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A NEW CONVERSION OF SILYL ENOL ETHERS INTO THE CORRESPONDING BORON ENOLATES WITH DIALKYLBORON HALIDES OR DIALKYLBORON TRIFLATES, AND CROSS ALDOL REACTIONS VIA THE BORON ENOLATES

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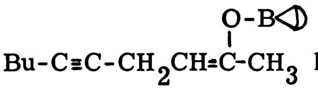
Silyl enol ethers react with dialkylboron halides or dialkylboron triflates to give the corresponding boron enolates quantitatively under mild conditions. Boron enolates thus generated are effectively used to afford cross aldol products with benzaldehyde.

The aldol condensation has attracted much attention of synthetic organic chemists$^{1)}$ and, most recently, diastereoselective aldol condensations via boron enolates were reported by several groups.$^{2)}$ It is desirable to develop a convenient method to generate boron enolates. This paper describes a promising method in which boron enolates are generated in situ through a new exchange between dialkylboron halides or triflates and silyl enol ethers which can be prepared easily.$^{3)}$

The reaction between 1-trimethylsiloxy-1-cyclohexene and B-bromo-9-borabicyclo [3.3.1] nonane (B-Br-9-BBN) in $CDCl_3$ at room temperature was monitored by ^1H NMR spectroscopy. The NMR signals at 0.10 ppm (s, O-Si$\underline{Me}_3$) and 4.73 ppm (t, vinyl-$\underline{H}$) disappeared within 1 h, and new signals appeared at 0.50 ppm (s, $\underline{Me}_3$SiBr) and 4.90 ppm (t, vinyl-$\underline{H}$). The ^{11}B NMR spectrum of the reaction mixture revealed a signal at 60.4 ppm (in $CDCl_3$). The ^{11}B NMR chemical shift of  $Bu\text{-}C{\equiv}C\text{-}CH_2CH{=}\overset{\overset{\text{O-B}}{|}}{C}\text{-}CH_3$ has been reported as 58.1 ppm (in THF).$^{4)}$ When CH_2Cl_2 was used as a solvent, the vinyl proton of 1-trimethylsiloxy-1-cyclohexene disappeared completely within 20 min. Aliquots of the reaction mixture were withdrawn at appropriate intervals of time, then added into 5% aq. $NaHCO_3$ solution in order to hydrolyze the generated boron enolate and analyzed for cyclohexanone by GC (carbowax, internal standard : undecane). The yields of cyclohexanone at the intervals are shown in Figure 1. Examination of the produced trimethylbromosilane by ^1H NMR (internal standard : benzene) revealed a yield of 85%. The above results illustrate that 1-trimethylsiloxy-1-cyclohexene reacts with B-Br-9-BBN to give the corresponding boron enolate almost quantitatively within 20 min in CH_2Cl_2 at room temperature. On the other hand, the reaction between 1-trimethylsiloxy-1-cyclohexene and dihexylchloroborane$^{5)}$ or dicyclopentylchloroborane in $CDCl_3$ at room temperature was found to be much slower, about 50% of the starting material being detected after 4 h by ^1H NMR.

Similar studies on a mixture of 1-trimethylsiloxy-1-cyclohexene and dialkylboron triflate, e.g., dibutylboron triflate, dicyclopentylboron triflate, or 9-BBN triflate, have demonstrated that the trimethylsilyl enol ether undergoes very rapid exchange with dialkylboron triflates : The NMR signals at 0.10 ppm and 4.73 ppm disappeared completely, and new signals at 0.45 ppm and 4.85 ppm appeared almost immediately in $CDCl_3$ at room temperature. Thus, the exchange with dialkylboron triflates takes place much more rapidly, compared with that using B-Br-9-BBN or dialkylchloroborane.

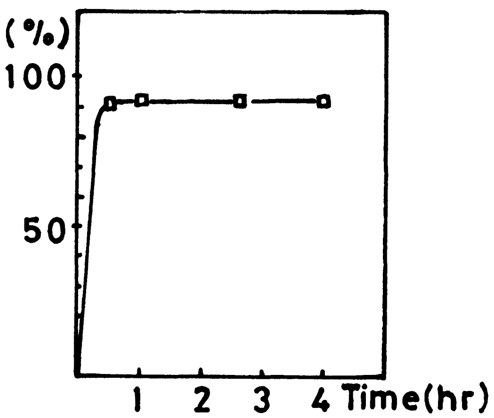
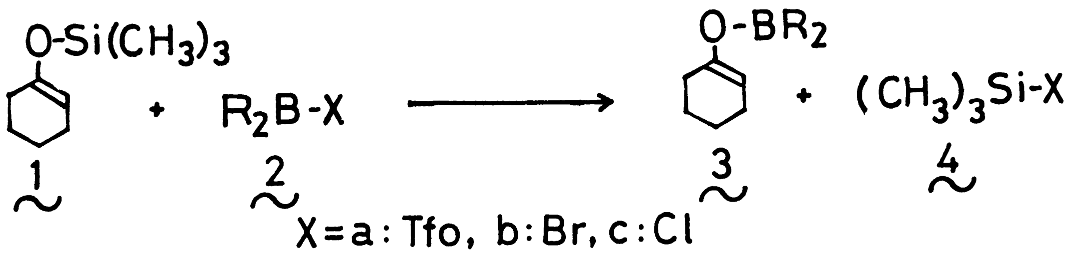
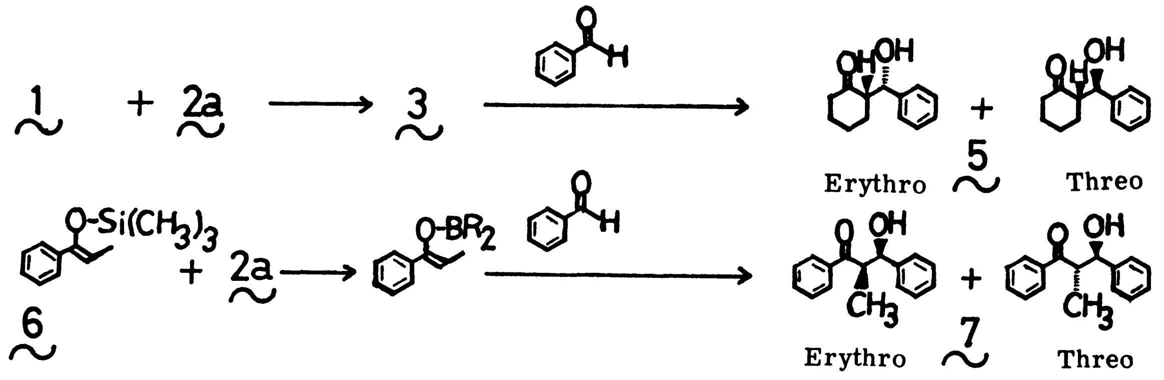


Figure 1 Yield of cyclohexanone

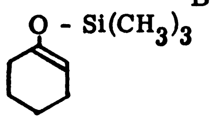
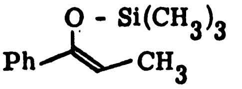


Then, diastereospecific aldol reaction using this exchange with dialkylboron triflates gave the results summarized in the table.



Table

The Condensation of Trimethylsilyl Enol Ethers with Benzaldehyde via the Exchange Reaction

Silyl Enol Ether	Boron Triflate	Exchange Reac. Cond.	Reac. Cond.	Solvent and Workup Method	Yield of **5** or **7** (%)	Threo/Erythro[a)]
	Bu_2B-OTf	-22 °C, 30 min	-78 °C, 1.5 h r. t. 15 min	Et_2O A	0[b)]	——
		-22 °C, 30 min	-78 °C, 3 h	Et_2O A	Low	——
		-22 °C, 30 min	-78 °C, 3 h	Et_2O B	90	75 : 25
		-22 °C, 30 min	-78 °C, 1 h -50 °C, 30 min	Et_2O B	89	78 : 22
		-22 °C, 30 min[c)]	-78 °C, 1 h -22 °C, 30 min	Et_2O B	90	83 : 17
	Bu_2B-OTf	-22 °C, 30 min	-78 °C, 1 h -50 °C, 30 min	Et_2O B	87	39 : 61
		-22 °C, 30 min	-78 °C, 1 h -50 °C, 30 min	CH_2Cl_2 B	88	30 : 70
	B-OTf	-22 °C, 30 min	-78 °C, 1 h -50 °C, 30 min	Pentane B	91	26 : 74

Workup Method A : The reaction mixture was treated with pH 7 phosphate buffer and methanol followed by addition of 30% H_2O_2. B : The reaction mixture was treated with pH 7 phosphate buffer followed by extraction with Et_2O. After removal of the ether, the residue was dissolved in methanol, then 30% H_2O_2 was added. a) The ratio of diastereomers was determined by ^1H NMR. b) No aldol product was detected by ^1H NMR. c) 0.1 equivalent of *N*, *N*-diisopropylethylamine was used.

A typical procedure of the aldol reaction utilizing *Z*-3-phenyl-3-trimethylsiloxy-2-propene (**6**) is as follows : To a solution of **6** (0.413 g, 2 mmol) in 4 ml CH_2Cl_2 was added dibutylboron triflate (0.548 g, 2 mmol) at -22 °C. The mixture was stirred for 30 min at the temperature then cooled to -78 °C. Benzaldehyde (0.212 g, 2 mmol) was added and the reaction mixture was stirred for 1 h at -78 °C and for 30 min at -50 ~ -55 °C. The resulting reaction mixture was treated with 20 ml pH 7 phosphate buffer, then extracted with Et_2O (30 ml × 2). After removal of the ether, the residual colorless oil was dissolved in methanol (5 ml), cooled to 0 °C and treated with 30% H_2O_2 (2 ml). The mixture was allowed to stand for 12 h at room temperature, then water was added (20 ml) and the milky mixture was concentrated *in vacuo* to remove most of the methanol.

The remaining mixture was extracted twice with ether and the ether layer was washed successively with 5% aq. sodium bicarbonate solution and brine. After drying the ether layer over anhydrous $MgSO_4$, the solvent was evaporated *in vacuo*. The crude product was purified on flash column chromatography with hexane : Et_2O = 7 : 3 as eluent to afford 0.421 g (88%) aldol product as a mixture of threo and erythro isomers (30 : 70).

In this reaction, the aldol products were obtained in good yields, however, stereospecificity is rather low (see Table). Experiments performed under similar conditions, but with the exchange at -78 °C, did not improve the stereospecificity. Further investigation of diastereospecific aldol condensation using this exchange is now in progress.

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References and Notes

1) a) H. O. House, "Modern Synthetic Reactions", Second Ed., W. A. Benjamin, Menlo Park, 1972, pp 629-682 ; b) K. Narasaka, J. Syn. Org. Chem. Jpn., 37, 307 (1979), and references cited therein.

2) a) S. Masamune, S. Mori, D. E. V. Horn, and D. W. Brook, Tetrahedron Lett., 1979, 1665 ; b) M. Hirama and S. Masamune, ibid., 1979, 2225 ; c) D. E. V. Horn and S. Masamune, ibid., 1979, 2229 ; d) M. Hirama, D. S. Garvey, L. D. L. Lu, and S. Masamune, ibid., 1979, 3937; e) D. A. Evans, E. Vogel, and J. V. Nelson, J. Am. Chem. Soc., 101, 6120 (1979) ; f) T. Inoue and T. Mukaiyama, Bull. Chem. Soc. Jpn., 53, 174 (1980).

3) Most recently, Professor I. Kuwajima, *et al.*, of Tokyo Institute of Technology discovered the same reaction described in this paper. Personal communication of I. Kuwajima.

4) Table of ^{11}B Chemical Shifts Relative to $BF_3 \cdot Et_2O$ (new convention) compiled by G. Molander and J. Cambell at Purdue University.

5) It was found that the reaction of dihexylchloroborane with acetophenone and *N*,*N*- diisopropylethylamine, followed by condensation with benzaldehyde, gave the corresponding aldol product in 92% yield.

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