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NEW DIRECTED CROSS-ALDOL REACTION USING 9-TRIFLUOROMETHYLSULFONYL-9-BORABICYCLO[3.3.1]NONANE

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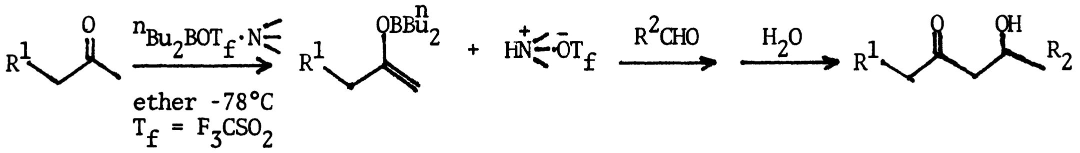
A directed cross-aldol reaction between two different carbonyl compounds by using 9-trifluoromethylsulfonyl-9-borabicyclo[3.3.1]-nonane and tertiary amine is described. The reaction of methyl ketones with the other carbonyl compounds takes place in regiospecific manner to afford the corresponding cross-aldols in good yields through intermediates, 9-(1-methyl-1-alkenyl)oxy-9-borabicyclo[3.3.1]nonanes.

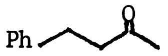
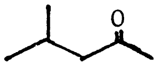
In the previous communication, the regiospecific preparation of various cross-aldols, only one regioisomer, from two different carbonyl compounds with di-n-butylboryl trifluoromethanesulfonate and tertiary amine through intermediate, 1-alkylvinyloxy-di-n-butylborane was reported[1] as depicted below.

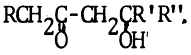


Now we wish to report here a cross-aldol reaction by use of 9-trifluoromethylsulfonyl-9-borabicyclo[3.3.1]nonane (9-BBN triflate)[2], derived from 9-BBN and trifluoromethanesulfonic acid, and tertiary amine.

A typical procedure is described for the reaction of 4-phenyl-2-butanone and benzaldehyde; to a solution of 9-BBN triflate (0.350g, 1.3mmol) and 2,6-lutidine (0.139g, 1.3 mmol) in 1.5ml of ether was added dropwise 4-phenyl-2-butanone (0.192g, 1.3mmol) at -78°C under argon. After the mixture was stirred for 3 hr, benzaldehyde (0.137g, 1.3mmol) in 1.5ml of ether was added at that temperature. The reaction mixture was allowed to stand for 3 hr, followed by addition of pH7.0 phosphate buffer (3 ml), methanol (7ml) and 30% H_2O_2 (3ml) at 0°C. After 15 min, the mixture was concentrated in vacuo to remove most of methanol followed by the extraction with dichloromethane, dried over Na_2SO_4 and the solvent was removed. The crude oil was purified by preparative tlc to give 3-benzyl-4-hydroxy-4-phenyl-2-butanone (0.234g, 88%) and 1,5-diphenyl-1-hydroxy-3-pentanone (0.005g, 2%). The results of the reaction of ketones with some carbonyl compounds by use of 9-BBN triflate and 2,6-lutidine are summarized in Table 1, according to the present procedure. The ratio of the resulted isomers is the reverse of that obtained by use of di-n-butylboryl triflate and tertiary amine[1].

Table 1. Yields and the ratio of regioisomers of cross-aldols

Ketone	Carbonyl compound	Yield, %	(I) : (II), %[c]
	PhCHO	90	98 : 2
		63[a]	100 : 0
		67[b]	100 : 0
		57[b]	100 : 0

a) In ether at room temperature for 1 day. Reactant ratio, ketone:acetone=1:1.5.
b) The regioisomers were separable on 10% QF_1 at 130°C.
c) All of the products gave satisfactory nmr, ir data for assigned structures of authentic samples. (I):  $CH_3\underset{O}{C}CHR\underset{OH}{C}R'R''$ (II):  $RCH_2\underset{O}{C}\text{-}CH_2\underset{OH}{C}R'R''$.

The effect of tertiary amines, acid captors, on the ratio of regioisomers was examined for the reaction of 4-phenyl-2-butanone and benzaldehyde. The reaction conditions are as follows. To a solution of 9-BBN triflate and amine in ether was added 4-phenyl-2-butanone at -78°C under argon. After the mixture was stirred for 15 min, benzaldehyde in ether was added at that temperature and stirred for 3 hr.

Table 2. The effect of amines

Amine	Yield, %	(I) : (II), %
tri-n-butylamine	72	81 : 19
ethyldiisopropylamine	73	62 : 38
2,6-lutidine	70	88 : 12
2,5-lutidine	34	44 : 56
pyridine	30	64 : 36

The ratio of the regioisomers depends on the nature of amines when the formation of vinyloxyborane is stopped within 15 min as shown in Tabel 2 and it is the reverse of that observed by using di-n-butylboryl triflate and ethyldiisopropylamine. The results can be reasonably explained by considering a key intermediate, 9-(1-methyl-1-alkenyl)oxy-9-BBN, formed by an interaction of the ammonium and pyridinium triflate with 9-(1-alkyl-1-vinyl)oxy-9-BBN initially generated from 9-BBN triflate and methyl ketone through thermodynamically controlled step.

It is noted that various directed cross-aldols are prepared in good yields by treating two different carbonyl compounds with 9-BBN triflate and tertiary amine under mild reaction conditions.

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Reference and Note

1) T. Mukaiyama and T. Inoue, Chem. Lett., 559 (1976).
2) The equimolar amounts of 9-BBN and trifluoromethanesulfonic acid were mixed in hexane at room temperature for one day. Distillation gave colorless oil, b.p. 38°C/0.03 mmHg. Yield 80%. ir (CCl_4): 1400, 1240, 1080, 640, 620 cm^{-1}.

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