Reduction of Alkylmercuric Hydroxides by Sodium Borohydride

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Abstract: A practical method for reduction of alkyl organomercurials of the type RHgY to RH has been developed using sodium borohydride in aqueous alkaline medium. Experiments with $NaBH_4$ in D_2O and with $NaBD_4$ in H_2O have shown that hydrogen for replacement of HgY comes from the borohydride and not from the water. These results, coupled with evidence that the replacement occurs with retention of configuration, are interpreted mechanistically in terms of a four-center transition state.

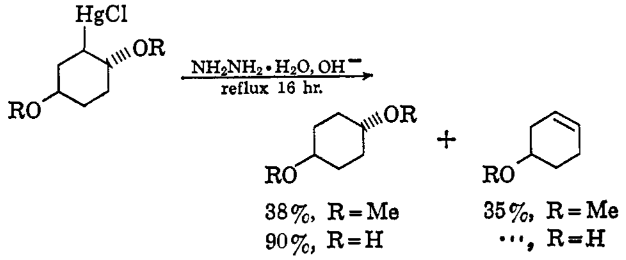
In connection with studies on the oxymercuration of cycloalkenes, it became desirable to replace the HgY group by hydrogen in order to determine the structures of the oxymercuration products. As a consequence, we became interested in the reduction of β-oxyalkyl mercurials and have developed a practical reduction method for these using sodium borohydride in alkaline solution. This paper discusses the scope and limitations of this method and presents some data relative to its stoichiometry, stereochemistry, and mechanism.

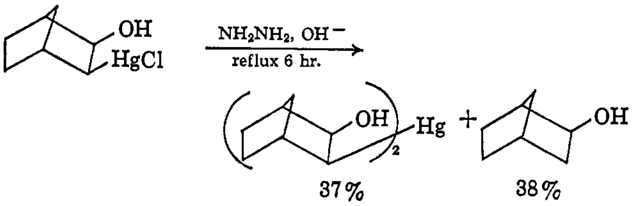
The reduction of alkyl mercurials has been carried out previously with a variety of reducing agents including sodium amalgam, hydrazine, sodium stannite, lithium and sodium borohydrides, and lithium aluminum hydride, as well as by electrolytic methods. The reduction can proceed from alkyl mercurials of the type RHgY to the dialkyl mercurial and/or to the hydrocarbon RH.

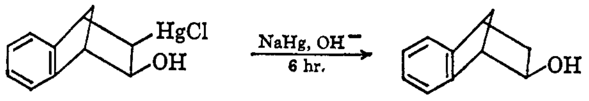
$$\begin{tikzcd} \text{R-Hg-Y} \arrow[r, "{[H]}"] \arrow[rr, bend right, "{[H]}"'] & \text{R-Hg-R} \arrow[r, "{[H]}"] & \text{R-H} + \text{Hg} \end{tikzcd}$$

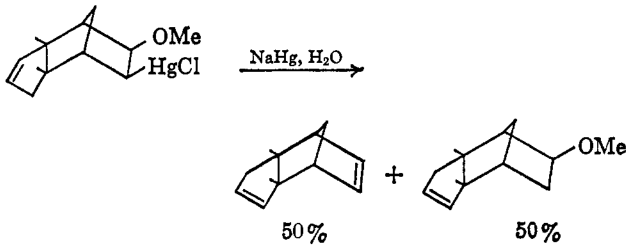
The extent of reduction depends primarily on the nature and amount of reducing agent, but the nature of R and of Y are sometimes of importance. When the R group contains a β-alkoxy group, deoxymercuration may become an important side reaction or the dominant reaction. This is true also with β-hydroxy groups, but to a lesser extent. Reduction to RH occurs most readily when Y in RHgY is a strongly electronegative group, such as Br, Cl, OAc, OR, or OH. When Y is R or Ar, reduction occurs slowly, or not at all, unless a strong reducing agent ($LiAlH_4$) is used.

Sodium stannite and hydrazine reductions generally proceed first to the dialkylmercury stage; with longer reaction times reduction proceeds further to the hydrocarbon state.[1,2] On the other hand, sodium amalgam reductions appear to involve direct replacement of the HgY group by H; formation of the dialkylmercury compound, if it occurs, is a side reaction. The examples of the application of the hydrazine and of the sodium amalgam methods shown below have been taken from the recent literature.[3-5]









Lithium borohydride and sodium borohydride have been used on a few occasions to reduce alkyl mercurials, either in nonaqueous medium[3] or for an extended time in aqueous medium.[6] Our experience is that reduction of β-alkoxyalkyl mercurials proceeds very rapidly in homogeneous aqueous alkaline medium with replacement of HgY by H and is relatively free of side reactions. Our results are comparable in this respect to those of Robson and Wright using sodium trimethoxyborohydride.[7]

Reduction of 2,5- and 2,6-epoxycylooctylmercuric derivatives (**1** and **2**) received most study in the present work. With **1**, reduction to 1,4-epoxycyclooctane (HgY replaced by H) was the major result in 0.5 *M* NaOH (Y = OAc, Cl), in water at pH 7 (Y = OAc), in absolute ethanol (Y = OAc), or in 1 *M* NaOEt in ethanol (Y = Cl). On the other hand, reductive deoxymercura-

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[1] G. F. Wright, *Can. J. Chem.*, 30, 268 (1952).

[2] T. G. Traylor and S. Winstein, *J. Org. Chem.*, 23, 1796 (1958).

[3] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959).

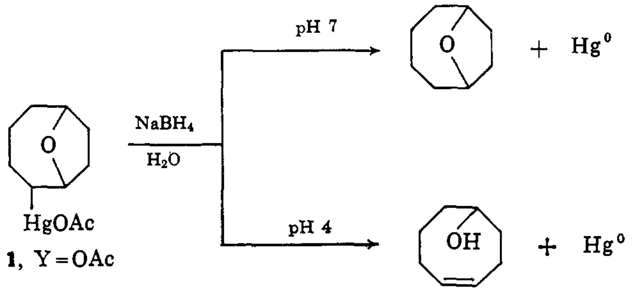
[4] T. G. Traylor and A. W. Baker, *J. Am. Chem. Soc.*, 85, 2746 (1963).

[5] J. K. Stille and S. C. Stinson, *Tetrahedron*, 20, 1387 (1964).

[6] T. G. Traylor, *J. Am. Chem. Soc.*, 86, 244 (1964).

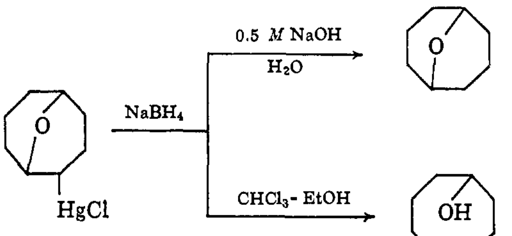
[7] J. H. Robson and G. F. Wright, *Can. J. Chem.*, 38, 21 (1960).

tion was the principal result in water at pH 4 (Y = OAc), in 50% ethanol–ether (Y = I), or in ethanol 1 *M* in pyridine (Y = Cl).



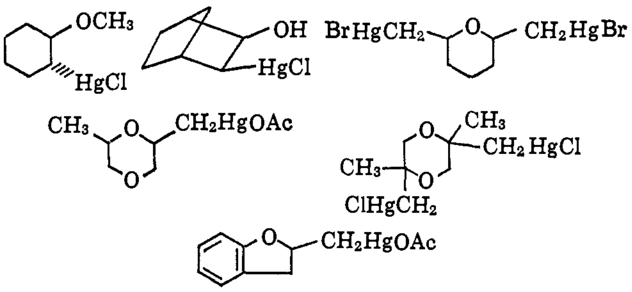
1, Y = OAc

Similarly, reduction with sodium borohydride in aqueous alkaline medium gave principally 1,5-epoxycyclooctane starting from **2** (Y = Cl) or from 1,5-bis(nitratomercuri)-2,6-epoxycyclooctane, whereas reductive deoxymercuration was the principal result when **2** (Y = ONO_2) was reduced in ethanol or when **2** (Y = Cl) was reduced in chloroform–ethanol.



2, Y = Cl

The reduction with sodium borohydride in alkaline medium has been applied successfully to a number of other β-oxy mercurials including the following.



These results together with those of Wright[7] suggest that this is a useful and convenient method for replacing HgY groups in alkyl mercurials by H. For example, *trans*-2-methoxy-1-chloromercuricyclohexane was reduced immediately to cyclohexyl methyl ether in 86% yield with no evidence of deoxymercuration. This may be contrasted with the results on a comparable system with the hydrazine method, which requires many hours of reflux and gives about equal amounts of deoxymercuration and reduction products.[3] The sodium borohydride reduction does not proceed by the route $RHgY \rightarrow R_2Hg \rightarrow RH$, since bis(2-methoxycyclohexyl)mercury proved to be inert to reduction under the conditions used for *trans*-2-methoxy-1-chloromercuricyclohexane.

The reduction of 2-halomercurimethyl-2,3-dihydrobenzofurans often takes an unusual course. Sodium stannite in water gives mainly deoxymercuration[8]; with sodium amalgam in ethanol the major product is the dialkylmercury compound.[9] The latter result represents one of the few examples where sodium amalgam reduction gives the dialkylmercury. This unusual behavior is probably associated with the unusually low water solubility of this mercurial. Even the acetoxymercuri derivative has very limited water solubility, which is in sharp contrast to the high water solubility of the 2,5- and 2,6-epoxycyclooctylmercuric acetates. 2-Acetoxymercurimethyl-2,3-dihydrobenzofuran fails to dissolve completely in aqueous alkali, and sodium borohydride reduction under these conditions gave 26% of 2-methyl-2,3-dihydrobenzofuran and 23% of bis[2-(2,3-dihydrobenzofuranyl)methyl]mercury. However, when the reaction mixture was rendered homogeneous by adding ethanol, the yield of 2-methyl-2,3-dihydrobenzofuran increased to 51%.

The function of the hydroxide (or alkoxide) in these reductions appears to be twofold. First, alkali promotes solubility (at least partly by effecting the transformation $RHgY \rightarrow RHg\text{-}OH$) and thereby reduces side reactions which are favored by a heterogeneous medium. Second, alkali prevents protonation of the oxygen in β-alkoxyalkyl mercurials and thereby inhibits deoxymercuration.

With phenylmercuric acetate and *p*-tolylmercuric chloride, sodium borohydride gave principally the diarylmercury. These diaryl mercurials were not reduced further by sodium borohydride, even with extended reaction times.

The route of oxymercuration followed by reduction is on occasion of preparative value for alcohols, ethers, or lactones. The utility of this method has been discussed by Henbest.[3] The use of sodium borohydride reduction in place of hydrazine should make this route more attractive. Examples of its application from work done in this laboratory include the conversion of methallyl alcohol to 2,2,5,5-tetramethyl-1,4-dioxane, 1-alloxy-2-propanol to 2,6-dimethyl-1,4-dioxane, 5-hexen-2-ol or 1,5-hexadiene to 2,5-dimethyltetrahydrofuran, 1,5-cyclooctadiene to 1,5-epoxycyclooctane, and 4-cycloocten-1-ol to 1,4-epoxycyclooctane. The two latter preparations are of particular interest because of the difficulty of obtaining these oxabicyclononanes by other routes[10] and the problems of stereochemistry and isomerism that arise.

Oxymercuration of 1,5-cyclooctadiene in aqueous medium with mercuric nitrate occurred with particular ease. Both the original hydroxymercuration and the subsequent mercuration (with hydroxyl participation) to give the cyclic ether must be rapid reactions. The resulting 1,5-bis(nitratomercuri)-2,6-epoxycyclooctane was reduced in 69% yield to 9-oxabicyclo[3.3.1]nonane. This constitutes a convenient route to this 1,5-epoxide.

Mercuration of 4-cycloocten-1-ol with mercuric acetate in the presence of sodium acetate was also rapid (participation of hydroxyl). Reduction of the resulting 2,5-epoxycyclooctylmercuric acetate (**1**, Y = OAc) gave 77% of 9-oxabicyclo[4.2.1]nonane, uncontaminated by the 1,5-epoxide isomer. In the absence of sodium acetate, **1** rearranged partly to the 1,5-epoxy isomer, and rearrangement was complete in the presence

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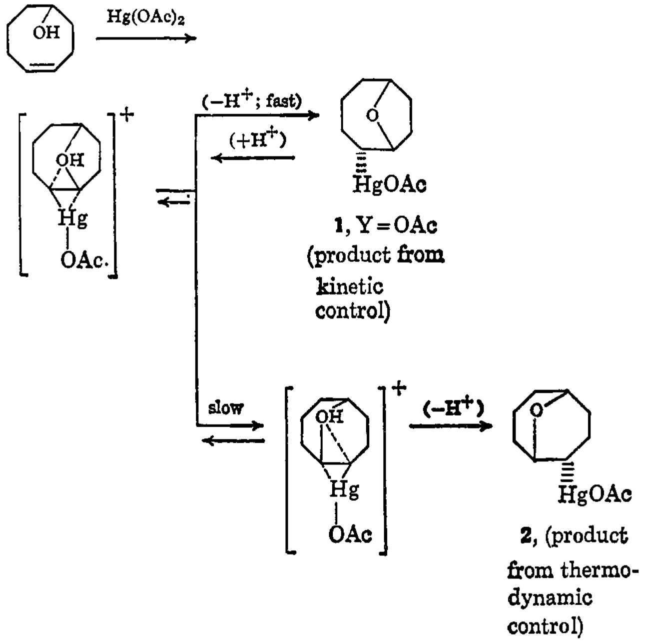
(8) L. E. Mills and R. Adams, *J. Am. Chem. Soc.*, **45**, 1842 (1923).

(9) R. Adams, F. L. Roman, and W. N. Sperry, *ibid.*, **44**, 1781 (1922).

(10) (a) A. C. Cope and B. C. Anderson, *ibid.*, **79**, 3892 (1957); (b) A. C. Cope and A. Fournier, Jr., *ibid.*, **79**, 3896 (1957).

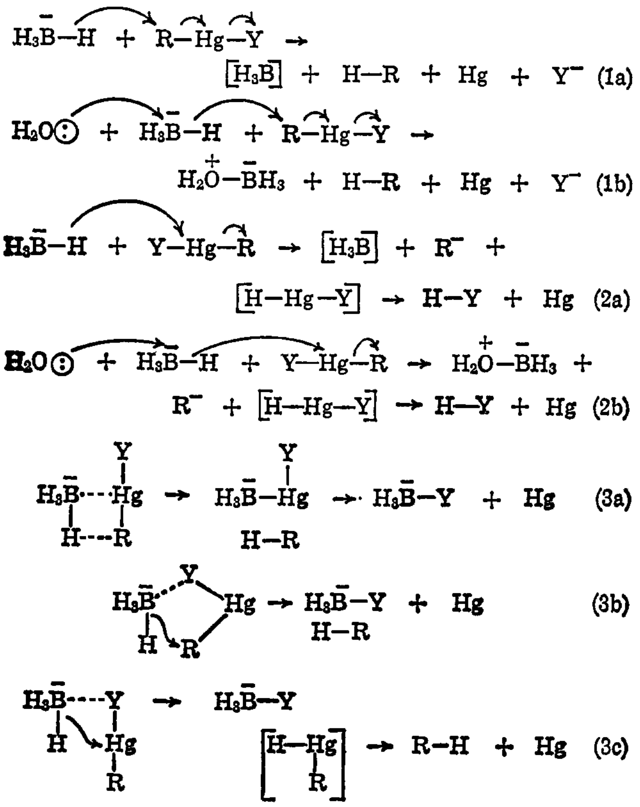
of strong acid (such as is present in the mercuration of 1,5-cyclooctadiene with mercuric nitrate). It is apparent from these results that the 1,4-epoxide is strongly favored under kinetic control and that the 1,5-epoxide is strongly favored at equilibrium. The mercuration and isomerization reactions no doubt involve a common intermediate as suggested in the following representation.



1, Y = OAc (product from kinetic control)

2, (product from thermodynamic control)

The stereochemistry of the oxymercuration products was not determined, but a *trans* structure is assigned on the basis of the usual *trans* addition mechanism,[6,11,12]



$$H_3\bar{B}{-}H + R{-}Hg{-}Y \rightarrow [H_3B] + H{-}R + Hg + Y^- \quad (1a)$$

$$H_2O: + H_3\bar{B}{-}H + R{-}Hg{-}Y \rightarrow H_2\overset{+}{O}{-}\bar{B}H_3 + H{-}R + Hg + Y^- \quad (1b)$$

$$H_3\bar{B}{-}H + Y{-}Hg{-}R \rightarrow [H_3B] + R^- + [H{-}Hg{-}Y] \rightarrow H{-}Y + Hg \quad (2a)$$

$$H_2O: + H_3\bar{B}{-}H + Y{-}Hg{-}R \rightarrow H_2\overset{+}{O}{-}\bar{B}H_3 + R^- + [H{-}Hg{-}Y] \rightarrow H{-}Y + Hg \quad (2b)$$

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[11] H. J. Lucas, F. R. Hepner, and S. Winstein, *J. Am. Chem. Soc.*, **61**, 3102 (1939).

[12] M. M. Kreevoy and F. R. Kowitt, *ibid.*, **82**, 739 (1960).

The borohydride reduction of mercurials, RHgY → RH + Hg + Y⁻, may be visualized as occurring by one of several mechanisms (1a–3c).

Mechanism 1a assumes nucleophilic attack of borohydride ion on carbon (SN2-type mechanism) with the formation of borine (BH_3). This mechanism predicts that the stoichiometry of the reaction will be 1 mole of mercurial to 1 mole of borohydride ion, since there is reason to believe that the reaction of borine with water (liberating hydrogen) is extremely rapid.[13] A test of the stoichiometry was made with three mercurials, namely, *trans*-2-methoxycyclohexylmercuric chloride and 2,5- and 2,6-oxidocyclooctylmercuric chlorides, by adding a weighed quantity of sodium borohydride to excess mercurial and determining the quantity of metallic mercury and the quantity of unreduced mercurial. In each instance 4 equiv of mercurial reacted with 1 equiv of borohydride; hydrogen was not evolved.

$$4RHgCl + 4OH^- + BH_4^- \longrightarrow 4RH + 4Hg + 4Cl^- + H_2BO_3^- + H_2O$$

The observed stoichiometry rules out mechanism 1a. Mechanism 1b is a variation of 1a in which a water molecule (or hydroxide ion) attacks boron as it releases its hydride ion to carbon. This mechanism would presumably lead to the correct stoichiometry since the $HOBH_3^-$ ion ultimately formed should be more reactive than BH_4^- as a source of hydride ions. Mechanism 1b is rendered highly unlikely, however, by the observation that 2,5-bis(chloromercurimethyl)-2,5-dimethyl-1,4-dioxane reacts as readily with borohydride as do other mercurials. Since the carbon atoms holding the mercury atoms in this compound are of a neopentyl type, one would expect these carbon atoms to be relatively inert to attack by an SN2-type process.[14]

Mechanisms 2a and 2b are more attractive than 1a or 1b inasmuch as they assume nucleophilic attack on the most electrophilic atom in the molecule, namely, mercury. Mechanism 2a is ruled out as such by the stoichiometry of the reduction (see above), but mechanism 2b remains as a possibility. The suggestion of a carbanion intermediate in this mechanism is comparable to that made by Traylor and Winstein to account for the deoxymercuration of *cis*-2-methoxy-1-chloromercuricyclohexane by lithium aluminum hydride.[15] Of course, in the reduction the carbanion need not be generated as such, since the developing carbanion could be forming a bond with a proton from a water molecule at the same time that the C–Hg bond is being broken (concerted-type mechanism).

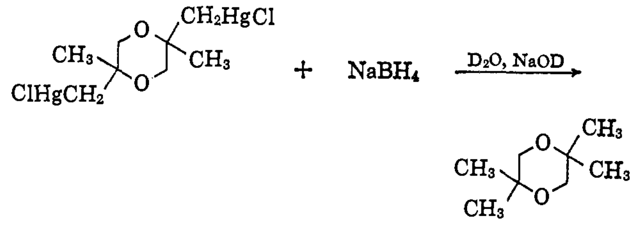
In order to test for a carbanion-type mechanism (carbanion or incipient carbanion), the sodium borohydride reduction of 2,5-bis(chloromercurimethyl)-2,5-dimethyl-1,4-dioxane was run in deuterium oxide in the presence of sodium deuteroxide. No deuterium was incorporated into the 2,2,5,5-tetramethyl-1,4-dioxane produced.

As a check on the source of the hydrogen, the reduction was also carried out with sodium borodeuteride

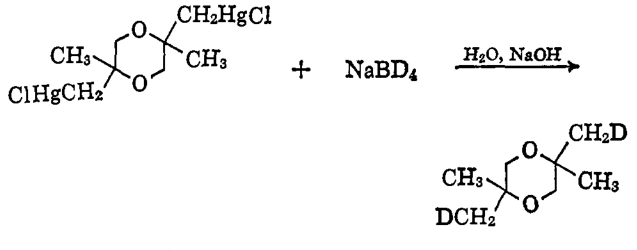
[13] R. E. Davis, E. Bromels, and C. L. Libby, *ibid.*, **84**, 885 (1962).

[14] This expectation is supported by the fact that the corresponding halo compound, 2,5-bis(iodomethyl)-2,5-dimethyl-1,4-dioxane, is highly resistant to nucleophilic attack (W. B. Hammond, unpublished results).

[15] T. G. Traylor and S. Winstein, Abstracts, 135th National Meeting of the American Chemical Society, Boston, Mass., April 1959, p 82-O.



in aqueous sodium hydroxide. In this instance nmr analysis showed the uptake of two deuterium atoms.

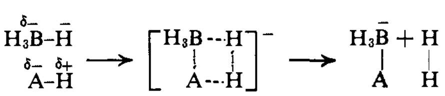


These experiments clearly rule out a carbanion or incipient carbanion intermediate. The most reasonable possibilities remaining are represented by mechanisms 3a, 3b, and 3c. These mechanisms are consistent with the experimental facts since they do not postulate the formation of either BH_3 or R^- in a free or incipient form.

In mechanism 3a, hydride initiates a frontal attack on carbon at the same time that a bond is being formed between boron and mercury. The $H_3\bar{B}$-Hg-Y species is then assumed to rearrange with the liberation of metallic mercury.

Mechanism 3b is a variation of 3a which assumes bonding in the transition state between the Y group and boron, rather than between mercury and boron. It is more attractive than 3a in this respect, but is less attractive on stereochemical grounds since mercury(II) appears to have linear bonds.[16]

There is little in the way of experimental evidence to allow a choice between mechanisms 3a, 3b, and 3c. However, consideration of the mode of cleavage of the hydrogen-boron bond in other reactions makes mechanism 3c much more attractive than 3a or 3b. For example, this mechanism may be compared to that suggested for the reaction of weak acids (HA) with borohydrides.[17] For this reaction Dessy suggested a four-center transition state in which the anion portion of the acid coordinates with the boron atom at the same time that a bond is being formed between the proton of HA and the (negative) hydrogen of the borohydride.

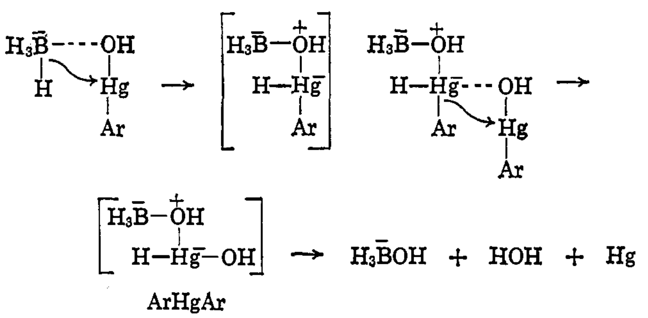


Mechanism 3c depicts a similar arrangement of the attacking electrophilic reagent for cleavage of the hydrogen-boron bond, the more negative atom (hydrogen) being associated with the more positive element (mercury) in the substrate. In mechanism 3a and 3b the more negative atom (hydrogen) is depicted as associating with the more *negative* atom (carbon) of the carbon-mercury bond.

The H-Hg-R intermediate in mechanism 3c is presumed to rearrange to R-H with the liberation of metallic mercury. This presumption is given credence by the fact that mercuric hydride could not be isolated by reduction of dimethylmercury with lithium aluminum hydride under conditions comparable to those used for the successful preparation of cadmium and zinc hydrides. Instead, hydrogen and mercury were produced, even at −80°, which suggests that mercuric hydride is quite unstable.[18]

The nature of the mercurial species present in the reduction medium (0.5 *M* in sodium hydroxide) can be estimated from the known dissociation constants of MeHgCl and MeHgOH in water, which are 3.5×10^{-6} and 3.1×10^{-10}, respectively.[19] Using these values the concentrations of the various species present in solution prepared as 0.1 *M* in RHgCl are: [RHgOH], 0.1 *M;* [RHgCl], 2×10^{-6} *M;* [RHg^+], 8×10^{-11} *M;* [OH^-], 0.4 *M;* [Cl^-], 0.1 *M*. The species most likely to be undergoing reduction is therefore RHgOH.

The failure of dialkylmercury compounds to be reduced by borohydride is understandable on the basis of mechanism 3c, since the structural change from RHgOH to RHgR makes mercury less electrophilic and, therefore, less prone to hydride attack. Furthermore, coordination of an unshared electron pair on OH with boron in the transition state is an integral part of mechanism 3c, and this possibility has been eliminated in RHgR by replacement of OH by R. The failure of phenylmercuric acetate or *p*-tolylmercuric chloride to be reduced to the hydrocarbon is not predicted by mechanism 3c, although the failure of the diarylmercurys, which are the actual products, to be reduced further is not unexpected. The mercury in C_6H_5HgOAc and *p*-MeC_6H_4HgCl (or the corresponding hydroxides) is more electronegative than in the aliphatic counterparts and should be more susceptible to attack by borohydride ion. One possible explanation for the formation of diarylmercurys is that hydride attack on mercury *does* occur as in mechanism 3c, but that an intermediate is formed which is sufficiently long-lived to undergo reaction with another molecule of arylmercuric hydroxide according to the general symmetrization mechanism suggested by Winstein.[20]



Mechanisms 3a and 3b are nucleophilic counterparts of the cleavage of mercurials by electrophilic reagents (hydrogen halides, mercuric halides, and the like).

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(16) (a) J. Kleinberg, W. J. Argersinger, Jr., and E. Griswold, "Inorganic Chemistry," D. C. Heath and Co., Boston, Mass., 1960, pp 609–610; (b) N. V. Sidgwick, "The Chemical Elements and Their Compounds," Vol. I, Oxford University Press, London, 1950, pp 298, 301.

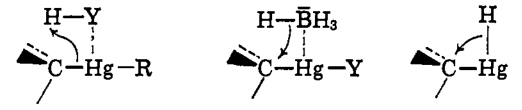
(17) R. E. Dessy and E. Grannen, Jr., *J. Am. Chem. Soc.*, 83, 3953 (1961).

(18) G. D. Barbaras, C. Dillard, A. E. Finholt, T. Wartik, K. E. Wilzbach, and H. I. Schlesinger, *ibid.*, 73, 4585 (1951).

(19) T. D. Waugh, H. F. Walton, and J. A. Loswick, *J. Phys. Chem.*, **59**, 395 (1955).

(20) S. Winstein, T. G. Traylor, and C. S. Garner, *J. Am. Chem. Soc.*, 77, 3741 (1955).

The observed retention of configuration in electrophilic cleavages is understandable on the basis of the four-center mechanisms proposed for these reactions,[21-23] since the electrophile (proton) is positioned at the front side of the carbon atom by coordination of Y with mercury. Similarly, in mechanism 3a (or 3b) the nucleophile (hydride) is held at the front side of the carbon atom by coordination of mercury (or Y) with boron, and retention of configuration should result. In mechanism 3c retention would also be expected since the stereochemistry is determined by an intramolecular rearrangement. In agreement with this expectation it was found that, in the reduction of *exo-cis*-2-hydroxy-3-chloromercurinorbornane with sodium borodeuteride, the replacement of the *exo*-chloromercuri group by hydrogen occurred with retention of configuration. The configuration of the resulting deuterated *exo*-norborneol was established using nmr spectroscopy. Previous studies of the nmr spectra of *exo*-norborneol and its derivatives have shown that the signal for the proton α to oxygen appears as a double doublet ($J_{AB} \cong$ 6-7 cps; $J_{AC} \cong$ 2 cps).[24,25] Reduction with sodium borohydride gave *exo*-norborneol, which displayed the reported double doublet centered at τ 6.23 (τ 5.54 in the acetate). Reduction with sodium borodeuteride gave *exo*-norborneol which gave a well-defined doublet at τ 6.30 (J_{AB} = 6.4 cps). The acetate gave an even sharper doublet at τ 5.45 (J_{AB} = 7 cps).

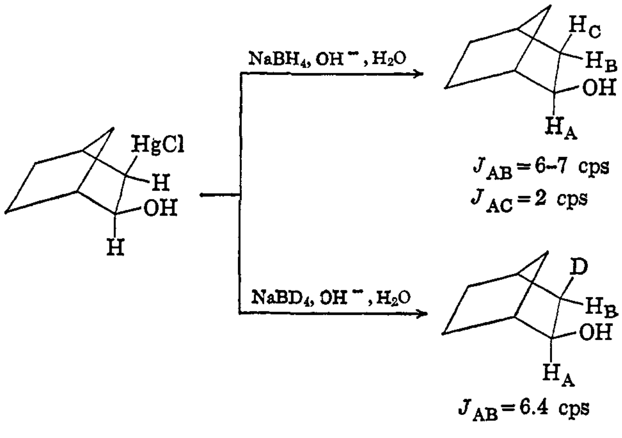


electrophilic cleavage

3a

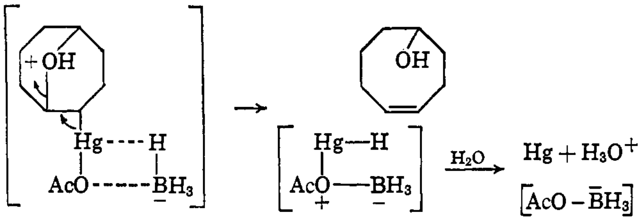
3c

nucleophilic cleavage



These results indicate that the reduction has occurred principally with retention of configuration.[26] The retention of configuration and the incorporation of deuterium rather than hydrogen observed in this experiment provide additional evidence against S_N2-type and carbanion mechanisms, and support the postulate of a four-center transition state.[27]

A similar type of mechanism can be used to represent reductive deoxymercuration by borohydride, which is the principal result for β-alkoxy mercurials at low pH. In acidic media reaction of the borohydride ion must occur almost exclusively with the protonated mercurial, which is not surprising. The intermediate mercuric hydride species probably releases a proton to water in the manner shown, although the possibility that borine is produced was not excluded.



At pH 7 or above, the concentration of the protonated species is reduced to the point where reduction of the nonprotonated mercurial by mechanism 3c takes precedence.

Experimental Section[28]

2,5-Epoxycyclooctylmercuric Acetate. 4-Cycloocten-1-ol (10.3 g, 0.082 mole), prepared from 1,5-cyclooctadiene monoxide,[29] was added dropwise over a 5-min period to a solution of 25.5 g (0.080 mole) of mercuric acetate and 6.56 g (0.080 mole) of sodium acetate in 100 ml of water. A negative test for mercuric ion[30] was obtained after 3 min of stirring. Cooling in an ice bath gave 24 g (78%) of the mercurial acetate. One crystallization from 10% (by volume) chloroform in hexane gave 19.9 g (65%) of product, mp 115–117°. An analytical sample melted at 116–117°. *Anal.* Calcd for $C_{10}H_{16}O_3Hg$: C, 31.21; H, 4.18. Found: C, 31.38; H, 4.03.

In the absence of sodium acetate the 1,4-epoxide (**1**) was contaminated by small amounts of the 1,5-epoxide (**2**) (formed by rearrangement). The results shown in Table I are representative (analysis by infrared).

Table I

$Hg(OAc)_2$, *M*	Solvent	Time	**1**, %	**2**, %
0.1	H_2O	10 min	Most	Trace
0.5	50% MeOH-H_2O	30 min	>90	<10
0.1	H_2O	65 min	80	20
0.5	H_2O	3.3 hr	<50	>50
0.1	H_2O^a	4.5 hr	Little	Most
0.1^b	H_2O	45 min	Little	Most

[a] Two equivalents of nitric acid added after 12 min. [b] Mercuric sulfate was used.

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(21) S. Winstein and T. G. Traylor, *J. Am. Chem. Soc.*, 77, 3747 (1955); 78, 2597 (1956).

(22) F. R. Jensen and L. H. Gale, *ibid.*, **82**, 148 (1960).

(23) R. E. Dessy and F. Paulik, *J. Chem. Educ.*, 40, 185 (1963).

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(26) The reaction may not be completely stereospecific, however, since comparison with an nmr spectrum (kindly supplied by Professor T. G. Traylor) of the deuterated product obtained by Traylor and Baker[4] from the reduction of this mercurial with sodium amalgam in deuterium oxide indicates that some of the isomer with the *endo* deuterium may be present.

(27) Further work on the stereochemistry of this reaction seems desirable, however, particularly since Professor T. G. Traylor has shown (unpublished results privately communicated) that in a closely related reaction, the reduction of methylcyclohexylmercuric chlorides with sodium borodeuteride, stereospecificity is not observed.

(28) Melting points were taken on a Fisher-Johns block and are uncorrected. Microanalyses were by Micro-Tech Laboratories, Skokie, Ill.

(29) J. G. Trayhnam and P. M. Greene, *J. Am. Chem. Soc.*, **86**, 2658 (1964).

(30) No yellow mercuric oxide precipitated when a few drops of the reaction mixture was added to 10% aqueous sodium hydroxide.

Reduction of 2,5-Epoxycyclooctylmercuric Acetate (1, Y = OAc) (a) **Reduction in 0.5 *M* Sodium Hydroxide.** A solution (64 ml) containing 4.16 g (0.108 mole) of 98% sodium borohydride (Metal Hydrides, Inc.) in 2.5 *M* sodium hydroxide was added dropwise to a rapidly stirred solution of 55.7 g (0.145 mole) of the mercurial, mp 114–115°, in 1 l. of 0.5 *M* aqueous sodium hydroxide. A dark gray precipitate separated during addition of the first 25 ml, which separated into shiny metallic mercury (27.5 g, 94%). No further reaction was apparent. The mixture was extracted three times with carbon tetrachloride, and the extract was dried over Drierite. Concentration and distillation gave 14.1 g (77%) of a waxy solid having a strong camphor-like odor, bp 71.1° (20 mm), mp 34–34.5°; reported for 1,4-epoxycyclooctane,[31] mp 31°. The infrared spectrum in carbon tetrachloride was identical with one published.[10a] The following bands differentiate this isomer from 9-oxabicyclo[3.3.1]nonane: 8.98, 9.4, 10.05, 10.8, and 11.54 μ.

(b) **Reduction at pH 7.** The pH of a solution of 0.60 g (0.00156 mole) of 2,5-epoxycyclooctylmercuric acetate in 50 ml of distilled water was found to be 4.1. The pH was brought to 7 by addition of 2.58 ml of 0.49 *M* sodium hydroxide. Addition of 0.036 g (0.00093 mole) of solid sodium borohydride in several portions gave an immediate reaction to form mercury; no hydrogen was evolved. The reaction mixture (pH 9.0) was extracted with carbon tetrachloride; concentration gave material with an infrared spectrum identical with that of 1,4-epoxycyclooctane.

A similar experiment in which the sodium borohydride was added in dimethylformamide solution gave comparable results.

(c) **Reduction at pH 4.4.** Addition of a solution of sodium borohydride in dimethylformamide to an aqueous solution of 0.363 g (0.000943 mole) of mercurial in 30 ml of water gave mercury (0.175 g, 93%) and 4-cycloocten-1-ol (identified by infrared). The characteristic odor of 1,4-epoxycyclooctane was absent.

(d) **Reduction in Absolute Ethanol.** Reduction by addition of a solution of sodium borohydride in absolute ethanol to the mercurial in ethanol gave 1,4-epoxycyclooctane and no 4-cycloocten-1-ol (infrared analysis).

2,5-Epoxycyclooctylmercuric Chloride. A solution (20 ml) containing 6 g (0.10 mole) of sodium chloride was added to 3.63 g (0.00945 mole) of 2,5-epoxycyclooctylmercuric acetate in 100 ml of 0.5 *M* sodium hydroxide. Acidification with carbon dioxide gave a nearly quantitative yield of the mercurial chloride. Crystallization from methanol gave colorless crystals, mp 138–139°. *Anal.* Calcd for $C_8H_{13}OHgCl$: C, 26.60; H, 3.63. Found: C, 26.38; H, 3.62. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ (μ) 3.41 (s), 6.79 (m), 6.84 (m), 7.31 (w), 7.46 (w), 7.64 (w), 8.0–8.3 (w–m), 8.75–9.0 (w–m), 9.56 (s), 9.98 (w), 10.2 (w–m), 10.77[32] (s), 10.98 (s),[32] and 11.9–12.1 (w).

Reduction in 0.5 *M* aqueous sodium hydroxide with solid sodium borohydride or in 1 *M* sodium ethoxide in ethanol gave 1,4-epoxycyclooctane with no evidence for 4-cycloocten-1-ol. Reduction in the presence of 1 *M* pyridine in ethanol gave 4-cycloocten-1-ol and no 1,4-epoxycyclooctane.

2,5-Epoxycyclooctylmercuric Iodide. This compound, prepared by the method used for the chloride, melted at 110–111° after two crystallizations from methanol. *Anal.* Calcd for $C_8H_{13}OHgI$: C, 21.22; H, 2.89. Found: C, 21.28; H, 2.76. The colorless crystals turned gray upon exposure to light.

Reduction of this mercurial in 50% ethanol–ether with solid sodium borohydride gave principally 4-cycloocten-1-ol.

1,5-Epoxycyclooctane. Addition of 14.0 g (0.129 mole) of 1,5-cyclooctadiene[33] to a rapidly stirred suspension of 82.3 g (0.24 mole) of mercuric nitrate monohydrate in 480 ml of distilled water resulted in a negative test for mercuric ion[30] after 7 min. After 2 hr of stirring, 180 ml of 10% sodium hydroxide was added slowly. A small amount of gray residue (mercurous oxide) was removed by filtration and the excess diene was removed from the basic filtrate by extraction with carbon tetrachloride.

Reduction by the method described for 1,4-epoxycyclooctane gave 10.5 g (69%) of 1,5-epoxycyclooctane as a camphor-like, waxy solid, bp 69.5–70.0 (20 mm), mp 52.5–53.5° (lit.[10b] mp 52.5–53.9°); $\lambda_{max}^{CCl_4}$ (μ) 3.42 (s), 6.69 (w), 6.87 (w–m), 6.95 (m), 7.27 (w), 7.35 (w), 7.61 (m),[34] 7.90 (w–m), 8.30 (m–s),[34] 8.89 (m–s), 9.18 (w–m), 9.69 (s),[34] 11.13 (m–s),[34] and 11.72 (s).[34]

2,6-Epoxycyclooctylmercuric Nitrate and Chloride. 4-Cycloocten-1-ol (6.7 g, 0.053 mole) was added dropwise over a 10-min period to a stirred suspension of 17.9 g (0.052 mole) of mercuric nitrate monohydrate and 5.25 g (0.052 mole) of potassium nitrate in 50 ml of water. The mercurial nitrate began to precipitate within 10 min, and after 14 hr was collected on a filter (15.7 g, 78%). A sample crystallized twice from ethyl acetate melted at 98.0–99.5°. Its infrared spectrum was identical with that of the chloride (see below), except for bands at 6.8–7.6, 8.2–8.4, and 11.96 μ, attributable to nitrate. Reduction of this nitrate in absolute ethanol with sodium borohydride in dimethylformamide gave 4-cycloocten-1-ol and no 1,5-epoxycyclooctane.

Solution of the mercurial nitrate in 10% aqueous sodium hydroxide, addition of sodium chloride, and acidification with carbon dioxide gave **2,6-epoxycyclooctylmercuric chloride**, mp 164–166°. An analytical sample recrystallized from 95% ethanol melted at 168–169°. *Anal.* Calcd for $C_8H_{13}OHgCl$: C, 26.60; H, 3.63. Found: C, 26.65; H, 3.69. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ (μ) 3.43 (s), 6.74 (m), 6.88 (m), 6.96 (w–m), 7.36 (w), 7.59 (w), 7.74 (w), 8.69 (s),[35] 8.91 (m), 9.17 (m),[35] 9.37 (m), 9.55 (m), 9.75 (s),[35] 10.23 (s), 11.12 (s),[35] 11.54 (s),[35] and 11.72 (s).[35]

Reduction of the mercurial chloride on 0.5 *M* aqueous sodium hydroxide gave 1,5-epoxycyclooctane (infrared analysis), but in 40% chloroform–ethanol the only detectable product was 4-cycloocten-1-ol.

2,5-Dimethyl-2,5-bis(chloromercurimethyl)-1,4-dioxane. Mercuric acetate (32 g, 0.10 mole) was stirred with 40 ml (0.47 mole) of methallyl alcohol for 15 min, and the resulting mixture was allowed to stand for 4 days. The thick gray paste was dissolved by adding 80 ml of 10% sodium hydroxide. After removal of a small amount of gray residue by filtration, an aqueous solution of sodium chloride (12 g, 0.21 mole) was added. An equal volume of water was added, and the solution was saturated with carbon dioxide. The resulting precipitate was removed and redissolved in 50 ml of 1.2 *M* sodium hydroxide. Repetition of the earlier procedure gave 15.8 g (52%) of colorless 2,5-dimethyl-2,5-bis(chloromercurimethyl)dioxane.[36]

(a) **Reduction with Sodium Borohydride.** A solution of 1.55 g (0.040 mole) of sodium borohydride in 20 ml of 2.5 *M* sodium hydroxide was added over a period of 45 min to a rapidly stirred solution of 43 g (0.070 mole) of the mercurial in 1 l. of 0.5 *M* sodium hydroxide cooled to about 15°. (In a prior small-scale reduction with a more rapid addition of sodium borohydride the initial precipitate was a gray, viscous liquid which decomposed in a mildly explosive manner.) After two extractions with carbon tetrachloride, 25.94 g (92%) of mercury was separated. The aqueous solution was saturated with sodium chloride and extracted once again with carbon tetrachloride. The combined extracts (600 ml total) were dried over Driertie. After removal of the solvent under reduced pressure, distillation gave 6.51 g (65%) of 2,2,5,5-tetramethyl-1,4-dioxane, bp 77.1° (90 mm), $n^{25}D$ 1.4184. *Anal.* Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.19. Found: C, 67.22; H, 11.24.

The nmr spectrum consisted of two sharp singlets, one at τ 6.66 assigned to the four equivalent ring methylene protons and the other at τ 8.88 assigned to the twelve methyl protons (relative areas 4:12.1). The infrared spectrum of the crude product gave no indication of the presence of alcohol (deoxymercuration product).

(b) **Reduction with Sodium Borohydride in Deuterium Oxide.** Eight pellets (*ca.* 0.9 g) of freshly opened 99.2% sodium hydroxide were added to 45 ml of 99.77% deuterium oxide (BIO-RAD Laboratories). A solution of 0.45 g (0.012 mole) of freshly opened sodium borohydride in 5 ml of the 0.5 *M* sodium deuterioxide solution was added slowly to a stirred, cooled solution of 4.0 g (0.0065 mole) of the mercurial in the remaining sodium deuterioxide solution. The infrared and nmr spectra of a concentrate from a carbon tetrachloride extraction were identical with those of the sample of 2,2,5,5-tetramethyl-1,4-dioxane prepared above. The relative areas of the nmr peaks were 4:12.1 (average of seven integrations).

(c) **Reduction with Sodium Borodeuteride in Water.** The reduction was repeated using 3.1 g (0.0050 mole) of mecurial dissolved in 40 ml of 0.5 *M* sodium hydroxide and 0.175 g (0.0042 mole) of sodium borodeuteride (Metal Hydrides, Inc.). The relative

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(31) H. Moell and F. Urbanek, *Festschr. Carl Wurster 60. Geburtstag, 1960*, 91 (1960); *Chem. Abstr.*, **56**, 9992*d* (1962).

(32) Not common to the spectrum of 2,6-epoxycyclooctylmercuric chloride (see below).

(33) Kindly furnished by Cities Service Research and Development Co.

(34) Not common to the spectrum of 1,4-epoxycyclooctane (see above).

(35) Bands not present in the spectrum of 2,5-epoxycyclooctylmercuric chloride.

(36) R. K. Summerbell and S. R. Forrester, *J. Org. Chem.*, **26**, 4834 (1961).

areas of the two nmr peaks were 4:9.8 (average of nine integrations).

Reduction of *trans*-2-Methoxycyclohexylmercuric Chloride. Reduction of 27.6 g (0.079 mole) of mercurial, mp 114–115°,[37] in 0.5 *M* sodium hydroxide gave 15.64 g (99%) of mercury and 86% of methoxycyclohexane collected in two fractions: (1) 1.12 g, bp 129–132°, $n^{20}\mathrm{D}$ 1.430; and (2) 6.58 g, bp 132°, $n^{20}\mathrm{D}$ 1.434 (lit.[38] bp 133.4°). The infrared spectrum of a crude sample of methoxycyclohexane obtained from a small-scale reduction was identical with that of the pure material; there was no evidence for the presence of cyclohexene.

Attempted Reduction of Bis(2-methoxycyclohexyl)mercury. The mercurial was obtained[1] as a light yellow, viscous liquid, $n^{20.2}\mathrm{D}$ 1.538 (lit.[1] $n^{20.5}\mathrm{D}$ 1.534). A stirred suspension of 0.8 g (0.19 mmole) of bis(2-methoxycyclohexyl)mercury in 30 ml of 0.5 *M* sodium hydroxide was treated with a solution of 0.087 g (2.2 mmoles) of sodium borohydride in 2.5 *M* sodium hydroxide. No reaction occurred in 24 hr.

Reduction of 2-Acetoxymercurimethyl-2,3-dihydrobenzofuran. Reduction of 45.8 g (0.116 mole) of the mercurial, mp 79–80° (lit.[9] mp 80–81°), suspended in 850 ml of 1 *M* sodium hydroxide by the addition of 3.3 g (0.085 mole) of sodium borohydride dissolved in 2.5 *M* sodium hydroxide gave 70% of mercury, 26% of 2-methyl-2,3-dihydrobenzofuran, bp 87.3–87.8° (19 mm), $n^{24.5}\mathrm{D}$ 1.5290 (lit.[39] bp 86.5–87.5° (19 mm), $n^{22}\mathrm{D}$ 1.5307), and 23% of bis[2-(2,3-dihydrobenzofuranyl)methyl]mercury, mp 92–94° (lit.[9] mp 93°).

Reduction of 14.6 g of the mercurial in 20% ethanol-water solution gave 91% of mercury and 51% of 2-methyl-2,3-dihydrobenzofuran. An infrared spectrum taken prior to distillation indicated that little or no 2-allylphenol was present.

Attempts to reduce bis[2-(2,3-dihydrobenzofuranyl)methyl]mercury in aqueous sodium hydroxide in the presence or absence of ethanol were unsuccessful.

Reduction of 2,5-Bis(bromomercurimethyl)tetrahydrofuran. The reaction of 42.6 g (0.0646 mole) of the mercurial, prepared by the method of Nesmeyanov[40] employing a 50-hr reaction time and dissolved in 1.2 l. of 0.5 *M* sodium hydroxide and 1.85 g (0.048 mole) of sodium borohydride, gave 97% mercury and an organic product isolated by carbon tetrachloride extraction of the reaction mixture. An infrared spectrum of the latter indicated the presence of *cis*-2,5-dimethyltetrahydrofuran[41] (most) and the *trans* isomer[41] (trace) and the absence of 1-hexen-5-ol.

Reduction of Phenylmercuric Acetate. A 3.0-g (0.0089 mole) sample of phenylmercuric acetate (Aldrich Chemical Co.) was dissolved in 200 ml of 0.5 *M* sodium hydroxide. After removing a small amount of residue by filtration, 3 ml of a solution containing 0.12 g (0.031 mole) of sodium borohydride in 2.5 *M* sodium hydroxide was added dropwise with stirring. The resulting gray precipitate was boiled with benzene and filtered to remove 0.43 g (48%) of mercury. The filtrate was concentrated and the resulting residue was washed with 95% ethanol to give 0.81 g (51%) of diphenylmercury, mp 120–123° (lit.[42] mp 124.5°).

Reduction of *p*-Tolylmercuric Chloride. A 10.0-g (0.0306 mole) sample of *p*-tolylmercuric chloride, mp 230–235°,[43] was reduced essentially as above to give 80% of mercury and 68% of di-*p*-tolylmercury, mp 237–238° (lit.[44] mp 238°).

Determination of Stoichiometry. The reductions were carried out using a large excess of mercurial dissolved in 0.5 *M* sodium hydroxide. The mercury produced was separated and weighed and the unchanged mercurial was recovered as the iodide by the addition of potassium iodide to the reaction mixture and acidification with carbon dioxide. The results are summarized in Table II.

Table II. Stoichiometry of Reductions of Mercurials with Sodium Borohydride in 0.5 *M* Sodium Hydroxide Solution

Mercurial	Concn, mmoles RHgY	Concn, mmoles $NaBH_4$	Stoichiometry	RHgI, %	Hg, %
2,6-Epoxycyclooctylmercuric chloride	9.39	1.63	4:1	89[a]	77
			3:1	56[a]	103
trans-2-Methoxycyclohexylmercuric chloride	14.4	1.22	4:1	97[b]	85
			3:1	86[b]	113
2,5-Epoxycyclooctylmercuric acetate	15.7	2.04	4:1	80[c]	91
			3:1	62[c]	121

[a] The crude iodide, mp 115–135°, was found to have an infrared spectrum identical with an authentic sample, m.p. 147°. [b] The iodide melted at 81–82° (lit[12] mp 81.5–82°). [c] The crude iodide, mp 92–95°, had an infrered spectrum identical with that of an authentic sample, mp 110–111° (some chloride is probably present in the crude iodide).

Reduction of *exo-cis*-2-Hydroxy-3-chloromercurinorbornane with Sodium Borodeuteride in 1 *M* Sodium Hydroxide. In a preliminary experiment a 51.9-g (0.150 mole) sample of mercurial, mp 127.9–128.9,[4] was suspended in 800 ml of 1 *M* sodium hydroxide, and a solution of 1.9 g (0.049 mole) of sodium borohydride in 40 ml of 2.5 *M* sodium hydroxide was added over a 1-hr period. Difficulty was experienced in the work-up, and part of the product was lost. (Better results could no doubt be obtained by using enough alcohol to make the medium homogeneous.) Sublimation allowed separation of 6.76 g (40%) of *exo*-2-norborneol, mp 125.8–126.5° (lit.[45] 127.6–128.5°); phenylurethan, mp 145.2–146° (lit.[46] mp 145–146°). The nmr spectrum (CCl_4) showed a double doublet at τ 6.23 (proton α to OH), a sharp singlet at τ 7.49 (hydroxyl proton—its position varied widely, depending on solvent and temperature), a broad singlet centered at τ 7.77, and a broad multiplet from τ 8.1 to 9.2; relative areas 0.93:0.92:2.0:8.2. The nmr spectrum of the acetate[47] displayed a double doublet at τ 5.54 (proton α to oxygen), a broad singlet at τ 7.78, and a multiplet from τ 7.93 to 9.17 containing a sharp peak at τ 8.12 (acetate methyl); relative areas 0.9:2.0:11.1 (average of our integrations).

A 3.06-g (0.00882 mole) sample of the mercurial was reduced in 100 ml of 1 *M* sodium hydroxide using 0.141 g (0.00337 mole) of sodium borodeuteride in 5 ml of 2.5 *M* sodium hydroxide. After three extractions with carbon tetrachloride, 1.07 g (60%) of mercury was isolated. The nmr spectrum of the product, after removal of the solvent under reduced pressure and dilution with chloroform, displayed the following peaks: a singlet at τ 5.99 (hydroxyl proton), a well-defined doublet centered at τ 6.30 (J_{AB} = 6.4 cps; proton α to hydroxyl), a broad singlet at τ 7.82, and a multiplet from τ 8.17 to 9.24; relative areas 0.9:0.8:2.0:7.3. The nmr spectrum of the acetate showed a sharp doublet centered at τ 5.45 (proton α to oxygen) with a coupling constant of 7 cps.

Acknowledgments. This investigation was supported by Public Health Service Research Grant CA-07351-01A1 from the National Cancer Institute. The investigation was originated under the direction of the late Professor R. K. Summerbell. We wish to thank Professor T. G. Traylor for providing us with information concerning his work in this area prior to publication.

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