

MERCURY IN ORGANIC CHEMISTRY

II*. A FAST REACTION OF SECONDARY ORGANOBORANES WITH MERCURY(II) ALKOXIDES

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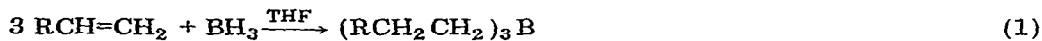
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Summary

Tri-sec-alkylboranes, readily available from internal olefins via hydroboration, undergo a rapid reaction at room temperature with mercuric methoxide in tetrahydrofuran to give the corresponding alkylmercuric salts. Although two of the three alkyl groups of the organoborane will react, excellent yields of only one group are feasible. Due to the rapid decomposition of mercuric methoxide in tetrahydrofuran, a considerable excess of the reagent must be used. A free radical chain reaction, initiated by the decomposition of the mercuric methoxide, is proposed. The reagent is much more thermally stable in methanol, but the mercuration of tri-sec-alkylboranes under these conditions often exhibits a considerable induction period prior to reaction. However, excellent yields in methanol can be obtained after a brief reflux period. The mercuration of tri-*exo*-norbornylborane gives an 85/15 mixture of *exo/endo*-norbornylmercuric chloride, lending support to a free radical chain mechanism.

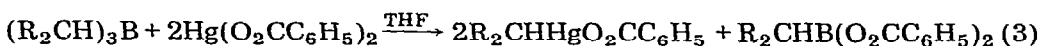
Introduction

Primary trialkylboranes, readily available from terminal olefins via hydroboration (eqn. 1), undergo a rapid quantitative reaction with mercuric acetate at room temperature to give the corresponding alkylmercuric acetate [1] (eqn. 2). This development makes a whole range of alkylmercuric salts and dialkylmercurials readily available for the first time.

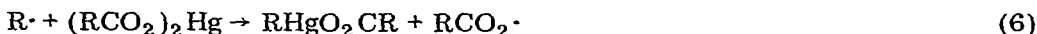


* For part I see ref. 19.

Although secondary trialkylboranes will react with a variety of mercury(II) salts to give organomercurials, these reactions are much more sluggish than those of primary trialkylboranes and require elevated reaction temperatures and extended reaction times [2] (eqn. 3). Due to the harsh reaction conditions considerable decomposition of the resulting product occurs, severely limiting the synthetic utility of the reaction. It thus proved impossible to obtain satisfactory yields of 2-norbornylmercuric chloride or sec-butylmercuric iodide from the corresponding trialkylboranes using this earlier procedure.



Ol'dekop and co-workers have recently developed a convenient synthesis of alkylmercuric carboxylates based on a free radical chain reaction of mercuric carboxylates [3] (eqns. 4 - 6). Since organoboranes have also recently been

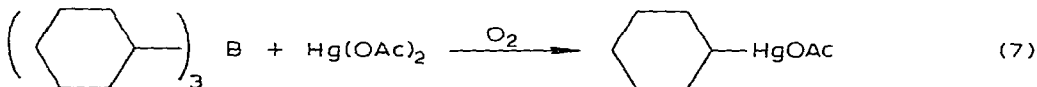


shown to be a convenient source of free radicals [4,5], the mercuration of trialkylboranes under free radical conditions would appear to offer an alternate route to organomercurials. We have investigated this possibility.

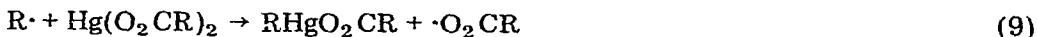
Results

Discovery

The addition of catalytic amounts of oxygen to organoboranes is known to generate free radicals [5]. The reaction of tricyclohexylborane and mercuric acetate in the presence of catalytic amounts of oxygen (1 ml/min of air) was investigated (eqn.7). Unfortunately, only a very low yield of cyclohexylmercurial could be obtained after 48 h at room temperature. No free radical chain reaction evidently occurs under these conditions. It would appear that the

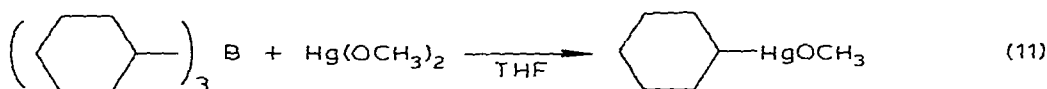


acetoxy radical is unable to displace an alkyl radical from the trialkylborane and thus bring about a chain reaction (eqns. 8 - 10). Alkoxy radicals, however, do undergo such a displacement reaction [4,5]. Thus we treated tricyclohexylborane with mercuric methoxide [6] (prepared from mercuric chloride and



solid sodium methoxide) in tetrahydrofuran (THF) in the presence of catalytic

amounts of oxygen (eqn. 11). A rather rapid reaction occurred under these conditions and approximately a 50% yield of cyclohexylmercuric chloride was isolated after work-up. A significant amount of metallic mercury was also present.



This facile mercuration reaction occurs with equal ease in the absence of oxygen. We then set out to investigate this intriguing new mercuration reaction of organoboranes and see if it might not be utilized for the conversion of secondary organoboranes to organomercurials.

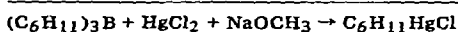
Stoichiometry

The stoichiometry of the reaction of tricyclohexylborane, mercuric chloride and sodium methoxide was examined to determine the nature of the reactants and the scope of this reaction. 100 ml of 0.5 M tricyclohexylborane (50 mmol) in THF was treated with varying amounts of solid sodium methoxide, followed either immediately by solid mercuric chloride or by the slow addition of varying amounts of 2M mercuric chloride in THF. The reactions were all allowed to proceed for 4 h at room temperature and the resulting organomercurial was converted to cyclohexylmercuric chloride upon work-up and separated by recrystallization from the elemental mercury which is always present. The results of these experiments are summarized in Table 1. It would appear from these results that only one of the three alkyl groups of tricyclohexylborane will react.

In order to determine the scope of this reaction, we have treated tricyclohexylborane, methyl dicyclohexylborinate and dimethyl cyclohexylboronate with 3, 2 and 1 equivalents of mercuric methoxide respectively. Bromination in the presence of acetic acid and GLPC analysis of the resulting cyclohexyl

TABLE 1

STOICHIOMETRY OF THE REACTION OF TRICYCLOHEXYLBORANE, MERCURIC CHLORIDE AND SODIUM METHOXIDE



Mercuric chloride (equiv.)	Sodium methoxide (equiv.)	Addition time (h) ^a	Cyclohexylmercuric chloride, isolated yield (%) ^b
1	0	0	0
1	1	0	1
1	2	0	51
1	2	2	65
1	3	2	61
1.5	3	2	75
2	4	0	97
2	4	2	93
3	6	0	94
6	12	0	88

^aTime of addition of mercuric chloride. ^bBased on reaction of one alkyl group.

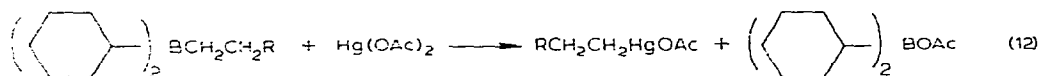
TABLE 2
STOICHIOMETRY OF THE MERCURATION OF ORGANOBORANES BY MERCURIC METHOXIDE

Organoborane	Mercuric methoxide (equiv.)	Cyclohexyl bromide (%) ^{a, b}
(C ₆ H ₁₁) ₃ B	3	100
(C ₆ H ₁₁) ₂ BOCH ₃	2	26
C ₆ H ₁₁ B(OCH ₃) ₂	1	trace

^aBased on reaction of one alkyl group. ^bGLPC analysis after bromination.

bromide indicated the extent of reaction. The results are presented in Table 2. Evidently, under these reaction conditions no more than one alkyl group of tricyclohexylborane will react. The modest yield of cyclohexyl bromide from the mercuration-bromination of methyl dicyclohexylborinate suggests, however, that the second alkyl group is not totally unreactive. This has since been confirmed in the mercuration of tri-*exo*-norbornylborane as well as the reaction of tricyclohexylborane in methanol.

A number of mercury(II) salts give a very fast reaction with primary trialkylboranes. Since secondary alkyl groups are much less reactive, one can use dicyclohexylborane for selective hydroboration-mercuration. Near quantitative yields of pure primary alkylmercuric salts can be obtained in this manner (eqn. 12). It was of interest to know if mercuric methoxide would also react rapidly with only the primary alkyl group in *n*-alkyldicyclohexylboranes or if the secondary alkyl groups would react competitively. The mercuration-bromination of *n*-hexyldicyclohexylborane using 1 equivalent of mercuric methoxide gave only *n*-hexyl bromide and no cyclohexyl bromide. Evidently mercuric methoxide also reacts preferentially with primary alkyl groups.



Mercuric methoxide mercuration of representative tri-sec-alkylboranes in THF

In order to determine the generality of this new mercuration procedure, several representative tri-sec-alkylboranes were treated with varying amounts of mercuric methoxide. The resulting organomercurials [7 - 9] are given in Table 3.

Stability of mercury(II) alkoxides

The mercuration of tri-sec-alkylboranes with mercuric methoxide in THF gives considerable amounts of metallic mercury. Consequently, a considerable excess of the reagent must be used in order to obtain good yields of organomercurial. The mercury apparently is produced by rapid thermal decomposition of the reagent in THF. In fact, a 98% yield of elemental mercury can be obtained by simply stirring the reagent overnight in THF. However, suspensions of mercuric methoxide in methanol are considerably more stable than in THF and can be kept for 24 - 48 h without significant decomposition.

TABLE 3
MERCURIC METHOXIDE MERCURATION TRI-SEC-ALKYLBORANES IN THF

Tri-sec-alkylborane	Mercuric methoxide (equiv.)	Addition time ^a (h)	Product	Isolated yield, ^b (%)	M.p. (lit. m.p.) (°C)	Ref.
Tricyclohexylborane	2	0	Cyclohexylmercuric chloride	97	160 (158)	[7]
Tricyclopentylborane	2	2	Cyclopentylmercuric chloride	65	112 (110.5)	[8]
	3	4		85		
Tri-sec-butylborane	3	4	Sec-butylmercuric iodide	76	54.7-55.0 (54)	[9]
Tri- <i>exo</i> -norbornylborane	2	2	2-Norbornylmercuric chloride ^d	80		
	3	2		78		
	3	4		111		

^aTime of addition of mercuric chloride. ^bBased on reaction of one alkyl group. ^cRecrystallized from 95% ethanol. ^dMixture of *exo* and *endo*.

We have also investigated the stability of mercuric *t*-butoxide, which was prepared by mixing mercuric chloride and potassium *t*-butoxide (eqn. 13).



This reagent appears reasonably stable at room temperature in THF, but gives less than a 10% yield of cyclohexylmercuric chloride upon treatment with tricyclohexylborane under these conditions. This reagent is also stable in *tert*-butanol but again gives very low yields of cyclohexylmercurial.

Mercuration of tri-sec-alkylboranes by mercuric methoxide in methanol

Because of the increased stability of mercuric methoxide in methanol, we have also attempted to use this reagent for the mercuration of tri-sec-alkylboranes, but the reaction is quite erratic. A mixture of tricyclohexylborane and 3 equivalents of mercuric methoxide in methanol has been allowed to sit as long as 24 h at room temperature without giving any apparent sign of reaction. Subsequent work-up gave only an 8% yield of cyclohexylmercuric chloride. On other occasions, this same reaction has gone smoothly and given up to 141% isolated yield of organomercurial after only 4 h reaction time (yield based on

TABLE 4
MERCURATION OF TRI-SEC-ALKYLBORANES BY MERCURIC METHOXIDE IN METHANOL

Tri-sec-alkylborane	Mercuric methoxide, (equiv.)	Product	Isolated yield ^a (%)
Tricyclohexylborane	1	Cyclohexylmercuric chloride	56
	2		108
	3		144
	4		159
Tricyclopentylborane	4	Cyclopentylmercuric chloride	88
Tri- <i>exo</i> -norbornylborane	4	2-Norbornylmercuric chloride	90

^aBased on reaction of one alkyl group.

one alkyl group). This reaction appears to have an induction period as do many free radical reactions.

This reaction would appear to have certain synthetic advantages if it could be more easily controlled. We have been able to control this reaction by refluxing for a brief time, which initiates the decomposition of the mercuric methoxide apparently necessary to bring about reaction and good yields of organomercurials can be obtained (Table 4). Although this procedure gives greatly improved yields for tricyclohexylborane, it does not appear to have any advantages for other tri-sec-alkylboranes.

Stereochemistry

In order to more fully understand the nature of the reaction, we have investigated the stereochemistry of the mercuration of tri-*exo*-norbornylborane. The 2-norbornylmercuric chloride derived from the mercuration of tri-*exo*-norbornylborane in THF was treated with bromine in pyridine at -40° , conditions which reportedly lead to strict retention of configuration in the resulting alkyl bromide [10]. NMR analysis of the reaction product indicated approximately $85 \pm 5\%$ *exo*-norbornyl bromide, which corresponds closely to that expected for the free radical mercuration of the organoborane.

Discussion

All previous reactions of secondary organoboranes with mercury(II) salts proceeded very sluggishly [2]. The reactions showed all the characteristics of an electrophilic cleavage reaction. However, the mercuration of tri-sec-alkylboranes with mercuric chloride in the presence of sodium methoxide leads to a remarkably facile conversion of these compounds into the corresponding sec-alkylmercuric salts. Present indications are that this is a free radical mercuration reaction.

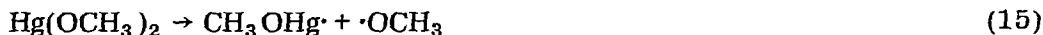
The stoichiometry of this reaction is most revealing. Mercuric chloride itself is inert towards both primary and secondary trialkylboranes [11]. Addition of 1 equivalent of sodium methoxide does not bring about reaction, suggesting that this is probably not the reaction of a boron "ate" complex with mercuric chloride (eqn. 14). Addition of a second equivalent of sodium methoxide gives a 51% isolated yield of cyclohexylmercuric chloride. This yield



can be improved slightly (65%) by adding the mercuric chloride slowly to the reaction mixture over 2 h. A third equivalent of sodium methoxide gives no improvement in yield (61%). Substitution of mercuric acetate for mercuric chloride gives similar yields, but more viscous reaction mixtures. All these results suggest that it is mercuric methoxide itself, $\text{Hg}(\text{OCH}_3)_2$, which is responsible for the reaction.

Mercuric methoxide undergoes a relatively rapid thermal decomposition at room temperature in THF. It is, however, fairly stable in methanol. This decomposition leads to elemental mercury. This reaction probably proceeds through homolytic scission of the weak mercury-oxygen bond to produce methoxy and methoxymercury radicals which subsequently decompose to mer-

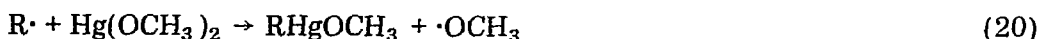
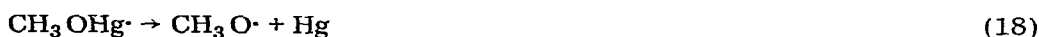
cury(0) and more methoxy radicals (eqns. 15 and 16). The thermal decomposition of alkylmercuric alkoxides is also reported to proceed by homolytic scission of the mercury—oxygen bond [12].



Several features of this new mercuration reaction of organoboranes indicate a free radical chain process. The unusually rapid rate of this reaction compared to previously attempted mercurations of tri-*sec*-alkylboranes [2] suggests that it is not an electrophilic cleavage reaction. The unusual induction periods observed when the reaction is carried out in methanol are also reminiscent of many free radical reactions. Finally, the stereochemistry of the mercuration of tri-*exo*-norbornylborane is that expected of a free radical reaction. The selectivity observed in the reaction of *n*-hexyldicyclohexylborane, however, suggests that mercuric methoxide undergoes a more rapid electrophilic cleavage reaction with primary alkylboranes and the free radical reaction is too slow to compete.

The stereochemistry of the mercuration provides the strongest evidence for a free radical reaction. Whereas most of the earlier discovered reactions of organoboranes proceed with strict retention of configuration [13], the more recently discovered free radical reactions generally proceed with some loss of stereospecificity. For example, the free radical autoxidation of tri-*exo*-norbornylborane by oxygen gives a 76/24 mixture of *exo/endo*-norbornyl-oxygen linkages [14]. Similar mixtures of *exo*- and *endo*-norbornyl compounds have been observed in other reactions of the norbornyl radical [15, 16]. The 85/15 mixture found in the mercuric methoxide mercuration of tri-*exo*-norbornylborane lends support to a free radical chain reaction.

We propose the following free radical chain mechanism for this new mercuration reaction (eqns. 17 - 20). The failure of the reaction to proceed with-



out initial decomposition of the mercuric methoxide and the formation of elemental mercury support this mechanism. Evidently the chain length in this reaction is not very long, necessitating the decomposition of considerable amounts of mercuric methoxide. Furthermore, although the second alkyl group of the trialkylborane will react, it must react significantly slower than the first. So far we have been unable to find a suitable free radical inhibitor to test on this reaction. Attempts to initiate the reaction by addition of oxygen or photolysis have also proved inconclusive.

Previously, we had been able to obtain good yields of cyclohexyl- and cyclopentylmercuric chlorides by refluxing the corresponding trialkylboranes with mercuric benzoate in THF [2]. This procedure was most unsatisfactory,

however, for the conversion of more hindered tri-sec-alkylboranes to organomercurials. In fact, we had a most difficult time finding sufficient 2-norbornyl bromide from the mercuration-bromination of tri-*exo*-norbornylborane for GLPC determination of the stereochemistry of this reaction. The new mercuric methoxide mercuration procedures offer obvious synthetic advantages over the previous method and appear to be much more widely applicable, as evidenced by the high yields of 2-norbornylmercuric chloride. Although the second alkyl group of tri-sec-alkylboranes will react, due to the rapid rate of decomposition of mercuric methoxide, it does not appear feasible at present to convert completely this second alkyl group to organomercurial.

Experimental

Materials

Mercuric chloride (Mallinckrodt), sodium methoxide (Harshaw), potassium tert-butoxide (MSA Research Corp.), methanol (Mallinckrodt) and tert-butyl alcohol (J.T. Baker) were used directly as obtained commercially. All other materials have been described previously [2].

Mercuric methoxide mercuration of tri-sec-alkylboranes

All preparative mercuration reactions were carried out as follows. 100 ml of 0.5 M tri-sec-alkylborane (50 mmol) in THF was prepared in the usual manner [17]. The appropriate amount of solid sodium methoxide was added with cooling and rapid stirring to the solution while backflushing with nitrogen. This was followed either immediately by solid mercuric chloride or by the slow addition of the appropriate amount of 2 M mercuric chloride in THF over the appropriate time span. The reaction mixture was then stirred 4 h at room temperature and poured into a large volume of ice water containing sufficient HCl to make the suspension slightly acidic. The gray solid was then collected by vacuum filtration, washed with large amounts of water and two 100-ml portions of cold pentane (0°), dissolved in hot 95% ethanol, filtered free of metallic mercury and allowed to crystallize. Filtration and further concentration of the mother liquor generally gave two good crops of alkylmercuric chloride.

Several modifications of this procedure were used to obtain sec-butylmercuric iodide. In order to obtain the higher melting alkylmercuric iodide instead of the chloride, 200 mmol of sodium iodide was added to the initial aqueous suspension, and the mixture was acidified with 10% sulfuric acid. The THF was then removed on a vacuum pump in order to obtain a solid product. Rapid filtration of the cold solution and a quick wash with two 100-ml portions of -50° pentane gave the solid product. Recrystallization from ethanol completed this procedure.

The reactions in methanol were accomplished as follows. The THF was removed from the organoborane on a vacuum pump, being careful to replace the nitrogen atmosphere upon release of the vacuum. Methanol (200 ml) was added to give a suspension of the insoluble organoborane in methanol. Solid sodium methoxide was added to this suspension while cooling in an ice bath. Solid mercuric chloride was added with vigorous stirring and the reaction mix-

ture was brought to reflux for 30 min. After cooling, the gray solid obtained was poured into ice water and worked-up as described above.

Mercuration-bromination of organoboranes

The mercuration-bromination of tricyclohexylborane, methyl dicyclohexylborinate, dimethyl cyclohexylboronate and n-hexyldicyclohexylborane were carried out as follows. Ten ml of 0.5 *M* organoborane (5 mmol) in THF was prepared. The appropriate amounts of solid sodium methoxide and mercuric chloride were added and stirred 4 h at room temperature. The n-hexyldicyclohexylborane was seen to react immediately. The solution were then cooled to 0° and 10 ml of acetic acid was added to avoid possible base induced bromination of the organoborane [18]. Sufficient bromine was then added to maintain an orange color for several minutes. Water (5 ml) and sufficient sodium thiosulfate were added to decolorize the bromine. The acid was neutralized with sodium hydroxide and enough sodium chloride added to separate the layers. n-Decane was added as an internal standard and GLPC analysis was carried out on a 10% SE-30 column.

Stability of mercuric alkoxides

The various mercuric alkoxides used in this study were prepared by adding 10 mmol of the appropriate mercuric salt to 10 ml of the solvent used. The alkali metal alkoxide was then added and any variations in color (namely yellow to black) were noted.

Stereochemistry

The stereochemistry of the 2-norbornylmercuric chloride was determined by bromination. Recrystallized organomercurial (10 mmol) was dissolved in 30 ml of pyridine at -40°. Ten ml of 1 *M* bromide in pyridine was added dropwise at -40° and the solution maintained at that temperature 30 min and then allowed to warm to room temperature. Ten ml of CCl₄ and 25 ml of 10% HCl were added and the CCl₄ layer separated. This layer was washed with water and filtered free of solid mercuric bromide. This solution was subsequently washed with water, 10% HCl, 5% sodium bicarbonate and finally water, dried over magnesium sulfate and concentrated. NMR could readily distinguish between the *exo* and *endo* hydrogens next to bromine and indicated a mixture of 85 ± 5% *exo*- and 15 ± 5% *endo*-norbornylbromide. The melting point of the twice recrystallized (95% ethanol) 2-norbornylmercuric chloride was not distinct, but appeared to be approximately 170 - 180°.

Analysis: (Found: C, 25.22; H, 3.31; Hg 60.80. C₇H₁₁ClHg calcd.: C, 25.39; H, 3.35; Hg, 60.56%.)

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