Chemistry of Heterocyclic Compounds, Vol. 45, No. 11, 2009

MICROWAVE-ASSISTED SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME PYRAZOL-1-YLQUINOXALIN-2(1H)-ONE DERIVATIVES

Olayinka O[1]. Ajani[1]*, Craig A[1]. Obafemi[2], Chinwe O. Ikpo[1], Kehinde O.[1] Ogunniran[1], and Obinna C. Nwinyi[3]

3-Hydrazinoquinoxalin-2(1H)-one was prepared from quinoxaline-2,3-dione and subsequently used for the synthesis of some potentially biologically active 3-(pyrazol-1-yl)quinoxalin-2(1H)-one derivatives. While 3-(3,5-dimethylpyrazol-1-yl)quinoxalin-2(1H)-one showed a comparative effect with streptomycin, 3-(5-oxo-3-phenyl-4,5-di- hydropyrazol-1-yl)quinoxalin-2(1H)-one was found to be the most active with an MIC value of 7.8 μg/ml.

Keywords: 3-hydrazinoquinoxalin-2(1H)-one, imines, Gram-positive bacteria.

Over the years it has been established that quinoxalines are, in general, relatively easy to prepare [1-3], and many derivatives have been synthesized with the aim of obtaining biologically active materials [4, 5]. Some quinoxaline and quinoxalinone derivatives have been reported to show antimicrobial [6, 7], antiinflammatory [8], antifungal [9], anticancer [10], antiviral [11], antimalarial [12], anticonvulsant [13], antidepressant [14], antitubercular [15], antibacterial [16], and antithrombotic [17] activities.

Thermal and chemically stable polyquinoxalines (PQs) find potential applications as films, coating adhesives [18], ultrafiltering materials, and composite matrices that demand stability in harsh environment [19]. In a similar manner the synthesis of novel pyrazole derivatives [20] and evaluation of their chemical behaviors have gained more importance in recent decades for biological [21–23], medicinal [24], and agricultural [25] purposes. Although numerous methods are available for construction of pyrazoles [26, 27], only little attention has been given to the pyrazolysis of quinoxalinone derivatives [28]. For instance, 1,3-dipolar cycloadditions of azomethine imines, available by acid catalyzed treatment of 3-pyrazolidinone with acetone and butyraldehyde, respectively, were studied [29]. The photoluminescence and electroluminescence of some new 1H-pyrazolo-

* To whom correspondence should be addressed, e-mail: wajanfresh@yahoo.com.

[1]Chemistry Department, College of Science and Technology, Covenant University, Canaanland, Km 10, Idiroko Road, P.M.B. 1023, Ota, Ogun State, Nigeria.
[2]Department of Chemistry, Faculty of Science, Obafemi Awolowo University, Ile-ife, Osun State, Nigeria.
[3]Department of Biological Sciences, College of Science and Technology, Covenant University, Canaanland, Km 10, Idiroko Road, P.M.B. 1023, Ota, Ogun State, Nigeria.

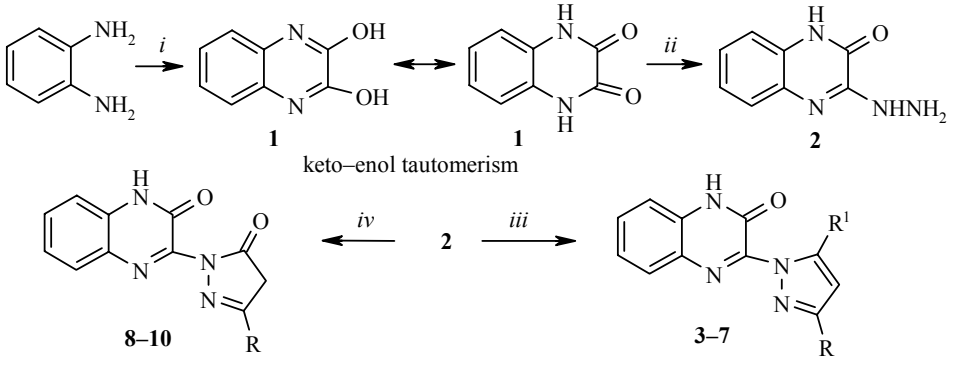
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1703-1713, November, 2009. Original article received April 17, 2009.

[3,4-*b*]quinoxaline derivatives have been investigated [30], while the biological properties of such moieties have been understudied [31]. From this point of view it is of great interest to synthesize some pyrazolylquinoxalinone derivatives with the aim of investigating their antibacterial properties.

3-Hydrazinoquinoxalin-2(1H)-one **(2)** was prepared from hydrazinolysis of 1,2,3,4-tetrahydroquinoxaline-2,3-dione **(1)**, which existed as a keto-enol tautomer (Scheme 1). The starting material **1** was prepared by the modified Obafemi and Pfleiderer procedure [32]. To a heated (100°C) solution of oxalic acid dihydrate in water, acidified *o*-phenylenediamine was added cautiously with vigorous stirring at 100°C for 20 min. The resulting mixture was cooled and then filtered off. The crude solid obtained was purified by crystallization from water to afford colorless needles of compound **1**. 3-Hydrazinoquinoxalin-2(1H)-one **2** underwent condensation reaction with various β-diketones to afford (3,5-disubstituted pyrazol-1-yl)quinoxalin-2(1H)-one derivatives **3–7** in excellent yields (Scheme 1). For instance, the reaction of compound **2** with 2-thenoyltrifluoroacetone gave 97% of 2-trifluoromethyl-substituted pyrazole **7** as a single product. This is because the carbonyl next to CF_3 is more reactive than the carbonyl next to thiophene due to the high electron withdrawing ability of the trifluoromethyl side chain. Therefore, the nucleophilic attack by NH_2 of hydrazine was initiated first on the carbonyl next to CF_3.

Furthermore, condensation of compound **2** with α-keto esters followed by thermal cyclization of the reaction intermediate in the presence of ethanol solvent gave the target structure of (3-alkyl(aryl)-5-oxo-4,5-dihydropyrazol-1-yl)quinoxalin-2(1H)-one derivatives **8**, **9**. The carbonyl of ketone is attacked first since it is more reactive than the carbonyl of ester. Finally, upon treatment of compound **2** with ethyl cyanoacetate the main product obtained was 3-(3-amino-5-oxo-4,5-dihydropyrazol-1-yl)quinoxalin-2(1H)-one (**10**) in moderate yield (Scheme). Melting points of all compounds were on the high side (177 to > 360°C) as a result of the presence of amide bonds and the probable existence of intramolecular hydrogen bonding.

Scheme 1



i: oxalic acid/HCl/H_2O; *ii*: $H_2NNH_2 \cdot H_2O$; *iii*: pentane- or hexane-, or heptane-2,4-dione, or heptane-3,5-dione, or 2-thenoyltrifluoroacetone; *iv*: ethyl acetoacetate or ethyl benzoylacetate, or ethyl cyanoacetate; **3** R = R^1 = Me, **4** R = Me, R^1 = Et; **5** R = Me, R^1 = Pr; **6** R = R^1 = Et; **7** R = CF_3, R^1 = Th; **8** R = Me, **9** R = Ph, **10** R = NH_2

The IR spectra of compounds **1**–**10** showed absorption bands due to the stretching vibrations of N–H, C=O, C=C, and C=N at 3470-3132, 1705-1648, 1620-1600, and 1580-1509 cm^{-1}, respectively. The IR spectrum of compound **9** showed a broad band at 3302 cm^{-1} due to the stretching vibration of N–H, while its two carbonyl stretching vibration appeared at 1703 and 1648 cm^{-1}, respectively. The IR absorption band at 1600 cm^{-1} depicted the presence of aromatic C=C, while C=N band was observed at 1509 cm^{-1}. The UV-visible spectrum of compound **9** gave rise to the wavelength (λ_{max}) at 208 and 352 nm, while a shoulder was observed at 244 nm. The wavelength at 208 nm is a result of $\pi \rightarrow \pi^*$ transition of the phenyl ring, while 352 nm is a result of contribution from the pyrazolyl ring. The electronic transition in the UV-visible spectra gave rise to the wavelength