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THE DIMESITYLBORON GROUP IN ORGANIC SYNTHESIS 2. THE C-ALKYLATION OF ALKYLDIMESITYLBORANES

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It is demonstrated that anions α to the dimesitylboron group are alkylated at carbon in excellent yields. The alkylations may be repeated, so allowing for one-pot, one, two or three insertion reactions.

We have previously shown that stabilised carbanions may be readily formed by the action of either lithium dicyclohexylamide or mesityl lithium on alkyldimesitylboranes[1] and that such species are readily methylated.[2] We now report on extensions of these observations, and the release of the organic moieties from the borane products.

We chose the anion 1, derived from methyldimesitylborane, 2, as our first substrate. With whichever base the anion was produced, alkylations proceeded satisfactorily (Table 1) (eq. 1) but the rates were enhanced in the presence of dicyclohexylamine.

$$\underset{2}{\mathrm{Mes_2BCH_3}} \longrightarrow \underset{1}{\mathrm{Mes_2B\bar{C}H_2}} \xrightarrow{\mathrm{RX}} \underset{3}{\mathrm{Mes_2BCH_2R}} \longrightarrow \underset{4}{\mathrm{RCH_2OH}} \qquad (1)$$

Benzyl iodide is clearly a superior alkylating agent to either the bromide or chloride (Table 1, exp. 5-7) but primary alkyl bromides may be used as well as the iodides (Table 1, exp. 1-4,[12]). Primary alkyl iodides react in 15m. no matter what the base used, but the rate of reaction of primary alkyl bromides is considerably enhanced in the presence of dicyclohexylamine. The products from alkyation with primary alkyl halides (3, R = prim. alkyl) are readily oxidised to the corresponding alcohols, 4, which are separated from the accompanying 2,4,6-trimethylphenol by column chromatography. Attempts to remove the weakly acidic phenol by means of base are only partly successful and are not recommended. The process represents an efficient homologation sequence.

Table 1

Alkylation/oxidation of $Mes_2BC\bar{H}_2$

Experiment	Electrophile	Product[a]	Yield %[b]	
			g.c.	isolated
1	$C_6H_{13}Br$	$C_7H_{15}OH$	96	83
2	$C_7H_{15}I$	$C_8H_{17}OH$	94	80
3	$C_8H_{17}I$	$C_9H_{17}OH$	92	83
4	$C_8H_{17}Br$	$C_9H_{17}OH$	90	-
5	$PhCH_2I$	$PhCH_2CH_2OH$	85	74
6	$PhCH_2Br$	$PhCH_2CH_2OH$	62	-
7	$PhCH_2Cl$	$PhCH_2CH_2OH$	45	-
8	$CH_3CHBrC_5H_{11}$	$CH_3CH(C_5H_{11})CH_2OH$	26	-
9	$CH_3CHOTs.C_2H_5$		0	-
10	$CH_3CHOMesylC_2H_5$		0	-
11	Cyclohexyl bromide	Mainly cyclohexene	0	-
12	MeI	$MesBCH_2CH_3$[c]	-	92[c]

[a] All products compared with authentic samples. [b] Yields are of alcohol, 4, and based on starting borane. [c] Oxidation not carried out, yield based on isolated borane.

As expected reactions with secondary halides and sulphonates led mainly to elimination rather than substitution (Table 1, exp. 8-11).

We then attempted to generalise the reaction by examination of the alkylation of anions 5, $Mes_2B\bar{C}HMe$ and 6, $Mes_2B\bar{C}HEt$ derived from ethyl- and propyldimesitylborane respectively. It was found advantageous to use mesityl lithium to produce the anion and to carry out the alkylations at 0°C (Table 2).

Table 2

Alkylation/oxidation of anions 5 and 6

Experiment	Anion	RX	Product[a]	% Yield[b]
13	5	BuI	BuCHOHMe	76
14	5	BuI	BuCHOHMe	96[c]
15	5	HexI	HexCHOHMe	84 (68)
16	5	HeptI	HeptCHOHMe	85 (70)
17	5	OctI	OctCHOHMe	82
18	5	$PhCH_2I$	$PhCH_2CHOH$ Me	78 (60)
19	6	PrI	PrCHOHPr	80[d]
20	6	PentI	PentCHOHPr	66[e]

[a] Based on comparison with authentic samples. [b] All yields are by g.c. except the one given in parenthesis, given as an example of isolation yield. [c] Two more equivalents of 5 used, yield based on butyl iodide. [d] Refluxed for 12h. at oxidation stage. [e] Heated for 72h. at 68°C for oxidation.

For anion **5** both the alkylation and oxidations proceed in a satisfactory fashion to give secondary alcohols in good yields. (Table 2, exp. 13-18). However increasing difficulty was experienced in the oxidations as the bulk of the groups around boron was increased. (Table 2 exp. 19-20).

We decided to check whether it was possible to proceed directly from Mes_2BCH_3 to $Mes_2BCHR^1R^2$, **7**, without isolation of the intermediate borane, **3**. For this purpose we alkylated **2** first with heptyl iodide and then with methyl iodide to give, after oxidation a 77% g.c. yield of HexCHOHMe. This compares well with the composite two stage process and shows that (1) can be used as a one carbon unit for double insertion reactions.

We then, in a hopeful frame of mind, attempted to prepare the very hindered boranes $Mes_2BCR^1R^2R^3$, **8** directly from $Mes_2BCH_2CH_3$. The first alkylation was carried out with butyl iodide and the second with ethyl iodide. To our surprise the reactions proceeded well and we isolated **8** (R^1 = Me, R^2 = Et, R^3 = Bu) in 66% overall yield! Not surprisingly the oxidation of this borane was difficult and the tertiary alcohol (Me.Et.Bu. C.OH) was only produced in 19% overall yield (based on $Mes_2BCH_2CH_3$) after oxidation for 3h. at 65°C. Indeed the efficient release of organic groups from very hindered organoboranes represents a challenge that we are attempting to meet. In view of the efficient production of $Mes_2BCH_2CH_3$ from Mes_2BCH_3 **2** (Table 1, exp. 12) it is clear that all <u>three</u> protons of **2** can be replaced by alkyl groups, if required, this representing a new threefold insertion process.

The alkylation of carbanions α- to the dimesitylboron group is an efficient and general process leading to a wide range of alkyldimesitylboranes and hence to the corresponding homologated alcohols.

<u>General procedure for the one carbon homologation of primary alkyl halides</u>.

n-Butyl lithium (5mmole, *ca* 1.6M in hexane) is added to a solution of dry dicyclohexylamine (5 mmole) in anhydrous THF (25ml.) in a nitrogen flushed, serum capped, round bottomed flask at 0°C. The mixture is stirred for 15m. then transferred using a double ended needle to methyldimesitylborane (5 mmole) at 25°C in a nitrogen flushed round bottomed flask. Reaction is exothermic to give generally pale orange to red solutions. After 15m. the dry alkyl halide (5 mmole) is added using a syringe. Reactions with primary alkyl iodides, tosylates and mesylates and benzyl bromide and iodide are exothermic and complete in 15m. at 25°C. Reactions with primary alkyl bromides are slightly exothermic and are best left for 12h. at 25°C.

Methanol (5ml.) is then added followed by sodium hydroxide (2.5ml. 5N) and then 50% hydrogen peroxide (5ml. care!) and the mixture either left at room temperature overnight or heated under reflux for 1h. The reaction mixture is salted out with saturated aqueous potassium carbonate, the organic layer separated and the aqueous layer extracted with ether (2 x 30ml.). The combined organic extracts are washed with 10% aqueous citric acid (30ml.) (use of hydrochloric acid leads to emulsions), followed by water (20 ml.), dried ($MgSO_4$) filtered and concentrated (max. temperature of evaporation is 40°C).

Products are purified by gradient elution (CH_2Cl_2, $CHCl_3$, Et_2O) on columns of 100-120 mesh silica gel (20g/g. crude product). 2,4,6-Trimethylphenol is eluted with dichloromethane and dichloromethane/chloroform mixtures and primary alcohols with 90% chloroform/10% ether. The primary alcohols are finally distilled using a kugelrohr apparatus and compared directly with authentic samples.

General procedure for the alkylation oxidation of alkyldimesitylboranes Mes_2BR, R = Et,Pr, Oct.

Dry mesityl bromide (5.5 mmole) is made up to a 0.5M solution in anhydrous THF under nitrogen, cooled to -78°C and two equivalents of standardised tertiary butyl lithium (*ca* 1.5M) in hexane are added. The solution becomes pale yellow and a white precipitate separates. After stirring for 15m. at -78°C, the mixture is placed in a bath at 25°C for 15m. then transferred *via* a double ended needle using nitrogen pressure to the alkyldimesitylborane (5 mmole) at 25°C. When R of Mes_2BR are Et, Pr then anion formation takes 1h. and when R = Oct, 2h. are required. The reaction mixture is cooled to 0°C and the anhydrous alkyl iodide (5.5mmole) added using a syringe. In all cases the pink reaction mixture is left for 30 m. and then oxidised with alkaline hydrogen peroxide as before. When R = Et, then 1h. under reflux or 12h. at 25°C suffices for complete oxidation but for higher alkyl groups longer times under reflux are required (see Table 2). Isolation of alcohol products is as outlined in the previous procedure.

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