

## Sulfide-Mediated Peptide Ligation in Water

Category

Peptide Chemistry

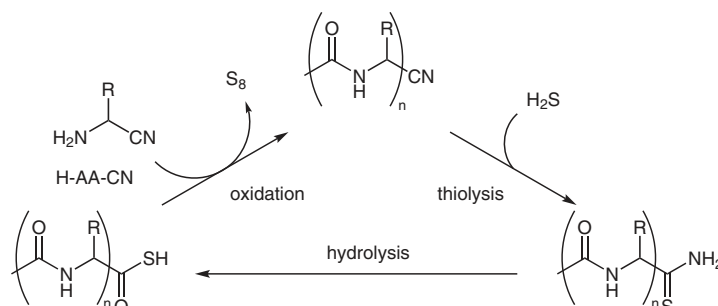
Key words

peptide ligation  
 aminonitriles  
 hydrogen sulfide  
 thioacetates  
 ferricyanides  
 aqueous media

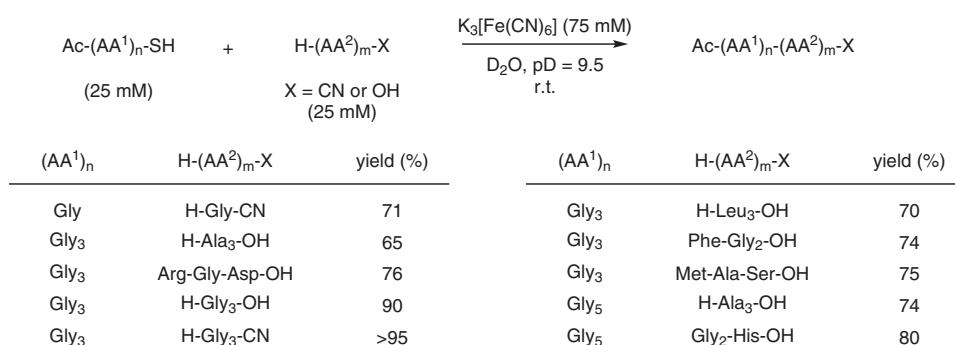
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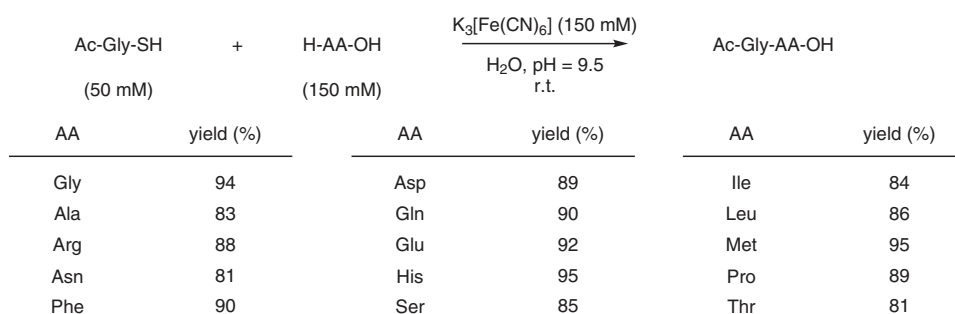
### Ligation cycle:



### Synthesis of oligomeric *N*-acetyl peptides and peptide nitriles by oxidative fragment ligation:



### Synthesis of *N*-acetyl dipeptides:



**Significance:** This work provides a method for achieving  $\alpha$ -peptide ligation in water that tolerates all 20 proteinogenic amino acids. This is extremely important, especially in biochemistry and the life sciences.

**Comment:** The authors have developed a method for chemoselective  $\alpha$ -aminonitrile ligation in water that uses prebiotically plausible molecules such as hydrogen sulfide, thioacetate, and ferricyanide. The  $\alpha$ -peptides are obtained in good to high yields. The model suggests that short *N*-acyl peptides might have served as plausible substrates during the early evolution of life.