## Category

## Peptide Chemistry

## Key words

native chemical ligation

amide bond

thioester link

polypeptides

proteins



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Extending the Applicability of Native Chemical Ligation *J. Am. Chem. Soc.* **1996**, *118*, 5891–5896.

## **Extension of Native Chemical Ligation**



.CO<sub>2</sub>H  $H_2N$ 1 - Boc 3 2. (BrCHRCO)<sub>2</sub>O (or) NO<sub>2</sub> peptide (resin) resir H₂N 4. HF 5. reduction (for n = 1) peptide peptide resin  $n = 1, X = CH_2, PG = S(3-HO_2C-4-O_2NC_6H_3)$  $n = 1, X = CH_2$ n = 2, X = O  $n = 2, X = O, PG = CH_2(4-MeC_6H_4)$ 

Synthesis of (aminooxy)ethanethiol derivative:



**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<sub>1</sub>]<sup> $\alpha$ </sup>COSR reacts with a second peptide having an N<sup> $\alpha$ </sup>-[(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.

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