**Thiopyridone-Derived Reagents for Peptide Coupling Reactions**

**Preparation of the coupling reagents:**

1. (COCl)\(_2\) (1.2 equiv) in DMF (cat.)
2. CH\(_2\)Cl\(_2\) r.t., 1 h to reflux, 4 h

\[
\begin{array}{c}
\text{Me,N}  \\
\text{O}  \\
\text{NMe}_2
\end{array}
\]

\[
\text{Cl}
\]

\[
\begin{array}{c}
\text{Me,N}  \\
\text{O}  \\
\text{NMe}_2
\end{array}
\]

1. KPF\(_6\) or NaBF\(_4\) (1.2 equiv) in MeCN r.t., 24 h

\[
\begin{array}{c}
\text{N}  \\
\text{R}_3
\end{array}
\]

\[
\text{Cl}
\]

\[
\begin{array}{c}
\text{O}  \\
\text{Me}
\end{array}
\]

\[
\begin{array}{c}
\text{N}  \\
\text{R}_4
\end{array}
\]

**Selected examples for peptide coupling reactions:**

\[
\begin{array}{c}
\text{R}_1
\end{array}
\]

\[
\begin{array}{c}
\text{R}_2
\end{array}
\]

\[
\text{OH}
\]

\[
\begin{array}{c}
\text{R}_3
\end{array}
\]

\[
\text{HCl-NH}_2
\]

\[
\begin{array}{c}
\text{R}_4
\end{array}
\]

\[
\text{OMe}
\]

\[
\begin{array}{c}
\text{N}  \\
\text{R}_3
\end{array}
\]

\[
\text{Cl}
\]

\[
\begin{array}{c}
\text{OMe}
\end{array}
\]

\[
\begin{array}{c}
\text{N}  \\
\text{R}_4
\end{array}
\]

(A or B (1.0 equiv) in MeCN r.t., 3–9 h)

\[
\text{Me}_2\text{N}
\]

\[
\text{NMe}_2
\]

**Significance:** Peptide coupling reagents are extremely important in peptide synthesis. In 1999, Nájera and co-workers reported a method for synthesizing thiopyridone-derived uronium salts as coupling reagents. The reagents were prepared from cheap starting materials, making them more economical than conventional coupling reagents such as HOBt.

**Comment:** By using the thiopyridone-derived reagents as coupling reagents, various dipeptides were synthesized in moderate to excellent yields.