

Cysteine Thioaldehydes : Photolytic Generation and Reactivity

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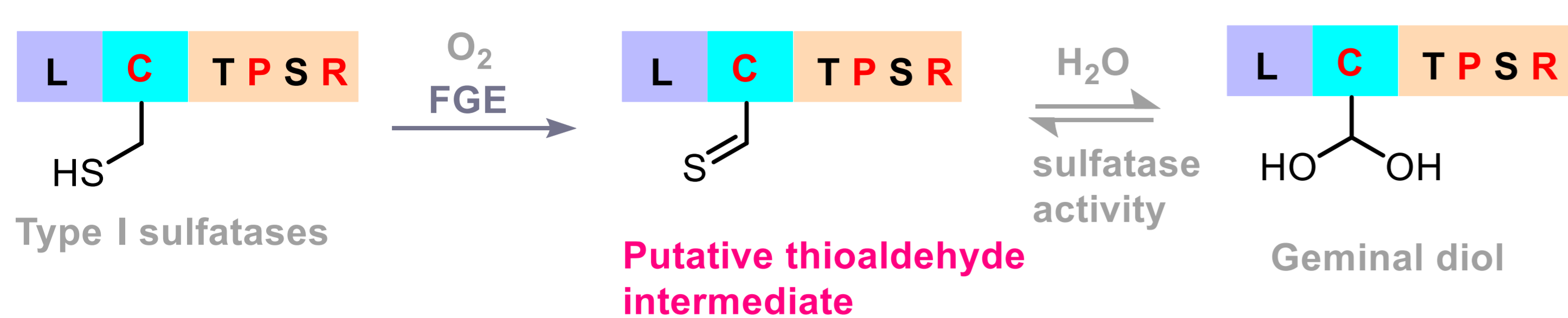
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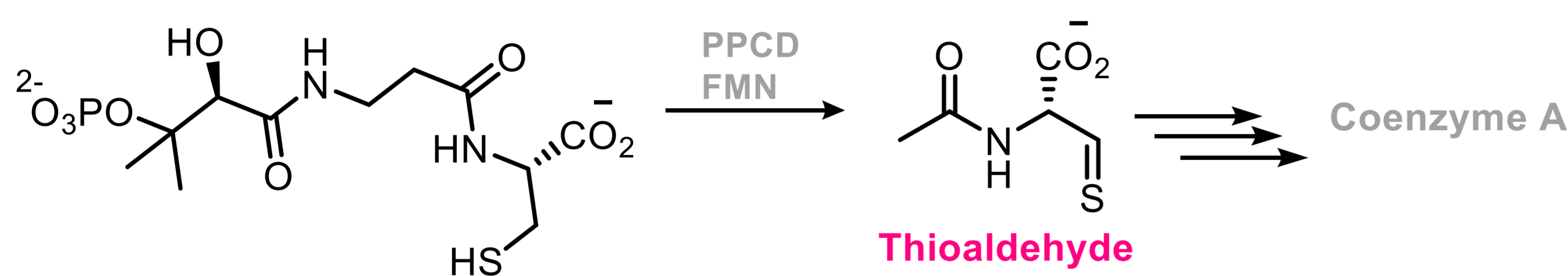
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<https://doi.org/10.17952/37EPS.2024.P2025>

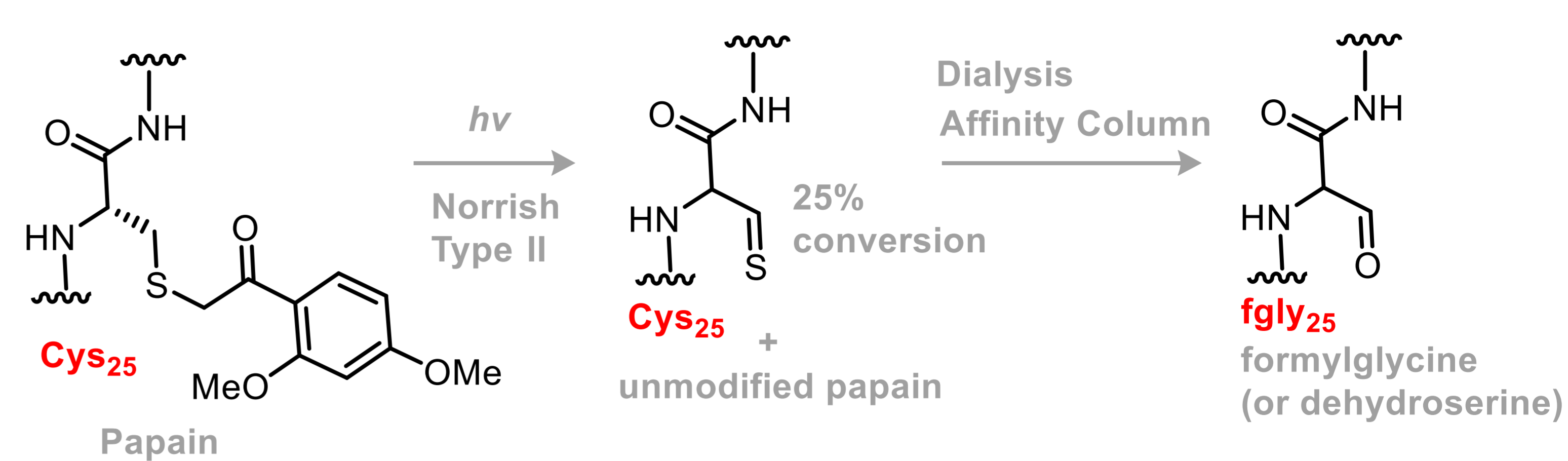
Formylglycine Generating Enzyme¹



Coenzyme A Biosynthesis³

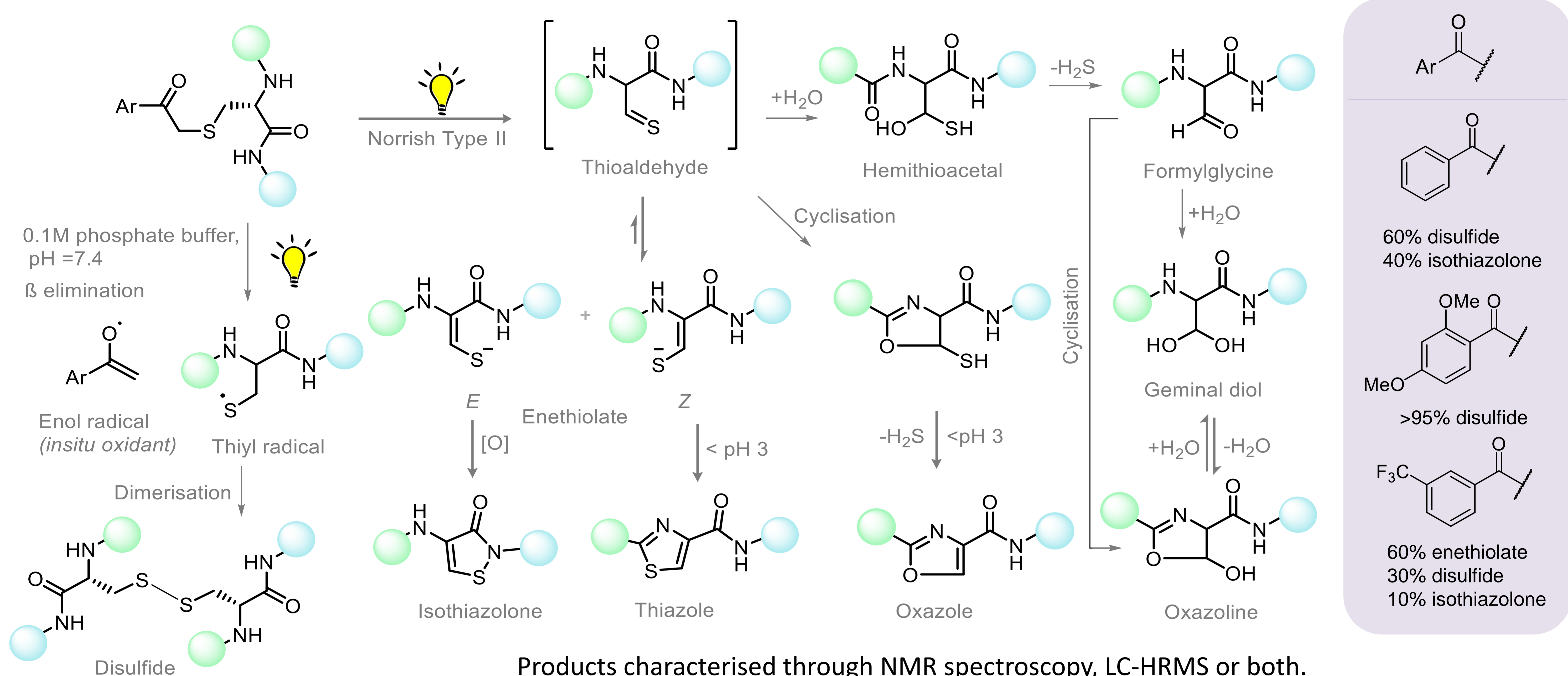


Lowe's Chemical Mutation of Papain²



- Products characterised through enzyme turnover assay
- Multiple rounds needed for complete alkylation and photolysis

Photolytic generation of thioaldehyde⁴



Products characterised through NMR spectroscopy, LC-HRMS or both.

Photolysis of alkylated peptide – AACTPSRGSLFTGRG

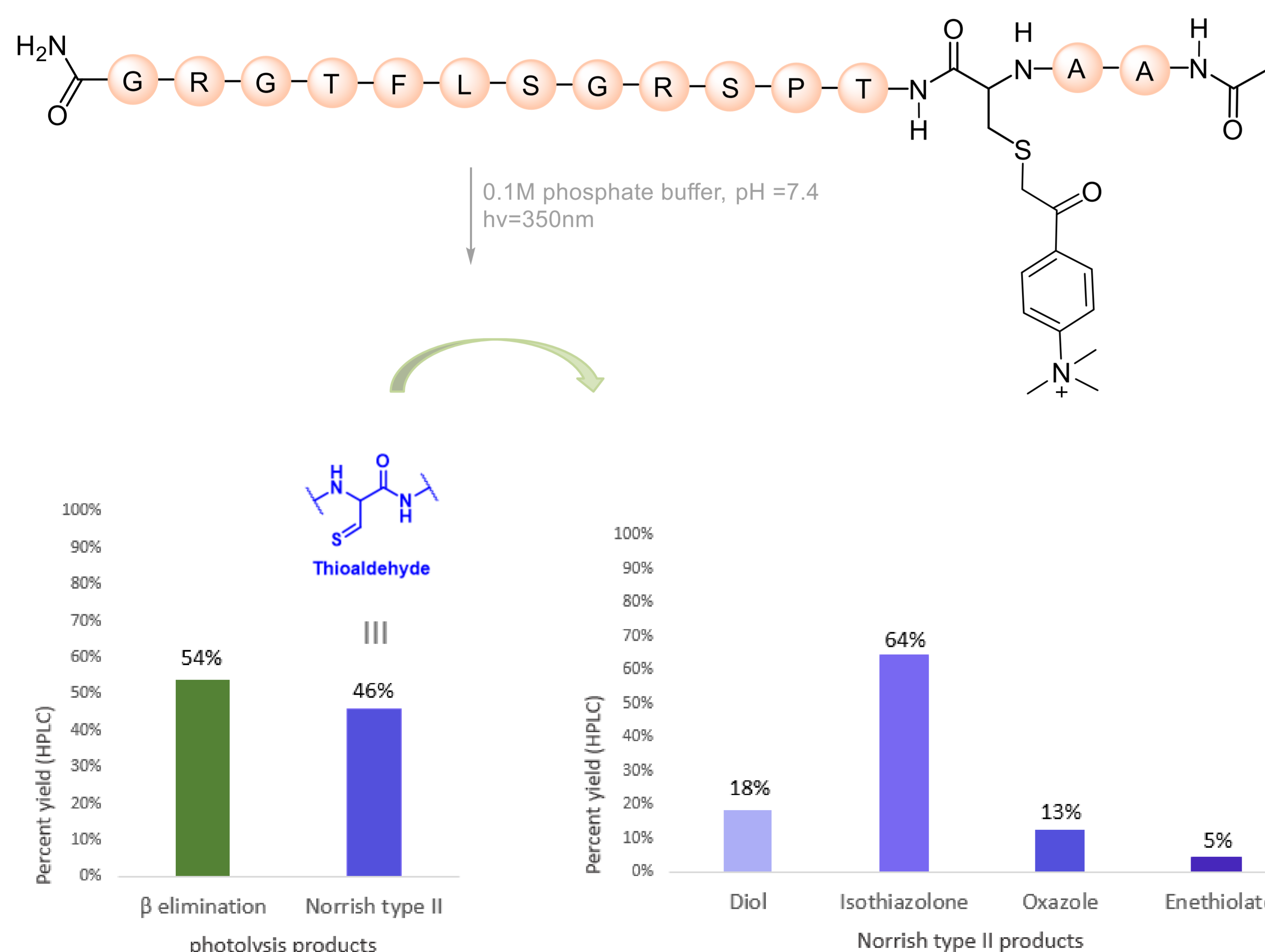


Figure 1: (Left) Partitioning of photolysis pathways, (Right) Distribution of products arising from further reaction of thioaldehyde.

Efficiency of thioaldehyde hydrolysis depends on sequence of peptide.

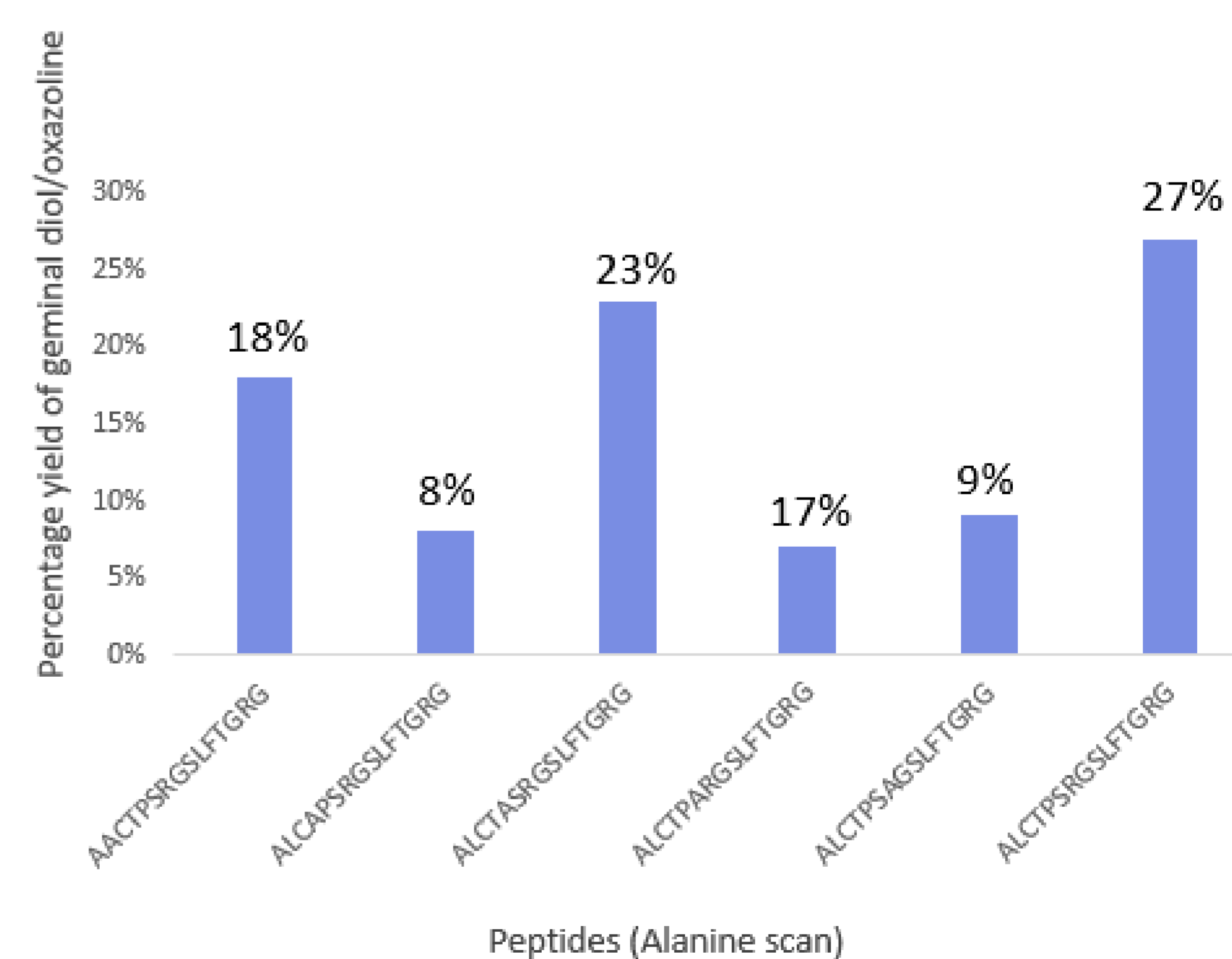


Figure 2: Percentage yield of geminal diol/oxazoline for peptides having the consensus sequence of FGE substrate, where each amino acid in the consensus sequence is replaced by alanine.

Conclusion

1. Cysteine thioaldehydes are highly reactive, undergoes rapid hydrolysis to thiohemiacetals and then to formylglycine. They also undergo tautomerisation to the enethiolate E, which is susceptible to oxidation to form isothiazolone and enethiolate Z, which undergoes cyclisation under acidic conditions to form thiazole.
2. Structure of the peptides have a profound effect on the yield of geminal diol/oxazoline formed from thioaldehyde, where each amino acid contributes to the formation and stability of geminal diol/oxazoline.
3. Hydrolysis of thioaldehyde to formylglycine by FGE is not trivial but carefully designed by enzyme in such a way that the thioaldehyde formed is completely hydrolysed to formylglycine/geminal diol in the active site in the presence of a water molecule thereby preventing all other possible reaction pathways.

References

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