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Boron Trifluoride Etherate Mediated 1,4-Addition of (1-Alkynyl)diisopropoxyboranes to α,β-Unsaturated Ketones. A Convenient New Route to 3-Alkynyl Ketone Synthesis

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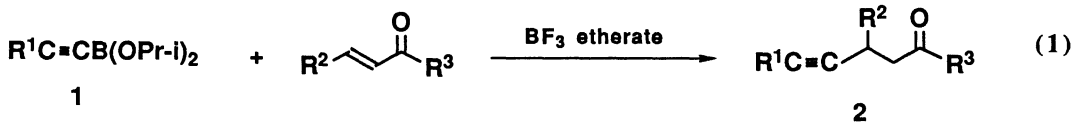
In the presence of BF_3 etherate, (1-alkynyl)diisopropoxyboranes react with α,β-unsaturated ketones to give 1,4-addition products selectively in good yields.

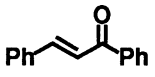
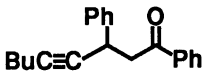
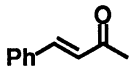
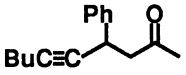
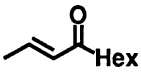
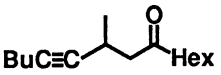
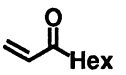
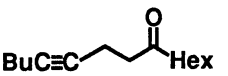
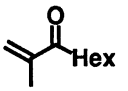
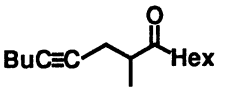
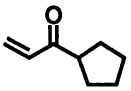
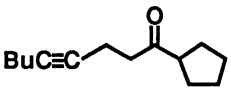
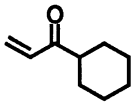
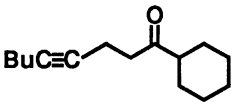
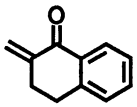
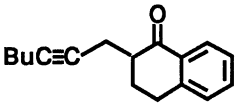
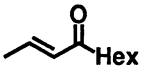
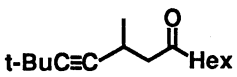
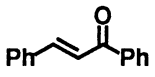
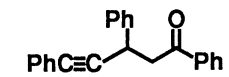
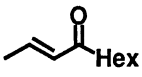
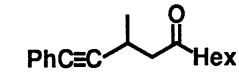
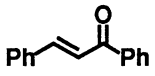
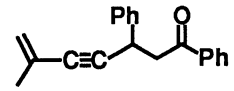
Conjugate addition of alkenyl or alkynyl metals to α,β-unsaturated carbonyl compounds is one of the most efficient methods for the extension of carbon chains with functional groups.[1,2] Recently, we found[2d] that alkenyldialkoxyboranes react with α,β-unsaturated ketones by activation with BF_3 etherate to give corresponding 1,4-addition products selectively. In this paper, we wish to report that (1-alkynyl)diisopropoxyboranes (**1**) also react with α,β-unsaturated ketones via 1,4-addition manner under such conditions to provide 3-alkynyl ketones (**2**) (Eq. 1).



(1) (1)

(1-Alkynyl)diisopropoxyboranes (**1**) can be prepared readily from triisopropoxyborane and 1-alkynes[3] and are conveniently used because being more stable than corresponding dialkylborane derivatives.[4] Furthermore, although copper reagents, which are often employed for the introduction of alkyl and alkenyl groups to α,β-unsaturated carbonyl compounds by 1,4-addition reaction, alkynylcopper derivatives are recognized to have no tendency for such conjugated addition.[5] Consequently the present method is useful for the synthesis of alkynyl ketones (**2**). As shown in Table 1, **1** reacted with a variety of unsaturated ketones to give the corresponding 1,4-addition products (**2**) in good yields. When alkyl vinyl ketones were used (Entries 4, 6, and 7 in Table 1), the formation of by-products, resulted from the reaction of **1** with two equiv.

Table 1. Reaction of (1-Alkynyl)dialkoxyboranes (1) with α,β-Unsaturated Ketones

Entry	Borane	Ketone	Product	Reaction conditions Temp/°C	Time/h	Yield/%[a]
1	$BuC{\equiv}CB(OPr\text{-}i)_2$			40	8	85
2				rt	48	60
3				0	120	70
4				rt	12[b]	60
5				rt	96	60
6				rt	48[b]	65
7				rt	12[b]	85
8				rt	3	86
9	$t\text{-}BuC{\equiv}CB(OPr\text{-}i)_2$			0	88	76
10	$PhC{\equiv}CB(OPr\text{-}i)_2$			40	3	81
11				0	88	84
12				40	3	68

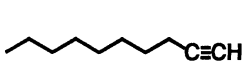
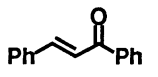
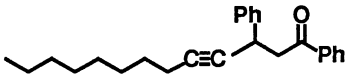
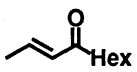
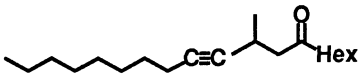
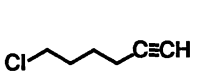
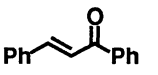
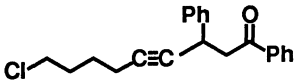
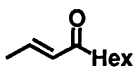
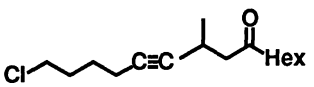
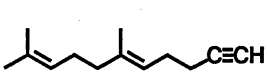
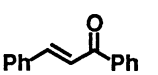
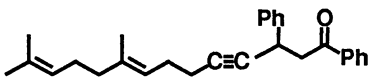
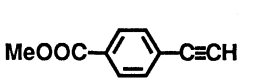
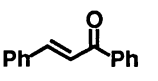
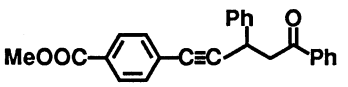
a) Isolated yield based on the ketone used.

b) The reaction was carried out in low concentration of the ketone, lower than 0.005 mol dm^{-3}, and 2 equiv. of borane and BF_3 etherate to ketone were used respectively. Otherwise, considerable amounts of by-products were formed.

of enones, was observed. This problem was overcome by carrying out the reaction under dilute conditions as indicated in Table 1.

A typical procedure is as follows: A mixture of (1-hexynyl)diisopropoxyborane (315 mg, 1.5 mmol), chalcone (208 mg, 1 mmol), and BF_3 etherate (142 mg, 1 mmol) in dichloromethane (20 mL) was stirred under reflux for 8 h. The consumption of chalcone was confirmed by tlc analysis and then the product was extracted with ether. The purification by preparative tlc (silica gel, 10% benzene in hexane) gave phenyl 2-phenyl-3-octynyl ketone in 85% yield.

Table 2. Synthesis of Alkynyl Ketones without the Isolation of (1-Alkynyl)diisopropoxyboranes

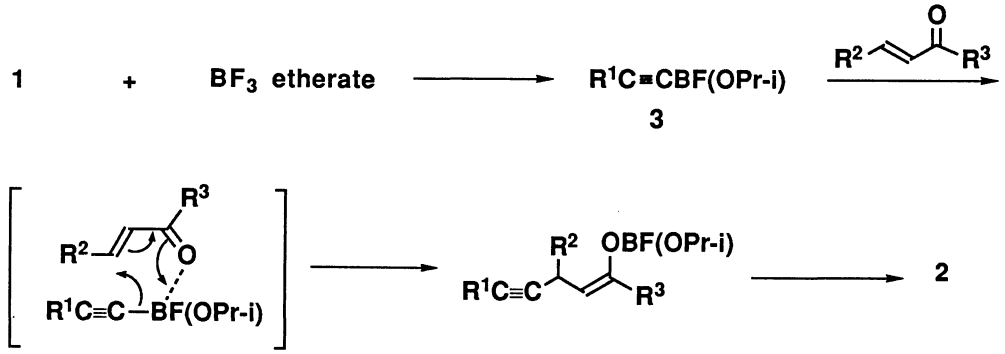
Alkyne[a)]	Enone	Product	Reaction conditions Temp/°C	Time/h	Yield/%[b)]
			40	15	81
			rt	72	80
			40	8	78
			rt	53	83
			40	14	70
			40	8	55

a) Three equiv. of alkyne and triisopropoxyborane to enone were used.
b) Isolated yield based on ketone used.

The reaction can be carried out without the isolation of **1**. An ethereal solution of **1** was prepared from 1-lithio-1-alkyne,[6)] triisopropoxyborane, and an ethereal solution of HCl according to the literature.[3)] The generated solid was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was dissolved in dichloromethane and used for the reaction with α,β-unsaturated ketones. By this method, the alkynes having high boiling points or functionalities can be used as shown in Table 2.

The reaction seems to proceed as follows. By the disproportionation reaction with BF_3 etherate, **1** changes to the fluoroborane derivative (**3**), which has higher Lewis acidity than **1**.[7)] After the coordination to carbonyl

oxygen, the alkynyl group of **3** adds to the α,β-unsaturated ketone through a cyclic transition state as shown in Eq. 2 to give the 1,4-addition product. The cyclic enones such as cyclohexenone which can't have such conformation, give no 1,4-addition products. This result supports the proposed mechanism.



(2)

References

1) S. Kim and J. M. Lee, *Tetrahedron Lett.*, **31**, 7627 (1990) and references cited therein.

2) a) P. Jacob and H. C. Brown, *J. Am. Chem. Soc.*, **98**, 7832 (1976); b) Y. Satoh, H. Serizawa, S. Hara, and A. Suzuki, *ibid.*, **107**, 5225 (1985); c) J. A. Sinclair, G. A. Molander, H. C. Brown, *ibid.*, **99**, 954 (1977); d) S. Hara, S. Hyuga, M. Aoyama, M. Sato, and A. Suzuki, *Tetrahedron Lett.*, **31**, 247 (1990).

3) H. C. Brown, N. G. Bhat, and M. Srebnik, *Tetrahedron Lett.*, **29**, 2631 (1988).

4) Most of alkynyldiisopropoxyboranes can be used under air for a short time, although they decompose gradually.

5) H. O. House and W. F. Fischer, *J. Org. Chem.*, **34**, 3616 (1969).

6) When 1-alkyne is insoluble in ether, THF is used as a solvent. In that case, lithium chloride is not precipitated and after the reaction, removal of solvent under vacuum, followed by the addition of hexane is necessary to remove lithium chloride.

7) Without BF_3 etherate, **1** does not react with α,β-unsaturated ketones at all. In the reaction of alkenyldialkoxyboranes, fluorinated borane derivatives, corresponding to **3**, were isolated.[2d] As to the disproportionation reaction between BF_3 etherate and alkoxyboranes, see, H. G. Cook, J. D. Liett, B. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, **1950**, 3125.

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