The Stereochemistry of Organoborane Formation from Grignard Reagents

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Summary The replacement of magnesium with boron in steroidal Grignard reagents proceeds with retention of configuration.

THE reaction of Grignard reagents with diborane in tetrahydrofuran (THF) gives organoboranes in good yields, and these can be converted to the corresponding hydroxy-compounds by treatment with alkaline hydrogen peroxide.[1] The reaction is applicable to aromatic, aliphatic and alicyclic halides. To examine the stereochemical course of the reaction, a pair of epimeric steroidal halides were chosen, and converted to alcohols by the reported procedure.[1]

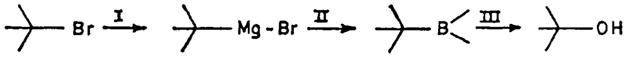
Following the method of Roberts, Shoppee and Stephenson[2] 3α-bromo-5α-cholestane (1) and 3β-bromo-5α-cholestane (2) were prepared and reacted with magnesium in the presence of excess BH_3 in refluxing THF until all the halide had been consumed. After decomposition of the excess diborane, the organoboranes thus formed were oxidised to the corresponding alcohols by standard methods.[3] The alcohols formed were separated by chromatography on alumina following the methods of Shoppee[4] (see Table for yields).

TABLE

	Percentage yields	
Products [a]	from 3α-bromo-5α-cholestane (1)	from 3β-bromo-5α-cholestane (2)
2α-hydroxy-5α-cholestane (3)	5	6
3α-hydroxy-5α-cholestane (4)	11	7
3β-hydroxy-5α-cholestane (5)	48	51

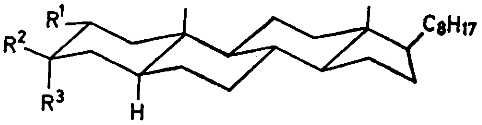
[a] Substantial quantities of bicholestanyl accompanied the products from both reactions.[2]

There are two main features of the result that require explanation, the fact that irrespective of the halide used the main product in both reactions is the same, the equatorial alcohol 3β-hydroxy-5α-cholestane (5), and the formation of the minor products, especially the 2α-hydroxy-5α-cholestane (3). The alcohols are formed through a series of reactions in which the carbon at the reaction centre is attached successively to bromine, magnesium, boron, and oxygen. The prime interest in this study is reaction II since it is known that the oxidation of organoboranes with alkaline hydrogen peroxide (reaction III) proceeds with retention of configuration,[3] and there is evidence[5] that in optically active systems the formation of the Grignard reagent (reaction I) is accompanied by loss of configurational identity although, once formed, the Grignard reagents are configurationally quite stable.[6,7]



In the present case it is known[2] that carbonation of the Grignard reagents from both (1) and (2) gives the same product, 3β-carboxy-5α-cholestane (6), showing that they were the same equatorial magnesium bromide (7). Since the organoborane (8) was oxidised to the equatorial alcohol (5) (reaction III) with retention of configuration, the replacement of magnesium with boron (reaction II) must also have gone with retention of configuration. This follows the normal course of the stereochemistry of electrophilic substitution of an aliphatic Grignard reagent,[7] which is the most likely mechanism for this reaction.

The most likely explanation for the origin of the minor products in the reaction of 3β-bromo-5α-cholestane (2) is the isomerisation of the organoborane (8) after the displacement of magnesium. Since the isomerisation of organoboranes is known to proceed by an elimination–addition mechanism[8] and the most stable olefin in ring A of the 5α-cholestane series is the 5α-cholest-2-ene,[9] the products of the hydroboration of this compound can be taken as a guide to the by-products expected from isomerisation of the organoborane. Hydroboration of 5α-cholest-2-ene with diborane[10] gave comparable amounts of 2α-hydroxy-5α-cholestane (3) and 3α-hydroxy-5α-cholestane (4) with a small preponderance of the latter, in agreement with the 3β-bromide (2) reaction. In the 3α-bromide (1) reaction the slightly larger 3α-alcohol (4) to 2α-alcohol (3) ratio may be due to the fact, that the diborane is present during the Grignard reagent formation, and the replacement of the magnesium by boron may compete to a small extent with the epimerisation to the preferred isomer in the tight radical pair, postulated[5] as an intermediate in the Grignard reagent formation. This could raise the proportion of 3α-alcohol above that expected from simple isomerisation of the organoborane (8).



(1) $R^1 = R^2 = H, R^3 = Br$
(2) $R^1 = R^3 = H, R^2 = Br$
(3) $R^1 = OH, R^2 = R^3 = H$
(4) $R^1 = R^2 = H, R^3 = OH$
(5) $R^1 = R^3 = H, R^2 = OH$
(6) $R^1 = R^3 = H, R^2 = CO_2H$
(7) $R^1 = R^3 = H, R^2 = MgBr$
(8) $R^1 = R^3 = H, R^2 = B <$

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