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Short Commentary Open Access

Replacement of "Amide Chemistry" with "Click Chemistry": Current Trend in Proteomics

Rituraj Dubey[1] and Ravi Bhushan[2]

[1]*Department of Chemistry, National Cheng-Kung University, Tainan, Taiwan*
[2]*Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee, India*

Short Commentary

In the past decades of proteomics research, amide chemistry played a vital and indispensable role. Presence of amino and carboxylic groups in proteins, availability of respective amide/carboxyl and amine labeled ligands and mild reaction environment for corresponding amide chemistry have fulfilled the requirement of advanced proteomics research. We have used the amide chemistry for enantioseparation of biologically important amino acids in recent years [1-3]. But in recent years amide chemistry has lost its importance to quite an extent due to its one drawback: on account of ample presence of amino and carboxylic groups it has become kind of "non-selective" reaction. The use of liquid chromatography-mass spectrometry and its variations in proteomics research [4,5] has widen the gap of conventional amide chemistry protocol and current click-chemistry protocol.

Copper(I)-catalyzed synthesis of 1,4-disubstituted 1,2,3-triazoles *via* Huisgen 1,3-dipolar cycloaddition of terminal alkynes and organic azides is termed as "click chemistry" reaction [6-8]. It involves alkyne and azide reactants which are chemically stable to common functional groups of organic reagents and biomolecules [9,10]. These reactants react irreversibly and regiospecifically to yield triazoles under mild conditions with few byproducts. Since it utilizes Cu(I)-catalytic environment, stable to variations in pH and the solvents, it has been significantly applied to modify a vast range of complex functionalities of biomolecules. Besides, it is also unaffected to the presence of other functional groups in the reactants. Thus click chemistry has become a fruitful and emerging area in the field of organic modification in biochemistry due to its excellent "super-selective" behavior. Hence it has been incorporated, developed and significantly utilized in the vast fields of chemistry and biology, especially proteomics as specific reactivity of azide and alkynes minimizes off-target effects and produces very low background.

As the research in proteomics progressed, some drawbacks of copper(I)-catalyzed reactions were discovered, e.g. Cu(I) is toxic to cells [11,12] possibly binds to some active sites of enzymes, reduces biological activity of enzymes, and easily disproportionate in aqueous environment which leads to reduction in the rate of reaction. These problems in proteomics research has given birth to Cu-free 1,3-dipolar cycloaddition reactions which has led to the development of strain-promoted cyclooctyne, oxanorbornadiene or dibenzocyclooctyne systems, for fast and "super-selective" reactions with azide-labeled biomolecules.

With incorporation of highly sensitive fluorescence molecules (as markers) and their respective sophisticated detection instruments in recent times [13,14] "super-selective" behavior of "click chemistry" has made it as an indispensable feature in proteomics research. There is expected a growth in this current trend of wide replacement of "amide chemistry" with "click chemistry".

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***Corresponding author:** Ravi Bhushan, Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee-247667, India, Tel: +91-1332-285795; Fax: +91-1332-286202; E-mail: rbushfcy54@gmail.com; rbushfcy@iitr.ac.in

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