Phosphate-Reagent-Mediated Peptide Coupling Reactions

**Preparation of the coupling reagent:**

\[
\text{EtOCl} + \text{Ph} = \text{N} - \text{N} - \text{O} \xrightarrow{\text{EtN (1.0 equiv)}} \text{EtN} \text{C}(0 \text{C}, 3 \text{h}) \rightarrow \text{N} - \text{N} - \text{O} \xrightarrow{\text{82\%}} \text{DEPBT}
\]

**Selected examples for peptide coupling reactions:**

\[
\text{CbzHN} \xrightarrow{\text{DEPBT (1.1 equiv)}} \text{EtN (2.0 equiv)}} \xrightarrow{\text{THF r.t., 2 h}} \text{CbzHN} \text{OEt}
\]

94\% yield

\[
\text{BocHN} \xrightarrow{\text{DEPBT (1.1 equiv)}} \text{EtN (2.0 equiv)}} \xrightarrow{\text{DMF r.t., 4 h}} \text{BocHN}
\]

82\% yield

**Significance:** Peptide coupling reagents are extremely important in peptide synthesis. In 1999, Goodman and co-workers reported the development of the phosphate reagent 3-(diethoxyphosphoryloxy)-1,2,3-benzotriazin-4(3H)-one (DEPBT) as a coupling reagent that can be easily prepared from diethyl chloridophosphate and 3-hydroxy-1,2,3-benzotriazin-4(3H)-one.

**Comment:** By using DEPBT as a coupling reagent, various peptides can be synthesized in excellent yields.