

International Journal of Pharmaceutical Science and Research

www.pharmacyjournal.net

ISSN: 2455-4685

Received: 25-06-2022, Accepted: 13-07-2022, Published: 26-07-2022

Volume 7, Issue 3, 2022, Page No. 1-6

Review. nomenclature systems of tetrazine and its pharmacology application

Israa Jirjees Neamah¹, Farqad M Baqer², Bassam A Hassan²

¹Lecturer, Thi-Qar General Directorate of Education, Iraq

² Department of Pharmaceutical Chemistry, College of Pharmacy, Thi-Qar University, Iraq

Abstract

In the presence study tetrazine naming according four naming system of heterocyclic nomenclature as common nomenclature, method of replacement, Hantzsch-Widmann Systematic or IUPAC and fused system. each system contain special rules for naming which are different from the other as following explaining with example structures. Tetrazine pharmacological activity as Antibacterial, antifungal, anticancer, antiviral, antimalarial, and antimicrobial activities found in several tetrazine compounds. Some tetrazineees derivatives are not bad analgesics and anti-inflammatories, other 1,2,4,5 -tetrazines exhibit significant antimalarial activity. A number of tetra hydro-s-tetrazines have been shown to have antibacterial and antifungal properties, with several 1, 4-dihydro-s-tetrazine derivatives possessing antiviral and anticancer properties.

Keywords: application, nomenclature, pharmacology and tetrazine

Introduction

Nomenclature of tetrazine

The name of tetrazin is based on the following systems for naming heterocyclic compounds:1) The common **nomenclature:** (Funny name) that conveys little or no structural information but is still commonly used.2) The method of replacementt.3) The Hantzsch-Widman (IUPAC or Systematic) technique, which, on the other hand, is intended 4) Hantzsch-Widman (Systematic or IUPAC. (1)

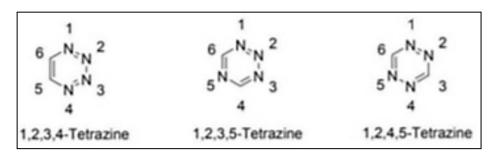


Fig 1

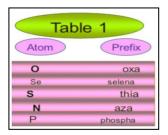
Common nomenclature (Trivial name)

Despite the fact that it conveys little or no structural information, it is commonly utilized. We haven't able to come up with a common naming for tetrazine yet. (1)

Replacement nomenclature

The name of the heterocyclic in replacement nomenclature is made up of the name of the matching carbocyclic and an elemental prefix for the heteroatom added (if more than one heteroatom is present, they should be mentioned in the priority order provided in the table) (table 1). Tetrahydrofuran, for example, is referred to as oxacyclopentanee in this nomenclature. (2)

Table 1



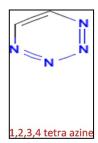


Fig 2

Hantzsch-Widman nomenclature (IUPAC)

Three to ten-membered rings are named using this system, which combines the appropriate prefix (or prefixes) that denote the type and position of the heteroatom presence in the ring with a suffix that determines both the ring size (depending on the total number of atoms in the ring) and the degree of unsaturation (note that fully saturated and fully unsaturated have certain rules for nomenclature while partially unsaturation will be indicated in certain ways).

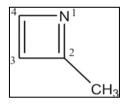


Fig 3

IUPAC name = locants +Prefix + suffix *The word (aza) is used to the nitrogen atoms and as in Table No. 1 distinguishes between nitrogen-containing heterocyclic and heterocyclic that do not include nitrogen.

In a monocyclic molecule, the numbering is controlled by the position of a single heteroatom. Position 1 is always allocated to the heteroatom, and any substituents present are tallied around the ring in order to get the lowest possible values as shown in figure (3) *. When there are two or more comparable heteroatoms in the ring (two nitrogen indicated by diazaa) and the numbering preferable starts with a saturated rather than an unsaturated atom, a multiplicative prefix (di, tri, ect.) and locants are employed, as seen in the following example: 1,2,3,4 tetracycline (3). Starting with the highest priority heteroatom, the numbering is done in such a way that the remaining heteroatoms in the ring receives the least possible numbers (the substituents are irrelevant). The prefix 4-Methyl-1, 3- Thiazaa, for example, corresponds to the following chemical (4).

Results and Discussion

Results of root and shoot length measurement -

The mung plants were raised hydroponically in Hogland solution having 10, 50,100, 500, 1000 mg/l concentrations of iron nanoparticles. Proper aeration was given by using air pumps in the solutions having suspended nanoparticles. Root and shoot length were measured on alternate day upto 14th day by using ruler with the help of box. Dhoke *et al.* (2013) [5] studied the effect of iron oxide nanoparticles on *Vigna radiata* seedling and good growth was observed. Same significant effects were observed in Ocimum basilicum L. growth characteristics (branches, leaves number) by Souad A. Elfeky *et al.* (2013). Root and shoot length were found increased as the concentration of nanoparticles increased from 10 to 1000 mg/l as shown as in Table 2. So we can say that iron had stimulatory effect probably on growth of plantsas shown in figure (7) Tetrazine willl take the suffix becausee it is a hexa ring unsaturated chemical with a nitrogenn atom(ine)

Examples

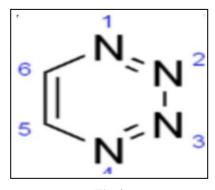


Fig 4

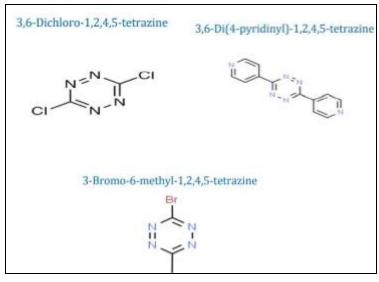


Fig 5

Nomenclature of Fusedd Systems: Fusion: This word referss to the process of merging twoo independent rings with the most non-cumulativee double bonds possible using twoo atoms and one common linkk. Rings with only two common atoms and one link, such as naphthalenee, are known as ortho-fused rings. Naphthalene Ortho-and peri-fusedd rings are those found in a polycyclicc molecule having a ring that is ortho-fused to two additionall rings that are ortho-fused together on opposite sides (i.e. there are three common atoms between the first ring and the other two). This naming system provides systematic names for fused heterocycles. The fused heterocyclic systemm is made up of two or more cyclicc structural units that have been fused together (components). The cyclicc structural units have the most non-cumulativee double bonds and are fused together so that each structural unit (component) has one bondd in common. The names of structural units might be simple or complex. The followinge rules are used to name the fusedd heterocyclic system:

Note: We will just discuss tetrazine namingg conventions.

- 1. The fused heterocyclic systemm is dissected into its constituentss, one of which is the base componentt and the other(s) is/are the attached componentt(s).
- 2. Base Component Selection: The foundation is formed first. To this purposee, the criteria listed beloww are applied in the order listedd below, one by onee, to arrive at a choice. The foundational elementt is
- 1. Nitrogen-containing componentt: As the base componentt, a nitrogen-containing component is usedd.
- 2. In the case of ringss of uneven size in a fusedd heterocyclic system, the component with the biggest ringg size is chosen as the basee component.
- 3. Rings of equal sizee but various numbers of heteroatomss: in a heterocyclic system with ringss of equal size but varyingg numbers of heteroatoms, the ringg with the most heteroatomss of any kind is regarded the base componentt.

Note: If two heteroatoms of the same groupp are present, the base components with the ring with heteroatoms that appearr first in Table 1 is favoredd. (6-11)

Heteroatom	Symbol (Valence)	Prefix
Oxygen	O(11)	Oxa
Sulfur	S(11)	Thia
Seleniun	Se(11)	Selena
Telluriun	Te(ll)	Tellma
Nitrogen	N(III)	Aza
Phosphorus	P(III)	Phospha
Arsenic	As (ill)	Arsa
Antimony	Sb(III)	Stiba
Bismuth	Bi(III)	Bisma
Silicon	Si(IV)	Sila
Gennaniun	Ge(IV)	Genna
Tin	Sn(IV)	Stanna
Lead	Pb(IV)	Plwnba
Boron	B(III)	Bora
Mercury	Hg(II)	Mercura

Table 2: prefixes for heteroatoms

- 4. Rings of the same sizee, number, and type of heteroatomss: if the components contain rings of the same sizee, number, and type of heteroatomss, the component containing the ringg with the lowest locant numberss is favored as the base componentt. (7)
- 5. **Notes:-1-**The associated component'ss (second component's) name is appended as a prefix to the base component's name (table 2). By altering the terminal 'e' of a triviall or HantzschWidman name of a component to 'o,' the prefix identifying an attachedd component is generated. When followedd by a vowel, this 'o' is not droppedd.
 - **2-**The base component's bondss are alphabetized using italic characters, commencing with 'a' for a 1,2-bondd 'b' for a 2,3-bondd, 'c' for a 3,4-bondd, 'd' for a 4,5-bondd, and so on.
 - **3-**The atoms that are commonn to both rings (side of fusionn) are denoted by the relevantt letters and numberss, which are surrounded in a squaree bracket and placed immediatelyy after the associated component's prefixx. The second component's numberss (positions of attachment) are arranged in the orderr in which they are attached to the base component.
 - **4-** Common heteroatom: If a heteroatomm occupies a fusion point, bothh components (ring systems) are saidd to have that heteroatom. (12-19)

Examples

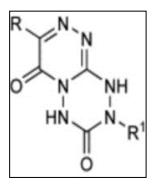


Fig 7: 1,2,4-triazino[4,3-e]-1,2,4,5-tetrazin..

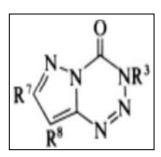


Fig 8: pyrazolo [5, 1-d]]-[1, 2, 3, 5] tetrazin--4-ones

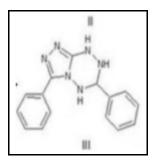


Fig 9: hexaydro [1, 2, 4] triazolo [4, 3 b] [1, 2, 4, 5] tetrazine

Application of tetrazine

1, 2, 4, 5-tetrazine derivatives or their n-hydroo form have a high potentiall for biological activityy, possessing a wide range of antivirall and antitumor These derivatives have also been widely used in pesticidess and herbicides. According to the literaturee, 1,2,4,5-tetramethyl-3,6-bis(phenylethynyll)-1,2,4,5-tetrazine has been suggestedd as an antitumor agent77,78,799; 3-amino-6-aryl-1,2,4,5-tetraziness showed modestt antimalariall activity800 a series of ttetrahydro--s-tetrazines have evaluatedd for their antibacteriall and antifungall activities81, and somee analgesicc hexahydro-s-tetrazines provedd to have useful and antiflammatoryy.activitiess. Recently, in addition to antibacteriall, antifungall, anticancerr, antivirall, antimalarial, and antimicrobiall activities are found in severall tetrazinee compounds. Some hexahydro-s-tetraziness are goodd analgesicss and anti-inflammatoriess, while 3- arylamino-6- benzylamino-1,2,4,5-tetraziness exhibited good significace antimalarial activityy. A number of tetrahydro-s-tetraziness have been shown to have antibacteriall and antifungal propertiess, with several 1,4 -dihydro-s-tetrazine derivativess possesse anticancer and antivirall propertiess. (19-25)

Conclusion

Tetrazines are heteroaromatic compounds with four nitrogenss in a six membering ring like to aromatic ring of benzeneer. There are three major isomerss, 1,2,3,4-tetrazine,1,2,3,5-tetrazinee and 1,2,4,5-tetrazine, depending on the placement of nitrogens in the ringg, of which the 1,2,4,5-tetrazine system is the only stablee isomer. There are many ways to synthesiss tetrazines one of which is the reactionn between benzohydrazide with KOH, CS2, and Hydrazinee hydrate to produce 4-amino-5phenyl-4H-1, 2, 4-triazole-3-thioll (I) then 3- hydrazine-5-phenyl-4H-1,2,4-triazole -4-amine is formedd when a mixture of produced compoundss (I) reacts with hydrazine hydrate in pyridinee (II). The reaction of compoundd (II) with benzaldehyde in alcoholic KOH to yields 3,6-diphenyl-1,5,6,7,8,8a-hexahydro--1,5,6,7,8,8a-hexahydr 1,5,6,7,8,8a-hexa[1,2,4] triazolo[4,3-b][1,2,4,5] tetrazine(III). Tetraziness plays an important rule in medical field. They have manyy applications as Antibacteriall, antifungal, anticancerr, antiviral, antimalariall, and antimicrobiall activities. Some hexahydro-s- tetraziness are not bad analgesics salso aanti-inflammatoriess, Also tetrazines derivatives exhibit highly significance antimalariall activity. A numberr tetrazines derivatives have shown to antibacteriall and antifungal propertiess, with several tetrazine derivativessshowen antiviral and anticancer properties. Tetrazines containing pyrrole, thiophene, or 3,4 ethylenedioxythiophene rings, which makee them ideal polymerizationn candidatess. also, tetrazine-alkene ligation has been used for imaging biomoleculess like proteins and DNA In cells, Furthermoree, these chemicals have long been employedd as pesticides and herbicides

Refrences

- 1. Kamaleddin Haj MET, Farzad K, Parisa A, Maryam M, Zohreh S, Ghazaleh G, Sorous S. Iranian J.of Pharma.Res.,2013:12(2):331-346.
- 2. Postovskii I Ya, Ershov VA, Sidorov EO, Serebryakova NV, Khimiya, Geterotsiklicheskikh Soedinenii.1997:(11):1564-8.
- 3. Balaha MF, El-Hamamsy MH, Sharaf El-Din NA, El-Mahdy NA, Journal, of Applied Pharmaceutical Science, 2016:6(4):028-045.
- 4. Smicius R, Burbuliene MM, Jakubkiene V, Udrenaite E, Vainilavicius P, Het. Chem J, 44, 279.
- 5. Hassan SM, Emam HA, Abdelall MM, Chem. Res. (S), 2000, 544.
- 6. Authors, Maitham Mohamed Abdulridha Alabody Bassam Abdulhussein HasanAlsafee Ahmed Abbas Saheeb Alsafee, Introduction of Heterocyclic Chemistry, 2018, 10-5.
- 7. Synthesis, characterization and photochemical study of potentially emitting tetrazine derivatives Sachin D Vahile Submitted to Graduate College of Bowling Green State University in Partial Fulfillment of the Requirements for the Degree of august 2009 master of science Committee:Dr. Pavel Anzenbacher Jr., Adviser Dr. Thomas H. Kinstle Dr. Douglas C Neckers.
- 8. Synthesis of Novel Triazoles, Tetrazine, Thiadiazoles and Their Biological Activities Mohammed A Al-Omair 1, Abdelwahed R Sayed 1,2.* and Magdy M Youssef 1,3.
- 9. 3,6-dichloro-1,2,4,5-Tetrazine Assayed at High Doses in the Metastatic Breast Cancer Cell Line MDA-MB-231 Reduces Cell Numbers and Induces Apoptosis Author(s): Mohamed Abdelkarim*, Khaoula Ben Younes, Ines Limam, Refka Guermazi, Amel Ben Ammaar ElGaaied and Fatma Ben Aissa-Fennira. Design, synthesis, cytotoxicity and 3D-QSAR analysis of new 3,6-disubstituted-1,2,4,5-tetrazine derivatives as potential antitumor agents A Ivaro Can ete-Molina a, Christian Espinosa-Bustos a, Marcos Gonza lez-Castro a, Mario Fau ndez b, Jaime Mella c, Ricardo A. Tapia a, Alan R. Cabrera a,d, Iva n Brito e, Adam Aguirre b, Cristian O. Salas a,*.
- 10. Synthesis and antimycobacterial activity of imidazo[1,2 b][1,2,4,5]tetrazines Dmitry A Maslov *et al*. Eur J Med Chem., 2019.
- 11. Bassam A. Hassan, Fadil Mohsen Hamed, Maitham M. Abdulridha, Farqad M.Baqer 2022. Phytoconstituents Screened of Grapefruit Peels with Antimicrobial Properties of Naringin and Naringenin Extracted and Isolated from its. *Annals of the Romanian Society for Cell Biology.*,2022:26(01):1160–1168.
- 12. Hussain, Maitham Y, Bassam A Hassan, Zaman K. Hanan. "Synthesis and Characterization of a new Schiff basses (3Z, 3Z)-3, 3'-((oxybis (4, 1-phenylene)) bis (azanylylidene)) bis (indolin-2-one)." Turkish Journal of Computer and Mathematics Education (TURCOMAT),2021:12(14):3341-3351.
- 13. Hassan Bassam A, Fadil Mohsen Hamed, Farqad M Baqer. "Green Chemistry. Review." EFFLATOUNIA-Multidisciplinary Journal, 2021, 5(2).
- 14. Hamed Fadil Mohsen, Bassam A Hassan, MAITHAM M Abdulridha. "The antitumor activity of sulfonamides derivatives." Int. J. Pharm. Res,2020:12:2512-2519.
- 15. Hassan Bassam A, Hameedi N Nasera, Maitham M Abdulridha. "Synthesis and antimicrobial evaluation of fused heterocyclic compound [1, 2, 4] triazolo [4, 3-b][1, 2, 4, 5] tetra zine.", 2019.

- 16. Shalaal Semma H, *et al.* "Maceration Techniques Extraction of Thymus Vulgaris and Laurel (Laurus Nobilis) Leaves with Antibacterial Study." Plant Archives, 2019:19(2):4041-4044.
- 17. Hamed Fadil M, *et al.* "Phytochemical and antimicrobial study of acetone extracts of menthe and olive leaves." The Journal of Research on the Lepidoptera, 2019:50(2):51-6.
- 18. Abdulridha Maitham M, *et al.* "Phytochemical and Antibacterial Activity of The Pegnum Harmala Seeds and Its Alkaloids." Plant Archives.2019:19(1):1439-1444.
- 19. Hassan Bassam A, Fadil Mohsen Hamed, Firas F Alyaseen. "Phytochemical screened, characterization and antibacterial activity of hesperetin and hesperidin extracted and isolated from dried oranges peels", 2018.
- 20. Abdulridha Maitham M, Bassam A Hassan, Fadil M Hamed. "Synthesis and Antibacterial Evaluation of 1, 3, 4-Thiadiazole Containing 1, 3, 4-Oxadiazole Bearing Schiff Bases." International Journal of Pharmaceutical Research, 2018.
- 21. Alyaseen Firas F, Bassam A Hassan, Haider S Abdulhussein. "Extraction, Isolation And Chemical Identification of Piperine Alkaloid from Black Pepper Seeds And Its Antibacterial Activity." Plant Archives, 2018:18(2):2171-2176.
- 22. Hasan, Bassam Abdul Hussein, *et al.* "Antimicrobial activity of ethanolic and aqueous extracts of pomegranate peel against Extended Spectrum Beta-Lactamase producing bacteria." University of Thi-Qar Journal, 2017:12(4):1-14.
- 23. Alsafee Bassam Abdulhussein Hasan. "Synthesis, Identification and Antibactrial Activity of Some New Heterocyclic Compounds Containing 1, 3, 4-Thiadiazole and 1, 3, 4-Oxadiazole Bearing Schiff Base." Iraqi National Journal of Chemistry, 2017, 17(2).
- 24. Alsafee Bassam Abdulhussein Hasan, Maitham Mohamed Abdulridha. "Synthesis and characterization of Cu (II) and Fe (II) metal complexes of oxazepine derivative via Schiff base [Fe (HPOHBOT) Cl2] and [Cu (HPOHBOT) Cl2]." African Journal of Pharmacy and Pharmacology, 2016:10(35):728-736.
- 25. Alsafee Bassam Abdulhussein Hasan. "Preparation and characterization of some transition metal complexes of 4-amino-N-(5-sulfanyl-1, 3, 4-thiadiazol-2-yl) benzenesulfonamide." International Journal of Scientific & Engineering Research, 2016:6(1):37-45.
- 26. Alsafee Bassam Abdulhussein Hasan. "Preparation and characterisation of some transition metal complexes of new 4- [(5-ethyl-1, 3, 4-oxadiazol-2-yl) sulfanyl] aniline." The Swedish Journal of Scientific Research, 2014:1(6):11-23.
- 27. Hasan Bassam A, Maitham M. Abdulridha. "Preparation and Characterisation of Sometransation Metal Complexes of New [Butanal (5-Ethyl-1, 3, 4-Oxadia-Zol-2-Yl) Hydrazone]." The Swedish Journal of Scientific Research, 2014:1(5):23-36.
- 28. Hamed, Lecturer Dr Fadil Mohsen, Assis Lectu, and Bassam A. Hassan. "The non-antibacterial activity of sulfonamide derivatives المنافقة عند المنافقة ال
- 29. Hassan Bassam A, Farqad M Baqer, Maitham M Abdulridha. "Design, Synthesis and Characterization of Benzoxazepine Thiourea New Derivatives."
- 30. Jabir Najim A. "Ruta Graveolens (Hurb Of Grace)-Anti Bacterial Effects, A."25-