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Unusual Regiochemistry in the Hydroboration of 3,3-Dibenzylcycloalkenes

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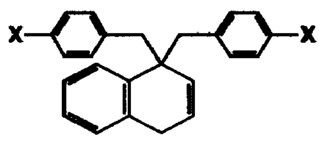
Abstract: Reaction of 3,3-dibenzylcycloalkenes with diborane results in predominant attack by boron at the more crowded ends of the double bonds.

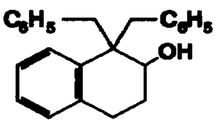
The hydroboration of alkenes is one of the most frequently used processes in synthetic organic chemistry – in part because the regiochemistry of the reaction is considered to be reliable and predictable. Boron atoms normally add to the less crowded ends of double bonds, and hydrogens to the more crowded ends. Steric effects are greatest for bulky hydroborating agents such as Sia_2BH and 9-BBN, but are also significant for reactions with diborane, which have invariably formed the same principal products, after oxidation, as have hydroborations by bulkier agents.[1] Electronic effects, which direct attack of boron to the more "nucleophilic" ends of double bonds,[2] may partially offset steric effects of substituents, but it appears that only in the hydroboration of 3,3,3-trifluoropropene[3] has boron added predominantly to the (slightly) more crowded end of a double bond.

We have now found that hydroborations of 3,3-dibenzylcycloalkenes by diborane are highly regioselective, but proceed with regiochemistries opposite from those that would be predicted from either steric or electronic effects of substituents.

Addition of a solution of 1,1-dibenzyl-1,4-dihydronaphthalene (**1a**) to a solution containing 5 moles of diborane in THF at -5°C, followed by oxidation with alkaline hydrogen peroxide, consistently yielded mixtures containing alcohols **2** and **3** in a 91:9 ratio. In contrast, hydroboration of **1a** by Sia_2BH^4 or 9-BBN yields



1 (a, X = H)



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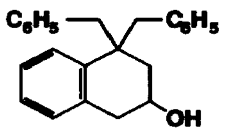

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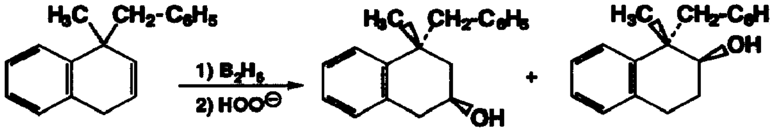
exclusively alcohol **3**, the product of boron attack at the less crowded site. Similarly, reaction of Sia_2BH with the other benzylcycloalkenes shown in the Table invariably yielded only the C-3 alcohols, although less than 0.5% of the C-2 alcohol would have been detected in each case.

If, instead of **1a** being added to a large excess of borane, borane solutions were added slowly to solutions of **1a**, the product mixtures contained only 75-80% of **2**, while if the alkene was added to solutions containing ca. 0.5-1.5 moles of diborane (1-3 moles of borane) per mole of **1a** the percentage of **2** increased from ca. 80 to 90% as the ratio of diborane to alkene increased. The higher percentages of **3** formed using lower ratios of diborane to **1a** are presumably due to the initially formed 1:1 adduct of **1a** and borane acting as a hydroborating agent in further reaction with **1a**.

In order to identify the factors controlling regioselectivity in the hydroboration of **1a**, a series of 3,3-disubstituted cycloalkenes were reacted with diborane under conditions similar to those used for hydroboration of **1a**.

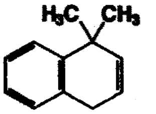
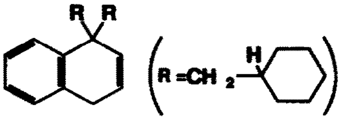
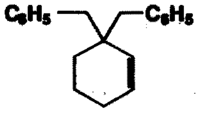
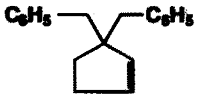
As is shown in the Table, hydroborations of 3,3-dibenzylcyclohexene and 3,3-dibenzylcyclopentene by diborane yield principally the C-2 alcohols. Therefore, it appears that the structures of the cycloalkene rings play little role in determining the regiochemistries of the hydroboration reactions. However, the unusual regioselectivity observed in the reaction of diborane with **1a** is clearly dependent on the presence of benzyl groups, rather than alkyl groups, at an allylic position, since reaction of 1,1-dimethyl or 1,1-di(cyclohexylmethyl)-1,4-dihydronaphthalene with diborane yielded product mixtures containing more of the C-3 than of the C-2 alcohols. Furthermore, two benzyl groups are necessary, since the C-3 alcohol is also the predominant regioisomer formed from cycloalkene **4**. The same C-3 alcohol was obtained from reaction of **4**



4

with Sia_2BH, and is therefore assigned the geometry with the hydroxy group *anti* to the benzyl substituent. The C-2 alcohol from hydroboration of **4** was stereoisomeric with the alcohol obtained from $LiAlH_4$ reduction of the C-2 ketone, suggesting that in the hydroboration product the hydroxy group was *syn* to the methyl. This assignment of geometry was confirmed by comparisons of Nuclear Overhauser effects in the spectra of the two C-2 alcohols. Thus, borane appears to attack **4** exclusively from the direction *anti* to the benzyl group, as would be expected from the fact that 1,1-dimethyl-1,4-dihydronaphthalene undergoes hydroboration appreciably faster than does **1a**.

Table. Reactions of Cycloalkenes with Diborane[a]

	Cycloalkene	% 2-Hydroxy Isomer[b]
1)	**1**, X = H	90, 91
2)	**1**, X = CH_3	88, 88
3)	**1**, X = Cl	96, 96
4)	**4**	42,44
5)		47, 43
6)		38, 41
7)		75, 73
8)		66, 71

[a] Additions of a 0.2 M solution of the alkene in THF to an equivalent volume of an 0.5 M solution of diborane at -5°C. Reaction time = 2 hrs.

[b] Determined from areas of ^1H NMR signals of carbinol hydrogens.

The exclusive formation of C-3 alcohols from reaction of 3,3-dibenzylcycloalkenes with Sia_2BH demonstrates that, as expected, C-2 is significantly more crowded than C-3. Since benzyl groups (s_p = -0.09)[5] are apparently somewhat more electron-donating than hydrogens, the electronic effects of the two benzyl groups should actually enhance attack by boron at C-3. Furthermore, if the benzyl groups did exhibit some unexpected electronic influences, such as powerful electron-withdrawing hyperconjugation effects, hydroboration of 4 should show regioselectivity intermediate between those of **1a** and its dimethyl analog, rather than regioselectivity almost identical with that of the dimethyl compound.

We have previously shown that 3,3-dibenzylcycloalkenes react with bromine to form bicyclo[3.3.1]nonane or bicyclo[3.2.1]octane derivatives, as a result of interaction of benzyl groups with the initially formed bromonium ions.[4,6] We initially suspected that a similar interaction in the course of hydroboration might account for formation of **2** by hydroboration of **1a**. Alternatively, it seemed possible that the vacant orbital of boron might interact with p-electrons of a benzyl group. However, both hypotheses predict that electron-donating substituents on benzyl groups would tend to increase the percentages of the 2-hydroxy isomers, whereas the percentages of the 2-hydroxy isomers are actually lowered by the presence of electron-donating substituents on the benzyl group.

An adequate explanation for the regiochemistry of hydroboration of 3,3-dibenzylcycloalkenes does not seem to be immediately obvious.

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