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AN INSIGHT FEATURES OF QUINOXALINE: A SHORT REVIEW

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ABSTRACT

A quinoxaline, also called a benzopyrazine, in organic chemistry, is a heterocyclic compound containing a ring complex made up of a benzene ring and a pyrazine ring. It is isomeric withother naphthyridines including quinazoline, phthalazine and cinnoline.Quinoxa lines are used as dyes, pharmaceuticals and antibiotics such as echinomycin,levomycin and actinoleutin.Some studies were carried out in order to explore the antitumoral properties of quinoxaline compounds: Recently, quinoxaline and its analogs have been investigated as the catalyst's ligands: They can be formed by condensing *ortho*-diamines with 1,2-diketones. The parent substance of the group, quinoxaline, results when glyoxal iscondensed with 1,2-diaminobenzene. Substituted derivatives arise when α-ketonic acids, α-chlorketones, α-aldehyde alcohols and α-ketone alcohols are used in place of diketones. Quinoxaline and its analogues may also be form by reduction of amino acids substituted 1,5-difluoro-2,4-dinitrobenzene (DFDNB):

KEYWORDS: benzopyrazine, quinazoline, phthalazine and cinnoline.

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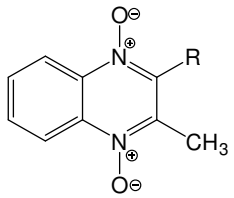
INTRODUCTION

BIOLOGICAL ASPECTS OF QUINOXALINE

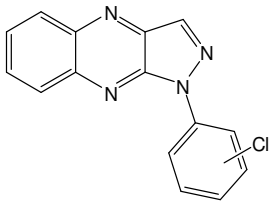
The literature survey revealed that substituted quinoxaline derivatives exhibit a wide variety of biological activities. It has been reported that some quinoxalines demonstrated antibacterial[1-2], antifungal[3-4], antiviral[5], antineoplastic[6], antidepressant[7], hypoglycemic, anti-inflammatory[8], excitatory aminoacid antagonistic[9], antiglaucoma, antiparasitic, antitubercular[10], anticancer[11] and anti HIV-1[12] activities. Many quinoxaline-1, 4-di-N-oxide derivatives have been described as antibacterial agents. Thus, 2-hydroxymethyl-3-methyl quinoxaline-1, 4-di-N-oxide (**1.001**, R=CH_2OH) and a metabolite of 2, 3-dimethyl quinoxaline -1, 4-di-N-oxide (**1.001**, R=CH3) are highly active against gram negative bacteria[3](fig. 1.2)



1.001

Figure 1.1

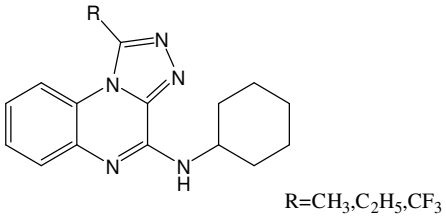
Kurasawa and co-workers prepared a series of pyrazoloquinoxalines 1.002 (fig. 1.2) which was found to possess antifungal activity[5]



1.002

Figure. 1.2

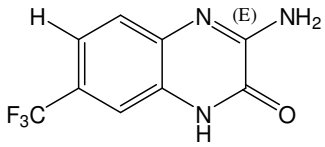
Several [1, 2, 4]-triazolo-[4, 3-a]-quinoxalines 1.003 (fig. 1.3) have been synthesized and found to possess potent antidepressant activity by virtue of their selective adenosine antagonistic activity[9]



1.003

Figure 1.3

In 1999, a group of research workers[10]have synthesized a new series of quinoxaline and submitted to preliminary in vitro evaluation for anticancer and results showed interesting anticancer activity for compound 1.004 (fig. 1.4)



1.004

Figure. 1.4

Recently, several 3, 3-disubstituted-quinoxalinones derivatives were prepared and evaluated as HIV-1 reverse transcriptase inhibitors[11]

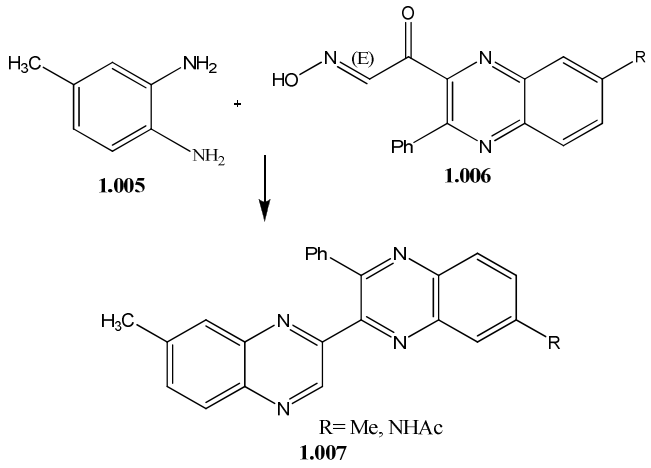
Synthetic aspects of quinoxaline

Synthesis of substituted quinoxalines:

Several routes are available for synthesis of quinoxaline ring, depending on the starting nuclei. These include:

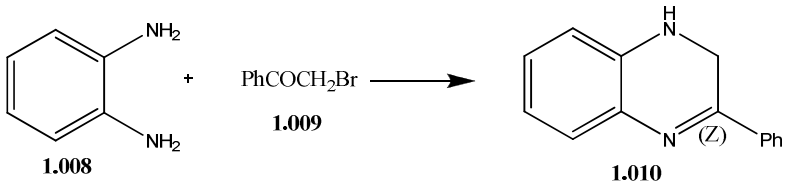
From 1, 2-diamino compounds and 1, 2-bis-electrophiles

The reaction between-1, 2-diamino 4- methyl benzene 1.005 and quinoxalinylglyoxal oximes 1.006 yielded the 2, 2-biquinoxalines 1.007 [Scheme-1.1]. The reaction between 1, 2 diamino compounds and 1, 2 dicarbonyl compounds provide a facile method for quinoxaline synthesis.



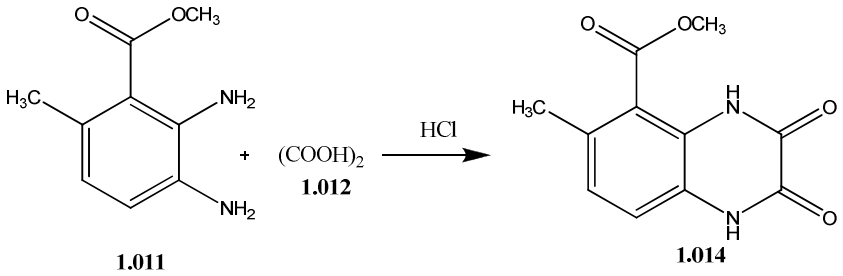
Scheme-1.1

It was also reported that phenyl dihydroquinoxaline 1.010 could be obtained through reaction of phenacyl bromide 1.009 with 1, 2-phenylenediamine 1.008 [Scheme-1.2].

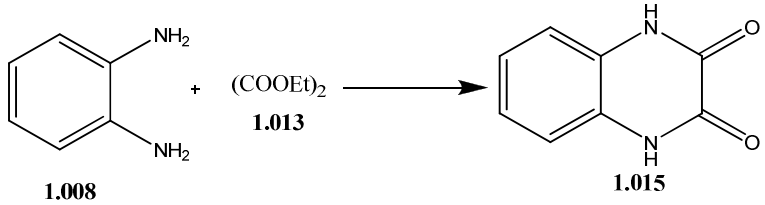


Scheme-1.2

The substituted quinoxalinedione 1.014 and 1.015 have been prepared[13-14]from the reaction of o-phenylene diamine 1.011 or 1.012 with oxalic acid 1.013 or its ester 1.015 following the [Scheme-1.3 and 1.4] respectively.



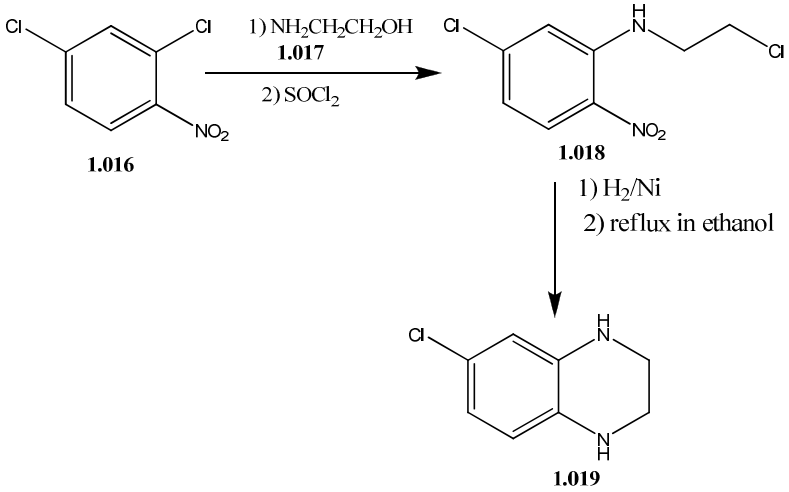
Scheme-1.3



Scheme-1.4

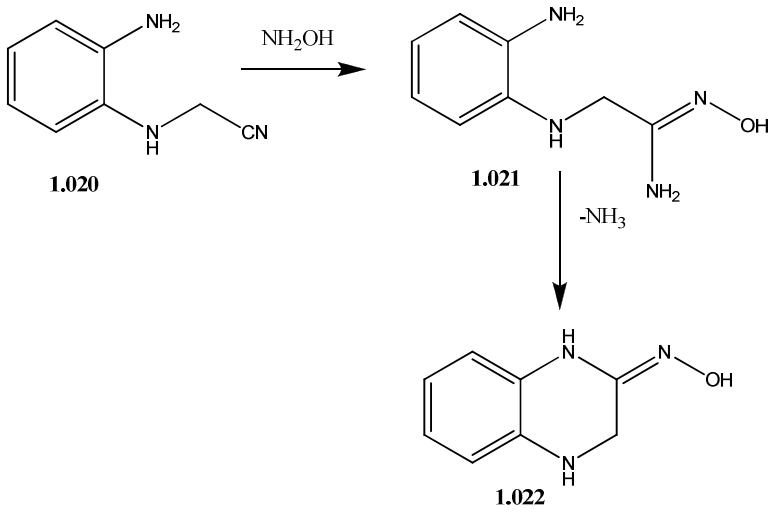
By intramolecular cyclization reactions

2, 4-Dichloronitrobenzene 1.016 was used as the starting material for the preparation of substituted 1, 2, 3, 4-tetrahydroquinoxaline 1.019 (Scheme-1.5). Interation of 1.016 with 2-aminoethanol followed by reaction with $SOCl_2$ formed 1.020. Reduction followed by subsequent cyclocondensation of 1.028 afforded 1.019 [15][Scheme-1.5].



Scheme-1.5

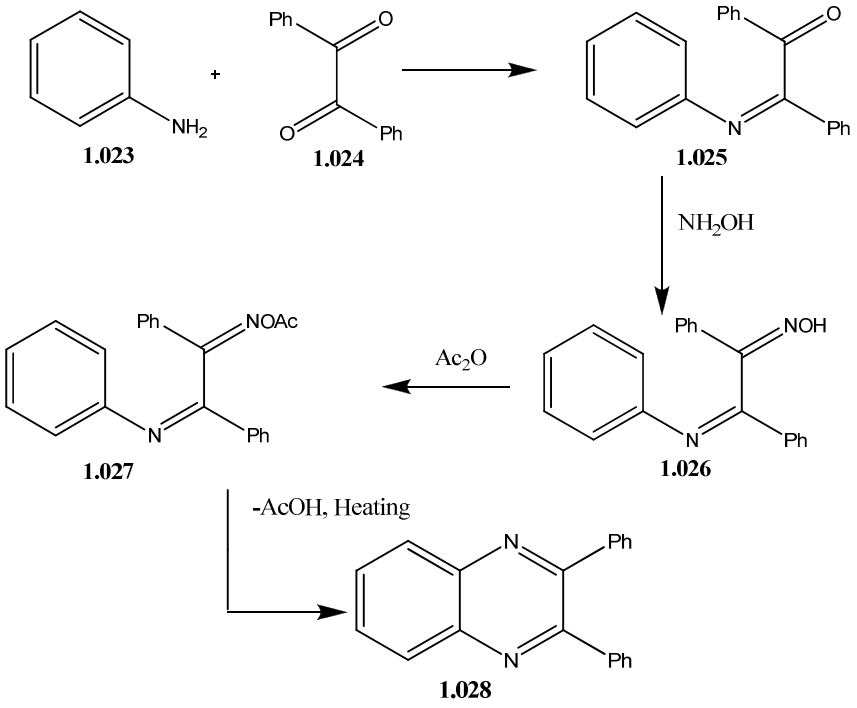
On the other hand,addition of hydroxylamine to N-(cyanomethyl) 1,2-phenylenediamine 1.020 , formed 1.021, which underwent cyclization with loss of ammonia to give 2-(hydroxyimino)-1,2,3,4-tetrahydro quinoxaline 1.022 [Scheme-1.6].



Scheme-1.6

From α-arylimino-oximes of α-dicarbonyl compounds

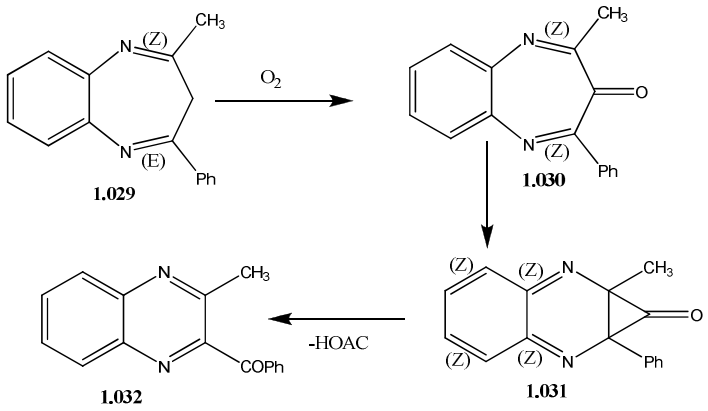
In 2000, a new method for quinoxaline synthesis[16] was developed which involved condensation of a primary aromatic amine 1.023 with α-dicarbonyl compound 1.024 to give 1.025 whose oxime 1.026 on treatment with Ac_2O formed the corresponding acetyl derivative 1.027, which on thermal cyclization afforded 1.028 [Scheme- 1.7].



Scheme-1.7

From diazepines

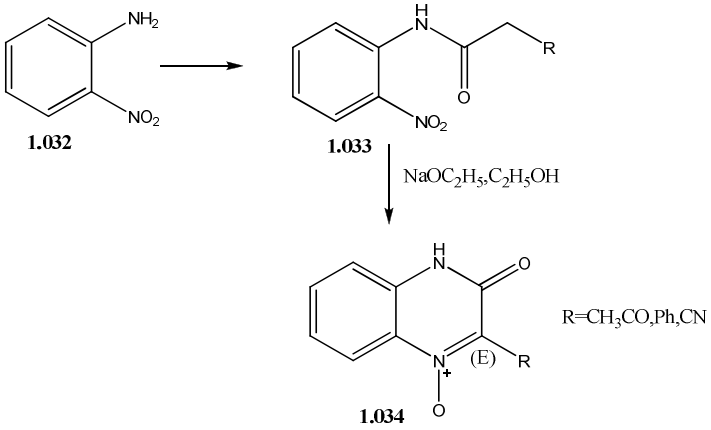
Ring contraction of diazepines to quinoxalines has been reported[17]thus, a photoxidation reaction, 2-methyl 4-phenyl -1, 5-benzodiazepine 1.029, gave 2-benzoyl-3-methyl quinoxaline 1.032 through the intermediacy of 1.030 and 1.031 respectively [Scheme-1.8].



Scheme-1.8

Preparation of quinoxaline-N-oxides

Cyclization of α-substituted o-nitroacetanilide 1.033, obtained from o-nitroaniline 1.032 and substituted acetyl chloride, gave quinoxaline-N-oxide [18]1.034 [Scheme-1.9].

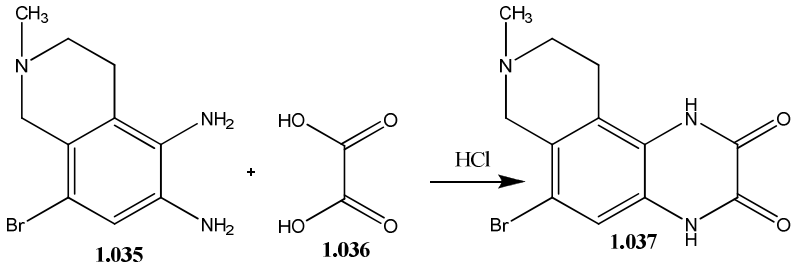


Scheme-1.9

Synthesis of fused quinoxalines

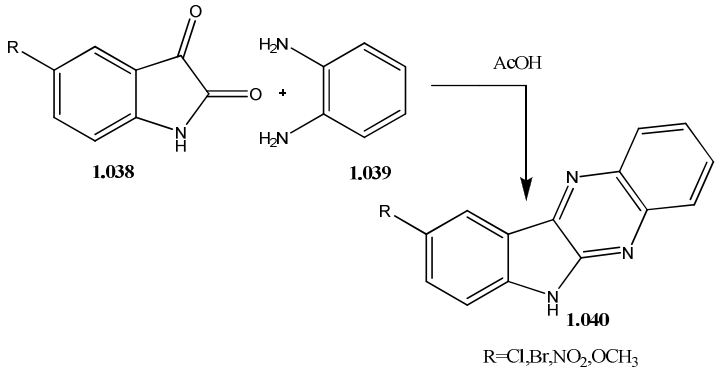
From 1,2-diamino compounds and 1,2-bis-electrophiles

8-Bromo-1, 2, 3, 4-tetrahydro 2-methyl 5, 6 isoquinolinediamine 1.035 condensed with oxalic acid **1.036** to provide quinoxaline [19] 1.037 [Scheme-1.10].



Scheme-1.10

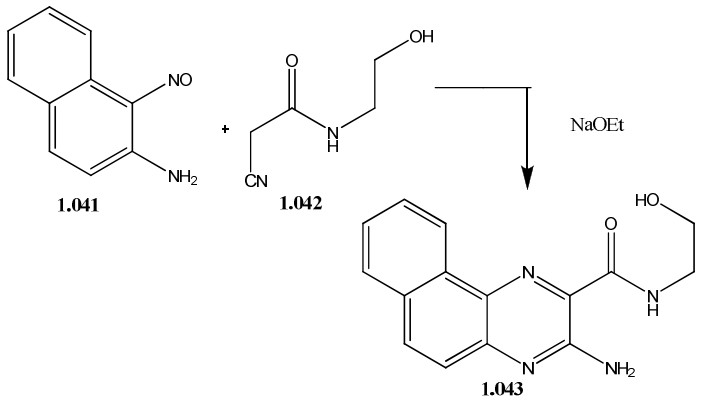
Fused quinoxalines were also prepared using cyclic 1, 2-dicarbonyl compounds[20]. Thus, indoloquinoxalines 1.040 were obtained via condensation of substituted isatins 1.038, with 1, 2-phenylenediamine 1.039, in glacial acetic acid [Scheme-1.11].



Scheme-1.11

From nitroso aromatic amines and active methylene compounds

Santilli and Osdene[21] showed that 1-nitroso 2-naphthylamine 1.041, when reacted with N-substituted cyanoacetamide 1.042, in sodium ethoxide, the substituted benzoquinoxaline derivative 1.043, were obtained [Scheme-1.12].



Scheme-1.12

CONCUSION

In this article we have synthesized qunoxaline in different types of methods which is further useful to differen biological activities etc.

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