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BF_3 ETHERATE MEDIATED 1,4-ADDITION OF 1-ALKENYLDIALKOXYBORANES TO α,β-UNSATURATED KETONES. A STEREOSELECTIVE SYNTHESIS OF γ,δ-UNSATURATED KETONES

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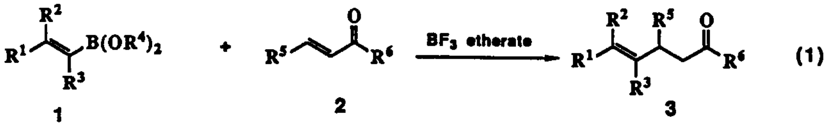
Abstract: 1-Alkenyldialkoxyboranes react with α,β–unsaturated ketones in the presence of BF_3 etherate through a facile 1,4-addition manner to give γ,δ-unsaturated ketones stereoselectively. As an application of this reaction, δ,δ- or γ,δ-disubstituted γ,δ-unsaturated ketones have been synthesized regio- and stereoselectively in good yields.

It is well known that B-(1-alkenyl)-9-borabicyclo[3.3.1]nonanes, readily obtainable by the hydroboration or haloboration reaction of alkynes, react with α,β-unsaturated ketones by 1,4-addition to give γ,δ-unsaturated ketones stereoselectively[1]. However, the application of this method is restricted because the regio- and stereoselective synthesis of the B-(1,2- or 2,2-disubstituted-1-alkenyl)-9-BBN compounds is generally difficult. On the other hand, dialkoxyborane derivatives are more stable than 9-BBN ones, and (1,2- or 2,2-disubstituted-1-alkenyl)dialkoxyboranes can be synthesized regio- and stereoselectively via haloboration-alkylation sequence of 1-alkynes[2] or hydroboration-alkylation sequence of 1-bromo-1-alkynes.[3] However, such dialkoxyboranes are less reactive than the corresponding 9-BBN derivatives and do not react with α,β-unsaturated ketones under the same reaction conditions. We wish to report here that alkenyldialkoxyboranes **1** react with α,β-unsaturated ketones **2** in the presence of BF_3 etherate to provide γ,δ-unsaturated ketones **3** in good yields regio- and stereoselectively (eq. 1).



Without BF_3 etherate, this reaction does not occur at all and other Lewis acids, such as $AlCl_3$, $TiCl_4$, $SnCl_4$, and $ZnCl_2$, are found to be less effective. The representative results are shown in Table 1. Dihydroxyborane derivatives also react as well as dialkoxyborane derivatives[4] (entries 12 and 13 in Table 1).

Table 1. The Synthsesis of γ,δ-Unsaturated Ketones[a]

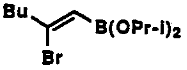
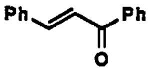
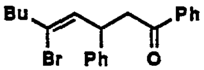
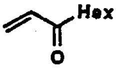
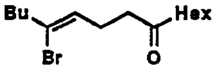
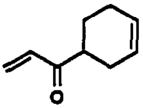
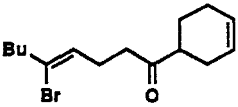
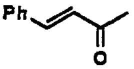
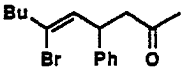
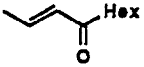
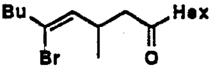
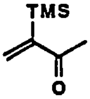
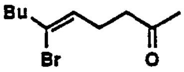
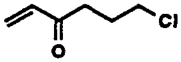
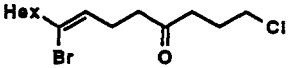
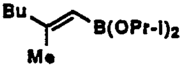
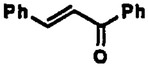
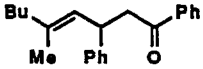
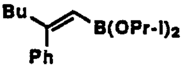
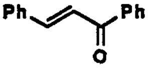
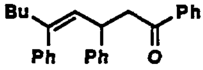
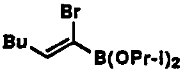
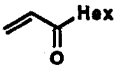
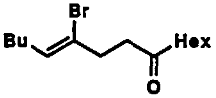
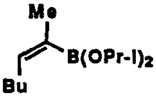
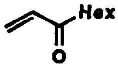
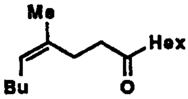
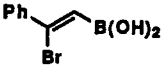
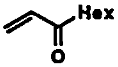
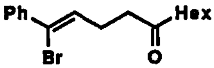
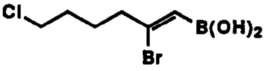
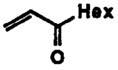
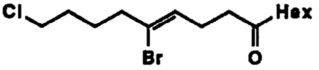
Entry	Borane, 1	Ketone, 2	Method[b]	Product[c], 3	Yield, %[d]
1			A		72
2			B		77
3			B		84
4			C		80
5			B		84
6			D	 e	60
7			B		70
8			E		69
9			F		78
10			B		63
11			D[f]		60
12			B		79

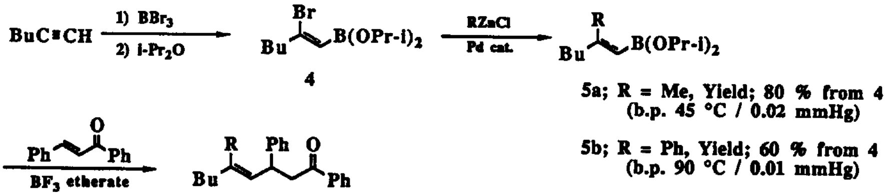
Table 1 continued.

13			B		62

a. The reaction was carried out in dichloromethane with 1.5 eq. of ketone and 1 eq. of BF_3 etherate to 1 were used unless otherwise mentioned.
b. Method A: The reaction was performed under reflux for 4 h. Method B: Under reflux over night. Method C: Under reflux for 2 days. Method D: At room temperature over night. Method E: At room temperature for 3 h. Method F: At room temperature for 2 days.
c. Isomeric purity, more than 98%.
d. Isolated yield based on the alkenylborane used.
e. Trimethylsilyl group was eliminated from the product during work up.
f. Toluene was used as solvent and 0.1 eq. of BF_3 etherate to 1 was employed.

The following procedure for the synthesis of (Z)-5-bromo-1,3-diphenyl-4-nonen-1-one is representative. To 10 ml of a dichloromethane solution of [(Z)-2-bromo-1-hexenyl]diisopropoxyborane[3a,5] (291 mg, 1 mmol) and chalcone (250 mg, 1.2 mmol) was added BF_3 etherate (142 mg, 1 mmol) at 0 °C and the mixture was stirred under reflux for 4 h. The reaction was quenched by the addition of water and the product was extracted with ether. The organic layer was washed with aq. $NaHCO_3$ and dried over $MgSO_4$. After the concentration and purification by preparative tlc (silica gel/ benzene : hexane = 95 : 5), the expected product was obtained in 72 % yield.

(2,2-Disubstituted or 1,2-disubstituted-1-alkenyl)dialkoxyboranes can be synthesized by the alkylation of bromoalkenylborane derivatives. For instance, (2,2-disubstituted-1-alkenyl)borane derivatives 5 were obtained by the alkylation of (2-bromo-1-hexenyl)diisopropoxyborane 4, prepared by the bromoboration reaction of 1-hexyne[5], with alkylzinc chloride in the presence of palladium catalyst. On the other hand, the alkylation of (1-bromo-1-hexenyl)diisopropoxyborane 7, obtained by the hydroboration reaction of 1-bromo-1-hexyne, with alkyllithium provided 1,2-disubstituted-1-alkenylborane derivative 8 regio- and stereoselectively.[3a] From 5 or 8, δ,δ- or γ,δ-disubstituted γ,δ-unsaturated ketones, 6 or 9, were obtained regio- and stereoselectively (eqs. 2 and 3).

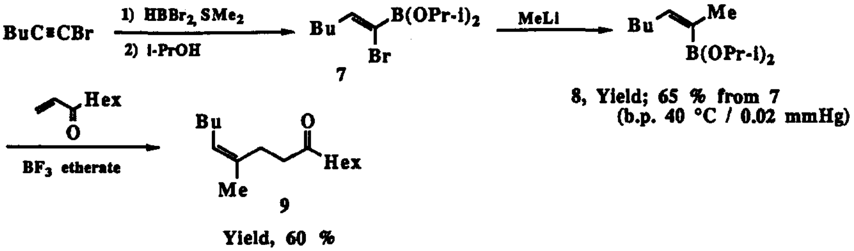


5a; R = Me, Yield; 80 % from 4 (b.p. 45 °C / 0.02 mmHg)

5b; R = Ph, Yield; 60 % from 4 (b.p. 90 °C / 0.01 mmHg) (2)

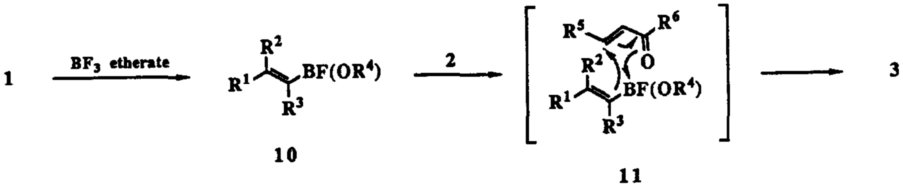
6a; R = Me, Yield; 69 %

6b; R = Ph, Yield; 78 %



(3)

The reaction seems to proceed as follows. One alkoxy group on boron of **1** is displaced by fluoride to give the borane **10**[6], which reacts with the α,β-unsaturated ketone **2** through a cyclic transition state **11** (eq. 4). Although there is no direct evidence to prove, the result that cyclic enones do not react with **1** at all[7], may support this mechanism, because they cannot have s-cis conformation, necessary for **11**.



(4)

References and Notes

1. a) P. Jacob, H. C. Brown, J. Am. Chem. Soc., **98**, 7832 (1976); b) Y. Satoh, H. Serizawa, S. Hara, and A. Suzuki, J. Am. Chem. Soc.,**107**, 5225 (1985)
2. Y. Satoh, H. Serizawa, N. Miyaura, S. Hara, and A. Suzuki, Tetrahedron Lett., **29**, 1811 (1988).
3. a) M. Satoh, N. Miyaura, and A. Suzuki, Chem. Lett., **1986**, 1329; b) H. C. Brown, T. Imai, N. G. Bhat, J. Org. Chem., **51**, 5277 (1986).
4. Other dialkoxyborane derivatives such as diethoxy-, 1,2-ethandioxy-, and 2,3-butanedioxyborane derivatives can be used similarly.
5. The preparation of **4** is as follows: To 30 ml of a dichloromethane solution of tribromoborane (7.5 g, 30 mmol) is added at - 78 °C, a dichloromethane solution of 1-hexyne (2.46 g, 30 mmol) dropwise and the mixture is stirred at - 78 °C for 1 h. After the addition of isopropyl ether (7.14 g, 70 mmol), the cooling bath is removed and the reaction mixture is stirred at room temperature over night. The volatile part is removed under reduced pressure and the distillation of the residue gives **4** in 73 % yield (b.p. 68 °C / 0.07 mmHg).
6. When **1** was stirred with BF_3 etherate without **2**, the formation of **10** was observed.
7. Cyclic enones such as 2-cyclohexenone and 2-cyclopentenone never gave the expected products in the reaction with **1** under the same conditions.

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