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ERYTHRO-SELECTIVE ALDOL CONDENSATION VIA ENAMINOSILANES

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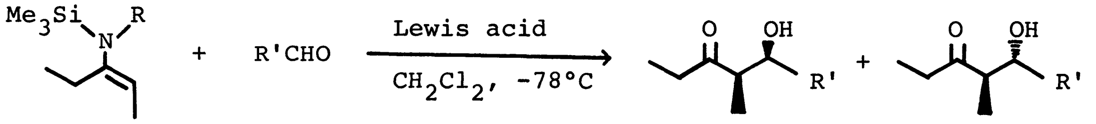
In the presence of $BF_3 \cdot OEt_2$, enaminosilanes derived from acyclic and cyclic ketones have been shown to undergo erythro selective kinetic aldol condensation.

The aldol condensation is one of the most important methods of forming a carbon-carbon bond, and it has been established that highly diastereoselective kinetic aldol condensation can be achieved using metal enolates.1) Reactions of metal enolates possessing a Lewis acidic metal counterion, such as Li,2) Mg,3) B,4) Al,5) Zn,6) and Si-Ti,7) which can chelate the two oxygen atoms proceed through the metal-linked six-membered transition state. In these cases, kinetic aldol diastereoselectivities depend upon the geometry of the metal enolates. (E)-Enolates generally favor threo aldols and (Z)-enolates preferentially give erythro adducts. On the other hand, the reactions using tris(dialkylamino)-sulfonium (TAS) enolate8) afforded kinetic erythro aldol products either predominantly or exclusively regardless of the geometry of the starting metal enolates via the acyclic mechanisms. Recently, Yamamoto reported that α-mercurio ketones react with aldehydes in the presence of $BF_3 \cdot OEt_2$ to give erythro aldols predominantly.9) Mukaiyama also reported the remarkably high erythro-selective aldol condensations using tin(II) enolates generated in situ by the oxidative addition of α-substituted α-bromoketones to metallic tin.10)

We would like to report herein that enaminosilanes,11) which are nitrogen-analogues of silyl enol ethers, react readily with aldehydes in the presence of an equimolar amount of Lewis acid catalysts under kinetic conditions to afford aldols in good yields.

Aldol reactions were carried out by adding a dichloromethane solution of enaminosilane (1 equiv.) to a mixture of aldehyde (1 equiv.) and Lewis acid



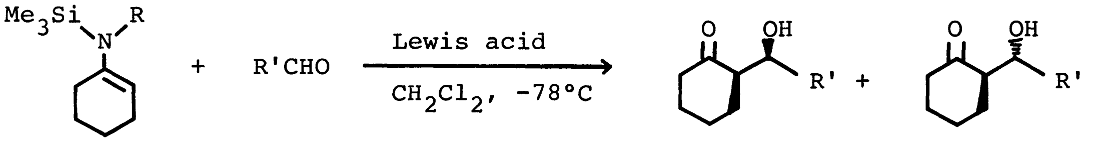
(1)

1-a ($R=n-C_4H_9$)

1-b ($R=c-C_6H_{11}$)

1-c ($R=n-C_8H_{17}$)

(erythro) (threo)



(2)

2 ($R=c-C_6H_{11}$)

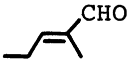
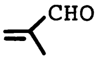
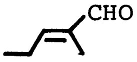
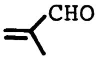
(erythro) (threo)

(1 equiv.) in dichloromethane at -78°C under anhydrous conditions. The reaction proceeds rapidly, and the conversion was almost quantitative. Details of the reaction conditions are given in Table 1. In the first place, enaminosilanes 1-a - 1-c derived from 3-pentanone which have (E)-geometry allowed to react with benzaldehyde to give aldol adducts in high yield when an equimolar amount of $BF_3 \cdot OEt_2$ was employed (Entries 1, 3, and 9). The preferences of the erythro adduct were obtained from (E)-enaminosilanes, and this ia a contrast to the report that (E)-silyl enol ethers react with aldehydes in the presence of $TiCl_4$ as the best Lewis acid-catalyst under kinetic control to afford threo aldols selectively.7) With enaminosilanes, $TiCl_4$ exhibited low levels of both threo-erythro diastereoselection and isolated yield (Entries 4, 10, and 13).

The influence of increased alkyl group bulkiness on N atoms reveals that the more hindered enaminosilane 1-b ($R=c-C_6H_{11}$) exhibited better kinetic selection than the less hindered one 1-a ($R=n-C_4H_9$). No significant difference in stereoselection, however, was noted between enaminosilanes 1-b ($R=c-C_6H_{11}$) and 1-c ($R=n-C_8H_{17}$) (Entries 3 and 9).

The aldol reaction of enaminosilane 2 derived from cyclohexanone also showed moderate erythro-selectivity (Eq. 2) (Entries 12 and 14). There is no simple way to prepare erythro aldols from cyclic ketones, because the enolates are geometrically fixed in the (E)-form, with notable exception that the reaction of triphenylstannyl-,12) bis(cyclopentadienyl)chloro-zirconium-,13) TAS- and

Table 1. Aldol condensation using enaminosilane

Entry	Enaminosilane	Lewis acid	Aldehyde	Reaction time/ min	Yield/% a)	Ratio of threo/erythro b)
1	1-a ($R=n\text{-}C_4H_9$)	$BF_3 \cdot OEt_2$	PhCHO	5	86	46/54
2	1-a	$BF_3 \cdot OEt_2$		5	86	30/70
3	1-b ($R=c\text{-}C_6H_{11}$)	$BF_3 \cdot OEt_2$	PhCHO	5	82	25/75
4	1-b	$TiCl_4$	PhCHO	5	65	35/65
5	1-b	$BF_3 \cdot OEt_2$	${}^{i}PrCHO$	5	86	15/85
6	1-b	$BF_3 \cdot OEt_2$	${}^{n}PrCHO$	5	93	20/80
7	1-b	$BF_3 \cdot OEt_2$		5	71	16/84
8	1-b	$BF_3 \cdot OEt_2$		5	79	28/72
9	1-c ($R=n\text{-}C_8H_{17}$)	$BF_3 \cdot OEt_2$	PhCHO	10	90	17/83
10	1-c	$TiCl_4$	PhCHO	5	60	38/62
11	1-c	$BF_3 \cdot OEt_2$		10	86	33/67
12	2 ($R=c\text{-}C_6H_{11}$)	$BF_3 \cdot OEt_2$	PhCHO	10	87	30/70
13	2	$TiCl_4$	PhCHO	5	50	48/52
14	2	$BF_3 \cdot OEt_2$	${}^{i}PrCHO$	5	91	35/65

a) Isolated yield by column chromatography or bulb-to-bulb distillation.

b) Aldol ratio determined by NMR.

trialkoxytitanium enolates[14)] afforded erythro product. Thus, the reaction presented here offers another method to obtain erythro aldols from cyclic ketones. While either a six-membered cyclic mechanism or an acyclic transition state is involved, the reason for the preferential formation of the erythro aldols is not clear.

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