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Article Review

Processes of 1,3-Dipolar cycloaddition in nucleoside, nucleotide and bio conjugation and its importance in medicinal chemistry

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Abstract: In the 1,3-dipolar cycloaddition, a 1,3-dipole and a dipolarophile interact chemically to produce a five-membered ring. The Huisgen cycloaddition occurs when an organic azide and an alkyne unite to form a 1,3-dipolar cycloaddition that results in a 1,2,3-triazole. 1,3-dipolar cycloaddition is an essential step in the regio- and stereoselective synthesis of five-membered heterocycles and their ring-opened acyclic derivatives. Some of the cycloadducts produced by these reactions were converted into enantiopure precursors known to exist in some biologically active chemicals as well as an active stereoisomer of a pine sawfly sex pheromone. The synthesis of several new enantiopure organocatalysts that were shown to be helpful in some The synthetic utility of these 1,3-dipolar cycloaddition processes with nitrones and a,b-unsaturated aldehydes was further demonstrated. There are times when these reactions have modest to moderate diastereofacial selectivity. the choose actual and nonracemic have improved. Compound collections are created in chemical biology research using the BIOS concept, which draws its inspiration from natural product scaffolds. In BIOS, the primary criterion utilized to develop hypotheses for the design and synthesis of targeted chemical libraries is biological relevance. Because they outline the chemical domains that nature has explored, the underlying scaffolds of natural product classes in particular serve as an inspiration for BIOS because they can be thought of as "trivet can often be achieved if both the azomethine ylide and the dipolarophile are chi privileged .

Keywords*: *Cycloaddition, Huisgen azide-alkyne reaction, biocongugation , nucleoside and nucleotide

1. Introduction

The dynamic nature of the pharmaceutical sector has given rise to numerous revolutionary technologies and creative concepts for the creation of new chemical entities. In the last two decades, scientists working in related fields have given per cyclic processes like electro cyclic addition , cycloaddition , and sigma tropic rearrangement a high priority.. Cycloaddition reactions continue to be the most notable among them [1] . Cycloaddition reactions come in a variety of forms, including (2+2), (4+2), (1+3), and others. The Diels-Alder reaction is an illustration of the (4+2) cycloaddition reaction. In this reaction, A dienophile's response to a dine at about (250)°C to produce an adduct of cycloaddition that contains Medicinal compounds called anthraquinones significant component found in numerous plants including Sienna, Cascara, rhubarb, and Laxative properties are provided by aloe.. 2-3 . These authors want to draw attention to a few uncommon or

recent cycloaddition reactions and their significance to the pharmaceutical community in the current work. When Sharp Less and others came up with the idea of "click chemistry," they brought back into focus the Acrylates and azides undergo a 1,3-dipolar cycloaddition process. [2] . This strategy, which is built on combining smaller parts, is similar to how nature produces chemicals. This idea uses reactions that are stereospecific, wide-ranging, modular, high yielding, and only produce harmless by-products to efficiently find new beneficial chemicals.. Also necessary for a process to be fully "click" are straightforward reaction conditions, easily accessible starting materials and reagents, the absence of solvents or the use of harmless or easily removed solvents [3].

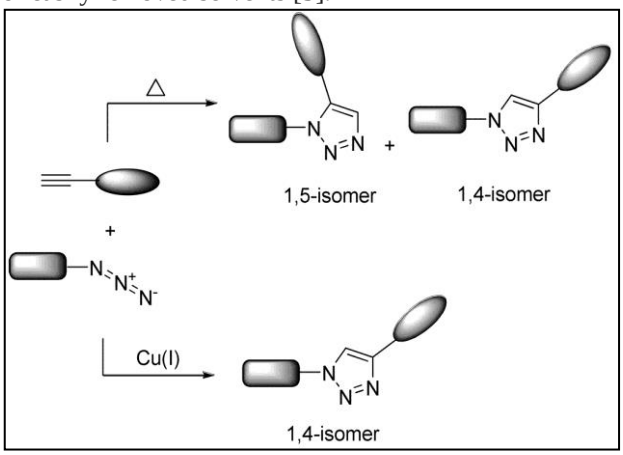
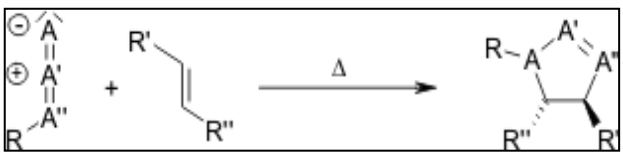


Fig (1) : Azides and Alkynes Under 1,3-Dipolar Cycloaddition

Heisenberg cycloaddition:

During the azide-alkyne Huisgen cycloaddition, an orthogonal coupling reaction occurs (often referred to as "Click chemistry"). does not conflict with the functionalities contained in proteins. Cu (I) or an alkyne that has been strained can both catalyze the production of triazole. With the help of a cysteine residue, this technique in particular enables the site-specific directed coupling of two distinct ligands (e.g., PEG, and a radio ligand or fluorophore) [4] . This method does call for the use of non-natural amino acids to introduce an alkyne or an azido functionality into the protein. By using a Met auxotroph strain, the D. Terrell group has demonstrated that the methionine analogs azidohomoalanine (Aha) or homopropargylglycine (Hpg) can be included in recombinant proteins in E. coli in high yields.



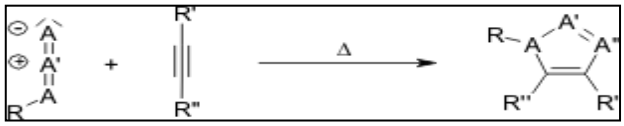


Fig (2): 1,3-Dipolar Cycloaddition

In the Huisgen Cycloaddition, a dipolarophile combines with a 1,3-dipolar molecule. to produce 5-membered (hetero)cycles. Alkenes, alkynes, and compounds with similar heteroatom functional groups are examples of dipolarophiles (nitriles and carbonyls, for example). Dipolar 1,3-compounds can be thought of as having a mesmeric structure at least that represents an electric dipole and one or more heteroatoms [5] .

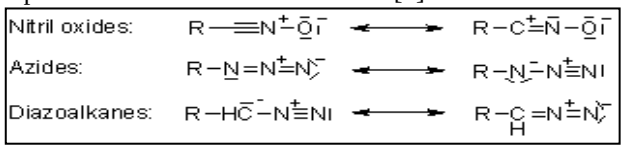


Fig (3): linear, propargyl-allenyl-type dipoles

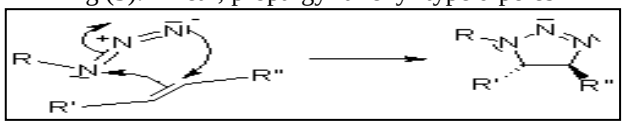


Fig (4): Mechanism of the Huisgen reaction

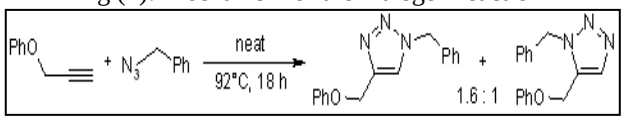


Fig (5): addition alkynes to azides

The cycloazide-alkyne reaction (Click Chemistry):

The "click" reaction, also known as the alkyne-azide cycloaddition, has been extensively used in the build-up of molecules and macromolecules and has enormous promise for the creation of a range of fields, including biology, could benefit from the usage of nanomaterials.. [6]. High efficiency and adaptability to the environment where the proposed covalent connecting of the azide and alkyne terminated moieties needs to be carried out are two benefits of this coupling. An ongoingly popular research topic involves the effective delivery of active pharmacological ingredients to particular organelles utilizing nanocarriers created using "click" chemistry and their very selective cycloaddition process produces 1,2,3-triazoles. [7] .

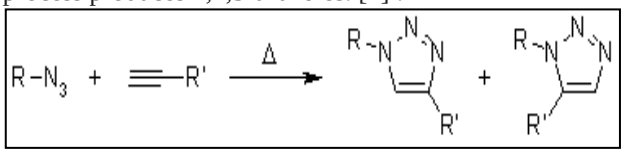


Fig (6): 1,2,3-triazoles

Click reactions occur in a single pot, are unaffected by water, generate a high yield of a single reaction product with a strong reaction specificity, and are "spring-loaded" defined by a strong thermo dynamic driving force that propels it fast and irreversibly to this

product (in some cases, with both regio- and stereo-specificity). These features make click reactions particularly suitable for the task of identifying and sorting molecules in complex biological contexts.. Products must be physiologically stable, and any byproducts cannot pose a risk under these circumstances. Click chemistry is widely used in business. The fluorophore rhodamine reacted with tetrazine and was related to norbonene in living systems [8]. In other cases, the selection of these proteins in cell lysates was assisted by SPAAC between a fluorophore with cyclooctyne modification and proteins with an azide tag.

Copper-Catalyzed Cycloaddition of Azide and Alkyne:

The reactions of organic azides and alkynes that are catalyzed by copper species are the classic examples of click chemistry.. Since then, improvements have been made to the so-called CuAAC reaction, also known as the copper-catalysed azide-alkyne cycloaddition, making it an ideal tool for organic synthesis. According to the kind of catalyst precursor, copper(I) or copper(II) salts or complexes, metallic or nano-particulated copper, and a number of solid-supported copper systems are divided into several categories [9].

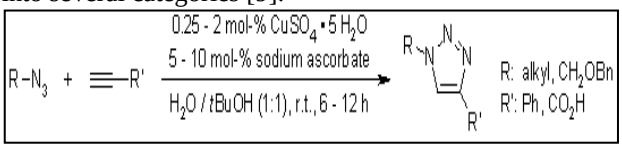


Fig (7): Copper-Catalyzed reaction

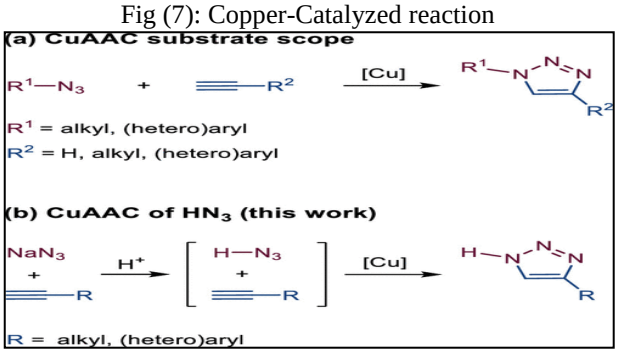


Fig (8) a/ CuAACS substrate scope /b/ Increasing the range of substrates for CuAAC

. The term "catalytic cycle" refers to a multistep reaction mechanism including a catalyst. The catalytic cycle is the primary method for explaining how catalysts work in fields such as materials science, biology, organometallic chemistry, and so forth.

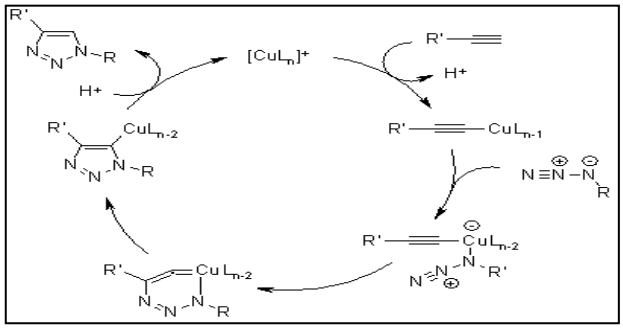


Fig (9): Mechanism of catalytic cycle.

Cu-catalyzed azide alkyl reaction for bio conjugation:

The copper-catalyzed cycloaddition reaction involving azides and alkynes takes place satisfactorily in aqueous solution in the presence of a tris (triazolyl) amine ligand. . This approach has been used to produce quick and trustworthy covalent connections to protein micromolar oncentrations decorated with any of the reactive moieties. The helating ligand is essential for maintaining the Cu (I) oxidation state and guarding against Cu (triazole)-induced denaturation of the protein. The ligation of the azide and alkyne groups is potentially useful as an universal bioconjugation technique because these groups themselves do not react with protein residues or other biomolecules. [10]. A key technique for the ligation of biomolecules is the Cu-catalyzed azide-alkyne cycloaddition (CuA AC) process. However, the biological value of these compounds is constrained by undesirable Cu-mediated oxidation and Cu-con tamination.

Discrete triazole bioconjugates can be formed quickly, reliably, and broadly spectrally using a general CuAAC flow platform, which is what we're reporting here.

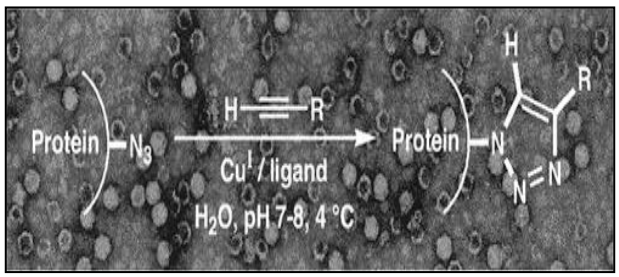


Fig (10): protein for bio conjugation

Biological conjugates, nucleosides, nucleotide and their use in medicine :

The biologically common chemicals nucleosides, nucleotides, and their derivatives are involved in almost all biochemical reactions. They serve crucial functions in the expression and storage of genetic information because they create the monomeric units of nucleic acids. When nucleic acids are broken down chemically or enzymatically, they produce glycosylamines called

nucleosides, which have two parts: a nitrogen base and a five-carbon sugar (ribose or 2' deoxyribose).. The heterocyclic, planar, aromatic nitrogenous bases are molecules. are primarily purine or pyrimidine derivatives [11]. Adenine (A) and guanine (G) residues make up the majority of the nucleic acids' purine components, and cytosine (C), uracil (U), which is mostly found in RNA, and thymine (C), which makes up the majority of the pyrimidine residues. The base compositions in double-helical DNAs and RNAs adhere to Chargaff's rules: A=T(U) and G=C1. Adenosine, guanosine, cytidine, uridine, and deoxythymidine are a few examples of nucleosides.. They serve as signaling molecules and serve as precursors for the nucleotides required for the production of DNA and RNA. Additionally essential to molecular biology and medicine, nucleosides are employed as antiviral or anticancer medicines. Especially in the liver, nucleotides can be converted into nucleosides, but they are more prevalent there. ingested and digested through the diet's nucleic acids, where nucleotidases transform nucleosides (such thymidine) and phosphate from nucleotides, such as thymidine monophosphate [12]. In the lumen of the digestive system, nucleosidases then transform the nucleosides into nucleobases and ribose or deoxyribose. Nucleotides can also be changed into ribose-1-phosphate or deoxyribose-1-phosphate, nitrogenous bases, inside the cell. In medicine, a number of nucleoside analogues are used as antiviral and anticancer drugs.These substances are combined with non-canonical bases by the viral polymerase. By becoming nucleotides, these substances are activated within the cells. Due to the difficulty charged nucleotides have in crossing cell membranes, they are supplied as nucleosides. The sugar backbone has several analogies in molecular biology. Because RNA has a limited degree of stability and is prone to hydrolysis, there are numerous more stable alternative nucleoside/nucleotide analogues that correctly bond to RNA... Utilizing a different backbone sugar allows for this. Included in these analogs are locked nucleic acids [13] .

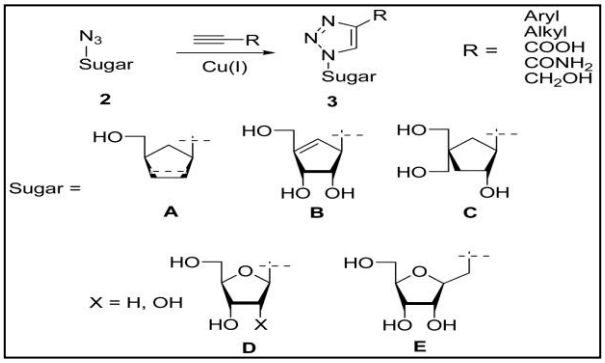


Fig (11): 1,2,3-Triazolo Nucleoside Synthesis

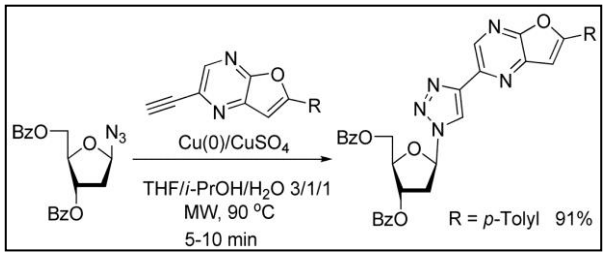


Fig (12): Synthesis of Nucleosides Analogs " Using Microwave Irradiation"

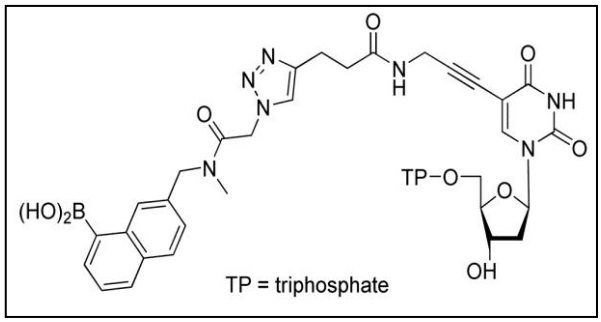


Fig (13): Structure of Boronic Acid

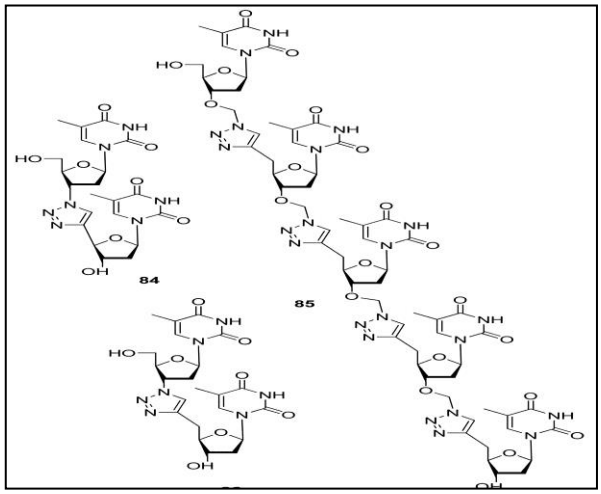


Fig (14): the oligonucleotide structures

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