samples and to Professor Seebach for the ^{13}C data for 2,2-bis(trimethylstannyl)-1,3-dithiane.

Registry No. 1,3-Dithiane, 505-23-7; 2-methyl-1,3-dithiane, 6007-26-7; 2-phenyl-1,3-dithiane, 5425-44-5; 2-(1,1-dimethylethyl)-1,3-dithiane, 6007-21-2; 2-(trimethylsilyl)-1,3-dithiane, 13411-42-2; 2-(trimethylgeranyl)-1,3-dithiane, 73119-27-4; 2-(trimethylstannyl)-1,3-dithiane, 68971-93-7; 2-(trimethylplumbyl)-1,3-dithiane, 75768-53-5; 2-methyl-2-(trimethylstannyl)-1,3-dithiane, 68971-99-3; 2-phenyl-2-(trimethylstannyl)-1,3-dithiane, 75768-54-6; 2-phenyl-2-(trimethylsilyl)-1,3-dithiane, 13411-45-5; 2,2-bis(trimethylsilyl)-1,3-dithiane, 13411-46-6; 2,2-bis(trimethylstannyl)-1,3-dithiane, 68971-97-1; *trans*-5-*tert*-butyl-2-(trimethylstannyl)-1,3-dithiane, 75768-55-7.

^2H Nuclear Magnetic Resonance Study of the Stereochemistry of Reduction of Some Organomercurials

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The stereochemical courses of the replacement of mercury by deuterium in a range of organomercury halides or acetates, by employing as reducing systems sodium borodeuteride/tetrahydrofuran/aqueous base and 1–2% sodium amalgam/deuterium oxide/sodium deuterioxide, have been investigated by ^2H nuclear magnetic resonance spectroscopy. The following organomercurials were examined: *cis*- and *trans*-(4-methylcyclohexyl)mercuric acetate (or bromide), *cis*-(3-methylcyclohexyl)mercuric bromide, *cis*- and *trans*-(2-methoxycyclohexyl)- and -(2-methoxycyclopentyl)mercuric chlorides, *exo,endo*-(2-norbornyl)mercuric acetate, (5-acetoxy-*exo,exo*-tricyclo[2.2.1.$0^{2,6}$]hept-3-yl)mercuric chloride [(5-acetoxy-3-nortricyclyl)mercuric chloride] and (*cis-exo*-2-acetoxynorborn-5-en-3-yl)mercuric chloride. The sodium borodeuteride reductions provide mixtures and unambiguous assignments of the ^2H spectra were possible either by synthesis of authentic deuterated compounds or on the basis of established ^1H chemical shifts. The signal intensities provide accurate measures of the preferred directions of abstraction by the radicals generally agreed to be involved in these borohydride reductions. In contrast, sodium amalgam reductions are completely stereospecific with retention at carbon, and no rearrangement was observed in the rearrangement-prone nontricyclyl–norbornenyl pair. These results support the idea that the ^2H-incorporating step is electrophilic cleavage of the C–Hg bond, probably in a subvalent organomercury species. The stereochemistries of the (deuterio)alkylcyclohexanes resulting from AIBN-initiated tributylstannane-*d* reductions of various alkylcyclohexyl bromides were also determined for comparison purposes.

The reduction of C–Hg bonds (eq 1) can be achieved

$$RHgX \xrightarrow{\text{reduce}} RH + Hg^0$$

with a variety of reagents.[1] However, sodium borohydride (usually in basic aqueous tetrahydrofuran) is attractive because of its technical ease and rapidity and represents the second stage of the oxymercuration–demercuration route to Markovnikov alcohols from alkenes.[2] In recent years increasing attention has been directed toward understanding the mechanism of this reduction, and the evidence is persuasive that free radicals (from an unstable RHgH) are involved.[3-9] The rearrangements accompanying reduction and the required stereolability of some intermediate are consistent with radical intervention. On the other hand, reduction of norbornyl[6,10] and dibenzobicyclo[2.2.2]octadienyl-type[6] mercurials with Na/Hg proceeds in a highly stereospecific fashion and has been recommended[6] as the method of choice for site specificity and stereospecificity of deuterium incorporation. Determinations of stereochemistry of ^2H incorporation have employed ^1H NMR spectroscopy, and adequate separation of resonances is necessary to permit evaluation.[6,7] The systems mentioned above, with some electronegative oxy function, normally provide adequately separated resonances. However, ^1H NMR analysis is more difficult to apply when the product is a simple cyclic hydrocarbon, e.g., reduction of alkylcyclohexyl mercurials, and yet these strain-free nonfunctionalized systems permit more generalized conclusions about stereochemistry and mechanisms. Infrared analysis has also been employed successfully in some cases,[7] but normally a C–^2H vibration characteristic of each pure isomer should be identified. Such vibrations for axial and equatorial C–^2H bonds have been employed for conclusions concerning the stereochemistry of deuterium incorporation.[11] We have found this approach tedious and sometimes unrewarding, and we

(1) For a general discussion see F. R. Jensen and B. Rickborn, "Electrophilic Substitution of Organomercurials", McGraw-Hill, New York, 1968, Chapter 6.
(2) H. C. Brown and P. Geoghegan, *J. Am. Chem. Soc.*, **89**, 1522 (1967); S. Bentham, P. Chamberlain, and G. H. Whitham, *Chem. Commun.*, 1528 (1970).
(3) F. G. Bordwell and M. L. Douglass, *J. Am. Chem. Soc.*, **88**, 993 (1966).
(4) G. A. Gray and W. R. Jackson, *J. Am. Chem. Soc.*, **91**, 6205 (1969); V. M. A. Chambers, W. R. Jackson, and G. W. Young, *Chem. Commun.*, 1275 (1970).
(5) D. J. Pasto and J. A. Gontarz, *J. Am. Chem. Soc.*, **91**, 719 (1969).
(6) F. R. Jensen, J. J. Miller, S. J. Cristol, and R. S. Beckley, *J. Org. Chem.* **37**, 4341 (1972).
(7) G. M. Whitesides and J. San Filippo, *J. Am. Chem. Soc.*, **92**, 6611 (1970).
(8) R. P. Quirk and R. E. Lea, *J. Am. Chem. Soc.*, **98**, 5973 (1976).
(9) K. Maskens and N. Polgar, *J. Chem. Soc., Perkin Trans. 1*, 109 (1973).
(10) T. G. Traylor and A. W. Baker, *J. Am. Chem. Soc.*, **85**, 2746 (1963); J. K. Stille and S. C. Stinson, *Tetrahedron*, **20**, 1387 (1964).
(11) (a) E. J. Corey, M. G. Howell, A. Boston, R. L. Young, and R. A. Sneen, *J. Am. Chem. Soc.*, **78**, 5036 (1956); (b) F. R. Jensen and L. H. Gale, *ibid*, **82**, 145 (1960); (c) P. A. Wiseman, *J. Org. Chem.*, **40**, 112 (1975); (d) W. N. Rogers and M. C. Baird, *J. Organomet. Chem.*, **182**, C65 (1979).

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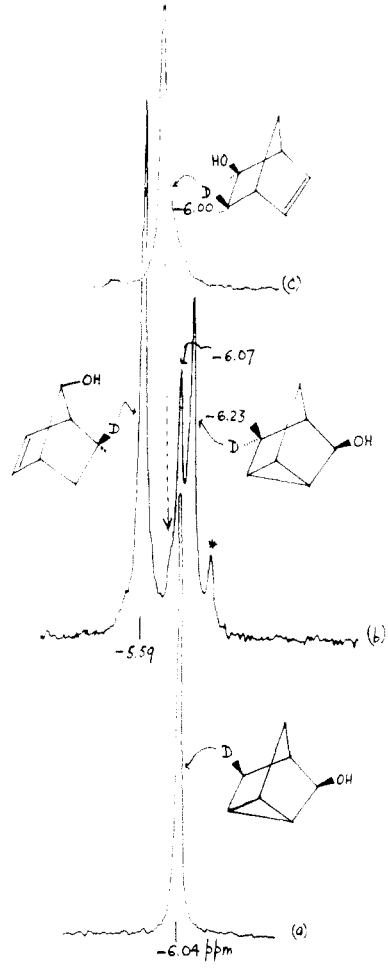


Figure 1. (a) 15.29-MHz ^2H spectrum of the sodium amalgam reduction product of (5-acetoxy-3-nortricyclyl)mercuric chloride, consisting of a lone signal (–6.04 ppm with respect to internal $CDCl_3$) confirming the stereospecific nature of this reduction. (The ^{13}C spectrum contained no signals for vinylic carbons.) (b) ^2H spectrum of the $NaBD_4$ reduction product of (5-acetoxy-3-nortricyclyl)mercuric chloride showing major signals at –5.59, –6.07 and –6.23 ppm, with a minor shoulder at ca. –5.97 ppm. (An essentially identical spectrum is obtained from $NaBD_4$ reduction of (*cis-exo*-2-acetoxynorborn-5-en-3-yl)mercuric chloride.) The chemical shifts of these major signals agree well with those based on available ^1H chemical shifts (see ref 4), and the signal at –6.07 is securely assigned by its essential coincidence with the signal in Figure 1a. The asterisked signal (ca. –6.50 ppm, corresponding to a ^1H shift of ca. 0.80 ppm) is unidentified. (c) ^2H spectrum of the sodium amalgam reduction product of (*cis-exo*-2-acetoxynorborn-5-en-3-yl)mercuric chloride, showing a single signal at –6.00 ppm, again confirming the stereospecific nature of this reduction. (The ^{13}C spectrum contained no signals for cyclopropyl carbons.) The essential coincidence of this signal with the shoulder in Figure 1b at ca. –5.97 ppm leads to the latter's assignment.

share House's scepticism[12] about the method.

We decided that ^2H NMR spectroscopy would be simpler and more accurate, and in this paper we report on the ^2H NMR examination of the sodium borodeuteride and sodium amalgam reductions of a range of mercurials, as well as the tributylstannane-*d* reductions of a few (alkyl)cyclohexyl bromides. The properties of ^2H from a magnetic resonance viewpoint, the acquisition of ^2H NMR spectra, and the chemical applications of the method have been reviewed recently.[13] It is worth mentioning that ^2H chemical shifts (in parts per million) are the same as those of the corresponding ^1H nucleus, and although the range of ^2H shifts is about 200 Hz, the spectra are usually well resolved. This is particularly so with ^1H decoupling, and integration of ^2H signals provides accurate results, because significant nuclear Overhauser enhancement does not accompany proton decoupling.[13]

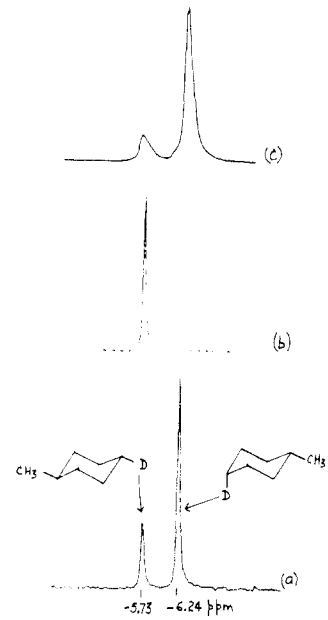
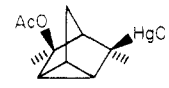


Figure 2. (a) 15.29-MHz ^2H spectrum of the $NaBD_4$ reduction product of *trans*-(4-methylcyclohexyl)mercuric acetate. The *cis*- and *trans*-4-(deuteriomethyl)cyclohexanes are in the ratio of 74:26. (b) ^2H spectrum of the sodium amalgam reduction product of *trans*-(4-methylcyclohexyl)mercuric acetate showing a lone signal for *trans*-4-deuteriomethylcyclohexane. (c) ^2H spectrum of the sodium amalgam reduction product of a 13:87 *trans*/*cis*-(4-methylcyclohexyl)mercuric acetate isomer mixture. The ^2H signals are in the ratio of ca. 14:86, confirming retention of configuration at carbon in the reduction of each isomer (when considered with the result in Figure 2b.

Results and Discussion

Sodium Borodeuteride Reductions. These reductions were conducted in the standard way (see Experimental Section), the reduction products were carefully extracted into chloroform, and these solutions examined directly by ^{13}C and ^2H NMR spectroscopy. The nature of the products, the level of ^2H incorporation,[14] and the product distributions were established by ^{13}C NMR, while the ^2H spectra provide accurate measures of the isomeric deuterated products.

(a) Norbornyl-Type Mercurials. (5-Acetoxy-*exo*-*exo*-tricyclo[2.2.1.$0^{2,6}$]hept-3-yl)mercuric chloride (I; see



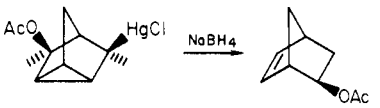
I

the Experimental Section for correction of some ^{13}C–^{199}Hg couplings for this compound) has been examined previously by three groups, all of whom report a product mixture. The initial report of Pasto and Gontarz[5] was corrected subsequently as to isomer distributions and was in agreement with that of Gray and Jackson.[4] The pertinent results are shown in eq 1 and 2. The major reported

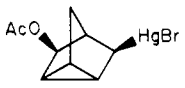
(12) See footnote 29 in H. O. House, B. A. Tefertiller, and H. D. Olmstead, *J. Org. Chem.*, **33**, 935 (1968).

(13) H. H. Mantsch, H. Saito, and I. C. P. Smith, *Prog. Nucl. Magn. Reson. Spectrosc.*, 11, 211 (1977).

(14) Determinations of the level of ^2H incorporation by mass spectrometry have been conducted[6-8] and the meaning of variations discussed.

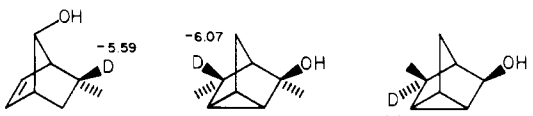


II (6%) III (34%) IV (60 ± 3%, Gray and Jackson)[4] (1)



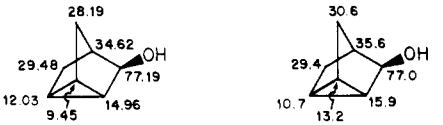
II (32%) III (7%) IV (61%, Whitesides and San Filippo)[7] (2)

difference (eq 1 and 2) concerns the proportions of *anti*-7-acetate and norbornenyl acetate. Our ^{13}C examination of the total product mixture showed that 2-*exo*-acetoxynorborn-5-ene (or its alcohol) was a very minor product component, in agreement with the finding of Gray and Jackson (who reported 6 ± 3%). The major components were clearly norticyclanol and *anti*-7-norbornenol (after hydrolysis). The ^2H spectrum (Figure 1) shows three major signals (in parts per million) assigned as shown in V–VII,



V VI VII

with the combined nortricyclanol (~54%) slightly exceeding the *anti*-7-alcohol (46%). (All ^2H chemical shifts are relative to internal $CDCl_3$.) Reduction of the isomeric (*cis-exo*-2-acetoxynorborn-5-en-3-yl)mercuric chloride provided an almost identical ^2H spectrum, as expected on the basis of Gray and Jackson's report.[4] What is clear is that ^2H incorporation into the nortricyclanol (5-exo and 5-endo positions) is not very selective. ^1H NMR data provided by Gray and Jackson[4] could be interpreted that H_{5x} (δ 1.25) was at lower field that H_{5n} (δ ~1.0–1.1) in line with chemical shift trends for H_x and H_n in norbornanes.[15] In nortricyclanol, H_{5x} and H_{5n} are located in almost identical environments with respect to the cyclopropane ring, and the normal shift sequence for exo or endo protons should apply. However, recourse to such imprecise considerations is not necessary. We have shown (vide infra) that Na–Hg reduction of the tricyclic mercurial is specific, the product yielding one ^2H signal (–6.03 ppm) and the ^{13}C spectrum (see below) for nortricyclanol. (No other organic material was present.) All the evidence from previous work[6,10,16] and herein is that such Na–Hg reductions proceed with retention of configuration at carbon, and the compound obtained was therefore 5-*exo*-deuterionortricyclanol. This now establishes that the major ^2H signal for the isomeric 5-deuterionortricyclanols (resulting from $NaBD_4$ reduction) was indeed due to the *endo*-^2H isomer. Our ^{13}C assignments (in parts per million) for 3-nortricyclanol (relative to the center of the triplet of $CDCl_3$ as 77.00 ppm) are shown in VIII and IX, and may be compared with those of Lipmaa.[17] Our assignments are based

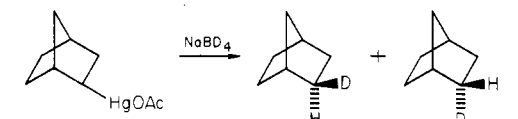


VIII IX (Lipmaa[17])

on considerations of one- and two-bond ^2H isotope effects (ca. 0.4 and 0.1 ppm, respectively) on the ^{13}C shifts. Although reduction with $NaBD_4$ led to no detectable undeuterated compound (^{13}C spectrum), reduction with a 3:1 mixture of $NaBD_4$ and $NaBH_4$ led to a spectrum of a mixture of 5-deuterionortricyclanol and 3-nortricyclanol itself.

Our (internal) comparisons of protio and specifically deuterated material requires the assignments of Lipmaa[17] for C_1,C_6 and C_5,C_7 to be reversed. (There appears to be a systematic difference of ca. 1–1.2 ppm between our shifts and those of Lipmaa.[17])

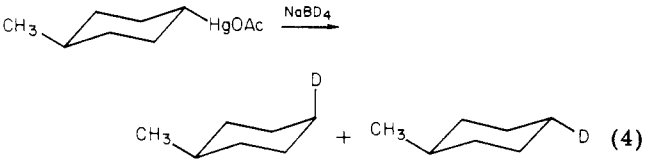
2-Norbornylmercuric acetate was prepared in the usual way from the Girgnard reagent from *exo*-2-norbornyl bromide and mercuric bromide,[7,18] followed by treatment with silver acetate. The sample was from ^{13}C NMR examination[19] a ca. 71:29 mixture of the exo and endo isomers. Reduction with $NaBD_4$ provided norbornane-2-*d*, as shown in eq 3. Previously, Whitesides,[7] on the basis



71:29 exo/endo 95.8 4.2 91.7 8.3 (3)

of IR spectroscopy, had reported that either isomer, separately, provided norbornane-2-*d* which was ~90:10 exo/endo. Our direct ^2H examination confirms this, and we made no further effort to separate and examine individually the starting (mercurial) isomers.

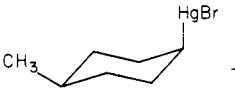
(b) Cyclohexyl-Type Mercurials. Pure *trans*-(4-methylcyclohexyl)mercuric acetate or bromide and predominantly *cis*-(4-methylcyclohexyl)mercuric bromide on $NaBD_4$ reduction yielded essentially the same mixture of *cis*- and *trans*-4-methylcyclohexane-1-*d* as shown in eq 4–6.



X (–6.55 ppm, 74%) XI (–6.05 ppm, 26%) (4)

duplicate →

X (–6.24 ppm, 76%) + XI (–5.73 ppm, 24%) (5)



X (–6.43 ppm, 74%) + XI (–5.94 ppm, 26%) (6)

cis-(3-Methylcyclohexyl)mercuric bromide provided

(15) See: L. F. Hines and J. K. Stille, *J. Am. Chem. Soc.*, **94**, 485 (1972); E. Vedejs and M. F. Salomon, *J. Org. Chem.*, **37**, 2075 (1972); D. R. Coulson, *J. Am. Chem. Soc.*, **91**, 200 (1969).

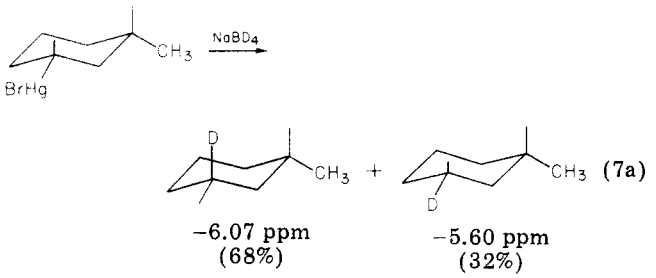
(16) S. Wolfe and P. Campbell, *Can. J. Chem.*, **43**, 1184 (1963).

(17) E. Lipmaa, T. Pehk, and J. Paasivirta, *Org. Magn. Reson.*, **5**, 277 (1973).

(18) S. Winstein, E. Vogelfanger, K. C. Pande, and H. F. Ebel, *J. Am. Chem. Soc.*, **84**, 4993 (1962).

(19) W. Kitching, D. Praeger, D. Doddrell, F. A. L. Anet, and J. Krane, *Tetrahedron Lett.*, 759 (1975).

largely *trans*-3-methylcyclohexane-*1-d*. Quenching of the 3-methylcyclohexyl Grignard reagent with D_2O provided *cis*-3-(deuteriomethyl)cyclohexane (−5.61 ppm) and the trans isomer (−6.06 ppm) in a 76:24 ratio (eq 7a,b).

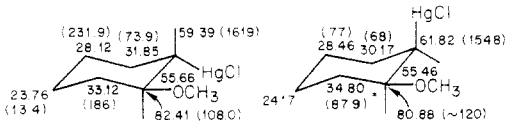


−6.07 ppm (68%) + −5.60 ppm (32%) (7a)

duplicate →

−6.13 ppm + (71%) + −5.68 ppm (29%) (7b)

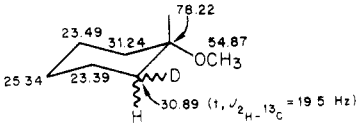
trans- and *cis*-(2-methoxycyclohexyl)mercuric chlorides were prepared, the former in the standard way by direct methoxymercuration of cyclohexene and the latter by acid-catalyzed equilibration of the former and selective (HCl) destruction of the trans isomer. The ^{13}C characteristics (in parts per million) of these isomers are summarized in structures XII and XIII. (The values in



XII XIII

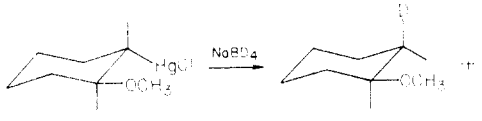
parentheses are ^{199}Hg–^{13}C couplings. The asterisked value was incorrectly was reported[19] as 102 Hz.) Significant differences also appear in the ^1H spectra of these isomers (see Experimental Section).

Reduction of each of the pure trans and cis isomers above provided only 2-(deuteriomethoxy)cyclohexane as judged by the ^{13}C spectrum of the total product (XIV).

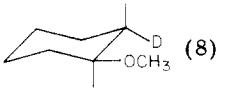


XIV

The ^2H NMR spectrum established that *trans*-2-(deuteriomethoxy)cyclohexane predominated, and the same mixture resulted from either starting isomer (eq 8 and 9).

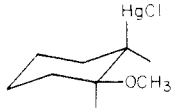


XV (−6.11 ppm, 44%)



(8)

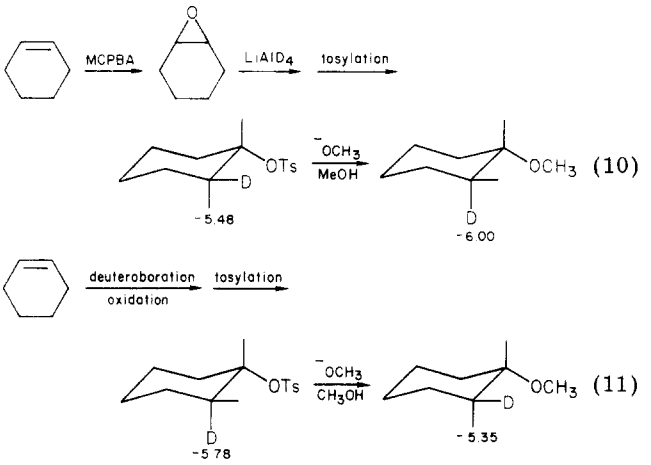
XVI (−5.48 ppm, 56%)



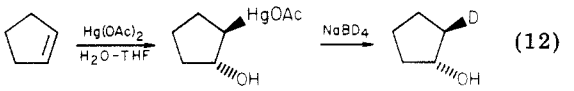
NaBD4 XV (−6.16 ppm, + 43%)

XVI (−5.52 ppm, 57%) (9)

That the ^2H assignments were correct followed from the spectra of authentic samples synthesized by standard procedures, as shown in eq 10 and 11.

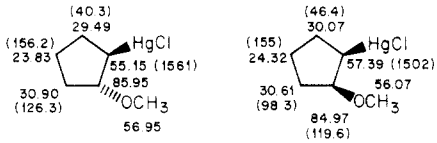


(c) Cyclopentyl-Type Mercurials. Pasto and Gontarz[5] have examined *trans*-(2-hydroxycyclopentyl)mercuric acetate (eq 12) and reported that the reduction step pro-



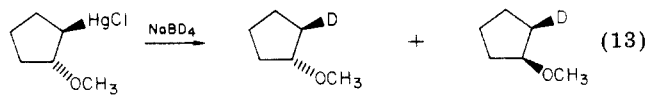
vided >95% *trans*-2-deuteriocyclopentanol, on the basis of IR comparisons (of the *p*-nitrobenzoate ester) with authentic *cis*- and *trans*-2-deuteriocyclopentyl *p*-nitrobenzoates. The cis oxymercurial was not examined. This intriguing stereochemical result was attributed to hydrogen atom transfer within the solvent cage before molecular reorientation.

Methoxymercuration of cyclopentene was conducted in the normal way to provide *trans*-(2-methoxycyclopentyl)mercuric chloride. Acid-catalyzed isomerization to the cis compound was performed, with the residual trans isomer being selectively destroyed by HCl-induced deoxymercuration. Both isomers were characterized by their ^{13}C and ^1H NMR spectra (see XVII and XVIII). Re-

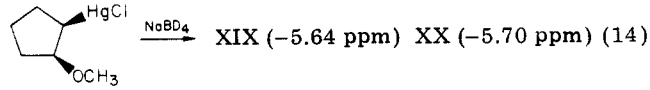


XVII XVIII

duction of either isomer or a 1:1 isomer mixture yielded essentially the same mixture of 2-deuteriocyclopentyl methyl ethers, with the lower field signal being far more intense and being assigned initially on the basis of the IR studies[5] to the trans isomer. A low-intensity signal appeared normally as a shoulder on the high-field side of the major signal (by ca. 0.06 ppm) and was assigned to the *cis*-2-deuteriocyclopentyl methyl ether. The results are summarized in eq 13–15.

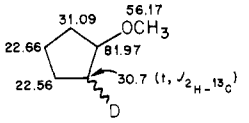


XIX (−5.84 ppm) XX (ca. −5.89 ppm, unresolved shoulder)



$$\text{1:1 mixture} \xrightarrow{NaBD_4} \text{XIX (-5.67 ppm) XX (ca. -5.70 ppm)} \quad (15)$$

We estimate the proportion of the *cis*-2-deuteriocyclopentyl product could be as high as 10–12%, somewhat greater than that reported by Pasto[5] (not greater than 5%). The small ^2H chemical shift difference for the isomers is not unexpected when the conformational profile of 2-methoxycyclopentane is considered.[20-22] (These ^2H assignments are fully consistent with the data from Na/Hg reductions of the isomers to be outlined later.) ^{13}C examination of the total chloroform extract confirmed quantitative production of 2-deuteriocyclopentyl methyl ether (XXI).



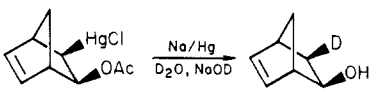
XXI

Sodium-Amalgam Reductions. A variety of structural types of mercurial were subjected to reduction by excess 1–1.5% Na/Hg in ca. 1 M $NaOD/D_2O$ by utilizing relatively long (1–2 days) reaction times. These conditions ensured that ester functions in the reactant mercurial were hydrolyzed, so that alcohols were the product actually examined spectroscopically.

Nortricycl–Dehydronorbornyl System. We have demonstrated that ^2H NMR provides deep insight into the $NaBD_4$ reductions in this system which afford identical product mixtures from either starting isomer. The available evidence[6,16] is that Na/Hg reductions of C–Hg bonds are highly stereospecific, proceeding with retention of configuration at carbon, and it seemed instructive to to test this presumed general specificity in a very rearrangement-prone system.

In our approach to the identification of the ^2H signals of the product resulting from $NaBD_4$ reduction of either the norbornenyl or the nortricyclyloxy mercurial, we discussed the specificity of the Na/Hg reduction of the latter oxymercurial, which provided 5-*exo*-deuterionortricyclanol, i.e., reduction with complete retention of configuration.

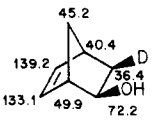
Sodium amalgam reduction of the isomeric norbornenyl (dehydronorbornyl) oxymercurial is also completely specific. Thus ^{13}C NMR examination of the product established that *no* tricyclic alcohol had formed (no cyclopropyl signals) and that the sole product was a deuterated norbornenol (hydrolysis of the acetate, eq 16). The ^{13}C NMR



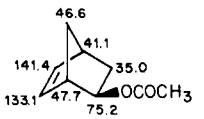
(16)

assignments are shown in XXII and are compared with those established for the corresponding acetate (XXIII).[23] That ^2H incorporation is site-specific is clear from the presence of one triplet (^{13}C–^2H coupling) at 36.4 ppm.

A single ^2H signal is observed at –6.00 ppm (to high field of $CDCl_3$) and was very similar to but nevertheless different from the shift (–6.03 ppm) found for 5-*exo*-deuterionortricyclanol. The closeness of these signals is



XXII



XXIII

consistent with the appearance of the ^2H spectrum for the $NaBD_4$ reduction of these mercurials, as a minor signal (shoulder) appears ca. 0.05 ppm to the low-field side of the signal ascribed to 5-*exo*-deuterionortricyclanol. This low-intensity signal confirms that norbornenol is a very minor product from the $NaBD_4$ reduction of either of the nortricyclyl or norbornenyl oxymercurials but that Na/Hg reduction of each is specific and that no rearrangement accompanies the Na/Hg reductions.

2-Norbornylmercuric acetate, obtained as a 71:29 exo/endo mixture (^{13}C NMR),[19] was also reduced in the normal way. The ^2H spectrum of the norbornane obtained consisted of two signals at –5.78 (70.4%) and –6.10 (29.6%) ppm (upfield) from internal $CDCl_3$. These shifts correspond to ^1H shifts of δ 1.49 and 1.17 for exo and endo protons, in excellent agreement with those (δ 1.49 and 1.18) reported.[24] The essentially identical ratios of exo/endo isomers in the reactant and product are logically interpreted with the supposition that Na/Hg reduction of each isomer proceeds with configurational retention at carbon.

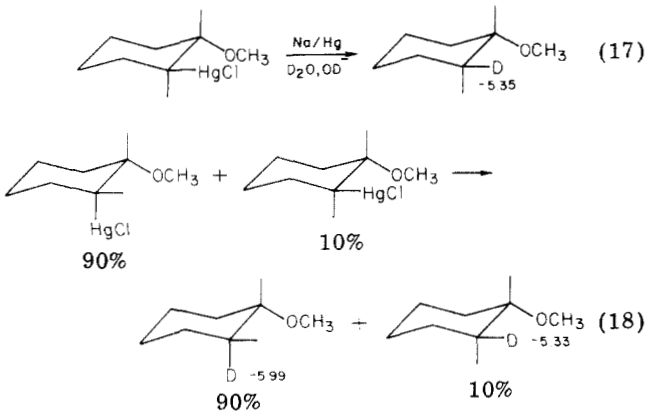
(4-Methylcyclohexyl)mercuric acetate was obtained in the pure trans form, and Na/Hg reduction was conducted. The ^{13}C NMR spectrum of the $CHCl_3$ extract of the reaction consisted of signals for methylcyclohexane-*d* and unreacted mercurial. This mercurial was exclusively trans, indicating that isomerization does not accompany this form of reduction. (The thermodynamic stabilities of *cis*- and *trans*-4-methylcyclohexyl mercurials would be extremely similar, perhaps slightly favoring the cis isomer.)[25,26] The ^2H spectrum was a single signal at –5.03 ppm, corresponding to *trans*-4-methylcyclohexane-*1-d* (the identical result, i.e., complete specificity, was observed on repetition).

A 13:87 trans/cis mixture (^{13}C NMR) of (4-methylcyclohexyl)mercuric bromide was converted directly to the acetates and reduced. The ^2H spectrum of the $CHCl_3$ extract consisted of two signals at –5.64 and –6.15 ppm, corresponding to *trans*- and *cis*-4-methylcyclohexane-*1-d*, in a ratio of ca. 14:86. Coupled with the result for the pure *trans*-4-methylcyclohexyl mercurial, these data demonstrate retention of configuration at carbon in the reduction of each isomer.

(2-Methoxycyclohexyl)mercuric Chlorides. Pure *trans*-(2-methoxycyclohexyl)mercuric chloride was reduced in the normal way, and the ^2H spectrum of the $CHCl_3$ solution of the extract consisted of one signal at –5.35 ppm, corresponding to *trans*-(2-deuteriomethoxy)cyclohexane (eq 17).

cis-2-(Methoxycyclohexyl)mercuric chloride, slightly contaminated with the trans isomer (ca. 90:10 by ^{13}C NMR) was subjected to the same procedure, and two ^2H signals at –5.33 and –5.99 ppm were observed (eq 18), corresponding to *trans*- and *cis*-2-(deuteriomethoxy)-cyclohexane. The intensity ratio was ca. 9.91, again requiring retention of configuration at carbon in the reduction of each isomer.

(20) R. L. Lipnick, *J. Am. Chem. Soc.*, **96**, 2941 (1974).
(21) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van-Catledge, *J. Am. Chem. Soc.*, **90**, 1199 (1968).
(22) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley, New York, 1965, p 44.
(23) P. F. Barron, D. Doddrell, and W. Kitching, *J. Organomet. Chem.*, **132**, 351 (1977).
(24) L. M. Jackman and S. Sternhell, "Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press, New York, 1969, p 230.
(25) F. A. L. Anet, J. Krane, W. Kitching, D. Doddrell, and D. Praeger, *Tetrahedron, Lett.*, 3255 (1974).
(26) F. R. Jensen and L. H. Gale, *J. Am. Chem. Soc.*, **81**, 6337 (1959).



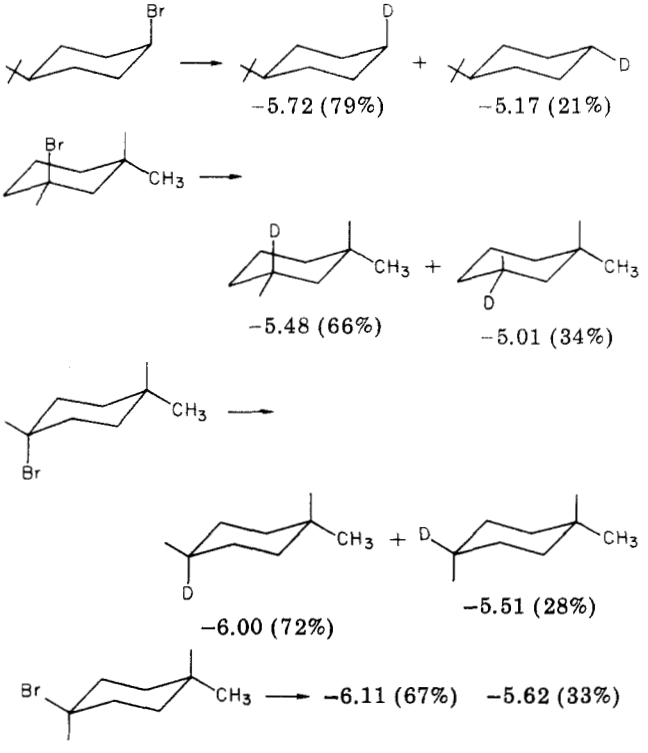
(2-Methoxycyclopentyl)mercuric Chlorides. Reduction of the pure trans isomer and workup in the normal way provided a single ^2H signal at −5.52 ppm. Reduction of the cis isomer, slightly contaminated with the trans isomer, afforded two ^2H signals at −5.54 and −5.62 ppm, with the latter (higher field signal) being far more intense. These data establish that the ^2H shift for *cis*- and *trans*-2-(deuteriomethoxy)cyclopentane are very close, with the *cis* slightly to higher field (by ca. 0.05 ppm), as observed in the 2-methoxycyclohexane system. These results, besides confirming the isomer distribution in the borodeuteride reduction, are in line with stereochemical retention at carbon in the Na–Hg reductions.

Reductions with Tributylstannane-*d*. A few alkylcyclohexyl bromides, of established structures, were reduced thermally by AIBN-induced reaction, in benzene, with *n*-$(C_4H_9)_3SnD$. Reaction (at 60 °C) was continued until the ^1H signal for the CHBr proton was completely absent. Direct examination by ^2H NMR provided the results shown in Scheme I [Wiseman[10c] has reported shifts of −5.98 and −5.42 (Δ = 0.56) ppm for *cis*- and *trans*-4-deuterio-*tert*-butylcyclohexane].

Sodium Borodeuteride Reductions. A free-radical chain mechanism is considered[3-8] to be involved in these reductions, and some of the more convincing evidence is based on rearrangements, particularly in the nortricyclyl–norbornenyl systems. Our ^2H study of the system confirms the general findings of Gray and Jackson[4] and San Filippo and Whitesides,[7] but we can add one further point. Gray and Jackson[4] establish that the abstraction step by the 5-nortricyclyl radical was nonselective (ca. 2:1 based on ^1H NMR integrations) but could not establish the preferred direction, which we show to be preferentially endo. Approximately equal amounts of the two products would be expected, as indicated in Scheme II. (The nortricyclene skeleton possesses C_{3v} symmetry.)

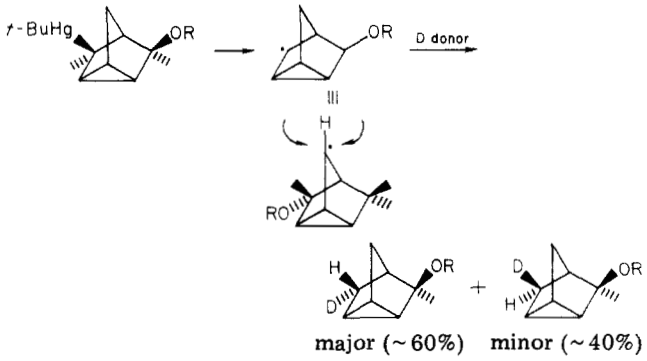
Our studies of the 3- and 4-methylcyclohexyl mercurials are of interest as the isomer distributions (of the deuterated methylcyclohexanes), easily established by ^2H NMR, allow comparison with those reported for other systems involving 4-alkylcyclohexyl radicals. The general position has been summarized and discussed by Jensen.[27] The distributions found in this study establish that the $NaBD_4$ reduction is characterized by predominant (~70:30) cis product in the 4-methyl series and trans product (~70:30) in the 3-methyl series. (In both series, the ^2H is predominantly axial.) Axial abstraction is favored by torsional effects when bond formation is significant in the transition state, and this would be consistent with the >90% product found in the norbornyl case. One might expect, then, that

Scheme I



[a] Chemical shifts in parts per million.

Scheme II



a measurable isotope effect would attend the H(D) abstraction step, and a value of *1.8* has been calculated[8] for transfer of hydrogen from 1-hexenylmercuric hydride to the hexenyl radical. These results are intriguing when it is considered that RHgH has defied characterization,[28] apparently due to low Hg–H bond dissociation energy.[29] Hence, H abstraction by R· from R'HgH would be expected to be highly *exothermic* with a low activation energy, with the transition state structurally resembling the reactants and exhibiting a very low or negligible isotope effect. In combination, the cis/trans ratio in the product and the k_H/k_D of ~1.8 are consistent with significant bond formation (R'Hg...D...R) in the abstraction step. A similar conclusion applies to our results for the alkylcyclohexyl bromide/tributyltin deuteride reductions, conducted under conditions where a free-radical chain reduction operates.[30]

(27) F. R. Jensen, L. H. Gale, and J. E. Rodgers, *J. Am. Chem. Soc.*, **90**, 5793 (1968).

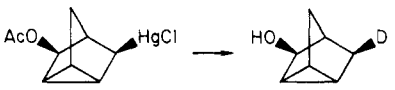
(28) The reaction of mercuric iodide with lithium aluminium hydride at low temperatures (−130 °C) provides a material thought to be a mercury hydride but which is extremely unstable. E. Wilberg and W. Herb, *Z. Naturforsch, B: Anorg. Chem., Org. Chem.*, **6**, 461 (1951).

(29) Bond energies of HgH and HgH^+ have been estimated as 8.6 and 53 kcal/mol. H. L. Roberts, *Adv. Inorg. Chem. Radiochem.*, **11**, 309 (1968).

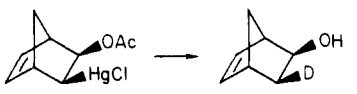
The cis/trans ratio (ca. 70:30), implying significant $R'_3Sn...D...R$ bond formation in the transition state, is consistent with $k_H/k_D \approx 2.7$–2.8 reported for H transfer from $R_3SnH(D)$ to cyclohexyl[31] and 5-hexenyl[8] radicals. The 2-methoxycyclohexyl radical provides predominantly (~55%) *trans*-2-methoxycyclohexane-*1*-d, while the 2-methoxycyclopentyl radical yields largely (~90%) trans abstraction product. In the absence of information regarding the geometries of these radicals, it seems reasonable that, if bond formation is significant in the transition state for ^2H abstraction, the methoxy group may exert a steric effect, promoting trans abstraction. The earlier suggestion of Pasto[5] that the 2-hydroxycyclopentyl radical achieved hydrogen transfer (in the solvent cage) before reorientation seems unlikely in view of our and other data[6,7] and the fact that a chain rather than a cage process is operative.

Sodium Amalgam Reductions. The evidence, without apparent exception, indicates that of the methods currently available for reduction of RHgX to RH (or RD), sodium amalgam (in D_2O, OD^-) is unique in proceeding with complete retention of configuration at carbon and essentially 100% ^2H incorporation.[6,10,16] Many of the earlier examples pertain to norbornyl moieties, but more recently cis and trans oxymercurials derived from the dibenzobicyclo[2.2.2]octatriene system have been examined[6] as well. An important earlier sample concerned reduction of the acetoxymercuration product of 3,3,6,6-tetradeuteriocyclohexene.[16] The stereospecificity observed in these reductions seems inconsistent with a free-radical pathway, and Jensen[6] has considered that in this heterogeneous system two closely linked one-electron transfers occur at the amalgam surface to yield RHg:, which would be particularly prone to hydrolytic (electrophilic) C–Hg bond cleavage to yield RD.

The results obtained in this study are particularly important as they indicate that specificity applies in a variety of systems and in particular, in a completely uncomplicated one, viz., the 4-methylcyclohexyl system, from which valid generalized conclusions may be drawn. Of particular interest, also, were the findings that separate reductions of the norbornenyl and nortricyclyl mercurials were completely regio- and stereospecific, on the basis ^{13}C and ^2H NMR (eq 19 and 20).



(19)



(20)

The complete specificities observed in the *cis*- and *trans*-2-methoxycyclohexyl and -cyclopentyl mercurials, as well as the above, confirms that "free" intermediates such as radicals or carbanions are not involved. Taken together, the evidence generates high confidence that all Na–Hg reductions will proceed with retention at carbon, and hence the claim that it is the method of choice for stereospecific introduction of ^2H for HgX is well founded.[6] (An apparent exception[32] has been reported, but intervention of an enolic intermediate appears very likely.) With the increasing use of organomercurials in synthesis, especially anion mercuration/demercuration and Hg^{II}-induced cyclizations,[33] a deeper understanding of the methods available for demercuration will be valuable, and the use of ^2H NMR provides an extremely straightforward analytical method. Additionally, hydroxymercuration (with acid-catalyzed equilibration to provide the alternative isomer, if necessary) followed by Na–Hg reduction (D_2O, ^-OD) may constitute a useful sequence for stereospecific synthesis of β-deuterio alcohols under some conditions.

Experimental Section

Compounds. *trans*- and *cis*-(4-Methylcyclohexyl)mercuric bromides were obtained as a mixture from the reaction of 4-methylcyclohexyl Grignard reagent and mercuric bromide, as detailed by Jensen and Gale.[11b] Crystallization from benzene provided pure *trans*-4-(methylcyclohexyl)mercuric bromide as the least soluble isomer.[11b] This had a melting point of 157–158 °C) in agreement with that reported,[11b] and its ^1H and ^{13}C NMR spectra[19] were appropriate, as described below. Successive crystallizations as described[11b] provided a mixture rich in the cis isomer, as judged by ^1H and ^{13}C NMR spectra.

In the ^1H NMR spectrum, the trans isomer is characterized by a signal at δ 2.70 (tt, $J \approx 11.15$ and 3.5 Hz), while the cis isomer exhibits a relatively narrow signal ($W_{1/2} \approx 10$ Hz) for CH(HgBr) at δ 3.43 (using $CHCl_3$ as δ 7.27).

The ^{13}C spectrum ($CDCl_3Me_4Si$) of the trans isomer consists of signals at 22.27 (CH_3), 32.70 (C_4), 33.68 ($C_{2,6}$), 37.55 ($C_{3,5}$), and 57.78 ppm (C_1), while under the same conditions, the cis exhibits signals at 22.66 (CH_3), 32.43 (C_4), 32.80 ($J_{^{199}Hg-^{13}C} = 59.8$ Hz, $C_{2,6}$), 37.99 ($J = 73.2$ Hz, $C_{3,5}$), and 61.31 ppm ($J = 1419$ Hz), C_1). The spectrum of the trans isomer was also recorded with $CDCl_3$–pyridine as solvent (better solubility) and signals at 22.44 (CH_3), 32.70 (C_4), 33.99 ($J = 65$ Hz, C_2, C_6), 37.67 ($J = 269$ Hz, $C_{3,5}$), and 54.95 ppm ($J = 1590$ Hz, C_1) were observed.

The mercuric acetates provide similar spectra except that C_1 (bearing HgOAc) appears to higher field, e.g., at 47.94 ppm, in the *trans*-4-methylcyclohexyl compound.

***cis*-(3-Methylcyclohexyl)mercuric bromide** was the predominant isomer, as expected, resulting from treatment of the 3-methylcyclohexyl Grignard reagent with $HgBr_2$, as described for the 4-series by Jensen and Gale.[11b] The crude mercurial exhibited a major ^1H signal (CCl_4–pyridine–Me_4Si) for CH(HgBr) at δ 2.64 (~80%) which was a triplet (with smaller couplings superimposed; $J \approx 11$ Hz), appropriate for an axially disposed proton. The minor CH(HgBr) signal was relatively narrow ($W_{1/2} \approx 9$ Hz) at δ 3.31, consistent with an equatorially disposed proton. [These ^1H shifts are very similar to those found for the trans (δ 2.70) and cis (δ 3.43) isomers in the 4-series.] One crystallization of this crude material from benzene provided the least soluble isomer, mp 99–102 °C. The ^1H spectrum now almost lacked the narrow signal at δ 3.31, and hence the major isomer *cis*-(3-methylcyclohexyl)mercuric bromide. [This material, which was ~90–95% cis, was cleaved with bromine in pyridine/air to provide ~95% *cis*-3-methylcyclohexyl bromide (on the basis of ^{13}C and ^1H NMR) for use in another study.][34] This cis mercurial exhibited ^{13}C signals at 22.61 (CH_3), 28.93 (C_5), 34.02 (C_3), 35.36 and 35.72 (C_4,C_6), 42.94 (C_2), and 57.46 ppm (C_1). (solvent $CDCl_3/Me_4Si$).

Anal. Calcd for $C_7H_{13}HgBr$: C, 22.22; H, 3.44. Found: C, 21.86; H, 3.38.

***trans*-(2-Methoxycyclohexyl)mercuric chloride** was prepared in the standard way by methoxymercuration of cyclohexene followed by treatment with aqueous sodium chloride; mp 115–116 °C (lit. mp 115–116 °C).[35] The cis isomer was obtained by treatment of the trans isomer with hydrazine hydrate, followed by limited exposure to hydrochloric acid.[36] Alternatively, the trans isomer can be subjected to perchloric acid catalyzed equilibration (in methanol) followed by selective destruction (HCl, deoxymercuration) of any remaining trans compound. The cis

(30) H. G. Kuivila, *Acc. Chem. Res.*, **2**, 299 (1969); L. W. Menapace and H. G. Kuivila, *J. Am. Chem. Soc.*, **86**, 3047 (1964).
(31) D. J. Carlsson and K. U. Ingold, *J. Am. Chem. Soc.*, **90**, 7047 (1968).
(32) P. A. Bartlett and J. L. Adams, *J. Am. Chem. Soc.*, **102**, 337 (1980).
(33) See footnote 13 in ref 30.
(34) W. Kitching and H. Olszowy, unpublished results.
(35) O. W. Berg, W. P. Lay, A. Rodgman, and G. F. Wright, *Can. J. Chem.*, **36**, 358 (1958).
(36) A. G. Brook, R. Donovan, and G. F. Wright, *Can. J. Chem.*, **31**, 536 (1953).

isomer has a melting point of 112–113 °C (lit.[35] 114.1–114.5 °C), and the ^{13}C spectral characteristics[19] are summarized in the text.

***trans*- and *cis*-(2-Methoxycyclopentyl)mercuric chlorides** were obtained by procedures similar to those outlined above for the cyclohexyl compounds. the trans isomer [mp 81 °C (lit.[36] mp 83.3–83.7 °C)] showed ^1H resonances at δ 3.27 (OCH_3), 2.87 (H_1), and 4.19 (H_2). The cis isomer [mp 57 °C (lit.[36] 59–59.5 °C)] exhibited ^1H signals at δ 3.20 (OCH_3), 2.85 (H_1), and 3.92 (H_2). These data are for pyridine solutions relative to internal Me_4Si. The ^{13}C NMR parameters for these isomers are listed in the text. In connection with another study, we have subjected the *cis*-2-methoxycyclohexyl and -cyclopentyl mercurials to cleavage by bromine in pyridine (air atmosphere) to provide the corresponding *cis*-2-methoxybromocycloalkanes, which are different from those obtained by treatment of the cycloalkenes with *N*-bromosuccinimide in methanol.[34]

(Bicyclo[2.2.1]hept-2-yl)mercuric bromide was obtained as an exo–endo mixture from the reaction of the 2-norbornyl Grignard reagent with mercuric bromide. This mixture was converted directly to the acetate mixture (silver acetate in methanol) which was examined directly by ^{13}C NMR to establish the exo/endo ratio at 71:29. The ^{13}C NMR characteristics of the 2-norbornyl mercurials have been reported[19] previously.

(2-Acetoxy-*cis-exo*-bicyclo[2.2.1]hept-5-en-3-yl)mercuric chloride was prepared in the manner described originally by Winstein[37] and detailed by Whitesides[7] for the bromide. The mercuric chloride exhibits a ^{13}C NMR spectrum very similar to that reported and assigned for the corresponding mercuric acetate.[23] Signals are observed at 21.81 (CH_3), 45.57 (C_4), 48.18 and 48.37 (C_1, C_7), 58.17 (C_3), 77.37 (C_2), 133.39 (C_6), 141.60 (C_5), and 170.14 ppm (CO). The ^1H spectrum (also for $CDCl_3$ with residual $CHCl_3$ at δ 7.27) consisted of signals at δ 1.81 (H_7, H_7'), 2.16 ($OCOCH_3$), 2.73 ($J_{^{199}Hg-^1H}$ = 180 Hz, H_3), 3.13 (H_1), 3.31 (J = 90 Hz, H_4), 5.00 (J = 84 Hz, H_2), and 6.03 and 6.27 (H_5, H_6).

(5-Acetoxy-*exo,exo*-tricyclo[2.2.1$0^{2,6}$]hept-3-yl)mercuric chloride [(5-acetoxy-3-nortricyclyl)mercuric chloride] was obtained in the manner outlined by Winstein;[37] mp 149–150 °C (lit.[37] mp 147–148 °C). This compound was fully characterized by its ^{13}C spectrum which is listed in detail below because our previous report[19] on the ^{13}C–^{199}Hg couplings in this compound (CW spectra) was (in part) tentative and now requires some revision (J refers to ^{199}Hg–^{13}C coupling constants): ^{13}C NMR δ 12.52 (J = 33.7 Hz, C_1), 14.01 (J = 178 Hz, C_6), 18.96 (J = 51.3 Hz, C_2), 21.24 ($OCOCH_3$), 33.84 (J = 39.6 Hz, C_7), 38.00 (J = 50.6 C_4), 54.00 (J = 1652 Hz, C_3), 79.16 (J = 300 Hz, C_5), 171.00 ($OCOCH_3$). In the ^1H spectrum ($CDCl_3/Me_4Si$) signals were observed at δ 4.64 (narrow t, $J \approx 1$ Hz, H_5), 2.68 and 2.44 (H_3 and H_4, 2 br s), 2.07 ($OCOCH_3$), 1.80–2.04 (H_7, H_7'), and 1.3–1.7 (cyclopropyl protons).

Reduction Procedures. (a) Sodium Borodeuteride. A standard procedure[6] was employed in which the mercurial (~250–300 mg, ~0.5 mmol) was dissolved in tetrahydrofuran (~2 mL) in a 10-mL, round-bottomed flask under a N_2 atmosphere. To this magnetically stirred solution was added ~3 mL of 2 M aqueous NaOH. Sodium borodeuteride (Merck; 98% D, ~0.25 mmol) was added as a solid, and immediate formation of mercury occurred. After about 30 min, water (3 mL) and reagent grade chloroform (2.3 mL) were added, and the solution was decanted from the mercury and transferred to a small separatory funnel. The chloroform layer was dried ($MgSO_4$) and examined directly (in a 10-mm NMR tube) by ^{13}C and ^2H NMR spectroscopy. For reactions involving ester functions, the reactions were allowed to proceed for longer times (3–4 h) to ensure conversion to the alcohols.

(b) Sodium amalgam (1.5%, large excess) was added to the mercurial (~0.5 mmol) which was suspended or dissolved in about 3 mL of 2 M NaOD in D_2O, and the mixture was vigorously stirred. After 15 h, additional quantities of amalgam were added, and this procedure was sometimes repeated. Chloroform (3 mL) was added, the liquid layers were removed, and the chloroform layer was separated and dried ($MgSO_4$) in the normal fashion. Again, direct NMR examination (^2H and ^{13}C) was conducted.

(c) Tributyltin deuteride was prepared in the normal way from tributyltin chloride and $LiAlD_4$ in ether; bp 80 °C (1 mm) [lit.[7,38] bp 76–81 °C (0.7–0.9 mm)]. The reduction of *cis*-4-methylcyclohexyl bromide is illustrative. This bromide (177 mg) was refluxed with Bu_3SnD (1 equiv, 293 mg) in benzene (2 mL) to which AIBN (3 mg) had been added. After 2.5 h, the CHBr ^1H resonance (δ ~4.55) was absent. To this solution was added 1 drop of $CDCl_3$, and a ^2H NMR spectrum was taken directly to obtain the signals established for *cis*- and *trans*-4-(deuteriomethyl)cyclohexane.

NMR Spectra. ^1H spectra were recorded on JEOL JNM-MH-100 or JNM-PS-100 spectrometers for the solvents and references indicated in the text. Broad-band, ^1H-decoupled ^2H and ^{13}C NMR spectra were recorded on a JEOL JNM-FX100 FT spectrometer fitted with a 10-mm multinuclear probe, which was tuned to observe ^2H at 15.29 MHz and ^{13}C at 25.05 MHz, with the field locked to an external ^7Li signal. ^2H spectra were accumulated by using 8K data points and a frequency width of 1 KHz (70° pulse, repetition time 4.19 s) whereas ^{13}C spectra were collected in the 8K double-precision mode with a frequency width of 5 KHz.

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