International Journal of Chemical Sciences

Short Communication| Vol 19 Iss 7

Recent Developments in the Synthesis of Biologically Active 1,2,4-Triazole Glycosides: A review

Hemat S Khalaf *

Department of Photochemistry, National Research Centre, Cairo, Egypt

***Corresponding author:** HS Khalaf, Department of S Photochemistry, National Research Centre, Cairo, Egypt.E-mail: hs_sci@rocketmail.com

Received: July 20, 2021; **Accepted:** August 03, 2021; **Published:** August 10, 2021

Abstract

Triazole was first synthesized over a century ago, but still attracts attention of chemists, biologists, technologists and other specialists. In recent years, antiviral, anti-inflammatory, anti-fertility, anti-tubercular activity, antimicrobial activities, anti-cancer and anti-corrosion properties of triazoles have been published. This review aims to describe the structures, synthesis, reactions and applications in several bioactive phenomena and Industrial uses.

Keywords: 1, 2, 4-Trizole; Thiole derivatives; Applications of 1,2,4-Triazole; Synthetic approaches of 1,2,4-triazole

Introduction

Nowadays, the heterocyclic chemistry brings reagents and synthetic methods of its own usual activity in synthesis of pharmaceutical researches drugs and material sciences. In the last decades, triazole heterocyclic ring system attracts much attention of many researchers all over the world owing to its presence in many naturally and synthetic bioactive compounds Triazole refers to heterocyclic ring having two carbons with three nitrogen atoms; the positions of this nitrogen give two sets of isomers. Each of this isomer has two tautomers that differ by which nitrogen has hydrogen atom. In the same manner, glycosides are a sugar molecule that is bounded by functional group via a glycoside bond, which is a covalent bond that joins carbohydrate hemiacetal or hemiketal group with hydroxyl group of another compound. There are extension in the term glycoside than hydroxyls to include the compounds such as thioglycosides (S-glycosidic bond), seleno glycosides (Se-glycosidic bond), Carba-glycosides (C-glycosidic bond) and even N-glycosides or glycosylamine (N-glycosidic bond).

Therapeutically some active compounds that contain triazole-glycoside moiety have been reported. Due to the presence of triazole-glycoside moiety in some important drugs, interest in the construction of such moiety (single or fused ring) has been aroused. Molecules have triazole ring system were shown to display a wide variety of biological activities such as antiviral, anti-inflammatory, antimicrobial or antitumor and thus potentials for therapeutic application and there are many review on the biological and therapeutic properties [1]. These bioactive properties of triazole ring system arise from its high dipole moment and its aptitude for strong hydrogen bond interaction. Among of these bioactive compounds that combine with triazole are those comprising carbohydrate moieties to form triazolyl glycoconjugates owing to its possession of biological effects such as anti-inflammatory, antimicrobial or antitumor properties.

Description

In many research strategies, triazole derivatives constructed on carbohydrate hetero-analog backbones, frameworks in which the sugar endo-cyclic oxygen atom has been replaced by nitrogen (imino sugars) sulfur (thio sugars) or carbon (carba sugars or cyclitols). These methods of synthesis are used to construct pseudo-sugar analogues to obtain more stable toward

endogenous degradative enzymes, efficient as they do not take part as typical carbohydrate, can inhibit important targets; they resemble sugars, so they can improve the structures of biological mimics and inhibit glycosidase.

Triazolyl glycoconjugates include molecules of triazole moiety linked to a carbohydrate at the anomeric or non-anomeric position. At these compounds, triazole ring lies between saccharide system and its serve as connecting unit, its name is triazole-linked pseudo oligosaccharide or it linked between sugar unit and another motif such as amino acids (glycopeptides) as well as larger compounds such as oligosaccharides (glycoclusters and glycodendrimers) [2].

1,2,4-Triazole-linked sugars *via N*-glycosidic bond

Organic synthesis and drug design techniques uses glycosides with high reactivity, so, (2S,3R,4S,5R)-tetrahydro-2*H*-pyran-2,3,4,5-tetrayl tetrakis (2,2-dimethylpropanoate) 13 reacted with dihalo triazole 14 in the presence of boron trifluoride (BF_3) as activator to afford glycosyl triazole 15 in good yield. Further investigations showed that *C*-alkylated product has been afforded *via C*-alkylation of the new compounds to open a new direction to obtain triazole that contains glycose *via* efficient *N*-alkylation. So, when 1-Iodo-perfluorohexane reacted with dibromo-1,2,4-triazole glycoside 16 (X = Br), it afforded 3-perfluorohexyl-1,2,4-triazole 19 by using cupper catalyst for coupling reaction while 5-position was replaced by hydrogen.

To introduce trifluoromethyl substituent at position 5 of triazole, glycoside triazole 16 is treated with trimethyl(trifluoromethyl)silane (Rupert's reagent), however, this reaction didn't occur while an Ullman-type coupling product was obtained [3]. So, it was generally considered 5-position of 1,2,4-triazole was the most reactive one to attach perfluoroalkyl substituent, instead, the competing hydrodebromination at 5-position proceeded at a faster rate than the coupling reaction, so the perfluoroalkyl group appeared at the 3-position. Preparation of new S-glycosides bearing 1,2,4-triazole moiety is a target to many research groups as antibacterial, anticancer and also because of its significance in many biological processes as presence of glycosides increases their solubility and guidance quality of the compounds are present in plant, animal and have involved properties. On the same line, aryl-mercapto-1,2,4-triazole-S-glycosides were synthesized *via* reaction of 3-aryl-5-mercapto-1,2,4-triazole 30 and tetra-*O*-acetyl- *α*-*D*-gluco-pyanosyl bromide. The resulted products 32 were tested as antibacterial agents. The investigation on the structure-activity relationship shows that hydroxyl group boosts the antibacterial activity of 3-aryl-5-mercapto-1,2,4-triazole-S-glycoside.

1,2,4-Triazole-linked sugars via C-glycosidic bond

Dields–Alder reaction of 1,4-diacetoxybutadiene with methyl cyanodithioformate 43 afforded sugar having sulfur in the ring. *Cis*-hydroxylation of 44 with OsO_4 in pyridine afforded the alcohol which on treatment in acetic anhydride gives tetra-acetate derivatives. Reaction of sugar with chloroazino cummulenes *via* cycloaddition afforded 5-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-D,L-arabino-pentulopyranos-1-yl)-3*H*-1,2,4-triazolium hexachloroantimonate 47 which by arising temperature gave 48. De-blocking of 48 with sodium methoxide in methanol afforded free thionucleosides [4].

Antiviral activity

Ribavirin (RBV) is a ribose-*N*-glycoside 6 that discovered in the beginning of 1970. It is used as antiviral agent containing 3-amino-1,2,4-triazole moiety. It is a broad antiviral agent against DNA and RNA viruses such as hepatitis C virus (HCV), and also it used in treatments of influenza, Hantann virus, in respiratory tract viral disease (RSV) and Lassa fever. While guanidine and amidine of ribavirin has a broad spectrum of antiviral activity.

Antibacterial activity

S-glycosides possessing 1,2,4-triazoles that synthesized from mercapto1,2,4-triazole and tetra-O-acetyl- α-D-glucopyanosyl bromide have screened for the antibacterial activity [5]. The investigation on the structure-activity relationship shows that hydroxyl group boosts the antibacterial activity of 3-aryl-5-mercapto-1,2,4-triazole-S-glycoside.

Conclusion

Heterocyclic 1,2,4-triazole glycoside derivatives possess unusually spacious potentiality as medicinal agents: antiviral, antitumor, antibacterial, antifungal and anti-inflammatory as well as many applications, and their various researches and developments have been being a quite rapidly developing and active highlight topic with an infinite space. Numerous efforts have been directed toward various types of possible applications of 1,2,4-triazole glycoside-based compounds and a lot of important progress has been made, especially their preparations have attracted increasing attention. This review systematically summarized the recent advances in the syntheses of 1,2,4-triazole glycoside derivatives. It was hoped that this review would be helpful for the design and development of highly efficient preparation of 1,2,4-triazole glycoside derivatives with various sorts and varieties of extensively potential applications.

REFERENCES

1. Wang XY, Wang JY, Pei J. BN heterosuperbenzenes: Synthesis and properties. Chem Eur J. 2015;21(9):3528-3539.
2. Chattopadhyay B, Gevorgyan V. Transition-Metal-Catalyzed Denitrogenative Transannulation: Converting Triazoles into Other Heterocyclic Systems. Angewandte Chemie International Edition. 2012;51(4):862-872.
3. Sunil Kumar Bhat, Jagjeet Singh. Simple and Eco-friendly Synthesis of Glycosides bearing triazolo[3,4-b][1,3,4]thiadiazole moiety linked through N atoms. IOSR J App Chem. 2017;10(4):46-49.
4. Malladi S, Isloor AM, Isloor S, et al. Synthesis, characterization and antibacterial activity of some new pyrazole based Schiff bases. Arab J Chem. 2013;6(3):335-340.
5. Prassas I, Diamandis EP. Novel therapeutic applications of cardiac glycosides. Nat Rev Drug Dis. 2008;7(11):926.