Extension of Native Chemical Ligation

**Significance:** The authors have extended the applicability of native chemical ligation (NCL) of unprotected peptide segments by the use of X-Gly and Gly-X ligation sites. This increases the number of suitable sites for NCL by a factor of three, to include more than 50 of the 400 dipeptide sequences found in proteins.

**Comment:** In this NCL method, the [peptide]$_1^{\text{Boc}}$COSR reacts with a second peptide having an N$^\alpha$-[oxy]ethanethiol group to afford the thioester-linked product, which rearranges to form a ligation product linked by an N-substituted amide bond. In addition, the substitution on the amide bond can be removed by treatment with Zn in acidic medium.