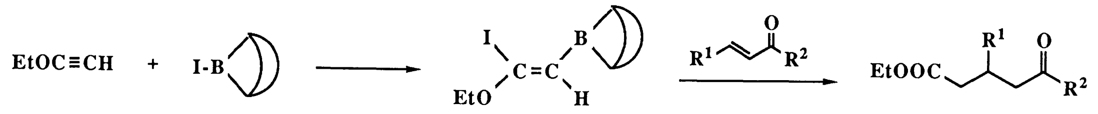
CHEMISTRY LETTERS, pp. 1723-1726, 1989.

The Michael-type Reaction of B-Iodo-9-BBN/Ethoxyethyne Adduct to α, β-Unsaturated Ketones. A Selective Synthesis of δ-Keto Esters[1)]

Fumitoshi KAWAMURA, Takao TAYANO, Yoshitaka SATOH, Shoji HARA,
and Akira SUZUKI*
Department of Applied Chemistry, Faculty of Engineering,
Hokkaido University, Sapporo 060

The adduct formed from B-iodo-9-borabicyclo[3.3.1]nonane and ethoxyethyne reacts with α,β-unsaturated ketones under mild conditions to give δ-keto esters in excellent yields selectively.

Recently we have reported that B-iodo-9-borabicyclo[3.3.1]nonane (B-I-9-BBN)/ethoxyethyne adduct (**1**) reacts with aldehydes under mild conditions to provide (E)-α, β-unsaturated esters, after the protic work up.[2)] That reaction showed the high chemoselectivity, and other carbonyl compounds such as ketones, esters, acid chlorides, and amides did not react with **1**. During the course of the study, we have found that the reaction of **1** with α,β-unsaturated ketones via a Michael-type addition proceeds smoothly to give δ-keto esters (**2**) in good yields (Eq. 1).



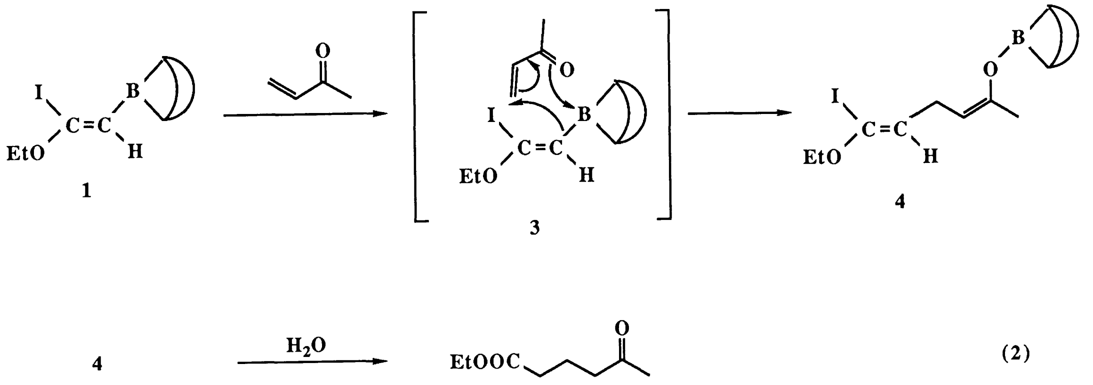
1 **2** (1)

The Michael reaction of carboxylic acid esters to α,β-unsaturated ketones is useful as one of carbon-carbon bond formation reaction. However, in the reaction of ester carbanions with enones, the 1,2-addition occurs competitively.[3)] Though the Lewis acid catalyzed reaction of ketene silyl acetals with enones was revealed to be effective to obtain Michael addition products selectively,[4)] acid sensitive ketones such as methyl vinyl ketone, gave poor results. On the other hand, the present reagent does not react with ketones via 1,2-addition, and the reaction is carried out under very mild conditions. Consequently, the Michael reaction products thus prepared are never contaminated with 1,2-addition products, and even in the case of methyl vinyl ketone, which polymerizes readily under acidic conditions, the reaction gives the expected product in a high yield.[5)]

The following procedure for the synthesis of ethyl 5-oxohexanoate is representative. To a pentane solution (5 mL) of B-I-9-BBN (0.372 g, 1.5 mmol) was added ethoxyethyne (0.105 g, 1.5 mmol) at -78 °C. After stirring at -78 °C for 1 h, methyl vinyl ketone (0.07 g, 1 mmol) was added. The reaction mixture was stirred at -78 °C for 30 min and then at room temperature for 1 h. Finally, 1 mL of ethanol and 2 mL of H_2O were added and the mixture was stirred at room temperature for another 1 h. The product was extracted with ether and purified by preparative tlc (silica gel/dichloromethane). Ethyl 5-oxohexanoate was isolated in 93% yield (137 mg). The representative results for the preparation of δ-keto esters are shown in Table 1.

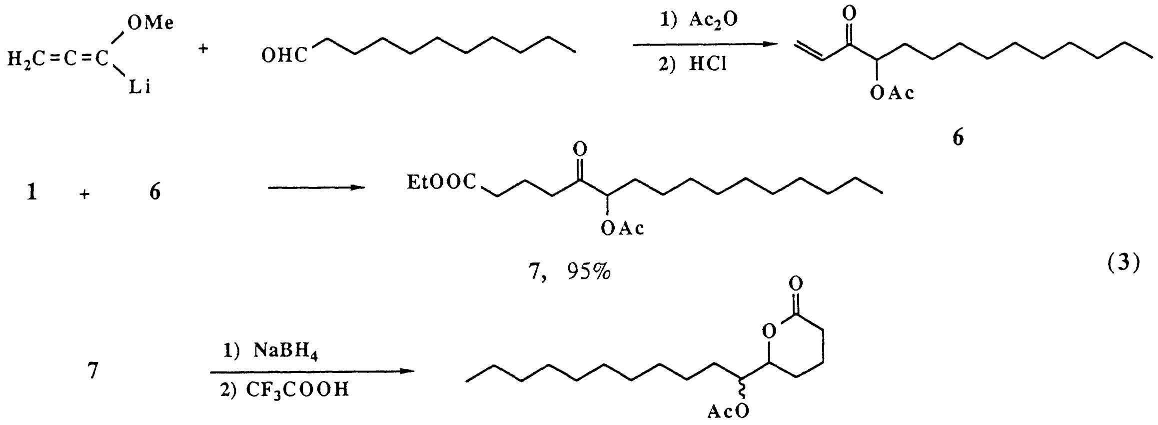
The Michael products were obtained in good yields from a variety of acyclic enones. However, cyclic enones such as 2-cylohexenone never provided the corresponding products in the reaction with **1**.

The reaction seems to proceed through the following pathway: 1) B-I-9-BBN adds to ethoxyethyne to give the adduct (**1**).[7)] 2) The adduct (**1**) reacts with methyl vinyl ketone via the cyclic transition state (**3**)[9)] to yield the intermediate (**4**). 3) The subsequent treatment with ethanol and water affords the keto ester. Since cyclohexenone is not able to have s-cis conformation, it can not react with **1** through the cyclic transition state.



(2)

Finally, in order to demonstrate the utility of this method, we attempted to synthesize 6-acetoxy-5-hexadecanolide (**5**), the major component of a mosquito oviposition attractant pheromone.[10)] The starting enone (**6**) was prepared from methoxy allene and undecanal in one-pot.[11)] The acetoxy enone (**6**) thus obtained, reacted with **1** selectively to give the acetoxy keto ester (**7**) in 95% yield. The desired pheromone (**5**) was synthesized from **7**, by the reduction with sodium borohydride, followed by lactonization (Eq. 3).[12)]



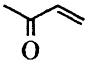
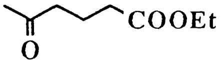
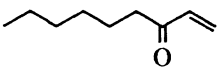
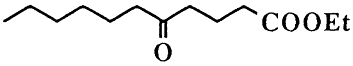
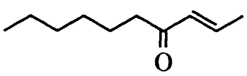
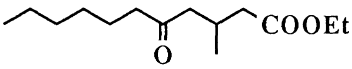
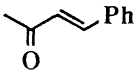
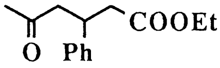
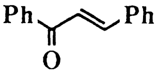
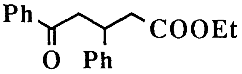
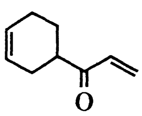
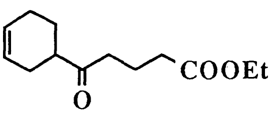
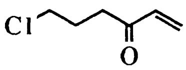
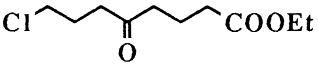
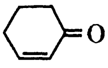
6

7, 95%

(3)

5, 60% (1:1 mixture of threo and erythro isomers)

Table 1. Synthesis of δ-Ketoesters

Enone	Product	Yield/%[a)]
		93
		90
		73
		75
		84
		74
		95
		no reaction

a) Isolated yield based on the ketone used.

References

1) Organic Synthesis Using Haloboration Reaction. 15.

2) Y. Satoh, T. Tayano, S. Hara, and A. Suzuki, Tetrahedron Lett., in press (1989)

3) C. H. Heathcock and D. A. Oare, J. Org. Chem., 50, 3022 (1985).

4) K. Saigo, M. Osaki, and T. Mukaiyama, Chem. Lett., 1976, 163.

5) Recently, the Michael reaction of ketene silyl acetals with α,β-unsaturated ketones under milder conditions has been reported.[6] Some of them also succeeded in overcoming these problems.

6) Y. Kita, J. Segawa, J. Haruta, T. Fujii, and Y. Tamura, Tetrahedron Lett., 21, 3779, (1980); Y. Kita, J. Segawa, J. Haruta, H. Yasuda, and Y. Tamura, J. Chem. Soc., Perkin Trans. 1, 1982, 1099; T. V. RajanBabu, J. Org. Chem., 49, 2083 (1984); C. H. Heathcock, M. H. Norman, and D. E. Uehling, J. Am. Chem. Soc., 107, 2797 (1985); S. Kobayashi, M. Murakami, and T. Mukaiyama, Chem. Lett., 1985, 953; T. Mukaiyama, M. Tamura, and S. Kobayashi, ibid., 1986, 1817.

7) As **1** is unstable, the full characterization is difficult. However it is derived to the alkynylated compound by the reaction with lithium acetylide and iodine.[8] The alkynylated compound thus obtained is stable enough to be identified.

8) S. Hara, Y. Satoh, H. Ishiguro, and A. Suzuki, Tetrahedron Lett., 24, 735 (1983)

9) For the Michael-type addition of B-alkenyl-9-BBN derivatives to α,β-unsaturated ketones, see: P. Jacob, III and H. C. Brown, J. Am. Chem. Soc., 98, 7832 (1976); Y. Satoh, H. Serizawa, S. Hara, and A. Suzuki, ibid., 107, 5225 (1985)

10) a) C. Fuganti, P. Grasselli, and S. Servi, Chem. Commun., 1982, 1285; b) Y. Masaki, K. Nagata, and K. Kaji, ibid., 1983, 1835; c) K. Mori and T. Otuka, Tetrahedron, 39, 3267 (1983); d) M. Ochiai, T. Ukita, Y. Nagao, and E. Fujita, Chem. Commun., 1985, 637; e) L. Guo-qiang, X. Hai-jian, W. Bi-chi, G. Guong-zhong, and Z. Wei-shan, Tetrahedron Lett., 26, 1233 (1985); f) K. Machiya, I. Ichimoto, M. Kirihata, and H. Ueda, Agric. Biol. Chem., 49, 643, (1985); g) C. W. Jefford, D. Jaggi, and J. Boukouvalas, Tetrahedron Lett., 27, 4011 (1986).

11) S. Hoff, L. Brandsma, and J. F. Arens, Rec. Trav. Chim., 87, 916 (1968); Idem., ibid., 87, 1179 (1968); J. A. Rompes, S. Hoff, P. P. Montijn, L. Brandsma, and J. F. Arens, ibid., 88, 1289 (1969).

12) The product (**5**) was identified by the direct comparison of the authentic sample prepared by the known procedure.[10g]

(Received June 19, 1989)