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Tetrazole Derivatives and Role of Tetrazole in Medicinal Chemistry: An Article Review

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Abstract

The review generalizes and systematizes in this review the results of research on the synthesis and properties of tetrazole derivatives and the properties of tetrazole compounds, and synthetic routes. In medical chemistry, the tetrazole compounds play a big role in medicinal applications such as antibacterial, anticancer, and effects on the central nervous system.

1. Introduction

Tetrazole is defined as a heterocyclic compound, a five-membered ring that contains carbon with four nitrogen atoms [1,2]. Three isomers of the parent tetrazole exist, differing in the position of the double bonds: 1H-, 2H-, and 5H-tetrazole [3] as shown in Figure 1.

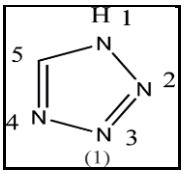


Figure 1. Structure of tetrazole.

2. Tetrazole Structure

The tetrazeride is defined as a five-membered aza structure with six π electrons as Huckel's rule is filled by four electrons from the ring and one pair of electrons from the nitrogen that are on loan. Similar to carboxylic acids, tetrazole is acidic, but the annular tautomerization of ring tetrazoles and carboxylic acids is different [4] as shown in Figure 2.

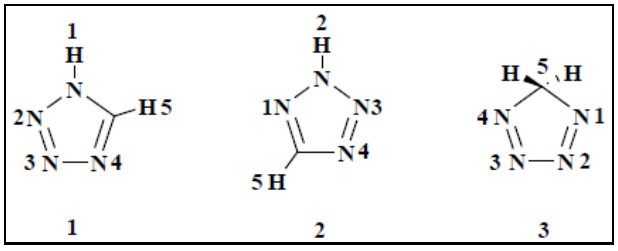


Figure 2. Structures of the regioisomeric tetrazole rings.

3. History of Tetrazole

Bladin discovered the tetrazole compound in 1885 [5]. Many scientists know about the work that American and European scientists have done in the field. Researchers would like to choose some of the following well-known scientists: R. Henry, R. Huisgen, R. Butler, E. Lippmann, M. Begtrup, B. Stanovnik, J. Plenkievich, J. Elguero, M. Palmer, A. Katritzky. Russian scientists have made a lot of progress in tetrazole chemistry [6].

4. Properties of Tetrazole

Tetrazoles have a lot of positive attributes, like low basicity, high acidity, a many of nitrogen atoms, high stability, as well as a high formation enthalpy. They are used as analytical reagents in science, as lipophilic spacers in drug design, as useful antitumor and anticancer agents, peptide inhibitors, beginning materials for making propellants,

energetic materials, and N-containing compounds [7-13]. Since the tetrazole ring is the heterocyclic analogue of compounds like cis-amide and carboxylic acid, it is used to create novel medications. In the metabolism of the body, it is also highly stable. Tetrazoles also work by piling up on top of sites in target tissues where receptors recognize them [14].

1H-Tetrazole looks like a light-yellow powder that is crystalline and has no odour. Tetrazole has a melting point between 155 and 157 °C. Tetrazoles break down when heated and release dangerous nitrogen fumes. Tetrazoles are vigorous acids and weak bases in comparison to other azoles. Unchanged tetrazole functions much like an organic acid, and its pKa value is similar to that of acetic acid [15].

5. Synthesis of Tetrazole

Numerous techniques for the manufacture of tetrazoles are published in the scientific literature. Figures 3-5 illustrate the main synthesis pathways for tetrazoles. There are several processes to produce tetrazoles, the majority of which use azides as either starting materials or reaction intermediates [16]. Various techniques are focusing on the production of new ways of obtaining this heterocycle, and even electrochemical approaches [17], where azides react with hydrazones to produce tetrazoles have been applied. The sections that follow discuss recent progress in the synthesis of tetrazole derivatives; the principal purpose is to report and discuss methods applicable to the development of novel active compounds with biological activity.

1. From amines compounds:

Tetrazoles may be generated by reacting amine compound with triethyl orthoformate within NaN_3 in DMSO as Figure 3 [18-20].

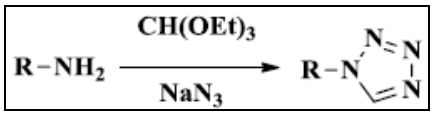


Figure 3. Synthetic route 1 for tetrazoles.

2. From cyano compounds:

It is generally known that the [3+2] cycloaddition combining that hydrazoic acid within cyanide compounds is an effective method as Figure 4 [21-23].

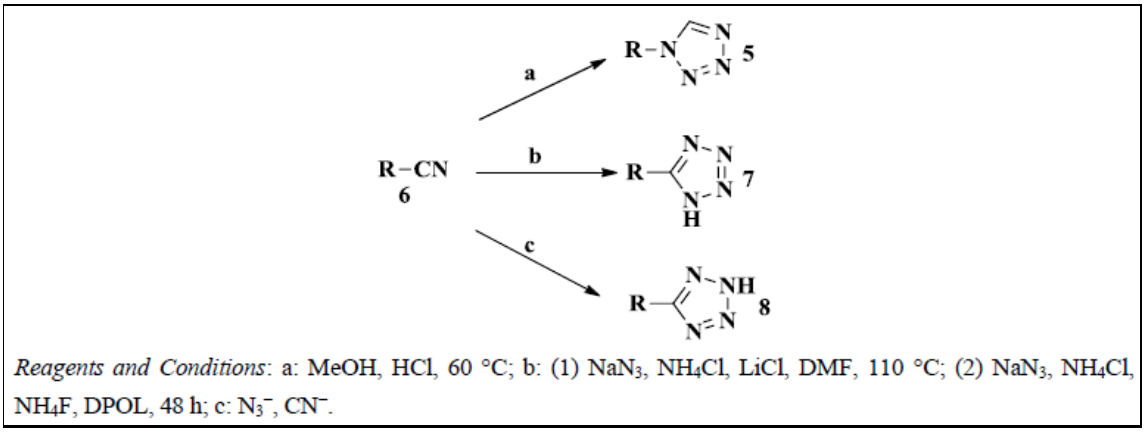


Figure 4. Synthetic route 2 for tetrazoles.

3. From amide compounds:

Under Mitsunobu conditions, an oxyphosphonium salt can be made from the corresponding amide compound. Then, a reaction with trimethylsilyl azide makes the needed in 1 and 2 position of tetrazoles as Figure 5 [24].

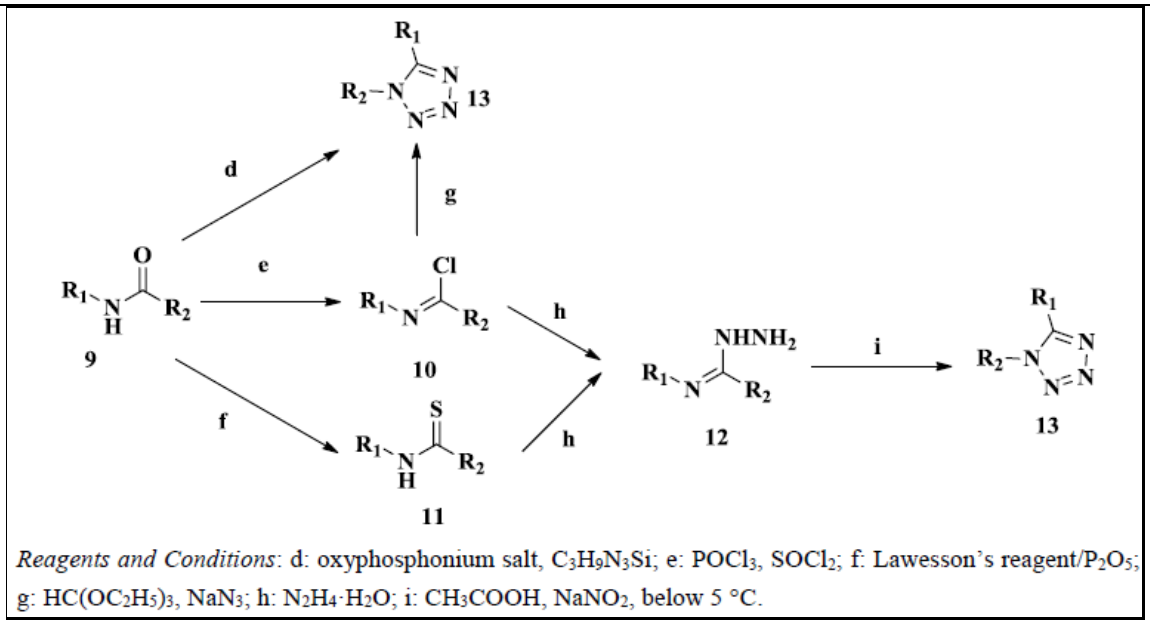


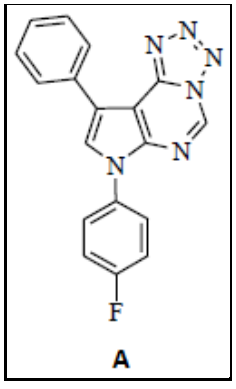
Figure 5. Synthetic route 3 for tetrazoles.

6. Biological Activity of Tetrazolium Derivatives

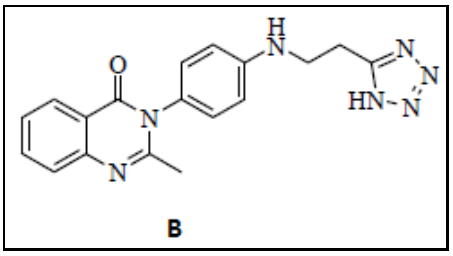
Tetrazole has a wide range of uses, including as catalysts, propellants, and even explosives. In spite of this, they earned a position in the field of medicinal chemistry owing to their unique electrical properties and vast spectrum of biological activities. These substances also have properties that make them anti-inflammatory, analgesic, anti-cancer, anti-convulsant, anti-hypertensive, hypoglycemic, anti-parasitic, and anti-viral [25].

6.1 Antibacterial and antifungal activity:

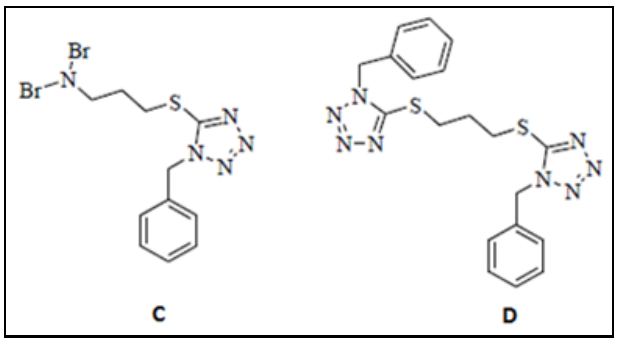
Dave C. G., et al., Synthesized new compound of tetrazole (A) and tested them for their antibacterial activity. From the results, Compound A is more active than ampicillin against all evaluated cultures, with the exception of S. aureus [26].



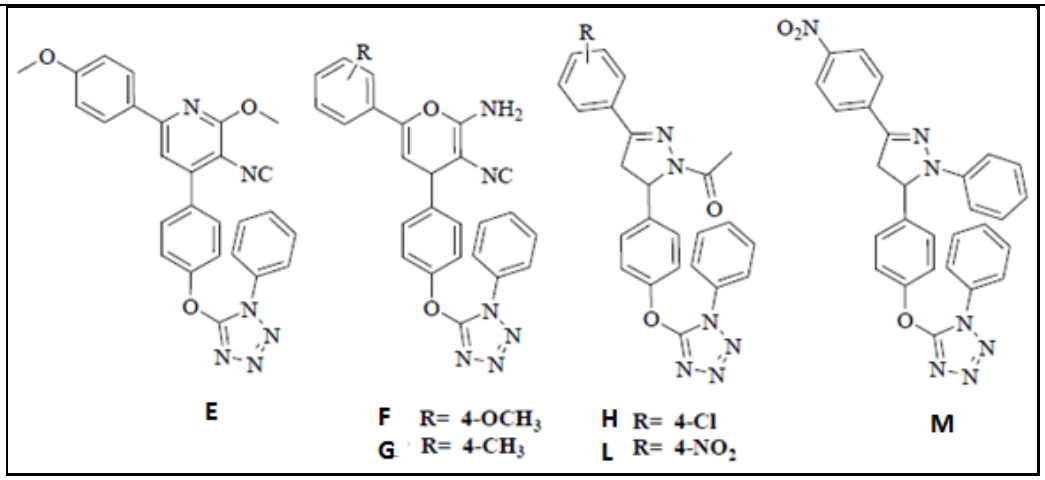
Arulmurugan S., et al., synthesized tetrazole compound (B) and tested it for antimicrobial activity using the disc diffusion procedure to measure inhibition zones [27].



Dhayanithi V. I., et al., produced tetrazole derivatives C and D and tested them as antimicrobial. Researchers found a modest level of action against the evaluated microorganisms [28].

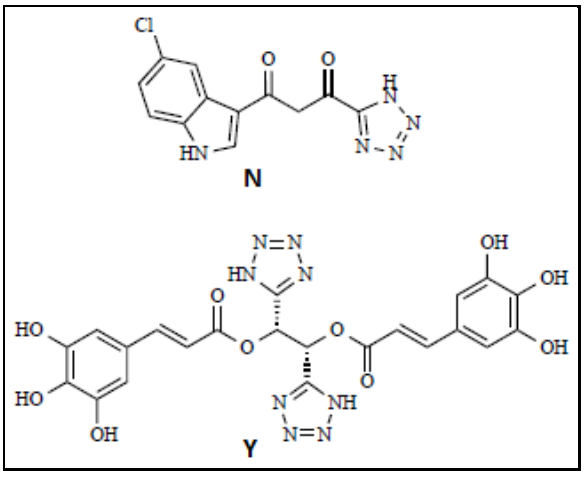


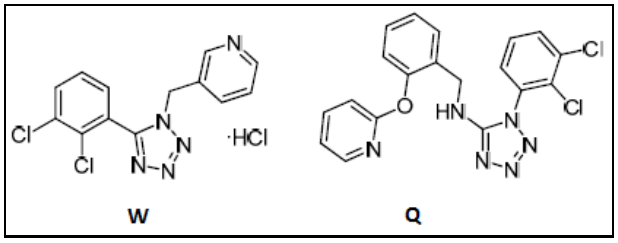
Moustafa M. A., et al., different compounds of heterocyclic derivatives (E, F, G, H, L, and M) were synthesized and tested as antimicrobial. From the results [29].



6.2 Antivirals:

The compounds (N and Y), synthesized and tested to inhibit the HIV-1 integrase [30].





6.3 Anti-inflammatory and analgesic activity:

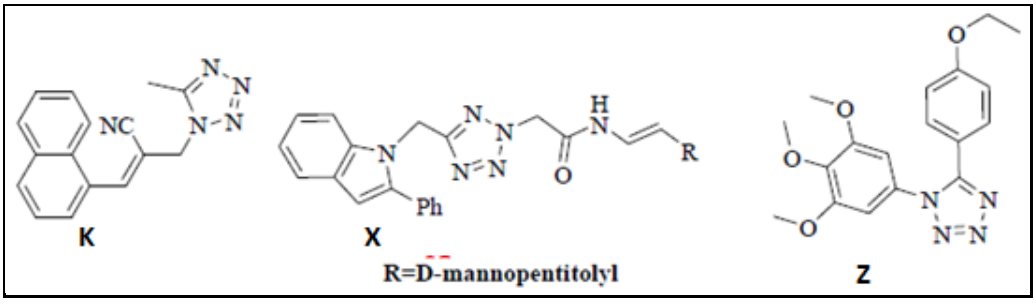
Falk S., et al. and Albalawi, et al., were prepared two kinds of compounds (W and Q) synthesized and used as anti-inflammatory agents [31, 32].

6.4 Anticancer activity:

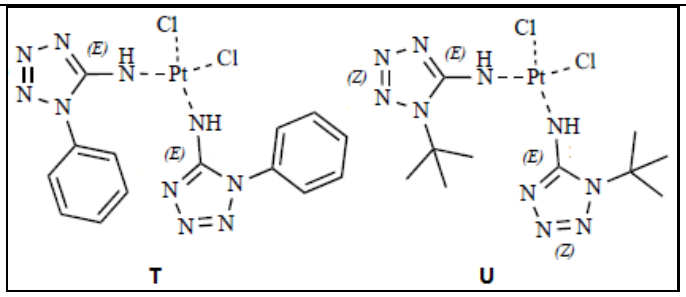
El-Sayed W. A., et al., found that compound K was more effective against liver carcinoma (Hep G2) and lung adenocarcinoma (A 549) cancer cell lines than other compounds [33].

While, Romagnoli R., et al., manufactured compound X, its anticancer efficacy against the human liver carcinoma cell line HepG2 was investigated [34].

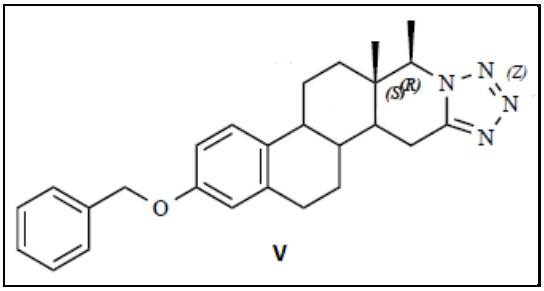
Finally, Kádár Z., et al., produced the second series of 1,2,3,4-tetrazole compound. Many of the produced compounds inhibited the development of multidrug-resistant cells as effectively as Compound Z [35].



Serebryanskaya, T. V., et al., synthesized a new groups of tetrazole complexes Pt(II) as complex E and Pd(II) as complex U these contained chlorine atoms and tested for antineoplastic activity [36].

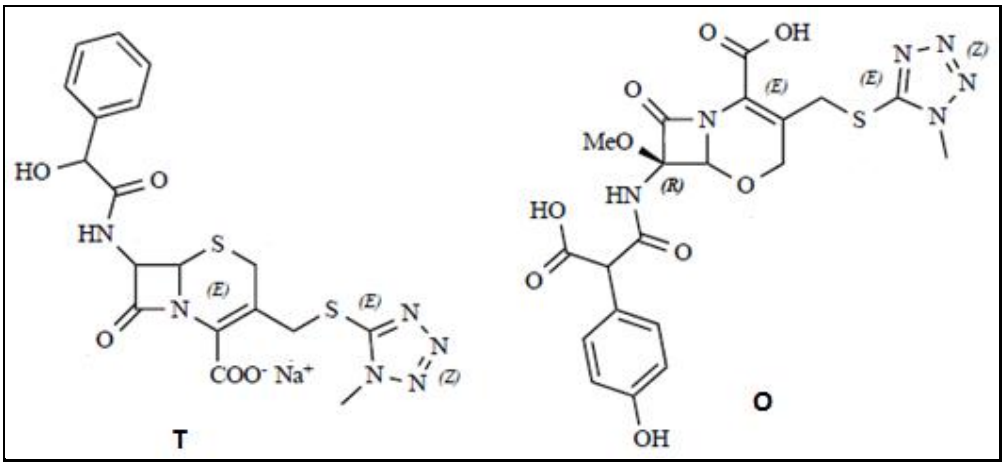


Penov-Gaši K. M., et al., synthesized the compound V and gives a big inhibition to breast cancer cell lines (MCF-7) [37].



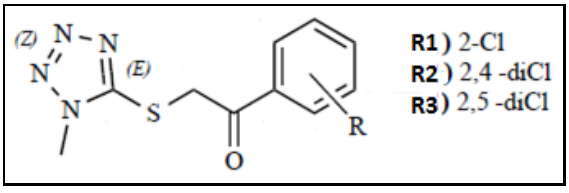
6.5 Antibacterial activity:

Crosby D. C., et al., synthesized a new series such as Cefamandole as compound T and Latamoxef as compound O, synthesized and tested against many types of bacteria [38].



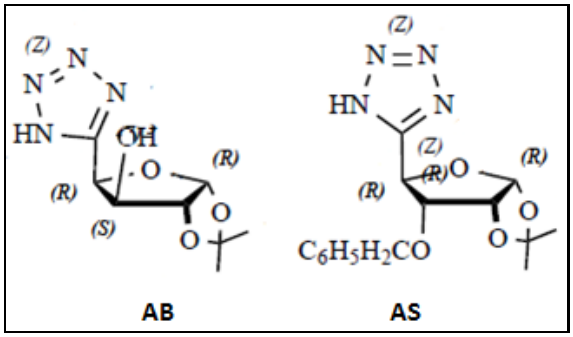
6.6 Antifungal:

Zhan P., et al, Synthesized the new compounds of tetrazole derivatives R1-R3 and tested as antifungal activity such as, against Candida albicans and Candida glabrata [39].



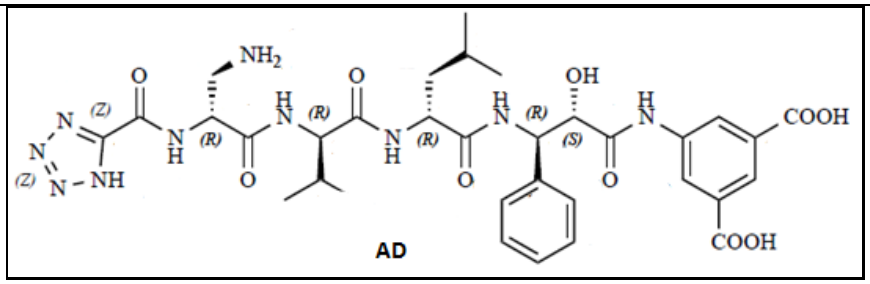
6.7 Antioxidants:

Seliverstova D. V., synthesized novel compounds AB and AS with antioxidant activity comparable to that of gallic acid and no cytotoxic effects on human lymphocytes [40].



6.8 Effect on the central nervous system:

Ostrovskii V.A., et al., prepared a compound AD that was a peptidomimetic, β-secretase inhibitor (BACE1) via used for a treat Alzheimer´s disease [41].



7. Conclusions

In this review, the history of tetrazol compounds was discussed, and some of their general properties were studied, in addition to the use of these compounds.

First, tetrazol compounds have wide applications in industry, agriculture, and the medical field because of their chemical structure, which has multiple properties.

Second, the medical uses of some compounds that have already been made have been looked into.

Lastly, this review comes to the conclusion that tetrazol compounds have a lot of different uses and can be made in many different ways, with the medical use being the main focus.

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