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The Reaction of Copper(I) Methyltrialkylborates with 1-(1-Pyrrolidinyl)-6-chloro-1-cyclohexene

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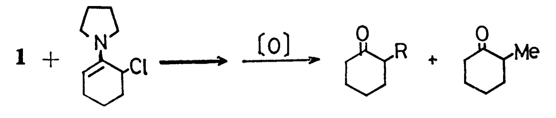
Synopsis. The reaction between copper(I) methyltrialkylborates readily obtainable from organoboranes and 1-(-1-pyrrolidinyl)-6-chloro-1-cyclohexene was found to give corresponding alkylation products which are readily hydrolyzed to alkylated cyclohexanones.

Recently, we have reported that lithium methyltrialkylborates readily undergo cation exchange reaction by copper(I) halides to give copper(I) methyltrialkylborates, which in turn successfully add to acrylonitrile, ethyl acrylate, 1-acyl-2-vinylcyclopropane[1] and ethyl propiolate.[2] These borate complexes also react with benzylic bromides,[3] aroyl chlorides,[4] allylic chlorides, propargylic bromides,[5] and ethyl β-bromoacrylates.[6] In an attempt to develop the reaction of such borate complexes, we examined the possibility of a coupling reaction with 1-(1-pyrrolidinyl)-6-chloro-1-cyclohexene.

To a solution of copper(I) methyltripropylborate obtained from lithium methyltripropylborate and copper(I) iodide (Eq. 1), 1-(1-pyrrolidinyl)-6-chloro-1-cyclohexene was addde at 0 °C and stirred at room temperature. After the reaction was complete, the residual organoborane was oxidized with alkaline hydrogen peroxide under the usual conditions. VPC analysis revealed the formation of 2-propylcyclohexanone (3) and 2-methylcyclohexanone (4) in 31 and 11% yields, respectivley (Eq. 2). Although the formation of an undesirable by-product, 2-methylcyclohexanone (4) formed by attack of methyl group in the borate was observed, it was found that such yields are markedly dependent upon copper(I) halides and solvents employed, as shown in Table 1. The reaction using copper(I) cyanide and 1,2-dimethoxyethane (DME) as a solvent was effective for the circumvention of formation of the by-product. This reaction is applicable to other representative organoboranes. In each case, the desired alkylated cyclohexanones were obtained in good yields (Table 1).

$$R_3B + MeLi \rightarrow (R_3BMe)Li \xrightarrow{CuX} \underset{\mathbf{1}}{(R_3BMe)Cu} \qquad (1)$$



(2)

2 **3** **4**

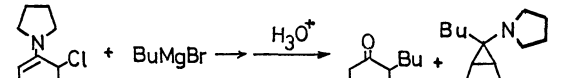
It is well known that enamines formed from cyclanones react with reactive alkyl halides at the β-carbon atom to afford an immonium salt, which is readily hydrolyzed to the monoalkylated ketone. Allylic, propargylic and benzylic halides as well as α-halo ketones, α-halo esters, and α-halo nitriles give good results, but yields are only fair with saturated alkyl halides[7]. On the other hand, the present reaction overcomes such a difficulty, which makes possible to introduce saturated alkyl groups at the α-carbon atom of cyclohexanones.

Table 1. Reaction of copper(I) methyltrialkylborates with 1-(1-pyrolidinyl)-6-chloro-1-cyclohexene

R_3B	CuX	Solvent	R′X	Yield (%)[a] of **3** or **6**
Propyl	CuI	THF		31 (11)
	CuBr	THF		32 (10)
	CuCl	THF		29 (7)
	CuCN	THF		53 (6)
	CuCN	DME		60 (13)
Butyl	CuCN	DME		81 (n. a.)[b]
Isobutyl	CuCN	DME		83 (n. a.)[b]
Hexyl	CuCN	DME		70 (n. a.)[b]
Propyl	CuCN	DME	Allyl bromide	59 (n. a.)[b]
	CuCN	DME	Benzyl bromide	59 (n. a.)[b]
	CuCN	DME	Dimethyl sulfate	37 (n. a.)[b]

a) Based on the chloroenamine (**2**) employed and the yields of methylcyclohexanone are shown in parentheses.
b) Not analyzed.

Recently, Cantacuzene *et al.*,[8] reported the alkylation of 1-(1-pyrrolidinyl)-6-chloro-1-cyclohexene (**2**) with Grignard reagents, For example, 2-butylcyclohexanone and 6-butyl-6-(1-pyrrolidinyl)bicylo[3.1.0]hexane were obtained in the ratio of 30:70: the ratio varied with different Grignard reagents (Eq. 3). However, any formation of such a cyclopropane derivative was not observed in the present reaction of copper(I) borates.



(3)

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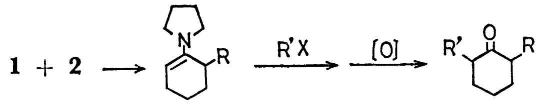
The present reaction, although the mechanism is still unknown, appears to proceed through the enamine (**5**) as an intermediate, because treatment of the reaction mixture, without alkaline hydrogen peroxide oxidation, with relatively active alkyl halides such as allylic and benzylic bromides or dimethyl sulfate pro-



(4)

5 **6**

duced the corresponding disubstituted cyclohexanone (**6**) (Eq. 4).

Combination of these two reactions, namely, the reaction of borate complexes with chloroenamine (**2**) and subsequent alkylation by alkyl halides, provides a convenient synthetic procedure for disubstituted cyclohexanones from organoboranes.

Experimental

Materials. Commercial copper(I) halides and alkyl halides were used. The solvents were purified by distillation before use. 1-(1-Pyrrolidinyl)-6-chloro-1-cyclohexene was prepared from 2-chlorocyclohexanone and pyrrolidine by the Blazejenski's method.[8] Trialkylbroanes were prepared from diborane and olefins *via* hydrobroation.[9]

The IR and NMR spectra were taken on a Hitachi-Perkin Elmer Model 125 spectrophotometer and a Hitachi R-22 spectrometer at 90 MHz using tetramethylsilane as an internal standard.

General Procedure. The following procedures for the preparation of 2-propylcyclohexanone and 2-allyl-6-propylcyclohexanone are representative.

A dry 100 ml-flask equipped with a septum inlet and a magnetic stirring bar was flushed with dry nitrogen. The flask was charged under dry nitrogen atmosphere with 0.89 g (9 mmol) of copper(I) cyanide and 12 ml of dry 1,2-dimethoxyethane. To this mixture was added lithium methyltripropylborate[1] (9 mmol in THF) at 0 °C and stirred for 5 min. Then 0.84 ml (6 mmol) of 1-(1-pyrrolidinyl)-6-chloro-1-cyclohexene was gradually added and the mixture was stirrred for 2 h at room temperature. After the reaction was complete, the residual organoborane was oxidized with 3 ml of 3 M aqueous NaOH and 3 ml of 30%-H_2O_2 at room temperature for 2 h. The products were extracted with ether. The combined extracts were washed with saturated NaCl solution and dried over anhydrous sodium sulfate. The ether solution thus obtained was analyzed by VPC, revealing the formation of 2-propylcyclohexanone (5.4 mmol, 60%).

The procedure for the preparation of 2-allyl-6-propylcyclohexanonone is as follows: To the reaction mixture obtained by the same procedure described above was added allyl bromide (3.06 g, 18 mmol), followed by refluxing for 3 h and allowed to stand over night at room temperature. Analysis by VPC after alkaline hydrogen peroxide oxidation indicated the presence of 3.54 mmol (59% yield) of 2-allyl-6-propylcyclohexanone. Although 2-allyl-6-methylcyclohexanone formed as a by-product was not analyzed, the quantity was little.

Identification of the Products. In all cases analytically pure samples were obtained by preparative VPC with Varian autoprep Model-2800 and characterized by NMR, IR, and mass spectra, refractive indices, and elemental analyses.

2-Propylcyclohexanone: $n_D^{20}=1.4558$ (lit,[10] 1.4538). Found: C, 76.96; H, 11.50%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%. Mass; $m/e=140$ (M^+). IR (CCl_4); 1710 cm^{-1}. NMR (CCl_4); δ, 0.91 (3H, t, $J=6$ Hz), 1.09—1.45 (4H, m), 1.46—2.50 (9H, m).

2-Butylcyclohexanone: $n_D^{20}=1.4576$ (lit,[10] 1.4545). Found: C, 77.30; H, 11.61%. Calcd for $C_{10}H_{18}O$: C, 77.56; H, 11.76%. Mass; $m/e=154$ (M^+). IR (CCl_4); 1710 cm^{-1}. NMR (CCl_4); δ, 0.90 (3H, t, $J=6$ Hz), 1.05—1.55 (6H, m), 1.60—2.50 (9H, m).

2-Isobutylcyclohexanone: $n_D^{20}=1.4477$. Found: C, 77.52; H, 11.62%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%. Mass; $m/e=154$ (M^+). IR (CCl_4); 1710 cm^{-1}. NMR (CCl_4); δ, 0.87 (6H, d, $J=5.5$ Hz), 1.1—2.4 (12H, m).

2-Hexylcyclohexanone: $n_D^{20}=1.4580$. Found: C, 78.74; H, 11.90%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%. Mass; $m/e=182$ (M^+). IR (CCl_4); 1700 cm^{-1}. NMR (CCl_4); δ, 0.90 (3H, t, $J=6$ Hz), 1.15—1.45 (8H, m), 1.50—2.40 (9H, m).

2-Allyl-6-propylcyclohexanone: Found: C, 79.43; H, 10.94%. Calcd for $C_{12}H_{20}O$: C, 79.74; H, 11.18%. Mass; $m/e=180$ (M^+). IR (CCl_4); 1700 cm^{-1}. NMR (CCl_4); δ, 0.90 (3H, t, $J=6$ Hz), 1.15—1.55 (4H, m), 1.55—2.60 (10H, m), 4.8—5.15 (2H, m), 5.5—6.0 (1H, m).

2-Benzyl-6-propylcyclohexanone: $n_D^{20}=1.5210$. Found: C, 83.47; H, 9.52%. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63%. Mass; $m/e=230$ (M^+). IR (CCl_4); 1700 cm^{-1}. NMR (CCl_4); δ, 0.90 (3H, t, $J=6$ Hz), 1.10—1.40 (4H, m), 1.55—2.60 (8H, m), 7.20 (5H, m).

2-Methyl-6-propylcyclohexanone: $n_D^{20}=1.4561$. Found: C, 78.04; H, 11.77%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%. Mass; $m/e=154$ (M^+). IR (CCl_4); 1710 cm^{-1}. NMR (CCl_4); δ, 0.96 (3H, t, $J=6$ Hz), 0.94 (3H, d, $J=5.5$ Hz), 1.1—1.5 (4H, m), 1.5—2.4 (8H, m).

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