Introduction

In 1980 Mukaiyama et al. published the first synthesis of di-\textit{n}-butylboryl trifluoromethanesulfonate (Bu$_2$BOTf) and demonstrated that this Lewis acid is particularly suitable for the generation of vinyloxyboranes (boron enolates).\textsuperscript{1} In the presence of a sterically hindered amine base (typically \textit{i}-Pr$_2$EtN, Et$_3$N or 2,6-lutidine) and Bu$_2$BOTf, vinyloxyboranes are conveniently prepared from active methylene-carbonyl containing compounds. The boron enolates turned out to be efficient intermediates for addition to carbonyls in cross-aldol reactions. With unsymmetrical ketones, use of Bu$_2$BOTf and \textit{i}-PrEt$_2$N results in the regioselective formation of the vinyloxyborane at the least hindered carbon. The relative stereochemistry of the new chiral centers formed in the aldol product is a direct consequence of vinyloxyborane enolate geometry with \textit{Z}-enolates affording the \textit{2,3-syn} aldol products and the \textit{E}-vinyloxyboranes leading to the \textit{2,3-trans} isomers. With Bu$_2$BOTf a remarkably high stereoselectivity towards the \textit{Z}-enolate is observed which results in highly \textit{syn}-selective aldol reactions. Probably the greatest utility of this reagent has been in the stereoselective formation of vinyloxyboranes attached to a chiral auxiliary.\textsuperscript{2} These are typified by the chiral oxazolidinones derived from \textit{\alpha}-amino alcohols initially developed by Evans. This modern methodology is a powerful tool for the highly enantioselective construction of two new chiral centers in an aldol addition under recycling of the auxiliary. Vinyloxyboranes also react with electrophiles other than aldehydes, furthermore it is possible to generate boryl azoenolates with Bu$_2$BOTf. In the area of macro lactonization Bu$_2$BOTf has also been used.

Preparation of Bu$_2$BOTf

Bu$_2$BOTf is commercially available as a 1 M solution in CH$_2$Cl$_2$ or Et$_2$O. However it is recommended that the reagent is freshly prepared and used pure, as the quality of stored Bu$_2$BOTf decreases quite rapidly due to its high moisture and air sensitivity. Bu$_2$BOTf is synthesised from tri-\textit{n}-butylborane and trifluoromethanesulfonic acid; the product is isolated by vacuum distillation under argon.\textsuperscript{1,3}

Abstracts

(A) In early applications Bu$_2$BOTf was used to form boron enolates, which undergo diastereoselective aldol additions (\textit{syn}). The stereoselectivity was found to be dependent on the temperature; the reaction at lower temperature (\textdegree\textit{78 C}) gave rise to a high stereoselectivity, a fairly good selectivity was observed at room temperature.\textsuperscript{1}
(B) Control of the regiochemistry is possible. Only one of the regioisomers of cross-aldols is produced without being accompanied by a detectable amount of the other regioisomers.1

\[
\begin{align*}
\text{Ph} & \quad \text{O} & \quad \text{Ph} \\
\text{C} & & \\
\text{H} & & \\
\text{O} & \quad \text{Ph} & \quad \text{OH} \\
\text{Ph} & & \\
\text{O} & \quad \text{Ph} & \quad \text{OH}
\end{align*}
\]
\[(1) \quad \text{Bu}_2\text{BOTf}, \quad \text{i}-\text{Pr}_2\text{NEt} \quad (2) \quad \text{PhCHO} \quad 84\% \quad \text{ratio} = 100 : 0\]

(C) The use of a chiral auxiliary attached to the vinyloxyboranes makes it possible to control the absolute stereochemistry of the new chiral centers formed in the aldol process. This chemistry initially developed by Evans,2,4 is nowadays an important tool in stereoselective synthesis and has found wide application in the field of total synthesis.

\[
\begin{align*}
\quad \text{O} & & \quad \text{Ph}
\quad \text{O} & \quad \text{N}\quad \text{Pr}
\quad \text{O} & \quad \text{Ph} & \quad \text{OH}
\quad \text{Ph} & & \\
\quad \text{O} & \quad \text{Ph} & \quad \text{OH}
\end{align*}
\]
\[(1) \quad \text{Bu}_2\text{BOTf}, \quad \text{i}-\text{Pr}_2\text{NEt} \quad (2) \quad \text{PhCHO} \quad \text{ratio} = 500 : 1 \quad 88\%
\quad \text{ratio} = < 1 : 500 \quad 89\%\]

(D) Vinyloxyboranes also react with electrophiles other than aldehydes. For example chiral bromides can be synthesised stereoselectively using \textit{N}-bromosuccinimide as the electrophile source.5

\[
\begin{align*}
\quad \text{O} & & \quad \text{Et}
\quad \text{O} & \quad \text{N}\quad \text{Pr}
\quad \text{O} & \quad \text{Br} & \quad \text{OH}
\quad \text{Br} & & \\
\quad \text{O} & \quad \text{Br} & \quad \text{OH}
\end{align*}
\]
\[(1) \quad \text{Bu}_2\text{BOTf} \quad \text{i}-\text{Pr}_2\text{NEt} \quad (2) \quad \text{NBS} \quad \text{ratio} = 94 : 4 \quad (\text{only one isomer shown respectively})\]

(E) The formation of boryl azaenolates proceeds smoothly, and they condense with various substituted benzaldehydes to yield \(\beta\)-hydroxy nitrile products.6 For instance 2-ethylpyridine gives predominantly the 2,3-\textit{syn} aldol product.7

\[
\begin{align*}
\quad \text{O} & & \quad \text{Et}
\quad \text{O} & \quad \text{N}\quad \text{Pr}
\quad \text{O} & \quad \text{Bn} & \quad \text{OH}
\quad \text{Bn} & & \\
\quad \text{O} & \quad \text{Bn} & \quad \text{OH}
\end{align*}
\]
\[(1) \quad \text{Bu}_2\text{BOTf}, \quad \text{Et}_3\text{N} \quad (2) \quad \text{PhCHO} \quad \text{ratio} = > 500 : 1 \quad 88\%
\quad \text{ratio} = < 1 : 500 \quad 89\%\]

(F) In the presence of 1 equivalent of \textit{Bu}_2\text{BOTf} trimethylsilyl \(\omega\)-trimethylsilyloxycarboxylates cyclize to the corresponding macrolides.8

\[
\begin{align*}
\quad \text{TMS} & & \quad \text{CO}_2\text{TMS}
\quad \text{TMS} & & \\
\quad \text{Bu}_2\text{BOTf} & & \\
\quad \text{toluene}, \Delta & & 50-83\%
\end{align*}
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References