The Mechanism of the Reduction of Organomercurials with Sodium Borohydride[1]

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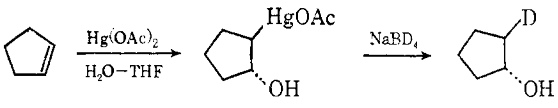
Abstract: The reduction of *trans*-2-hydroxycyclopentylmercuric acetate with sodium borodeuteride in basic aqueous tetrahydrofuran produces *trans*-2-deuteriocyclopentanol in >95% stereochemical purity. The pure diastereomeric hydroxymercuric acetates derived from *cis*- and *trans*-2-butene produce 50:50 mixtures of *erythro*- and *threo*-3-deuterio-2-butanols on reduction with sodium borodeuteride. Reduction of either 5-acetoxy-3-nortricyclylmercuric chloride or 3-acetoxy-5-norbornen-2-ylmercuric chloride produces a 64:36 mixture of 5-norbornen-2-yl acetate and 3-nortricyclyl acetate. Similar reduction of these mercuri derivatives with sodium borodeuteride indicates that no carbon skeletal rearrangements have occurred. Reduction of 3-phenyl-2-propen-1-ylmercuric bromide produces a 4:96 mixture of propenylbenzene and allylbenzene. The mechanism of the reduction is proposed to proceed *via* formation of an organomercuric hydride (RHgH) which undergoes homolytic dissociation to produce R· and ·HgH. Hydrogen atom transfer within the solvent cage occurs before molecular reorientation with the reactive cyclopentyl radical leading to retention; whereas central carbon–carbon bond rotation occurs faster with the 2-butyl radicals than hydrogen atom transfer leading to complete racemization. In the nortricyclyl and norbornenyl cases the intermediate equilibrating radicals have sufficient stability to undergo molecular reorientation before capturing the hydrogen atom. The results of both of these latter cases and the phenylpropenyl case, argue against a concerted intramolecular reaction.

The hydroxymercuration of olefins[3] followed by reduction with sodium borohydride[4] represents a highly facile synthesis of alcohols.[5] The alcohols derived *via* this route correspond to the Markovnikov addition of water to the double bond in contrast to the anti-Markovnikov addition achieved *via* hydroboration.[5] The stereochemistry of the oxymercuration reaction is *trans*[3] except for certain strained olefinic systems.[6] The only report describing the stereochemistry of the reduction step is that of Bordwell and Douglass[4] for the reduction of the *cis-exo* adduct of norbornene which occurs with retention. In view of the added potential of the oxymercuration and aminomercuration[7] reactions for the production of stereospecifically labeled β-deuterio- and tritioalcohols and amines (required for other investigations in our laboratories), and the fact that a stereochemical generalization based on reactions in the norborane system should be avoided due to the unique character of the system, we have investigated the sodium borohydride reduction of organomercurials in greater detail.

Results

Hydroxymercuration of cyclopentene produces the *trans*-2-hydroxycyclopentylmercuric acetate (**1**). Reduction of **1** with sodium borodeuteride in aqueous tetrahydrofuran in the presence of molar sodium hydroxide[5] produces 2-deuteriocyclopentanol. The alcohol was converted to the corresponding *p*-nitrobenzoate. Comparison of the infrared spectrum of the *p*-nitrobenzoate with the infrared spectra of authentic *cis*- and *trans*-2-deuteriocyclopentyl *p*-nitrobenzoates[8] indicated that reduction of **1** produced >95% stereochemically pure *trans*-2-deuteriocyclopentanol.



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Hydroxymercuration of *cis*- and *trans*-2-butenes produces exclusively the *threo* and *erythro* adducts **2** and **3**, respectively. The nuclear magnetic resonance spectra (see Table I) of **2** and **3** are sufficiently different to indicate that the additions were completely stereospecific. Reduction of both **2** and **3** with sodium borodeuteride produces a 50:50 mixture of *erythro*- and *threo*-3-deuterio-2-butanols as determined by infrared analysis of the corresponding benzoates.[9] Attempts to trap the *sec*-butyl radical and to observe radical intermediates by electron paramagnetic resonance techniques employing a flow cell[10] were unsuccessful.

Acetoxymercuration of norbornadiene under kinetic control, followed by treatment with aqueous sodium chloride, produced 3-acetoxy-5-norbornen-2-

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[2] Alfred P. Sloan Research Fellow, 1967–1969.

[3] For reviews of the hydroxymercuration of olefins see: J. Chatt, *Chem. Rev.*, **48**, 7 (1951); N. S. Zefirov, *Russ. Chem. Rev.*, **34**, 527 (1965).

[4] F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, **88**, 993 (1966).

[5] H. C. Brown and P. Geoghegan, Jr., *ibid.*, **89**, 1522 (1967).

[6] A. Factor and T. G. Traylor, *J. Org. Chem.*, 33, 2607 (1968), and references cited therein.

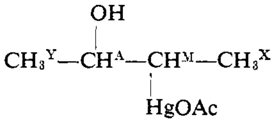
[7] A. Latter and J. J. Perié, *Tetrahedron Lett.*, 5165 (1967).

[8] *cis*-2-Deuteriocyclopentyl *p*-nitrobenzoate was prepared by deuterioboration of cyclopentene followed by esterification by *p*-nitrobenzoyl chloride in pyridine. The *trans* isomer was prepared by reduction of cyclopentene oxide with lithium aluminum deuteride followed by esterification. The infrared spectra, recorded in potassium bromide disks, showed differences in the 1200–1100-cm^{-1} region: *cis*, 1159 (medium) and 1111 cm^{-1}; *trans*, 1173 (weak) and 1111 cm^{-1} (D. J. Pasto, G. Cooper, and G. R. Meyer, unpublished results).

[9] D. J. Pasto, C. C. Cumbo, and J. Hickman, *J. Amer. Chem. Soc.*, **88**, 2201 (1966).

[10] The authors wish to acknowledge the assistance of Professor Robert G. Hayes, of our department, with the epr experiment.

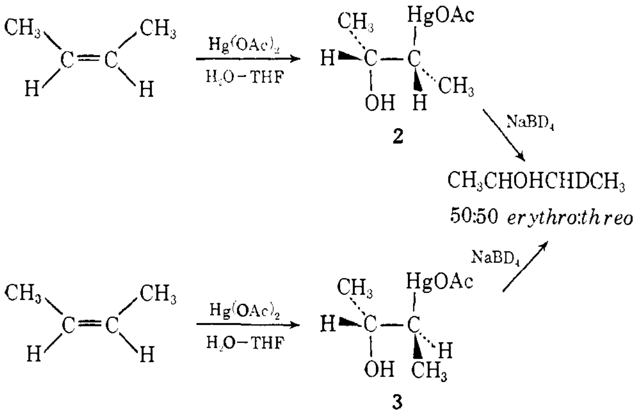
Table I. Nmr Parameters of Adducts **2** and **3**[a]



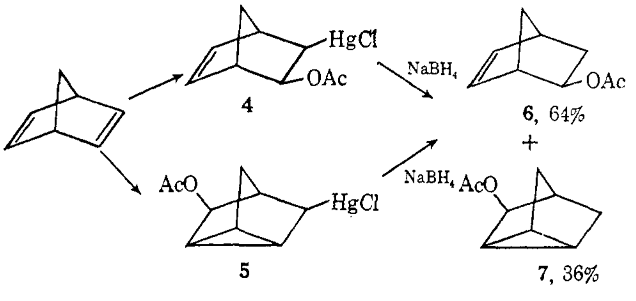
$$CH_3^Y\text{—}\underset{HgOAc}{\overset{OH}{C}H^A}\text{—}CH^M\text{—}CH_3^X$$

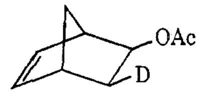
	2	3
	Chemical Shifts[b]	
H_A	3.91	3.98
H_M	2.74	3.02
H_X	1.47	1.37
H_Y	1.30	1.31
	Coupling Constants[c]	
H_YH_A	6.3	6.1
H_AH_M	4.1	4.4
H_MH_X	7.8	7.5
$^{199}HgH_A$	344	387
$^{199}HgH_M$	227	231
$^{199}HgH_X$	276	284

[a] Recorded 25% in deuteriochloroform. [b] Chemical shifts are in δ relative to TMS. [c] Coupling constants in hertz.



ylmercuric chloride (**4**).[11] The nmr spectrum of **4** displays an X–A–B–Y olefinic system at δ 5.98 and 6.30 with a doublet (J = 7.0 Hz) for >CHOAc at δ 4.80. Acetoxymercuration of norbornadiene under thermodynamically controlled conditions produces 5-acetoxy-3-nortricyclylmercuric chloride (**5**).[11] The nmr spectrum of **5** displayed no peaks in the olefinic region. Reduction of **4** and **5** with sodium borohydride and deuteride produces identical mixtures of acetates **6** and **7** in a 64:36 ratio. Samples of **6** and **7** derived from the sodium borodeuteride reduction were collected by preparative glpc and analyzed for deuterium content and position. The nmr spectra of these samples are consistent only with structures **8** and **9** in which deuterium resides only at the positions previously occupied by mercury.





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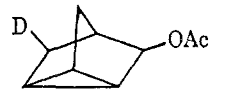

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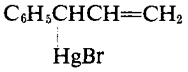
3-Phenyl-2-propen-1-ylmercuric bromide (**10**) was prepared by treating cinnamyl bromide with mercury in 95% ethanol.[12a] The nmr spectrum of the product showed no terminal vinyl resonance peaks that would be characteristic of **11**. Reduction of **10** produced a 4:96 mixture of propenyl- and allylbenzene.



$$C_6H_5\underset{HgBr}{C}HCH{=}CH_2$$

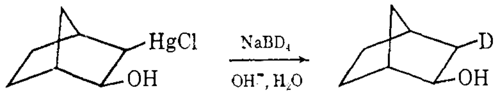
11

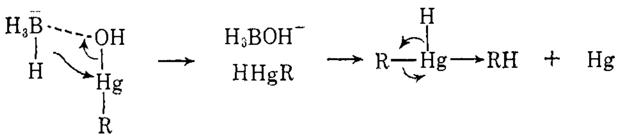
$$\underset{\mathbf{10}}{C_6H_5CH{=}CHCH_2HgBr} \xrightarrow{NaBH_4}$$

$$C_6H_5CH{=}CHCH_3 + C_6H_5CH_2CH{=}CH_2$$

Discussion

Bordwell and Douglass[4] have observed that di-*exo*-3-hydroxy-2-norbornylmercuric chloride undergoes reduction with sodium borodeuteride in aqueous base to produce di-*exo*-3-deuterio-2-norbornanol. Bordwell considered several possible mechanisms for this transformation and, based on the observation that the reducing agent was the sole source of the hydrogen (or deuterium) incorporated into the alcohol with retention of configuration, considered that the following mechanism was the most probable mechanism.[4] From a consideration of dissociation constants, Bordwell proposes that the chloride is converted to the mercuric hydroxide which then undergoes reduction *via* a four-centered transition state to give an alkylmercuric hydride (RHgH). The alkylmercuric hydride is proposed to undergo an intramolecular rearrangement with retention of configuration.





The data gathered in this study clarifies the conversion of the alkylmercuric hydride to hydrocarbon and free mercury. The observations of the complete loss of stereochemistry in the reduction of the 2-butyl cases, and the formation of rearranged product in the nortricyclyl, norbornenyl, and phenylpropenyl cases, are not consistent with a concerted intramolecular rearrangement of the alkylmercuric hydride.

A more consistent mechanism for the formation of the final products would appear to involve radical intermediates as follows.

$$RHgH \longrightarrow R\cdot + \cdot HgH \longrightarrow RH + Hg$$

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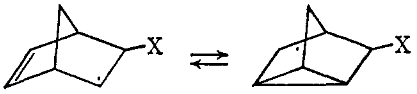
(11) K. C. Pande and S. Winstein, *Tetrahedron Lett.*, 3393 (1964).

(12) (a) O. A. Reutov and A. N. Mesmeyanov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 655 (1953); (b) H. G. Kuivila, L. W. Menapace, and C. R. Warner, *J. Amer. Chem. Soc.*, **84**, 3584 (1962).

Perhaps the most pertinent data is that derived from the reductions of the nortricyclyl and norbornenylmercuric chlorides. Kuivila, Menapace, and Warner[12b] have observed that the reduction of 2-bromonortricyclene with triphenyltin hydride produces a mixture of nortricyclene and norbornene (relative amounts not specified). This reaction has been shown to proceed *via* a chain radical mechanism.[13] Cristol, Brindell, and Reeder[14] have observed that the radical addition of aryl thiols to norbornadiene produces a 40:60 mixture of 3-nortricyclyl aryl sulfide and 5-norbornen-2-yl aryl sulfide *via* the equilibrating radicals **10** and **11**. The results of the reduction of **4** and **5** are remarkably similar to the results of Cristol and coworkers. Similarly, the reduction of **10** can be visualized as proceeding *via* the radical **12**.



10 **11**

$$C_6H_5CH{=}CH\dot{C}H_2 \longleftrightarrow C_6H_5\dot{C}HCH{=}CH_2$$

12

In the reduction of *trans*-2-hydroxycyclopentylmercuric acetate (**1**) greater than 95% of retention was observed. Assuming that this substrate goes to product by a radical mechanism, the very reactive 2-hydroxycyclopentyl radical must abstract the hydrogen atom from ·HgH before molecular reorientation within the solvent cage. In the 3-hydroxy-2-butylmercuric acetates, the intermediate radical must have a lifetime long enough to undergo central carbon–carbon bond rotation (not available with the 2-hydroxycyclopentyl system) before abstracting the hydrogen atom from ·HgH. With **4** and **5**, the intermediate radicals **10** and **11** (X = OAc) are more stable and may react at either position.

Summary

The stereochemistry of the reduction, and the structure of the product formed, is highly dependent on the carbon skeleton of the organomercurial.[15] It seems fairly obvious that the rearrangement of the organomercuric hydride occurs *via* a radical reaction.

Experimental Section

***trans*-2-Hydroxycyclopentylmercuric acetate (1)** was prepared by the method of Traylor and Baker.[16]

***threo*-3-Hydroxy-2-butylmercuric Chloride (2).** To a stirred solution of 22.8 g (0.07 mol) of mercuric acetate in 70 ml of water was added 0.07 mol of *cis*-2-butene. The reaction mixture was stirred for 1.5 hr at 25° and was concentrated under reduced pressure. The oily residue was extracted with ethyl acetate and the extract was dried over magnesium sulfate. Pentane was added to the ethyl acetate solution causing an oily layer to separate. The oily layer was removed and any excess solvent was removed under vacuum. The viscous residue was reasonably stable at 0°; slowly producing an insoluble white precipitate. The nmr spectrum (see Table I) of the material indicated a purity of >95%.

***erythro*-3-Hydroxy-2-butylmercuric acetate (3)** was prepared as described above using *trans*-2-butene. The nmr spectral data are given in Table I.

5-Acetoxy-3-nortricyclylmercuric chloride (5) was prepared as described by Pande and Winstein[11] by isomerization of **4** by mercuric chloride in dimethyl sulfoxide.

Cinnamylmercuric bromide was prepared as described by Reutov and Nesmeyanov.[12a]

Reduction of the Organomercurials with Sodium Borohydride or Borodeuteride. The reduction of the organomercurials was carried out employing the procedure of Brown and Geoghegan.[5] The products were recovered by extraction with ether.

The deuterated cyclopentanol and butanols were converted to the *p*-nitrobenzoate and benzoates, respectively, and their stereochemistry determined by infrared analysis.[8,9]

The crude acetate mixture derived from the borohydride reduction of **4** and **5** was analyzed by nmr spectroscopy (peak assignments were made by comparison with authentic materials[17]). The deuterioacetates formed by borodeuteride reduction of **4** and **5** were isolated by preparative glpc on a 20-ft 20% Carbowax 20M on Chromosorb W column, and the extent and position of deuterium incorporation determined by nmr spectroscopy.

The mixture of allyl- and propenylbenzenes derived by borohydride reduction of cinnamylmercuric bromide was analyzed by glpc on a 20-ft 20% DEGS on Chromosorb W column at 175° by retention time comparison with authentic compounds.

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(13) H. G. Kuivila, *Advan. Organometal. Chem.*, **1**, 76 (1964).

(14) S. J. Cristol, G. D. Brindell, and J. A. Reeder, *J. Amer. Chem. Soc.*, **80**, 635 (1958).

(15) In a footnote in ref 4 it is indicated that T. Traylor has observed that the reduction of 4-methylcyclohexylmercuric compounds occur with incomplete retention.

(16) T. G. Traylor and A. W. Baker, *J. Amer. Chem. Soc.*, **85**, 2746 (1963).

(17) J. Meinwald, J. Crandall, and W. E. Hymans, *Org. Syn.*, **45**, 74 (1965).