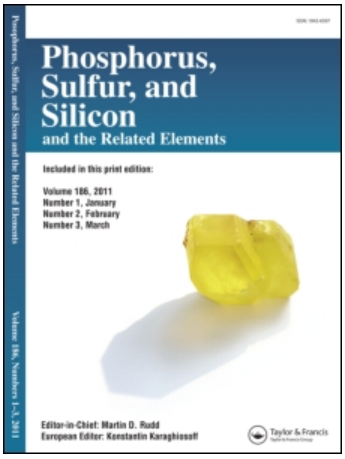

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The Development of Stable 3-Nitro-2-pyridinesulfenyl Reagents and Their Application to Peptide Chemistry

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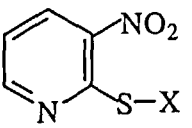
Development of 3-Nitro-2-pyridinesulfenyl (Npys) halide reagents and their application to peptide chemistry are discussed

Developing a new reagent or a reaction which can modify enzymes or receptors under biological conditions and can regenerate again their native forms and activities, is one of the challenging field of organic chemistry. 3-Nitro-2-pyridinesulfenyl (Npys) halide reagents were developed on this line and it was the first isolated solid among nitrogen-containing heterocyclic sulfenyl halides which was found to be extraordinarily stable.[1]



"PROTECTION AND ACTIVATION" CONCEPT OF FUNCTIONAL GROUP

Npys halide reacts smoothly with amino, hydroxyl, and thiol functional groups to afford sulfenamide, sulfenate, and disulfide, respectively. The Npys group was found to be useful for the protection and activation of these functional groups. The Npys group was stable against strong acids such as trifluoroacetic acid but was selectively removed under neutral conditions using triphenylphosphine or 2-pyridinethiol 1-oxide without affecting conventional protecting groups.[2]

Most importantly, the S-N or S-O bond of Npys derivatives could be activated by tertiary phosphine to form, in the presence of COOH function, a peptide or an ester linkage via oxidation-reduction condensation which is so called "Mukaiyama Reaction".

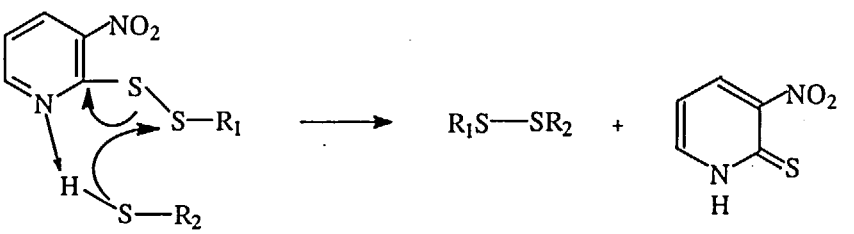
$$R^1COOH + Npys\text{-}NHR^2 + R^3{}_3P \longrightarrow R^1CONHR^2 + R^3{}_3P{=}O + NpysH$$

SOLID PHASE PEPTIDE SYNTHESIS USING NPYS-AMINO ACIDS

The solid phase peptide synthesis by the use of Npys-amino acids does not need a strong acid such as trifluoroacetic acid for t-butyloxycarbonyl(Boc)-strategy or strong base such as piperidine for fluorenylmethloxycarbonyl(Fmoc)-strategy, and it can be carried out under neutral or neutralized conditions.The whole reactions from the attachment of the first amino acids to the cleavage of peptide from the resin at the last step can be carried out in the same vessel, and all the procedures are fully automated.[3]

AFFINITY LABELING OF RECEPTORS OR ENZYMES WITH THIOL FUNCTIONS

The S-S bond of Npys-substituted thiol functions could be activated by another free thiol function to produce an asymmetrical disulfide bond by stoichiometric reaction.



This reaction took place over a wide pH range under biological conditions and specific affinity labeling ligands to each μ, δ, κ opiate receptor[4] and inhibitors to enzymes such as cathepsin B, calpain[5], endo-oligopeptidase A[6] were developed.

REFERENCES

1. R. Matsueda and K. Aiba, *Chem. Lett.*, 951 (1978).
2. R. Matsueda and R. Walter, *Int. J. Peptide Protein Res.*, **16**, 392 (1980).
3. S. Ikeda, T.Yokota, K. Watanabe, M. Kan, Y. Takahashi, T. Ichikawa, K. Takahashi, and R. Matsueda, *Peptide Chemistry 1985* (Peptide Research Foundation,Osaka, 1986), p. 115.
4. R. Matsueda, K. Koike, and I. Takayanagi, *Chem. Pharm. Bull.*, **41**, 1312 (1993).
5. R. Matsueda, H. Umeyama, R. N. Puri, H. N. Bradford,and R. W. Colman, Chem. *Lett.*, 191 (1990).
6. M. D. Gomes, L. Juliano, E. S. Ferro, R. Matsueda, and A. C. M. Camargo, *Biochem. Biophy. Res. Commun*, **197**, 501 (1993).