demercuration of the intermediate alkylmercuric salts, the mechanisms of these reductions have received careful scrutiny recently. The significant mechanistic observations are that reductive demercurations by sodium borohydride are characterized by loss of stereochemical integrity,⁵⁻⁸ rearrangement,^{6,7,9} and incomplete incorporation of label from sodium borodeuteride.^{7,8} These results as well as the efficient trapping of alkyl radical intermediates by molecular oxygen^{9,11} and 2,2,6,6-tetramethylpiperidoxyl¹¹ have been explained in terms of mechanisms for the reductive demercurations by sodium borohydride involving either solvent-cage reactions (eq 1-3) or radical-chain processes (eq 4-6); an alkylmercuric hydride, RHgH, is the assumed source of hydrogen for the radicals.⁷ Furthermore, the product distributions from reductions of norbornenyl-, nortricycyl-, and isomeric norbornylmercuric salts using a variety of metal hydrides (NaBH₄, (*n*-Bu)₃SnH, (C₆H₅)₃SnH, Et₂AlH, and HCup(*n*-Bu)₃) have been interpreted in terms of a common source of hydrogen (RHgH) for reductions using different metal hydrides.^{7,10}



or



We have been exploring the scope and limitations of using rearrangement as a mechanistic probe for radical intermediates. Earlier studies of the sodium borohydride reduction of 2,2,2-triphenylethylmercuric chloride provided the first evidence for relatively long-lived radical intermediates in reductive demercuration, since the major product in the absence of oxygen was the rearranged hydrocarbon, 1,1,2-triphenylethane.⁹ These studies also provide the first report of successful trapping of radical intermediates in these reactions; the major product of reductive demercuration of 2,2,2-triphenylethylmercuric chloride by sodium borohydride in the presence of oxygen was the rearranged alcohol, 1,1,2-triphenylethanol. However, the extrapolation of these results to simple alkyl systems was regarded as tenuous. As an extension of these studies, we report herein results obtained for the reductive demercuration of hex-5-enyl-1-mercuric bromide (**1**) by various metal hydrides.¹² These studies provide direct evidence regarding: (a) the lifetimes of the radical intermediates in reductive demercuration; (b) the nature of the common hydrogen source; and (c) the cause of the relatively low amounts of deuterium incorporation (80-90% *d*₁) reported for reductive

demercurations using sodium borodeuteride (94% *d*). An unexpected spin-off of these studies has been the development of a simple, accurate method of determining isotope effects for hydrogen-transfer reactions of radicals, taking advantage of the competing rearrangement in the 5-hexenyl system.

Experimental Section

General Methods. Melting points were obtained using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are uncorrected. NMR spectra were run in carbon disulfide using a Varian Model A-60 spectrometer; chemical shifts are reported in parts per million downfield from tetramethylsilane. Infrared spectra were obtained using a Perkin-Elmer Model 337 grating spectrometer with samples between sodium chloride plates. Combined GLC-mass spectra were obtained on a Hitachi Perkin-Elmer Model RMU-6E mass spectrometer interfaced with a Perkin-Elmer Model 881 gas chromatograph. Spectra used for deuterium analyses were obtained using an ionizing voltage of ca. 30 eV, since at this voltage no $M - 1$ peak was observed for 1-hexene. At least four scans of the molecular ion region were made for each deuterium analysis. Analytical GLC measurements were conducted on a Varian Aerograph Model 90-P gas chromatograph using the internal standard method for calibrations. Hydrocarbon products were separated and analyzed using both a 20 ft, 10% di-*n*-decyl phthalate on Chromosorb W-AW DMCS column and a 20 ft, 20% Carbowax 20M on Chromosorb W-AW DMCS column. Alcohol products were separated and analyzed using the Carbowax 20M column. Microanalyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, 5251 Elbach über Engelskirchen, West Germany and by Chemalytics, Inc., 2330 S. Industrial Park Dr., Tempe, Arizona.

Materials. Commercial samples of 6-bromo-1-hexene, hex-5-en-1-ol, tri-*n*-butyltin chloride, 1,2,6-trihydroxyhexane, 1,2,6-tribromohexane, and azobisisobutyronitrile were used without purification. Sodium borohydride was recrystallized from diglyme and stored as an aqueous solution in 3 M sodium hydroxide. Sodium borodeuteride (Alfa Inorganics, 94% *d*; Crescent Chemicals Co., 98% *d*), lithium aluminum hydride, and lithium aluminum deuteride (Alfa Inorganics, 98% *d*) were stored in an inert atmosphere glove box¹³ under an argon atmosphere and used without purification. Benzene was stirred over concentrated sulfuric acid, washed with water, dried over anhydrous $MgSO_4$, and then distilled from lithium aluminum hydride. Mercuric bromide, mercuric chloride, and phosphorus tribromide were used without purification. 1,2,6-Tribromohexane,¹⁴ 6-bromo-1-hexene,¹⁵ tri-*n*-butyltin deuteride,⁷ and tri-*n*-butyltin hydride¹⁶ were prepared using standard literature procedures.

Hex-5-enyl-1-mercuric Bromide. Ether solutions containing 3.7 mmol of 5-hexenylmagnesium bromide were prepared either from 6-bromo-1-hexene or 1,2,6-tribromohexane.¹⁴ A solution of 10.4 g (3.85 mmol) of mercuric chloride in 40 ml of tetrahydrofuran (freshly distilled from benzophenone sodium ketyl) was added dropwise to the Grignard solution. After stirring for 0.5 h, the ether solution was washed with water, dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The resulting solid was recrystallized to constant melting point from methanol to yield 3.5 g (25%) of hex-5-enyl-1-mercuric bromide: mp 100–101 °C; ¹H NMR (CS_2) δ 1.5 (m, 8 H), 4.8 (m, 2 H), 5.5 (m, 1 H); ir (KBr mull) 3080 (m), 2930 (s), 2850 (s), 1640 cm^{-1} (m); ir (Nujol mull) 915 (s), 690 cm^{-1} (m). Anal. ($C_{16}H_{11}HgBr$): C, H.

Cyclopentylmethylmercuric Bromide. A procedure similar to the method described for hex-5-enyl-1-mercuric bromide except using cyclopentylmethyl bromide was used for this preparation. The product was recrystallized from methanol and sublimed to give a yield of 22% of cyclopentylmethylmercuric bromide: mp 60–61 °C; ¹H NMR (CS_2) δ 1.6 (m), 2.2 (m); ir (KBr) 2950 (s), 2850 (s), 730 cm^{-1} (m). Anal. ($C_{16}H_{11}HgBr$): C, H.

Bis-1-hex-5-enylmercury. 5-Hexenylmagnesium bromide was prepared from 58.9 g (0.18 mol) of 1,2,6-tribromohexane and 13 g (0.54 mol) of magnesium in ether and quenched with 68 g (0.19 mol) of mercuric bromide. The oil resulting from workup was chromatographed on a 2 ft silica gel column using hexane as eluent. The resulting oil was identified as bis-1-hex-5-enylmercury on the basis of: (1) producing only one spot on TLC analysis (Silica Gel G) which did not develop with sodium borohydride unless pretreated with iodine vapor; (2) reaction with mercuric bromide in tetrahydrofuran to produce hex-5-enyl-1-mercuric bromide; and (3) no reaction with

sodium borohydride in 10 ml of tetrahydrofuran–15 ml of water: NMR (neat) δ 1.5 (m), 1.48 (m), 5.5 (m); ir (neat) 3080 (m), 2930 (s), 1640 cm^{-1} (m). Decomposition in transit precluded reliable elemental analysis. A literature report of the synthesis of this compound did not report physical properties.¹⁸

Demercurations of Hex-5-enyl-1-mercuric Bromide with Sodium Borohydride (Deuteride) in Degassed Solvents. Reductions were performed in three solvent systems: (a) 20 ml of tetrahydrofuran, 5 ml of water; (b) 10 ml of tetrahydrofuran, 15 ml of water; and (c) 5 ml of tetrahydrofuran, 20 ml of water. The procedures used for the reactions in these solvents were similar. Water (0–8 ml), 5–8 ml of 3 M aqueous sodium hydroxide, and 5 ml of 0.5 M aqueous sodium borohydride (2.5 mmol) or borodeuteride were mixed in a flask equipped with a side arm containing 100–200 mg (0.275–0.550 mmol) of hex-5-enyl-1-mercuric bromide and the flask was connected to a high vacuum manifold. After several freeze–evacuate–thaw cycles, a degassed flask of tetrahydrofuran over lithium aluminum hydride was opened to the manifold and tetrahydrofuran (5–20 ml) was flash distilled into the reaction flask. After isolating the reaction flask from the manifold, tetrahydrofuran (2 ml) was distilled into the side arm and the mercurial solution emptied into the stirred reaction flask. After a period of several hours, the flask was cooled to –70 °C and pentane (internal standard) was added. After warming, the aqueous layer was saturated with sodium chloride and the tetrahydrofuran layer was separated, dried with 4-Å molecular sieves, and analyzed by GLC and GLC–MS. Control experiments established the accuracy of this work-up procedure for hydrocarbon analyses.

Demercuration of Hex-5-enyl-1-mercuric Bromide with Sodium Borohydride in the Presence of Oxygen. Procedures for these reductions were similar to those in degassed solvents (10 ml of tetrahydrofuran–15 ml of H_2O) except that an oxygen atmosphere (1 atm) was introduced into the reaction flask prior to addition of the mercurial solution. 1-Pentanol was added prior to standard workup as an internal standard for GLC analyses. When the mercurial (1) was added abruptly as described for the degassed solutions, significant amounts of hydrocarbon products were obtained (16% 1-hexene and 8% methylcyclopentane) in addition to hex-5-en-1-ol (55%). When the mercurial solution was added dropwise, the hydrocarbon products were eliminated (<1% of each) and the yield of hex-5-en-1-ol rose to 68%. In no case were significant amounts of cyclopentylmethanol detected (<1%).

Peroxide product analyses were performed on the oil obtained by removing the tetrahydrofuran under reduced pressure after workup. This oil was chromatographed on a silica-gel column using low-boiling petroleum ether followed by 10% ether–90% petroleum ether as eluents. The peroxide fraction (yellow oil) gave a positive ferrox test for peroxides.¹⁹ This impure peroxide fraction yielded only hex-5-en-1-ol (GLC) after reduction with either lithium aluminum hydride or potassium iodide and was unaffected by treatment with dilute aqueous H_2SO_4 for 24 h. This oil produced 1.8 mol of hex-5-en-1-ol for each equivalent of peroxide titrated with standard potassium iodide and sodium thiosulfate solutions.²⁰ The ¹H NMR spectrum (CS_2) of the oil (free from 5-hexen-1-ol as shown by GLC) showed peaks at δ 5.5 (m, 1 H), 4.8 (m, 2 H), 3.8 (t, 2 H), 1.5 (m, ca. 6 H). The ir spectrum (neat) showed a hydroxyl band at 3600 cm^{-1} and peaks at 3080, 2930, 2850, and 1640 cm^{-1} . The ¹H NMR spectrum (CS_2) of 5-hexen-1-ol is similar except that it has a peak at δ 3.40 (t) vs. δ 3.8 for the unknown peroxide.

Reduction of Hex-5-enyl-1-mercuric Bromide with Sodium Amalgam. Hex-5-enyl-1-mercuric bromide (0.158 g, 0.43 mmol), 2 ml of tetrahydrofuran, 0.5 ml of D_2O (Stohler Isotope Chemicals, 99.8% D), and 3.06 g of sodium amalgam (1.2%)²¹ were stirred for 24 h. After adding pentane (internal standard), an aliquot was removed, dried over 4 Å molecular sieves, and analyzed by GLC and GLC–MS. A 60% yield of 1-hexene (>96% *d*₁ by GLC–MS) was determined by GLC. No other hydrocarbon products (<1%) were observed.

Demercuration of Cyclopentylmethylmercuric Bromide with Sodium Borohydride. Cyclopentylmethylmercuric bromide (0.200 g, 0.55 mmol) was reduced with sodium borohydride using the same procedure described for hex-5-enyl-1-mercuric bromide in degassed solvents in 10 ml of tetrahydrofuran–15 ml of water. Analysis by GLC indicated a 51% yield of methylcyclopentane and no detectable 1-hexene (<1%).

Reduction of Hex-5-enyl-1-mercuric Bromide with Lithium Aluminum Hydride (Deuteride). Tetrahydrofuran solutions of lithium aluminum hydride and lithium aluminum deuteride were standardized

Table I. Sodium Borohydride Reductions of Hex-5-enyl-1-mercuric Bromide^a

Run	Reducing agent	Solvent THF/ H ₂ O, ml	% Product yields and isotopic compositions ^b	
			1-Hexene	Methylcyclopentane
1	NaBH ₄	5/20	17	4
2	NaBH ₄	5/20	16	3
3	NaBH ₄	10/15	30	35
4	NaBH ₄	10/15	30	35
5	NaBH ₄	10/15	37	44
6 ^c	NaBH ₄	10/15	26	56
7 ^c	NaBH ₄	10/15	26	53
8	NaBH ₄	20/5	18	57
9	NaBH ₄	20/5	19	62
10	NaBD ₄ (94% <i>d</i>)	10/15	27 (86% <i>d</i> ₁)	55 (87% <i>d</i> ₁)
11	NaBD ₄ (98% <i>d</i>)	10/15	19 (94% <i>d</i> ₁)	40 (93% <i>d</i> ₁)
12	NaBD ₄ (48% <i>d</i>)	10/15	32 (27% <i>d</i> ₁)	41 (27% <i>d</i> ₁)
13	NaBD ₄ (94% <i>d</i>)	10/15	25	57

^a All reactions at ambient temperature using 2.5 mmol of NaBH₄ and 200 mg (0.55 mmol) of hex-5-enyl-1-mercuric bromide except where noted. ^b Remainder of the product mixture is bis-1-hex-5-enylmercury. ^c 100 mg (0.275 mmol) of mercurial used in these reactions.

by hydrolyzing aliquots and measuring the volume of hydrogen gas evolved.²² A 0.50-ml aliquot (0.402 M, 0.201 mmol) of the standardized solution of lithium aluminum hydride was added rapidly to a flask containing 0.154 g (0.42 mmol) of hex-5-enyl-1-mercuric bromide in 5 ml of tetrahydrofuran with rapid stirring. After the reaction was stirred for 1 h, the excess lithium aluminum hydride was destroyed using 2% aqueous NaOH until gas evolution ceased. After adding pentane (internal standard), the tetrahydrofuran solution was dried over 4 Å molecular sieves and analyzed by GLC and GLC-MS. No detectable deuterium incorporation into the hydrocarbon products was found when D₂O (99.8% D) was used to quench these reductions. Similar procedures were used for lithium aluminum deuteride reductions.

Reduction of Hex-5-enyl-1-mercuric Bromide with Tri-*n*-butyltin Hydride (Deuteride). Standardized solutions²³ (0.425 N) of tri-*n*-butyltin hydride and tri-*n*-butyltin deuteride²⁴ in benzene were utilized for these reductions. A 5-ml aliquot (2.13 mmol) of the benzene solution of tri-*n*-butyltin hydride was added by syringe into a flask containing 0.350 g (0.964 mmol) of hex-5-enyl-1-mercuric bromide under a positive pressure of nitrogen. After 30 min the solution was cooled in an ice-water bath and pentane (internal standard) was added. The resulting solution was analyzed by GLC and GLC-MS. Similar procedures were used for tri-*n*-butyltin deuteride reductions.

Reduction of 6-Bromo-1-hexene with Tri-*n*-butyltin Hydride (Deuteride). These reductions were carried out in a 50-ml glass bulb with a vacuum manifold adapter and a serum cap adapter. After flushing the flask with nitrogen, 5 ml of 0.45 M (2.25 mmol) tri-*n*-butyltin hydride and a 6-7-mm length of open-ended capillary tubing filled with azobisisobutyronitrile were added to the flask. The solution was cooled to -70 °C and then 0.130 ml (0.156 g, 0.96 mmol) of 6-bromo-1-hexene was added via syringe. After two freeze-evacuate-thaw cycles, the flask was placed in a 40 °C oil bath for 21 h. After cooling and adding pentane (internal standard), the solution was analyzed by GLC and GLC-MS.

Results

Table I lists products, yields, and isotopic compositions observed on reduction of hex-5-enyl-1-mercuric bromide (**1**) using sodium borohydride and sodium borodeuteride in degassed, alkaline, aqueous tetrahydrofuran. Table II lists products, yields, and isotopic compositions observed on reduction of hex-5-enyl-1-mercuric bromide using lithium aluminum hydride, lithium aluminum deuteride, tri-*n*-butyltin hydride, and tri-*n*-butyltin deuteride. Methylcyclopentane is formed in significant yields from reductive demercurations of

Table II. Lithium Aluminum Hydride^a and Tri-*n*-Butyltin Hydride^b Reductions of Hex-5-enyl-1-mercuric Bromide

Run	Reducing agent	% Product yields and isotopic compositions	
		1-Hexene	Methylcyclopentane
1	LiAlH ₄	33	36
2	LiAlH ₄	42	48
3	LiAlH ₄ ^c	36	60
4	LiAlD ₄ (98% <i>d</i>)	20 (>93% <i>d</i> ₁)	41
5	LiAlD ₄ (98% <i>d</i>)	20 (96% <i>d</i> ₁)	39
6	LiAlD ₄ ^d (54% <i>d</i>)	28 (37% <i>d</i> ₁)	40 (38% <i>d</i> ₁)
7	Bu ₃ SnH	68	20
8	Bu ₃ SnH	68	18
9	Bu ₃ SnD (98% <i>d</i>)	60 (96% <i>d</i> ₁)	28
10	Bu ₃ SnD (98% <i>d</i>)	59 (96% <i>d</i> ₁)	29
11	Bu ₃ SnD (65% <i>d</i>)	68 (44% <i>d</i> ₁)	27
12	Bu ₃ SnD (65% <i>d</i>)	70 (45% <i>d</i> ₁)	26

^a LiAlH₄ reductions were carried out at ambient temperature in 5 ml of tetrahydrofuran using 0.804 mequiv of LiAlH₄ and 0.150 g (0.41 mmol) of mercurial. ^b Bu₃SnH reductions were carried out at ambient temperature in 5 ml of benzene using 2.13 mequiv of Bu₃SnH and 0.350 g (0.96 mmol) of mercurial. ^c LiAlH₄ solution added dropwise to the mercurial, and D₂O (99.8% *d*) used to quench the reaction. No detectable deuterium incorporation in products. ^d 1.08 mequiv of LiAlH₄ used in this reaction.

Table III. Tri-*n*-butyltin Hydride Reductions of 6-Bromo-1-hexene^a

Run	Reducing agent	% Product yields and isotopic composition	
		1-Hexene	Methylcyclopentane
1	Bu ₃ SnH	64	17
2	Bu ₃ SnH	69	18
3	Bu ₃ SnD (98% <i>d</i>)	48 (94% <i>d</i> ₁)	31
4	Bu ₃ SnD (98% <i>d</i>)	52 (94% <i>d</i> ₁)	38

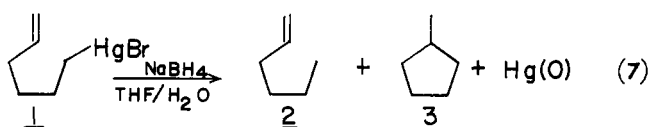
^a All reactions at 40 °C for 21 h using 2.25 mequiv of Bu₃SnH and 0.156 g (0.96 mmol) of 6-bromo-1-hexene in 5 ml of benzene using azobisisobutyronitrile as initiator.

1 using all of these hydride reducing agents. It is noteworthy that the amount of methylcyclopentane relative to 1-hexene is increased when deuterated reducing agents are employed, e.g., compare the ratios in runs 3, 4, and 5 to runs 10-13 (Table I).

Table III lists products, yields, and isotopic compositions resulting from the tri-*n*-butyltin hydride reduction of 6-bromo-1-hexene. In accord with the free-radical chain nature of this reaction and the previous results of Walling and Ciofari,²⁵ both methylcyclopentane and 1-hexene are produced from these reductions.

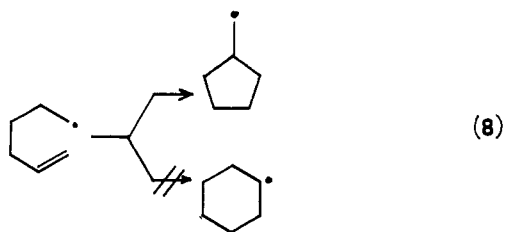
Discussion

Sodium Borohydride Reduction of 1. Examination of the data in Table I shows that under most reaction conditions methylcyclopentane is the major hydrocarbon product of reductive demercuration of hex-5-enyl-1-mercuric bromide using sodium borohydride (eq 7). The formation of methylcyclo-



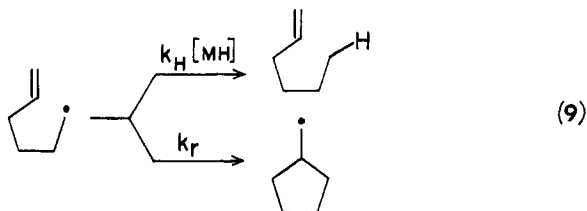
pentane is consistent with the formation of radical intermediates rather than carbenium ions in these reductive demer-

curations, since the 5-hexenyl radical is known to undergo cyclization to the cyclopentylmethyl radical (eq 8), whereas



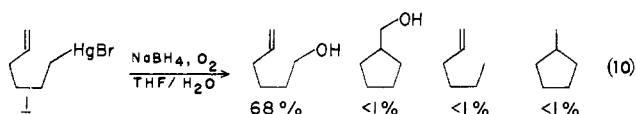
the 5-hexenyl cation cyclizes to the cyclohexyl cation.²⁶ Further support for this distinction was obtained by examining the sodium borohydride reduction of cyclopentylmethylmercuric bromide; the only hydrocarbon product was methylcyclopentane in 51% yield. This result is consistent with the known irreversibility of the ring closure of the 5-hexenyl radical to the cyclopentylmethyl radical;²⁶ however, the cyclopentylmethyl cation is known to rearrange to the cyclohexyl cation under solvolytic conditions.²⁷ These results also provide evidence concerning the lifetime of these radicals, since the rate constant for cyclization of the 5-hexenyl radical is known to have a value of $1 \times 10^5 \text{ s}^{-1}$ at 25 °C,²⁸ which is very slow compared to expected rates of reaction of radicals within a solvent cage. The observation of major amounts of the rearrangement product, methylcyclopentane, in these reductions indicates that the lifetimes of radical intermediates must be relatively long compared to cage processes. In terms of the mechanisms previously proposed for these reactions (eq 1-6), noncage processes such as a radical-chain mechanism (eq 4-6) are most consistent with these data. A similar conclusion was reached previously from studies of the sodium borohydride reduction of 2,2,2-triphenylethylmercuric chloride.⁹

The data in Table I also show that the product proportions are dependent on the solvent composition and the initial concentration of **1**. A reasonable hypothesis would be that the intermediate 5-hexenyl radicals are partitioned between hydrogen abstraction and rearrangement as shown in eq 9, where



MH is the hydrogen source for the radicals (presumably RHgH). The solvent and concentration dependence of the product proportions would then be associated with changes in the concentration of MH. Jensen et al.⁸ have considered previously the effect of the solvent on NaBH_4 reductions of organomercurials in terms of the mechanism outlined in eq 4-6. They concluded that the steady-state concentration of RHgH would be smaller in less polar media, which is consistent with the effect of solvent which we observe.

Sodium Borohydride Reductions of **1 in the Presence of Oxygen.** Hex-5-en-1-ol is the major product obtained when a tetrahydrofuran solution of the mercurial **1** is added dropwise to an aqueous tetrahydrofuran solution of sodium borohydride in the presence of molecular oxygen; only traces of cyclopentylmethanol, 1-hexene, and methylcyclopentane are formed



(eq 10).²⁹ These results are consistent with efficient trapping of 5-hexenyl radicals by molecular oxygen, i.e., much faster

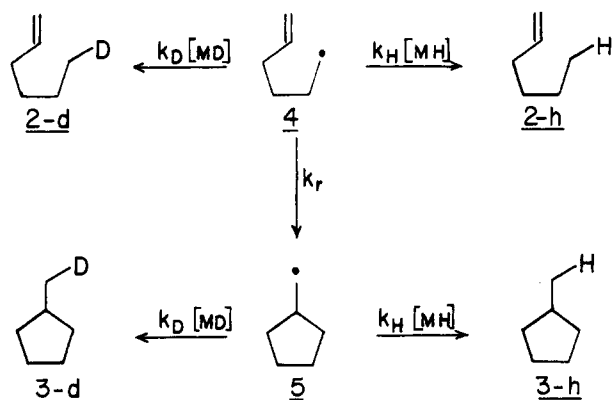
than the competing ring closure to give cyclopentylmethyl radical-derived products. A control experiment without added sodium borohydride established that little, if any, reaction takes place between the alkylmercurial and oxygen under the reaction conditions.³⁰ These oxygen-trapping results can be accommodated with the mechanism advanced previously by Hill and Whitesides.¹¹

Hill and Whitesides¹¹ have reported that alkoxyboron compounds as well as alcohols are produced from reductions of alkylmercurials by sodium borohydride in dimethylformamide in the presence of oxygen. We have obtained evidence for the formation of alkyl peroxides from analogous reactions in aqueous tetrahydrofuran.³¹ The peroxide product from the reaction of 5-hexenyl-1-mercuric bromide with sodium borohydride under an oxygen atmosphere could not be unambiguously identified because pure samples could not be obtained from the reaction mixtures. However, the peroxide-containing fraction, which did not contain 5-hexen-1-ol (GLC), was reduced to hex-5-en-1-ol using either lithium aluminum hydride or potassium iodide. When the product mixture resulting from reductions in an oxygen atmosphere was treated with potassium iodide, the yield of 5-hexen-1-ol increased from 68 to 91% and the peroxide was not detected (GLC). Furthermore, both the ^1H NMR and IR spectra of this material closely resemble those of hex-5-en-1-ol. Reasonable possibilities for the structure of this peroxide are 5-hexenyl hydroperoxide, a mixed borate ester, or (less likely) di-5-hexenyl peroxide.

Sodium Borodeuteride Reductions. The product distribution from reductive demercurations of **1** is significantly altered by substituting borodeuteride for borohydride, as shown by comparison of entries 3-5 with entries 10-13 in Table I; the yield of methylcyclopentane is increased and the yield of 1-hexene is decreased by this isotopic substitution. These results suggest that an isotope effect³² is operating in the hydrogen atom abstraction step which effectively increases the lifetime of the hex-5-enyl radicals with borodeuteride as reducing agent and thus leads to a higher proportion of rearranged hydrocarbon. Furthermore, the amount of deuterium incorporation in the hydrocarbon products is significantly lower than the deuterium content of the reducing agent, NaBD_4 .^{33,34}

The shift in product distribution can be rationalized in terms of the competing reactions outlined in Scheme I, where MH

Scheme I



and MD represent the sources of hydrogen and deuterium, respectively, for the radicals. If it is assumed that all cyclopentylmethyl radicals (**5**) give methylcyclopentane (**3-h** and **3-d**), the following rate expressions result

$$d[2\text{-h}]/dt = k_H[4][\text{MH}] \quad (11)$$

$$d[2\text{-d}]/dt = k_D[4][\text{MD}] \quad (12)$$

$$d[3\text{-h} + 3\text{-d}]/dt = k_r[4] \quad (13)$$

By dividing eq 11 by eq 13, eq 14 is obtained; the superscript "H" on the concentration brackets refers to NaBH₄ reactions.

$$d[2-h]^H/d[3-h]^H = k_H[MH]^H/k_r \quad (14)$$

If it is assumed that the concentration of the hydrogen source, MH, is effectively constant during the course of the reaction (i.e., steady-state approximation), then eq 14 can be integrated to give

$$[2-h]^H/[3-h]^H = k_H[MH]^H/k_r \quad (15)$$

Similarly, by dividing eq 12 by eq 13 and integrating, eq 16 is obtained; the superscript "D" on the concentration brackets refers to NaBD₄ reductions.

$$[2-d]^D/[3-h + 3-d]^D = k_D[MD]^D/k_r \quad (16)$$

Finally, by dividing eq 15 by eq 16 and rearranging terms, eq 17 is obtained.³⁵

$$k_H/k_D = \left(\frac{[2-h]^H/[3-h]^H}{[2-d]^D/[3-h + 3-d]^D} \right) \left(\frac{[MD]^D}{[MH]^H} \right) \quad (17)$$

All of the quantities required to calculate the isotope effect using eq 17 are readily available in Table I, except the ratio [MD]^D/[MH]^H, which represents the ratio of the steady-state concentrations of the hydrogen-transfer species in the NaBD₄ vs. NaBH₄ reductions.³⁵ A reasonable estimate of this ratio can be obtained, subject to the following assumptions: (1) MH is the alkylmercuric hydride, 5-hexenylmercuric hydride (RHgH); (2) RHgH is formed irreversibly from the alkylmercuric halide (eq 1); and (3) all RHgH is converted into hydrocarbon products. Using these assumptions, the ratio [MD]^D/[MH]^H can be determined from the deuterium content of the hydrocarbon products in the NaBD₄ reductions, since the NaBD₄ and NaBH₄ reductions were performed using the same reaction conditions.³⁷ The isotope effects³² calculated using eq 17 and the previous assumptions are shown in Table IV, entries 1 and 2. The calculated isotope effect on product proportions of 1.8 can be compared with the isotope effect of 4.4, which has been reported for hydrogen abstraction from BH₄⁻ by an alkyl radical.³⁸ This comparison tends to support the assumption that alkyl radicals abstract hydrogen from a reactive intermediate, presumably RHgH, and not directly from BH₄⁻.

The implications of these isotope-effect results are quite provocative, since the kinetic isotope effect of 1.8 for transfer of a hydrogen atom from the alkylmercuric hydride to the hex-5-enyl radical provides a means of characterizing the nature of the alkylmercuric hydride. Since no stable alkylmercuric hydride has been reported,³⁶ implying low Hg-H bond energies for this intermediate,⁷ the transition state for hydrogen transfer to a radical from RHgH would be expected to be less symmetrical (more reactant-like³⁹) than the transition state for abstraction from BH₄⁻. This would be expected to result in a smaller isotope effect for hydrogen transfer from RHgH vs. BH₄⁻, as observed.⁴⁰

These results provide an explanation for the less than quantitative amounts of deuterium incorporation reported by various groups.⁴¹ The operation of an isotope effect in either the step which forms RHgH (eq 1) or in the hydrogen-abstraction step (eq 5) would result in enrichment of the lighter isotope in the products for incompletely labeled borodeuteride of the type commercially available (94–98% D).

Lithium Aluminum Hydride and Tri-*n*-butyltin Hydride Reductions. Whitesides and San Filippo⁷ have proposed a common reaction pathway for all metal hydride reductions of alkylmercuric halides on the basis of the insensitivity of isomeric product ratios to variations in the metal hydride [NaBD₄, Et₂AlD, DCuP(*n*-Bu)₃, (*n*-Bu)₃SnD] for reductions

Table IV. Calculated Isotope Effects for Sodium Borohydride, Lithium Aluminum Hydride, and Tri-*n*-butyltin Hydride Reductions of **1** Using Equation 17

Entry	Reducing agent	Product ratios ^a		% <i>d</i> in products ^a	<i>k</i> _H / <i>k</i> _D
		[2-h] ^H / [3-h] ^H	[2-d] ^D / [3-h + 3-d] ^D		
1	NaBD ₄	0.85 ^b	0.42	0.86	1.7
2	NaBD ₄	0.85 ^b	0.45	0.94	1.8
3	LiAlD ₄	0.90 ^c	0.49	0.96	1.8
4	Bu ₃ SnD	3.6 ^d	2.06	0.96	1.7
5	Bu ₃ SnD	3.6 ^d	1.95	0.96	1.8

^a The product ratios and isotopic compositions of products were calculated from the GLC and GLC-MS data in Table I and II. ^b This value of [2-h]^H/[3-h]^H represents the average of this ratio for entries 3–5 in Table I. ^c This value of [2-h]^H/[3-h]^H represents the average of this ratio for entries 1 and 2 in Table II. ^d This value of [2-h]^H/[3-h]^H represents the average of this ratio for entries 7 and 8 in Table II.

of norbornyl-2-mercuric bromides as well as for a tricycloheptylmercuric bromide and the corresponding bicyclo[2.2.1]heptylmercuric bromide. Similar conclusions were reached independently by Gray, Jackson, and Chambers.¹⁰ If this hypothesis is correct, the isotope effect³² calculated from the shift in the product distributions for hydride reductions of 5-hexenyl-1-mercuric bromide should be independent of the nature of the metal hydride, since hydrogen transfer from 5-hexenylmercuric hydride to the 5-hexenyl radicals would be occurring for all metal hydride reductions. In order to test the postulated common reaction pathway for all metal hydride reductions of alkylmercuric halides, the reductions of hex-5-enyl-1-mercuric bromide by tri-*n*-butyltin hydride and lithium aluminum hydride have been investigated. The results in Table II show that the rearranged hydrocarbon, methylcyclopentane, is the major product of both the LiAlH₄ and (*n*-Bu)₃SnH reductions. As discussed previously, these results are consistent with the formation of noncage radicals for these reductions.⁴² As observed for NaBH₄ reductions, the product ratio (1-hexene/methylcyclopentane) decreases for the metal deuteride compared to the ratio observed for the corresponding metal hydride. The value for the corresponding hydrogen isotope effects³² can be calculated for each reducing agent using eq 7, assuming that the isotopic composition of the alkylmercuric hydride can be approximated by the isotopic composition of the hydrocarbon products.³⁷ The results of these calculations are also shown in Table IV. The kinetic isotope effects calculated for both reducing agents (1.8) are in remarkably good agreement with the analogous isotope effect obtained for the sodium borohydride reduction of **1**. Furthermore, since the isotope effect for hydrogen transfer from tri-*n*-butyltin hydride to alkyl radicals has been reported to be 2.7–2.8,⁴³ the mechanism of reduction of **1** by tri-*n*-butyltin hydride apparently does not involve hydrogen transfer from tri-*n*-butyltin hydride to the 5-hexenyl radical. Further support for this conclusion was obtained by determining the isotope effect for hydrogen transfer to 5-hexenyl radicals from tri-*n*-butyltin hydride using the shift in product distribution method described herein. The data are shown in Table III. The average value for the isotope effect determined using these data and eq 17 is 2.8 ± 0.2 at 40 °C, which is in good agreement with the value reported for transfer to the cyclohexyl radical (2.7–2.8 at 25 °C).⁴³

These isotope effect results provide support for the proposal^{7,10} that metal hydride reductions of alkylmercuric halides, in general, proceed via similar mechanistic pathways involving hydrogen atom transfer to alkyl radicals from a common hydrogen-transfer agent, presumably the alkylmercuric hy-

dride.⁴⁴ Furthermore, they demonstrate the mechanistic utility of competing rearrangement of hex-5-enyl radicals to determine isotope effects in hydrogen-transfer reactions of radicals.

Sodium Amalgam Reduction. Evidence has been presented which indicates that the sodium amalgam reduction of alkylmercuric salts does not proceed via a free radical pathway, unlike the metal hydride reductions.^{8,9} In accordance with these results, the sodium amalgam reduction of hex-5-enyl-1-mercuric bromide in a mixture of tetrahydrofuran and deuterium oxide produces only the unrearranged hydrocarbon 1-hexene in 60% yield. The lack of rearrangement in this system suggests either that radicals are not formed or that radicals, if formed, have very short lifetimes relative to the time required for rearrangement (i.e., 10^{-5} s). Furthermore, GLC-MS analysis of the 1-hexene from this reaction indicated that the deuterium content of this hydrocarbon (>96%) was much higher than the amounts observed in the hydride reductions. The previously reported stereospecificity of this reaction,⁸ as well as the high amount of incorporation of deuterium label and lack of rearrangement reported herein, support the use of sodium amalgam for structure proof, deuterium labeling, and synthesis in systems which are prone to free-radical rearrangement.

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References and Notes

- (1) (a) Taken in part from the Ph.D. Dissertation of R.E.L., University of Arkansas, 1975; (b) Presented in part at the 30th Southwest Regional Meeting of the American Chemical Society, Houston, Texas, 1974, Abstr. No. 77.
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- (30) See also ref 9 and 11 for further documentation of these results.
- (31) Precedent for the stability of alkyl peroxides in aqueous sodium borohydride solutions can be found in the recent work of Bloodworth and co-workers: A. J. Bloodworth and R. J. Bunce, *J. Chem. Soc., Perkin Trans. 1*, 1972 (1972), and references cited therein.
- (32) The term "isotope effect" is used in this paper to describe a differentiation which results in production of methylcyclopentane vs. 1-hexene. This should be contrasted with the general usage of this term to imply a differentiation between formation of R-H vs. R-D products. We are grateful to a referee for calling our attention to this distinction.
- (33) The fact that 94% monodeuterated hydrocarbon products are obtained using 98% deuterated NaBD₄ (Table I, run 11) argues against significant hydrogen abstraction from the solvent.
- (34) An isotope effect based on H vs. D discrimination for the NaBD₄ reductions can be calculated from the isotopic composition of the products in Table I. A value of ca. 2.6 is obtained for both runs 10 and 12 in Table I.
- (35) The critical assumption in this derivation is that of $d[MD]/dt = d[MD]/dt = 0$, i.e., that a steady-state approximation applies to the hydrogen-transfer species. Some support for this assumption can be derived from the failure of previous attempts to prepare species in solution with Hg-H bonds (ref 36). Furthermore, the calculated isotope effects utilizing eq 17 depend on the ratio of $[MD]^D/[MH]^H$. In this context the original steady-state assumption is not required; all that is required is that, if the concentrations of MD and MH are not constant during the course of a reaction, the changes in $[MD]$ and $[MH]$ have the same time-dependence function (which would cancel in eq 17). Under these circumstances the ratio $[MD]^D/[MH]^H$ is effectively constant when comparing reactions which differ only in isotopic composition.
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