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A Novel Synthesis of Internal Alkenyldialkylborane by the Reaction of 1-Halo-1-alkenyldialkylborane with Grignard Reagent

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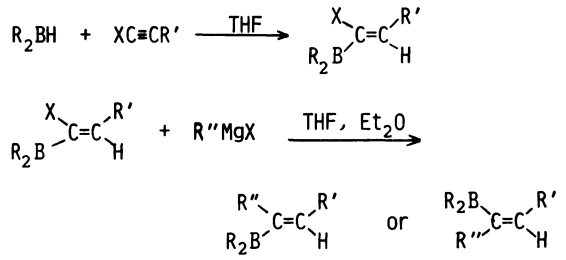
To synthesize internal alkenyldialkylboranes, coupling reactions were carried out by using 1-halo-1-alkenyldialkylboranes and Grignard reagents. Hydrogen peroxide oxidation and protonolysis with acetic acid of the reaction product revealed that internal (*E*)-alkenyldialkylborane was formed in 60—90% yield.

Organoborane is readily prepared by hydroboration, in which borane adds to a carbon-carbon double or triple bond in a regio- and stereoselective manner.[1] The skeleton of the alkyl or alkenyl group of organoborane formed by hydroboration is specified by the starting unsaturated compound. If the structure of the alkyl or alkenyl group of organoborane could be transformed to a desired one, the synthetic utility of organoborane would be greatly enhanced, although it is presently unavailable *via* hydroboration.

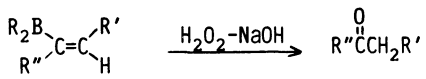
By the coupling reaction of 1-bromoalkyldialkoxyborane with alkylmagnesiumhalides, substitution of bromine with alkyl group has been reported,[2,3] and the application of this reaction to 1-halo-1-alkenylborane seems to be a successful route to regio- and stereoselective synthesis of internal alkenylboranes.[4] In this paper, we wish to report a synthesis of internal alkenyldialkylboranes by the coupling reaction of 1-halo-1-alkenylborane with a Grignard reagent (Scheme 1).



Scheme 1.

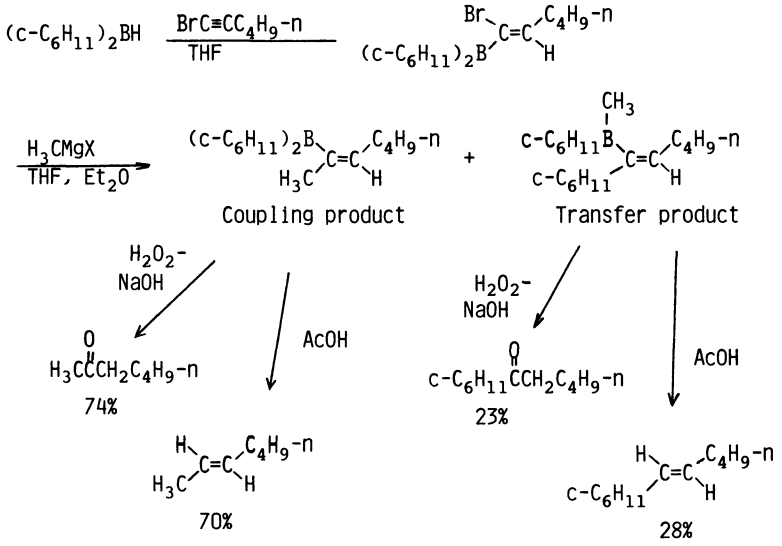
Results and Discussion

We have no suitable means to estimate directly the formation of internal alkenyldialkylborane at present. Fortunately, however, the internal alkenyl group of organoborane can be almost quntitatively transformed to the corresponding ketone by alkaline hydrogen peroxide oxidation.[5,6] Thus the yield of the internal alkenyldialkylborane was estimated indirectly from the amount of ketone formed by the above oxidation of the reaction product.



The reaction was carried out in the following way. To a THF solution of 2 mmol of 1-halo-1-alkenyldialkylborane, prepared from dialkylborane and 1-halo-1-alkyne,[7] diethyl ether solution of 2 mmol of alkylmagnesium halide was added at −50 °C and the solution was stirred at this temperature for 1 h. Then the reaction mixture was treated with alkaline hydrogen peroxide, and the product was analyzed by GLC.

In the reaction of 1-bromo-1-hexenyldicyclohexylborane with methylmagnesium iodide, 2-heptanone was obtained in 74% yield based on dicyclohexylborane employed. This result indicated that the expected 1-methyl-1-hexenyldicyclohexylborane was formed at least in this yield by the coupling reaction depicted in Scheme 2. In addition to 2-heptanone, cyclohexyl-

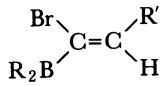
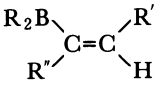
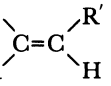
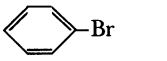
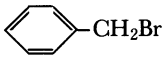
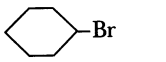


Scheme 2.

pentylketone was formed in 23% yield. This fact suggests that the transfer of the cyclohexyl group from the boron atom to the hexenyl carbon atom competed with the coupling reaction, to give 1-cyclohexyl-1-hexenylmethylcyclohexylborane (Transfer product in Scheme 2).

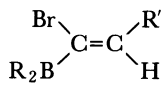
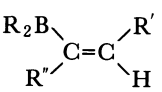
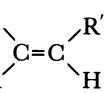
Brown *et al.* reported that the protonolysis of internal alkenylborane with carboxylic acid provided corresponding alkenes in retention of the configuration.[8] Thus to obtain further evidence for the formation of 1-methyl-1-hexenyldicyclohexylborane and to reveal the configuration of the alkenyl moiety of this com-

Table 1. 1-Alkyl-1-alkenyldialkylboranes obtained by the reactions of 1-bromo-1-alkenyldialkylboranes with Grignard reagents[a] and their yields[b]

R and R′ of 	R″X for the Grignard reagent	Product and yield/%  (Coupling)	 (Transfer)
R=cyclohexyl R′=n-C_4H_9	CH_3I[d]	74	23
	$CH_3CH_2CH_2Br$	60	36
	$(CH_3)_2CHBr$	12	40
	$CH_3(CH_2)_3CH_2Br$	52	35
	$CH_3(CH_2)_6CH_2Br$	54	37
	$H_2C{=}CHCH_2Br$	70	27
		0	88
		21	58
R=C_5H_{11}[c] R′=n-C_4H_9	$CH_3CH_2CH_2Br$	64	18
	$CH_3(CH_2)_3CH_2Br$	68	20
	$CH_3(CH_2)_6CH_2Br$	64	35
	$H_2C{=}CHCH_2Br$[d]	60	28
		9	34
R=cyclohexyl R′=n-C_6H_{13}	CH_3I[d]	72	24

a) Carried out by using 5 mmol of 1-bromo-1-alkenyldialkylborane and 5 mmol of the Grignard reagent in THF at −50 °C. b) Estimated from the amount of ketone in the oxidized solution and based on dialkylborane used. c) 1,2-Dimethylpropyl. d) Diethyl ether was used as the solvent for the Grignard reagent.

Table 2. 1-Alkyl-1-alkenyldialkylboranes obtained by the reactions of 1-iodo-1-alkenyldialkylboranes with Grignard reagents[a] and their yields[b]

R and R′ of 	R″X for the Grignard reagent	Product and yield/%  (Coupling)	 (Transfer)
R=cyclohexyl R′=n-C_4H_9	$CH_3CH_2CH_2Br$	70	30
	$CH_3(CH_2)_3CH_2Br$	66	31
	$CH_3(CH_2)_6CH_2Br$	66	30
	$H_2C{=}CHCH_2Br$[d]	90	9
R=C_5H_{11}[c] R′=n-C_4H_9	$CH_3CH_2CH_2Br$	75	8
	$CH_3(CH_2)_3CH_2Br$	70	8
	$CH_3(CH_2)_6CH_2Br$	70	12
	$H_2C{=}CHCH_2Br$[d]	62	10
R=cyclohexyl R′=n-C_6H_{13}	CH_3I[d]	85	13
R=C_5H_{11}[c] R′=n-C_6H_{13}	CH_3I[d]	82	14

a) Carried out by using 5 mmol of 1-iodo-1-alkenyldialkylborane and 5 mmol of the Grignard reagent in THF at −50 °C. b) Estimated from the amount of ketone in the oxidized solution and based on dialkylborane used. c) 1,2-Dimethylpropyl. d) Diethyl ether was used as the solvent for the Grignard reagent.

pound, the reaction mixture was treated with acetic acid at room temperature for 3 h, and the products were analyzed by GLC.

In this case (*E*)-2-heptene was formed in 70% yield based on dicyclohexylborane employed. The above fact supported the formation of (*E*)-1-methyl-1-hexenyldialkylborane. Thus, inversion of the configuration must be involved in the coupling reaction because 1-bromo-1-hexenyldicyclohexylborane has the *Z*-configuration as depicted in Scheme 2.[7]

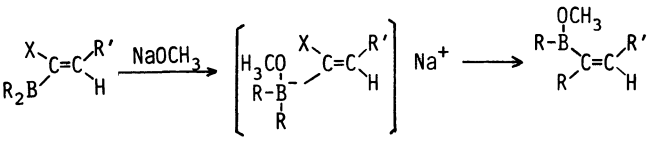
Several coupling reactions of 1-bromo-1-alkenyldialkylboranes with some Grignard reagents were examined. The results are shown in Table 1.

In most cases, two (*E*)-1-alkyl-1-alkenyldialkylboranes were formed. One was the expected coupling product and the other was the transfer product. The size of the alkyl group of the Grignard reagent had an appreciable influence on the distribution of these products. Thus in the case of small groups, such as methyl, propyl and allyl, the coupling reaction proceeded predominantly, while in the case of bulky groups, such as cyclohexyl, phenyl and benzyl, the transfer reaction proceeded predominantly.

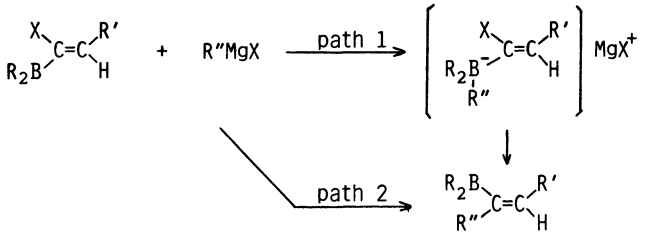
Much better results were obtained when 1-iodo-1-alkenyldialkylboranes were employed instead of 1-bromo-1-alkenyldialkylboranes. 1-Alkyl-1-alkenyldialkylborane formed in these reactions and their yields estimated in a similar manner as described above are presented in Table 2.

To clarify the configuration of the alkenyl moiety of these internal alkenylboranes, the reaction mixtures were protonolyzed with acetic acid and the resulting alkenes are presented in Table 3. In all cases examined, (*E*)-alkenes were formed, indicating that these internal alkenyldialkylboranes have the *E*-configuration.

Campbell *et al.* reported that in the reaction of (*Z*)-1-halo-1-alkenyldialkylborane with *t*-butyllithium, an inversion of the configuration occured *via* an ate-complex with hydride.[9] On the other hand, Zweifel *et al.* revealed that an internal (*E*)-alkenylborinate, having one alkyl group and one methoxl group on the boron atom, was formed in the reaction of 1-halo-1-alkenyldialkylborane with sodium methoxide.[10] In this reaction one of the two alkyl groups on the boron atom is transfered to the α-carbon atom of the alkenyl group *via* an ate-complex.



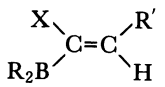
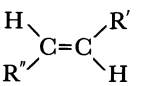
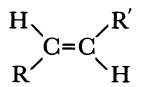
In the present reaction, it seems probable that a similar ate-complex of 1-halo-1-alkenyldialkylborane with the carbanion from the Grignard reagent would be formed at the first stage of the reaction, and then R'and R" may be transfered to the alkenyl carbon atom in a competitive manner, path 1 in Scheme 3. Initially, we attempted to couple directly 1-halo-1-alkenyldialkylborane and the Grignard reagent, path 2 in Scheme 3. However, we have no clear evidence for such a coupling reaction at the moment. In any event, it was revealed that (*E*)-1-alkyl-1-alkenyldialkylborane was formed in the present reaction.



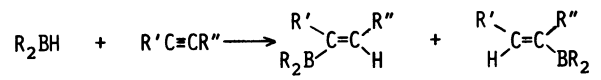
Scheme 3.

Internal alkenyldialkylborane can be synthesized by hydroboration of internal alkyne with sterically hindered dialkylborane.[7] However, in this reaction the regioselective addition of the boron atom to the triple bond is impossible for an internal alkyne whose two alkyl groups are of a similar structure. Thus the reac-

Table 3. (*E*)-Alkenes formed by the protonolysis of 1-alkyl-1-alkenyldialkylborane with acetic acid[a]

R and R' of 	R"X for the Grignard reagent	Product and yield/%[b] 	
R=cyclohexyl R'=*n*-C_4H_9	CH_3I[d,e]	70	28
	$CH_3(CH_2)_3CH_2Br$[e]	54	37
	$CH_3(CH_2)_6CH_2Br$[e]	56	38
	$CH_3(CH_2)_3CH_2Br$[e]	69	22
	$CH_3(CH_2)_6CH_2Br$[e]	69	22
	$CH_3(CH_2)_6CH_2Br$[f]	70	16
	$CH_3(CH_2)_6CH_2Br$[f]	73	18
R=cyclohexyl R'=*n*-C_6H_{13}	H_2=$CHCH_2Br$[d,f]	67	20

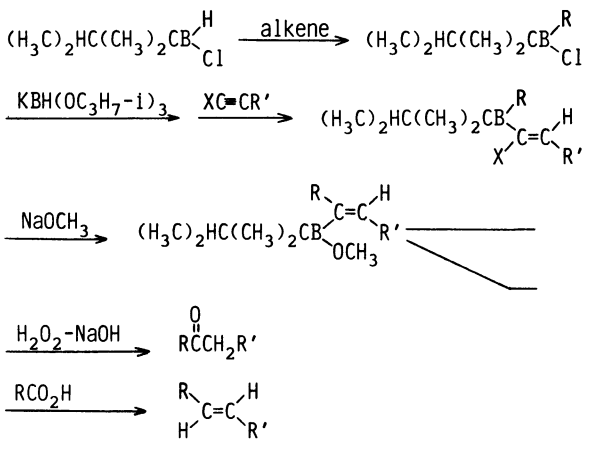
a) Protonolyzed at room temperature for 3 h. b) Based on dialkylborane used. c) 1,2-Dimethylpropyl. d) Diethyl ether was used as the solvent for the Grignard reagent. e) 1-Bromo-alkenyldialkylborane was used. f) 1-Iodo-alkenyldialkylborane was used.



tion can be successfully applied only for alkynes in which the steric hindrance and/or electronic character of the two alkyl groups differ largely from each other, or for completely symmetrical alkynes. Further, internal alkenyldialkylborane, thus obtained has the *Z*-configuration. The present reaction has the feature that two alkyl groups on the alkenyl double bond can be chosen arbitrarily. One is from relatively unhindered Grignard reagent and the other is from 1-halo-1-alkyne. In addition, the resulting internal alkenyldialkylborane has the *E*-configuration.

Several attempts were made to increase the yield of the internal alkenyldialkylborane. For, example, metal-triphenylphosphine compounds $NiCl_2(PPh_3)$[11] and $Pd(PPh_3)_4$,[12] known to have a remarkable promoting effect on the coupling reaction of alkenyl halide with the Grignard reagent, were added to the reaction mixture. Also 9-BBN was used as the hydroborating agent instead of dicyclohexylborane and bis(1,2-dimethylpropyl)borane. However, these failed to give satisfactory results.

Although the purpose of the present work is to synthesize internal alkenyldialkylborane, the regioselective formation of ketones and the regio- and stereoselective formation of internal alkenes observed in the examination of 1-alkyl-1-alkenyldialkylborane is also of interest to organic synthesis. Brown *et al.* obtained ketones or internal (*E*)-alkenes by the successive treatment of (1,1,2-trimethylpropyl)chloroborane with alkene, potassium triisopropoxyborohydride, 1-halo-1-alkyne and alkaline hydrogen peroxide or a carboxylic acid.[7,13] In this reaction the alkyl group introduced into the alkenyl double bond is derived from alkene *via* hydroboration.



However, in the present reaction such an alkyl group is derived from the Grignard reagent. Accordingly the reaction is applicable to the introduction of such alkyl groups as methyl and allyl, which cannot be introduced *via* hydroboration. For example, in the preparative scale experiment using 1-bromo-1-hexenyldicyclohexylborane and methyl magnesium iodide 2-heptanone was obtained in 68% yield by distillation of the oxidized products. Similarly (*E*)-2-heptene was also obtained in 65% yield by distillation of the protonolyzed products.

Experimental

Instruments. IR spectra (film) were recorded by using a Hitachi 285 spectrometer. ^1H NMR (CCl_4, TMS) spectra were run on a Hitachi R-20A spectrometer. Mass spectra were recorded by using a Hitachi M-52 mass spectrometer.

Reagents. Cyclohexene and 2-methyl-2-butene were distilled under argon stream after drying over lithium aluminium hydride. 1-Bromo-1-hexyne,[14] 1-bromo-1-octyne,[14] 1-iodo-1-hexyne,[15] and 1-iodo-1-octyne[16] were prepared by the methods described in the literatures. Dicyclohexylborane and bis(1,2-dimethylpropyl)borane[17] in THF were prepared as described in the literature. Alkyl halides were dried over Molecular Sieve 5A and distilled before use.

Representative Procedure. A 100-ml round bottomed flask, equipped with a gas inlet for argon, a septum inlet with a serum cap and a magnetic stirring bar, was flushed with argon. 1-Bromo-1-hexenyldicyclohexylborane was prepared by the addition of cyclohexene (0.82 g, 10 mmol) to BH_3 (5 mmol) in THF. 1-Bromo-1-hexyne (0.81 g, 5 mmol) was added slowly to the solution at −10 °C and the solution was stirred for 3 h at 0 °C. To this stirred solution, a diethyl ether solution of methylmagnesium iodide (5 mmol), prepared separately, was transfered with the aid of a syringe at −50 °C and the stirring was continued at this temperature for 1 h. Then the solution was allowed to warm to room temperature and oxidized with alkaline hydrogen peroxide, neutralized with hydrochloric acid, washed three times with NaCl-saturated water and dried over anhydrous magnesium sulfate. The solution was analyzed by GLC (10% PEG-20M, Diasolid M) using the internal standard method.

In the preparative reaction, the amounts of reagents and solvents used were four times those in the analytical reaction. After work-up diethyl ether and THF were evaporated, and the residue was put on a silica-gel column (Wako Q-50). From a mixture of two ketones, eluted by a mixture of benzene and diethyl ether (95:5), 1.55 g of 2-heptanone was distilled at 147 °C/753 Torr (68% yield) nearly free from cyclohexylpentyl ketone. ^1H NMR δ=0.88 (3H, t), 1.08—1.90 (6H, m), 2.05 (3H, s) and 2.31 (2H, t); IR 1712 cm^{-1}; MS *m/e* 142 (M^+).

The protonolysis was performed in the following way. To the reaction mixture, obtained as described above, 5 ml of acetic acid was added and the solution was stirred at room temperature for 3 h. Then the solution was washed three times with NaCl-saturated water and dried over anhydrous calcium chloride. The solution was analyzed by GLC (10% PEG-20M, Diasolid M) using the internal standard method. The preparative reaction was carried out by using four times the amounts of reagents and solvents used in the analytical reaction. After work-up 1.27 g of (*E*)-2-heptene was distilled at 97 °C/754 Torr (65% yield) uncontaminated by (*E*)-1-cyclohexyl-1-hexene. ^1H NMR δ=0.88 (3H, t), 1.00—1.50 (4H, m), 1.59 (3H, d), 1.70—2.25 (2H, m) and 5.00—5.72 (2H, m); IR 964 cm^{-1} (HC=CH); MS *m/e* 98 (M^+).

Analytical data of ketones and alkenes obtained in the examination of internal alkenyldialkylboranes are as follows.

2-Nonanone: ^1H NMR δ=0.88 (3H, t), 1.08—1.90 (10H, m), 2.05 (3H, s) and 2.30 (2H, t); IR 1713 cm^{-1}; MS *m/e* 142 (M^+).

4-Nonanone: ^1H NMR δ=0.83 (6H, t), 1.05—2.00 (8H, m) and 2.28 (4H, t); IR 1718 cm^{-1}; MS *m/e* 142 (M^+). Found: C, 76.01; H, 12.74%. Calcd for $C_9H_{18}O$: C, 75.99; H, 12.76%.

6-Undeuanone: ^1H NMR δ=0.83 (6H, t), 1.05—2.00 (12H,

m) and 2.28 (4H, t); IR 1718 cm^{-1}; MS *m/e* 170 (M^+). Found: C, 77.55; H, 13.00%. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02%

1-Nonen-4-one: ^1H NMR δ=0.83 (3H, t), 1.00—2.00 (6H, m), 2.30 (2H, m), 3.00 (2H, d) and 4.65—6.20 (3H, m); IR 1720 and 915 cm^{-1} (-CH=CH_2); MS *m/e* 140 (M^+). Found: C, 77.12; H, 11.50%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

1-Undecen-4-one: ^1H NMR δ=0.87 (3H, t), 1.00—2.00 (10H, m), 2.30 (2H, m), 3.00 (2H, d) and 4.65—6.20 (3H, m); IR 1719 and 916 cm^{-1} (-CH=CH_2); MS *m/e* 168 (M^+). Found: C, 78.48; H, 11.97%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%.

(E)-*5-Undecene*: ^1H NMR δ=0.81 (6H, t), 1.00—1.70 (10H, m), 1.70—2.20 (4H, m) and 5.18—5.40 (2H, m); IR 965 cm^{-1} (CH=CH): MS *m/e* 154 (M^+). Found: C, 85.66; H, 14.33%. Calcd for $C_{11}H_{22}$: C, 85.63; H, 14.33%.

(E)-*5-Tetradecene*: ^1H NMR δ=0.85 (6H, t), 1.00—1.70 (16H, m), 1.70—2.30 (4H, m) and 5.20—5.40 (2H, m); IR 964 cm^{-1} (HC=CH); MS *m/e* 196 (M^+). Found: C, 85.60; H, 14.34%. Calcd for $C_{14}H_{28}$: C, 85.63; H, 14.34%.

(E)-*1,4-Undecadiene*: ^1H NMR δ=0.84 (3H, t), 1.10—1.70 (8H, m), 1.70—2.20 (2H, m), 2.50—2.75 (2H, m) and 4.60—6.10 (5H, m); IR 914 (-CH=CH_2) and 965 cm^{-1} (CH=CH); MS *m/e* 152 (M^+). Found: C, 86.80; H, 13.21%. Calcd for $C_{11}H_{20}$: C, 86.76; H, 13.24%.

References

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