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# A Review of Synthesis of Aminoguanidine Derivatives and Some of their Biological Activities

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**Abstract:- Five-ring scaffolds are the most important and best-known heterocycles and are an essential component of many natural products and drugs. These scaffolds are centrally located and are the main str uctures of many different drugs. These medications inclu de antibiotics, antibiotics, antibiotics, antibiotics, antibiot ics, antibiotics, and antibiotics. In this review, we will ma inly talk about aminoguanidine bicarbonate derivatives due to their important medicinal properties. This is partl y because, unlike other isomers, they are chemically stabl e and heat stable and can be used as bioisosteres in phar maceutical production. We consider the modifications of different aminoguanidine bicarbonate derivatives, especially the anti-inflammatory and anti cancer drugs published in the last 5 years, as an importa nt research area. This article aims to provide an in-depth study and analysis of the latest developments in chemical aminoguanidine bicarbonate derivatives. This would be a good starting point for future research.**

## I. INTRODUCTION

Heterocycles are ring compounds that contain one or more different ring atoms. Five- and six-membered compounds are the most important heterocyclic systems. [1]Although they are heterocyclic compounds, the ring structure usually contains at least one carbon atom and one or more elements such as sulfur, oxygen,and n itrogen. Since it is generally thought that no carbon can be re placed by a carbon atom, they are called heteroatoms. This f ormula can be made from aromatic or non-aromatic rings.

Heterocyclic chemistry is a branch of chemistry that deals with compound s, products, reactions, and applications.[2]

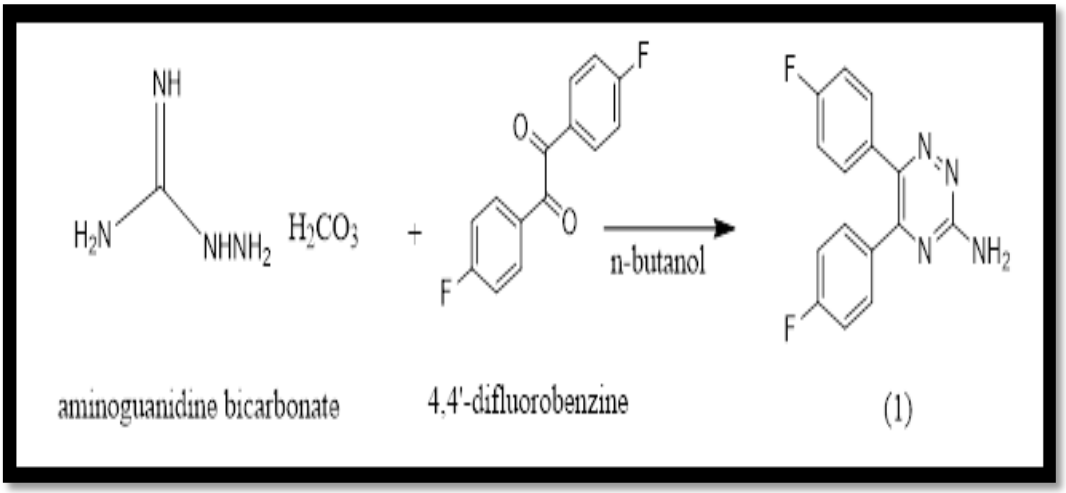
Aminoguanidine bicarbonate has attracted recent attent ion due to its practical preparation and important physical pr operties. Aminoguanidine bicarbonate not only forms salts with carboxylic acids, but also condenses with acids under a cidic conditions to form hydrazides.[3] Aminoguanidine bicarbonate has been subjected to extensive studies in recent years. The aminoguanidine bicarbonate scaffold is very versatile and has been part of several clinically used drugs. They have found use as antitubercular, antimicrobial, antifungal, anti-inflammatory, antibacterial, and antiviral agents, particularly anti-HIV agents. Many reports have appeared in the literature highlighting their chemical and pharmacological uses.

This review emphasizes the various pharmacological properties associated with aminoguanidine bicarbonate derivatives. The review covers the progress made over the last ten years.

## II. PREPARATION OF AMINOGUANIDINE DERIVATIVES

Several methods for synthesizing aminoguanidine bicarbonate derivatives are widely described in the literature. The various reported syntheses may be cyclization of aminoguanidine bicarbonate in a one-, two-, or three-step process.

A new route to the synthesis of 3-amino-5,6-di(4'fluorophenyl)-1,2,4triazine (1) was synthesized by an analogous route shown in Scheme 1. From refluxing 4,4'-difluoro benzylwith aminoguanidine bicarbonate in n-butanol and subjected to evaluation of their plant protection and antifungal activity.4




Scheme 1: 3-amino-5, 6-di(4’fluorophenyl)-1,2,4 triazine

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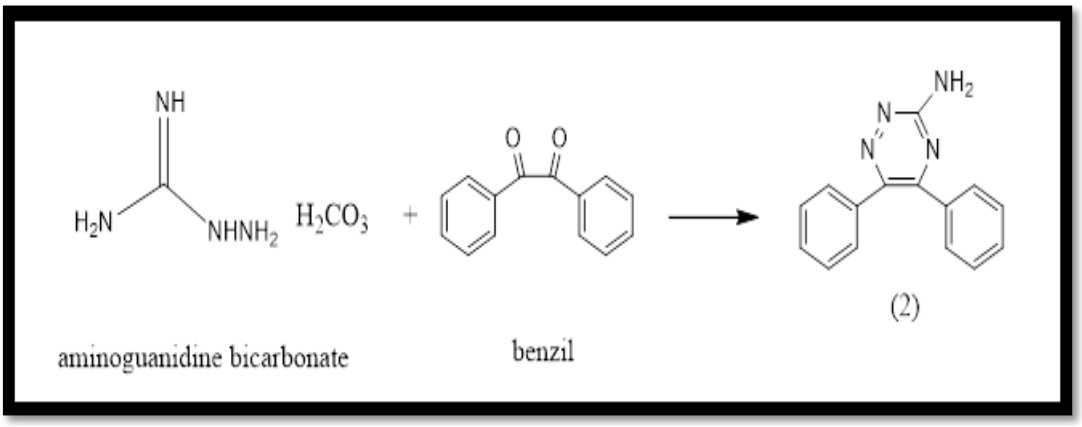
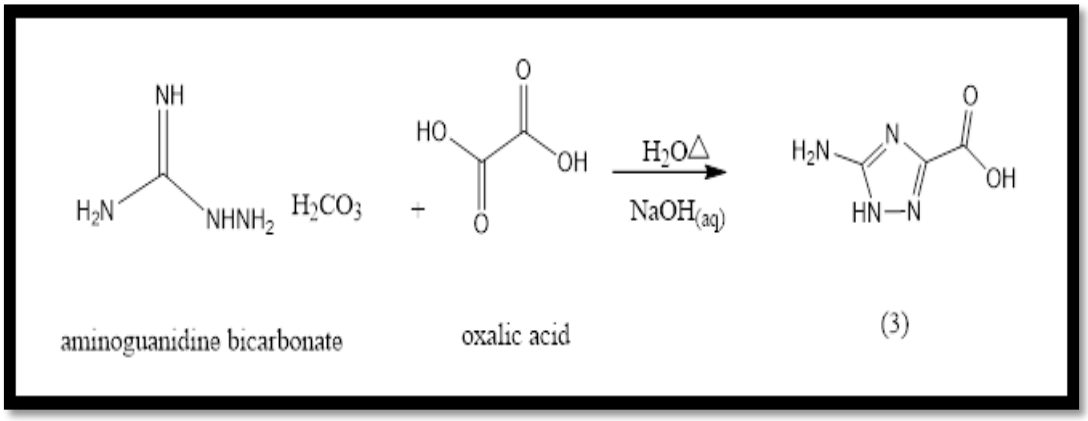
A series of new 5-6 diphenyl-(1,2,4)triazine-3-calamine (2) was synthesized in an analogous manner shown in Scheme 2. From refluxing benzyl with aminoguanidine bicarbonate in n-butanol and subjected to evaluation of their anticonvulsant activity.[5]



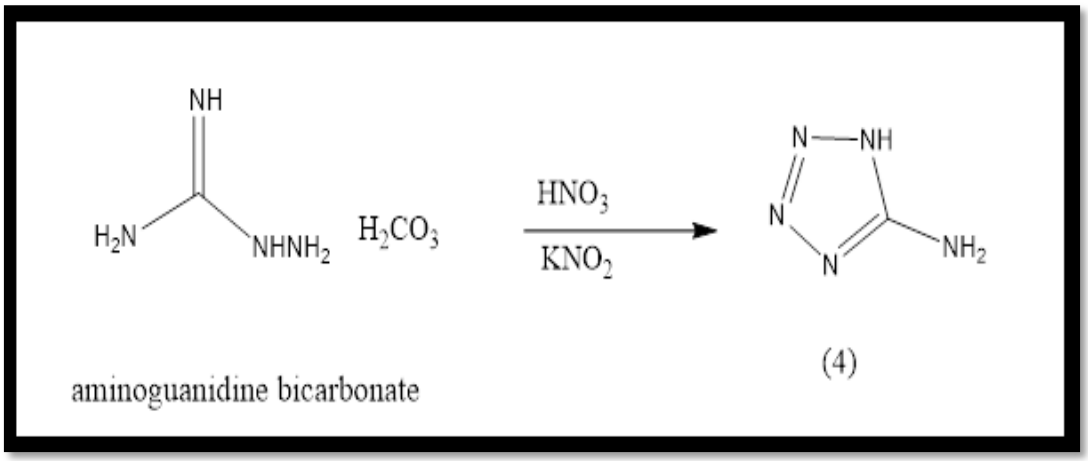

Scheme 2: synthesis of5-6 diphenyl-(1,2,4) triazine-3-yal-amine

A new heterocyclic system 5-amino-1H 1,2,4-triazole-3-carboxylic acid (3) was synthesized by an analogous route shown in Scheme 3. They were synthesized by reacting aminoguanidine bicarbonate with excess oxalic acid in the presence of a base and subjected to evaluation of their anticancer activity .[6]




Scheme 3: 5-amino-1H-1,2,4-triazole-3-carboxylic acid

A series of new n-amino tetrazoles (4) were synthesized by an analogous route shown in Scheme 4. The synthesis was based on Thiele's method, which involves the interaction of aminoguanidine bicarbonate with nitric acid produced in situ from potassium nitrite and nitric acid and subjected to evaluation of their anticonvulsant activity.[7]




Scheme 4: n-aminotetrazole

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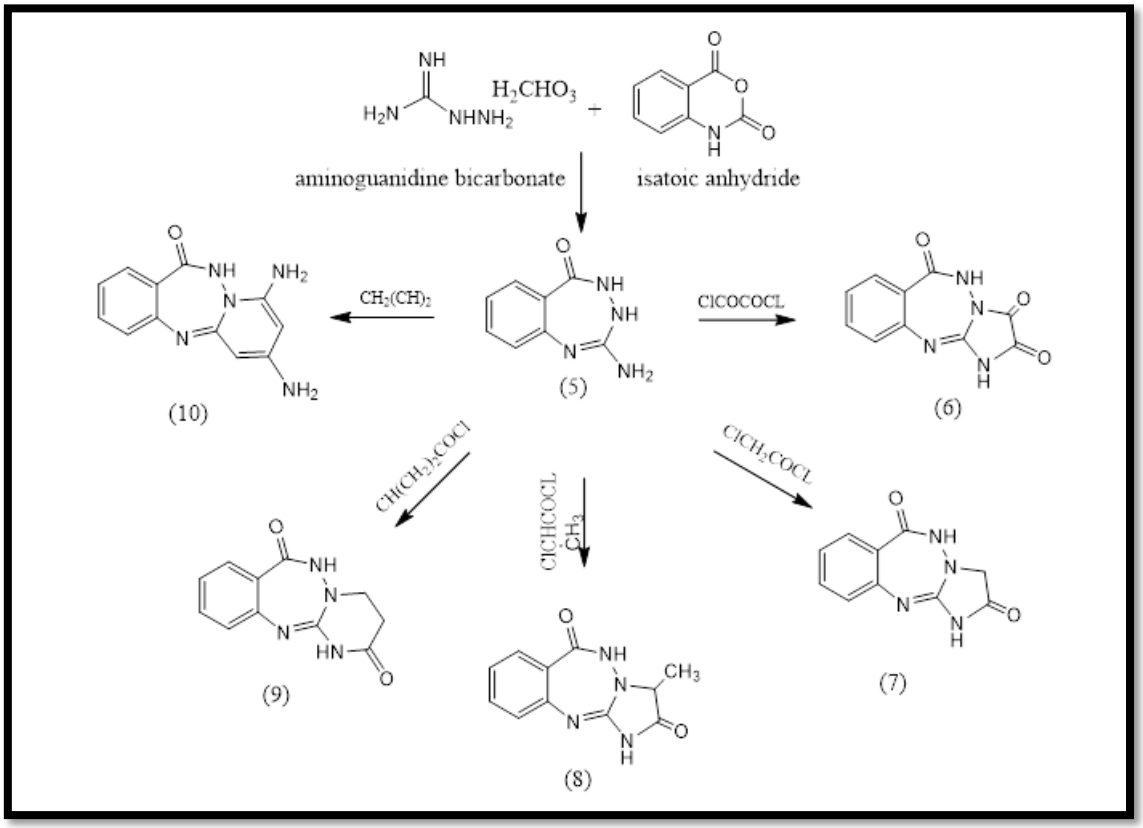
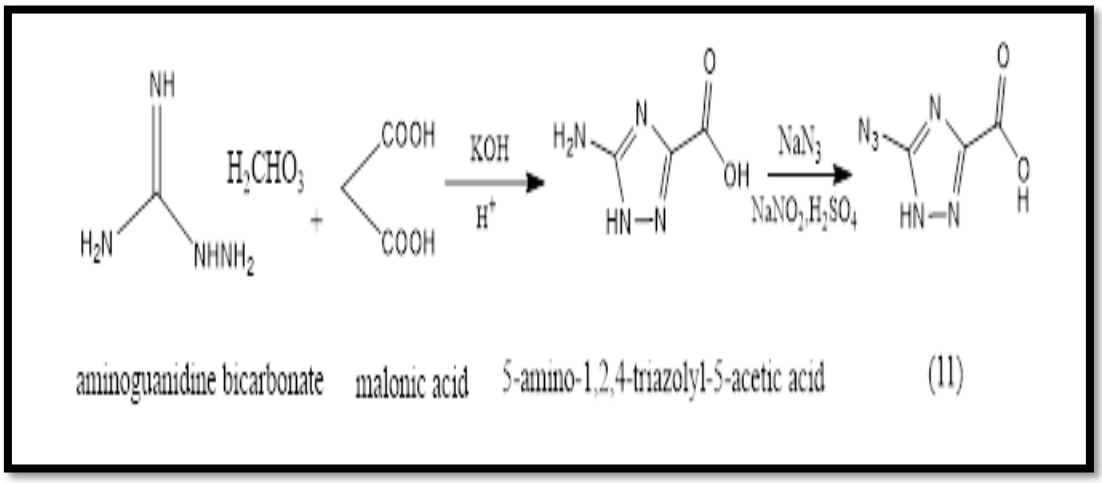
A series of novel benzodiazepine-1,2,4 (benzo TAP-1,2,4) compounds were synthesized analogously to those shown in Scheme 5, reaction of the isotonic anhydride with aminoguanidine bicarbonate in AcOHto obtain the triazine (5) and further reaction of this with oxalyl chloride, chloroacetyl chloride, 2-chloropropionyl chloride, 3-chloropropionyl chloride and malononitrile in dry benzene and anhydrous K2CO3 under reflux conditions at 6-10 and subjected to evaluation of their antitumor activity.[8]




Scheme 5: benzotriazepane-1,2,4 (benzoTAP- 1,2,4) compounds

A **new** series of **azidotriazole** compounds, **5-azido-1,2,4triazolyl-5-acetic** acid (ATAA) **(11) were synthesized** based on **the Sa ndmeyer reaction.** They are **produced** by **a similar metho d** in Scheme 6. **It is** synthesized by intramolecular condensat ion of malonic acid and aminoguanidine bicarbonate in analkaline medium. In general, **the** oxidation reaction is **carried out** at **05°C, followed by** diazotization in sodium nitrite and **sulfur ic** acid at **0°C to give 5-amino-1,2,4-triazolyl-5-acetic acid**, and **after testing.** with excess sodium azide at **5oC** to evalua te **its antibacterial** activity.[9]




Scheme 6: 5-azido-1,2,4 triazolyl-5-acetic acid (ATAA)

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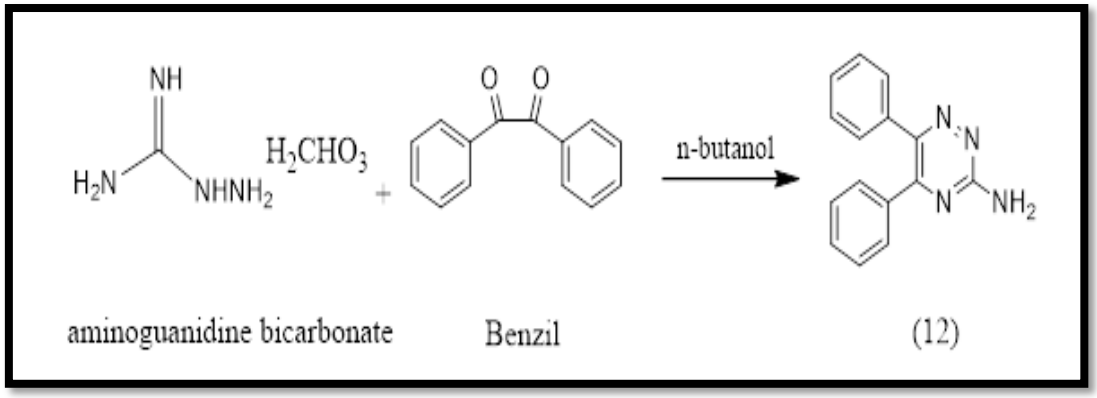
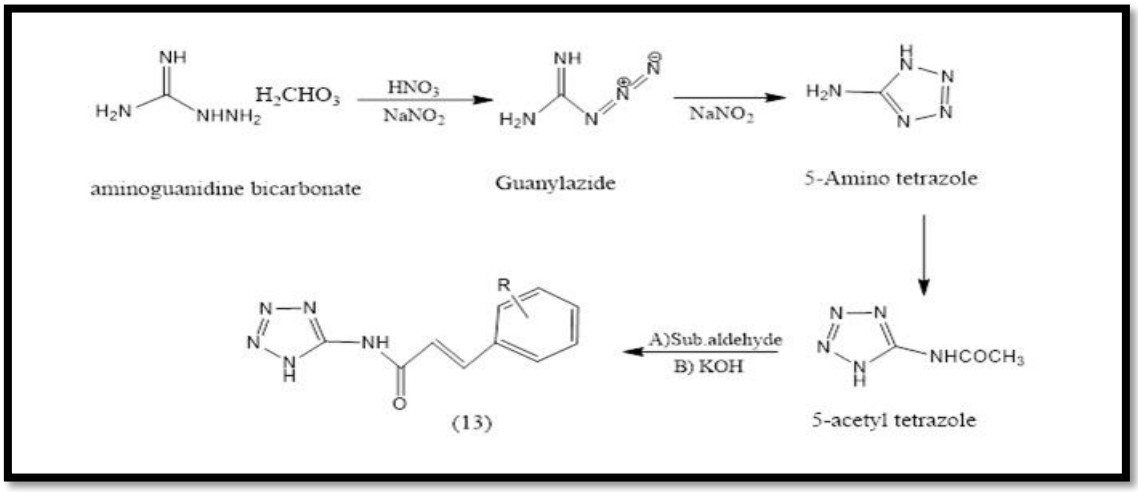
**One** of **the** new amino-5,6-diphenyl-1,2,4triazines (12) **was** synthesized by **a method similar to that** shown in Scheme **7 of cyclization condensation of** the benzyl **group** with aminoguanidine bicarbonate **under** reflu x. **n-butanol evaluated for HIV protection**.[10]



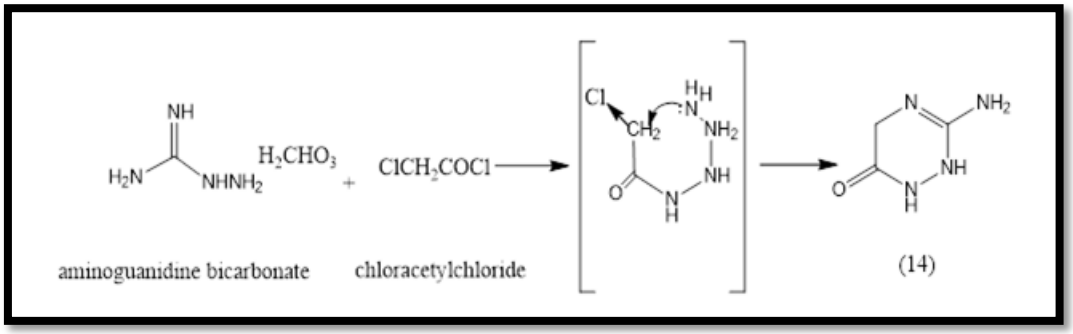

Scheme 7: amino-5, 6-diphenyl-1,2,4-triazines

A series of new (E)-N-(1H-tetrazol-5-yl)-substituted amide (13), synthesis of 5-amino tetrazole was based on Thiele's method. Synthesized by the analog shown in Scheme 8, by diazotization in sodium nitrite, then the synthesis of 5-acetyl tetrazole was achieved, the synthesis of (E)-N-(1H-tetrazole-5-yl)-substituted amide compound was subjected to evaluate their antifungal activity.[11]




Scheme 8:(E)-N-(1H-tetrazol-5-yl)-substituted amide.

A series of novel 3-amino-1,2,5,6-tetrahydro-1,2,4-trizain-6-ones (14) were synthesized analogously to those shown in Scheme 9. They are obtained from chloroacetyl chloride and aminoguanidine bicarbonate. Chloroacetylation takes place on the more basic atom N1, the resulting 1-chloroacetylaminoguanidine cyclizes to triazine as a result of a nucleophilic We cannot separate the nitrogen atom from the amino group of the methylene carbon atom i n the middle molecule. The reaction was carried out with hig h yield in glacial acetic acid, in the presence of sodium acetate as a cyclizing agent, in equimolar ratios of starters an d at room temperature, and its antifungal activity was evalua ted.12




Scheme 9: 3-Amino-1,2,5,6-tetrahydro-1,2,4-trizain-6-on

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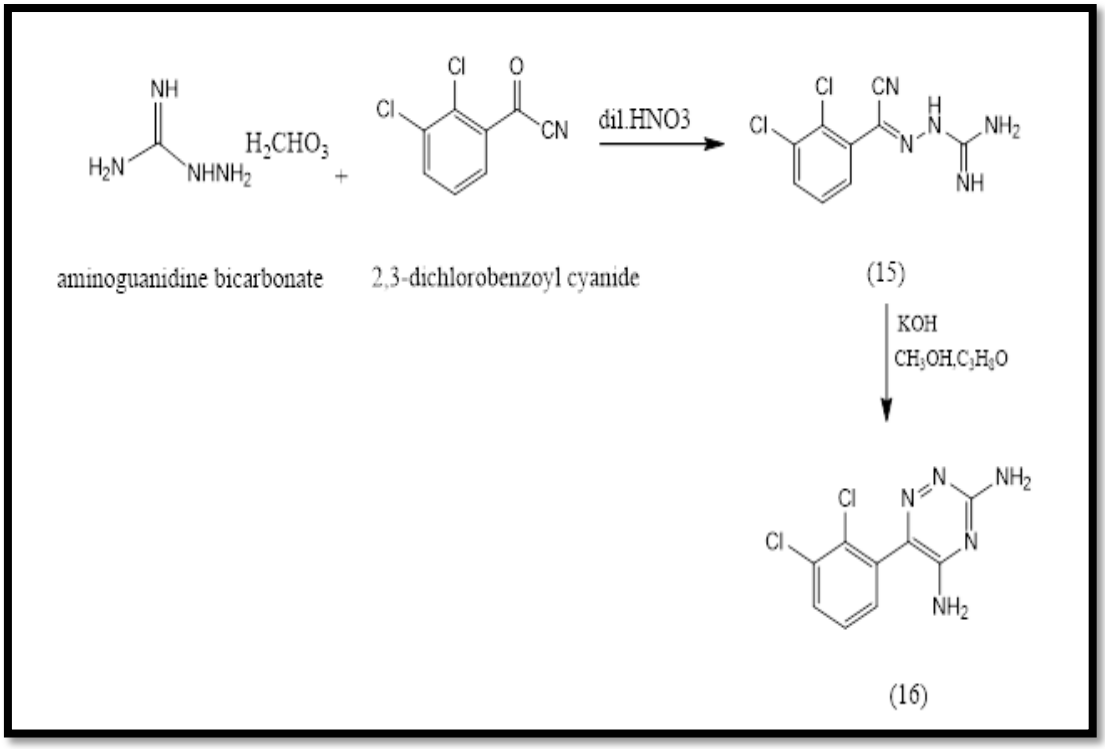
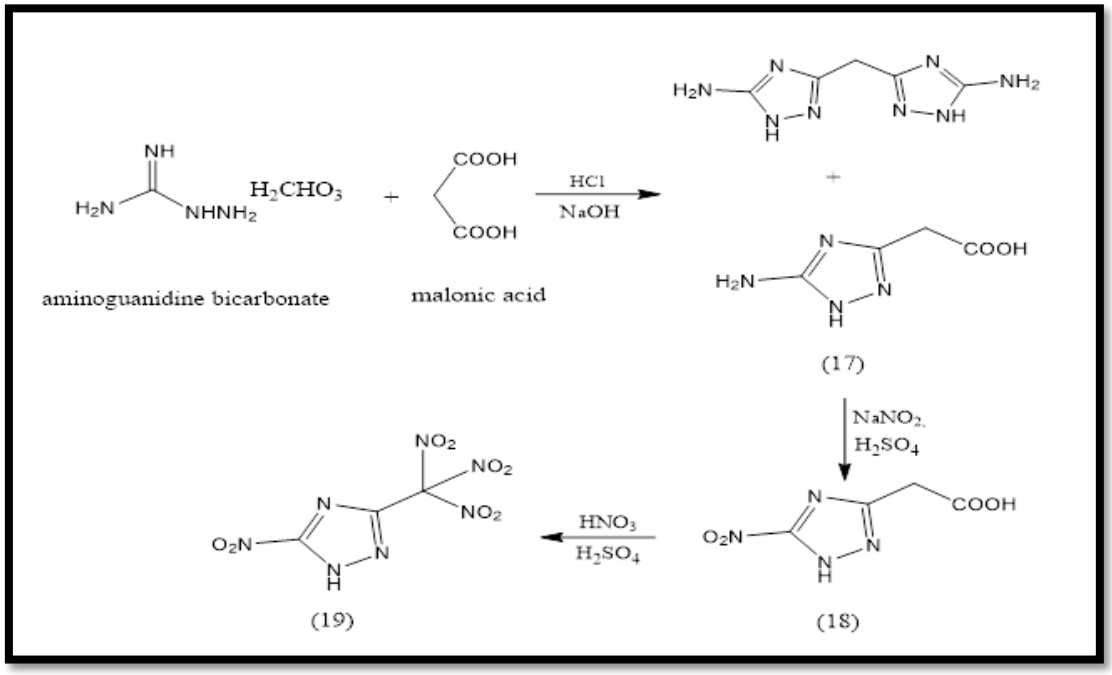
A series of novel lamotrigine (16) was synthesized by an analogous route shown in Scheme 10. Which involves 2-(2,3-chlorophenyl)-2-(guanidin-yl-imino)acetonitrile (15) Schiff base 2,3-dichloro benzoyl cyanide with aminoguanidine bicarbonate cyclization and subjected to evaluation of their anticonvulsant activity.[13]



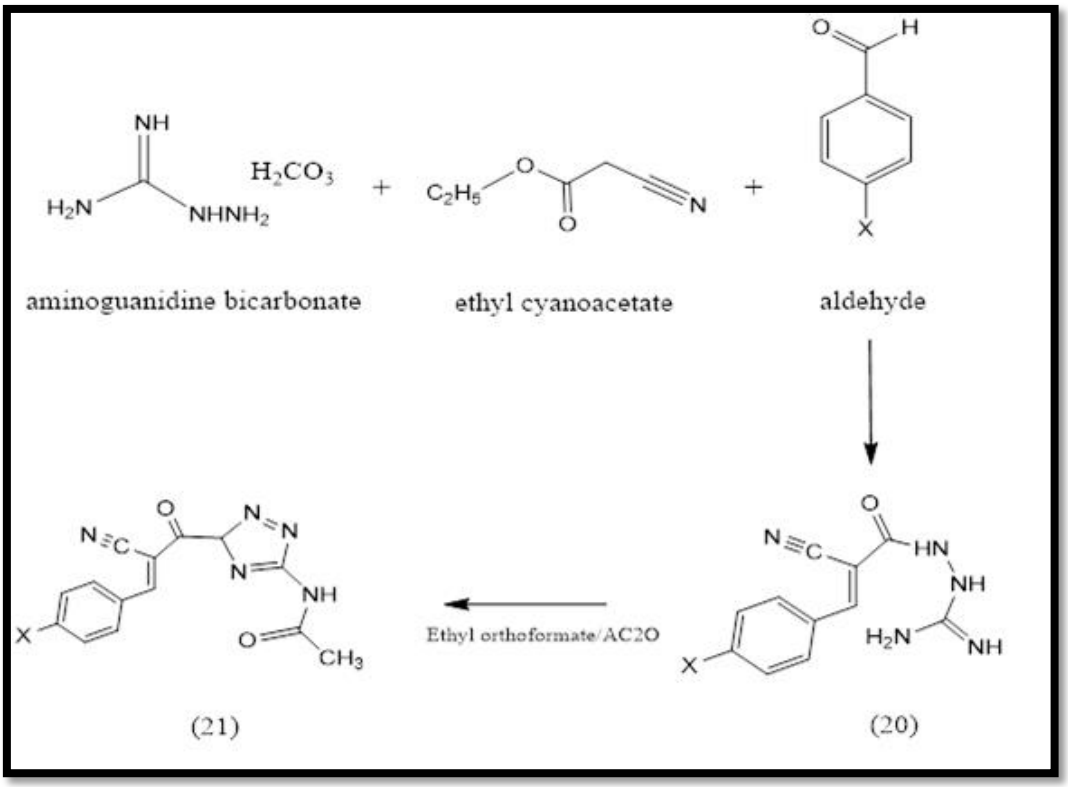

Scheme 10: Lamotrigine

**One** of **the new** trinitromethyl-substituted monocyclic 5-nitro-3-trinitromethyl-1H-1,2,4-triazoles (19) **was** synthesized by **a similar method to** Sche me **11. The precursor 5-amino-1,2,4-triazole-3-acid-ylacetic acid** (17) was prepared using an aqueous solution o f aminoguanidine bicarbonate and malonic **acid and treated with** an excess of nitrite **ions. Made** to form 5-nitro-1H-1,2,4-triazole. -3-yl-acetic acid (18).Attempts to oxidize the amino group to nitro using hydrogen peroxide and sodium tungate were unsuccessful. Nitration of 5-nitro-1H-1,2,4-triazol-3-ylacetic acid using 100% HN03/96% H2SO4 gave 5-nitro-3-trinitromethyl-H-1 in good (75%) yield. ,2,4-triazole (19), show high density, good thermal stability, an acceptable oxygen balance, excellent detonation properties, positive heat of formation, and are subject to evaluation of their energetic properties.



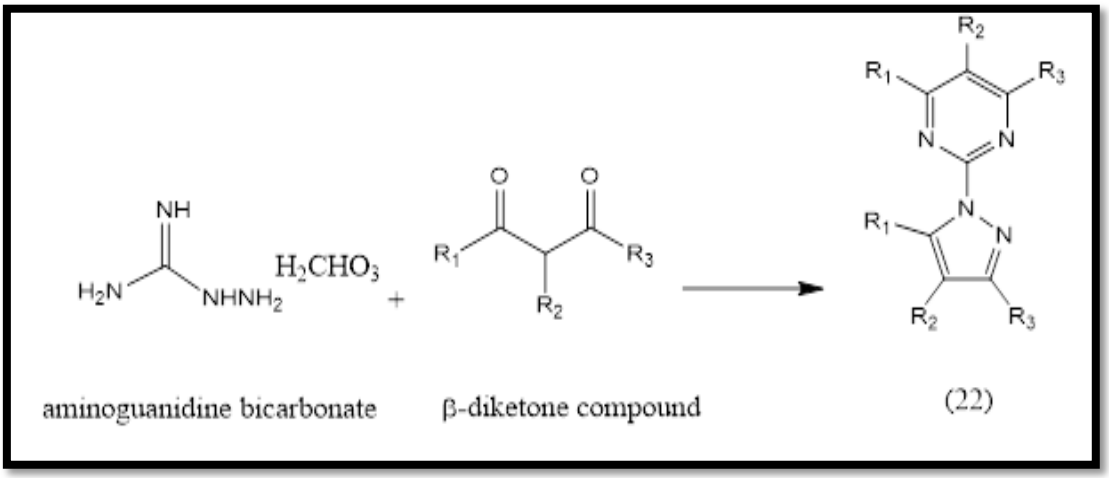

Scheme 11: tri-nitromethyl-substituted monocyclic 5-nitro-3-tri-nitromethyl-1H-l,2,4-triazole

A series of novel N-(1-(2-cyano-3-phenylacryloyl)-1H-1,2,4-triazol-3-yl)acetamide (21) was synthesized by an analogous route shown in Scheme 12. precursor 2-(2-cyano-3-substituted phenylacryloyl)hydrazinecarboximidamide (20) was prepared using aminoguanidine bicarbonate, ethyl cyanoacetate, anhydrous potassium carbonate and an aromatic aldehyde. The reaction is carried out using ethyl orthoformate and the formation of compound (21) and subjected to evaluation of their anticancer activity.[15]




Scheme 12: *N*-(1-(2-Cyano-3-phenylacryloyl)-1*H*-1,2,4-triazol-3-yl)acetamide.

A series of novel pyrimidinylpyrazole (21) was synthesized by an analogous route shown in Scheme 13. It can be obtained by a stepwise reaction of aminoguanidine bicarbonate and a diketone compound. R1, R2 and R3 are determined depending on the intended pyrimidinylpyrazole compound. This reaction in the absence of solvent or reaction in water is subjected to evaluation of their antitumor activity.[16]




Scheme 13:pyrimidinylpyrazole

A **new set** of **1H-1,2,4-triazol-3-ylbenzenesulfonamide** derivatives **(24)** was synthesized by **a method similar to that** shown in Scheme 14. The **precursor 3-amino-1H-1,2,4-triazole** (23) **)** was **obtained** by cyclization **condensation** of aminoguanidine bicarbonate and **a suitable** carboxylic **acid and** was used directly in the next step. **Nucleophilic** substitution **reaction of 3-amino-1H-1,2,4-triazole** and sulfonyl chloride derivatives. **Preparation of** compound (24) and **evaluation of its antibacterial** activity.[17]

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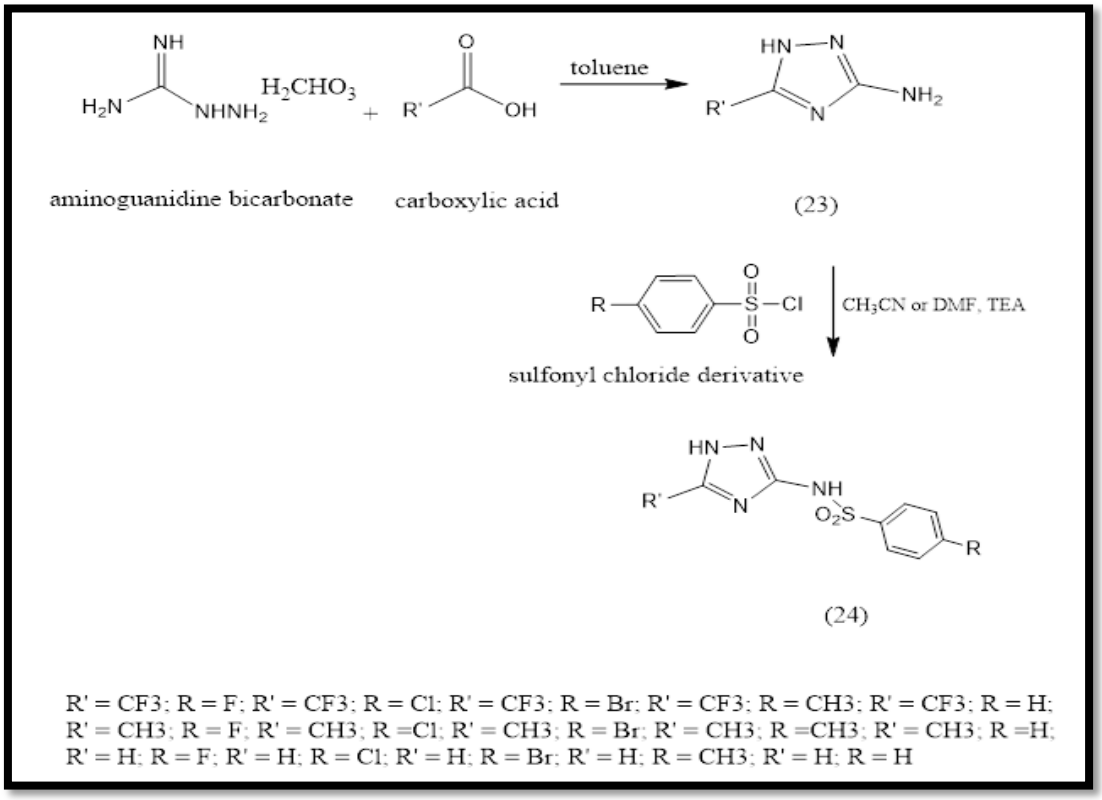
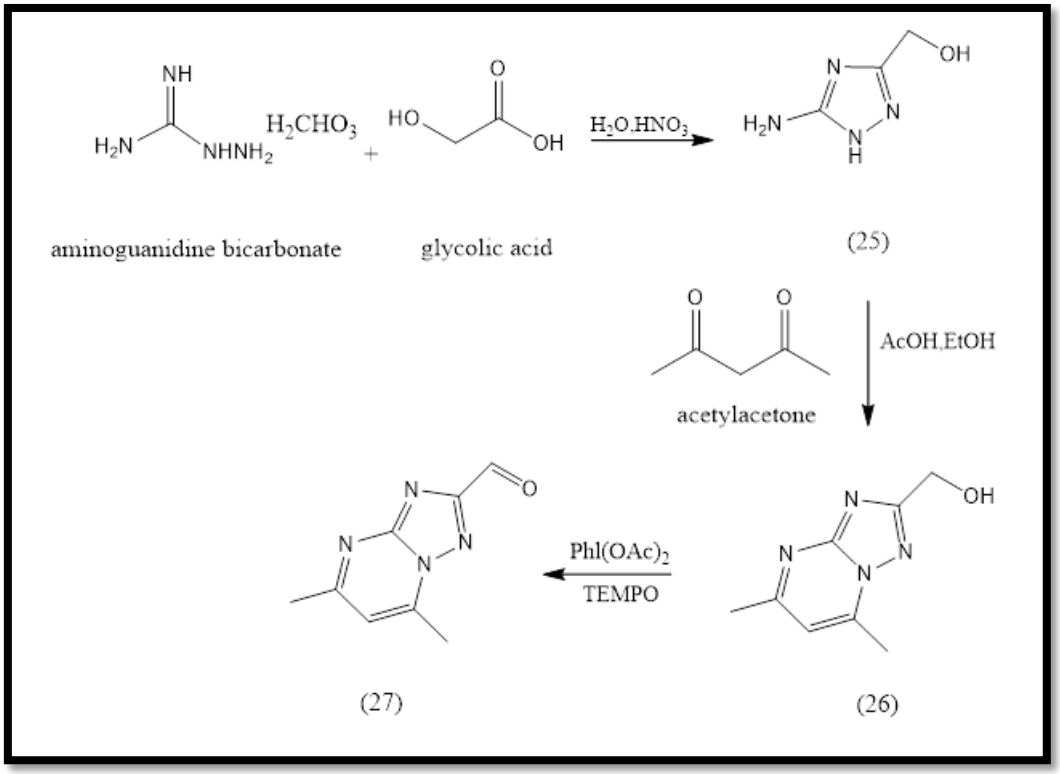



Scheme 14: 1H-1,2,4-triazol-3-yl benzenesulfonamide derivatives

A series of new 5,7-dimethyl-1,2,4-triazolo[1,5a(14C)]pyrimidine-2-carbaldehyde (27) were synthesized analogously to those shown in Scheme 15. The precursor (5-amino-1H-1,2,4-triazol-3-yl)methanol (25) was obtained by cyclization of aminoguanidine bicarbonate and glycolic acid. The next step was directly reacted with acetylacetone to give (5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methanol (26), then PhI(OAc)2/TEMPO mediated oxidation of compound (26) to prepare compound (27) and subjected to evaluation of their herbicidal activity and excellent fungicidal activity.[18]




Scheme 15: 5,7-dimethyl-1,2,4-triazolo[1,5a(14C)]pyrimidine-2-carbaldehyde

## III. CONCLUSION

Aminoguanidine bicarbonate remains an interesting area for researchers, as evidenced by the latest work from 2023. Many of the aminoguanidine bicarbonate derivatives described in this review show potent biological activities and deserve more detailed research in this area. We hope that this article, which synthesizes the knowledge about the biological activities of aminoguanidine bicarbonate, will increase scientific interest in these compounds and encourage the development of new derivatives and their introduction into research in further studies.

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