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**R E S E A E C H A R T I C L E**

# Synthesis of *N*-(3-Oxo-2,4-dihydro-1*H*-quinoxalin-2-yl)Benz amide

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**A B S T R A C T**

The title compound, N-(3-Oxo-2,4-dihydro-1H-quinoxalin-2-yl)benzamide2, was synthesized in high yield, via N-alkylation reaction of methyl 2-azido-2-benzamidoacetate or methyl 2-bromo-2-benzamidoacetate with o-phenylenediaminein acetone, with the presence of diisopropylethylamine(DIEPA) as a base. The structure of the prepared compound was characterized by 1H, 13C NMR in addition to MS.

**Keywords:** O-Phenylenediamine, heterocyclic compounds, Quinoxaline, N-alkylation.

**A R T I C L E I N F O**

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**C O N T E N T S**



## 1. Introduction

In recent years the heterocyclic compounds are very much used as anti-microbial agents [1-3]. Quinoxalines are an important class of nitrogen containing heterocyclic with wide variety of biological activities [4-8]. Quinoxalinone structure has good physico-chemical properties and drug-like properties. Many bioactive compounds contain this moiety [9,10]. It has received much attention as a potential pharmacophore in medicinal chemistry. Different derivatives of quinoxalines are found to posses antifungal [11], antimicrobial, bacteriostatic, antibacterial, plant fungicide, antiallergic [12], CNS depressant [13], antimalarial [14], antiviral [1], antileprotic [15], anti-inflammatory [16], antitumor activity [17]. Quinoxaline ring is a part of various antibiotics, such as Echinomycin,

Levomycin and Actinoleutin that are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors. Meanwhile, the incidence of drug resistance in gram positive bacteria is growing rapidly and has become a significant public health threat. Quinoxaline-2,3-Dione is used to treat Parkinsonism [18], epilepsy [19], Alzheimer's disease [20], Huntington's disease [21], anti convulsants [22] and also to treat anti thrombin, Bradykinin, anti-tumor. Quinoxaline-2,3-Dione is used for treating conditions such as a cerebral ischemia or cerebral infarction resulting from range of phenomena thrombo embolic or hemorrhagic stroke, cerebral vasospasms, hypoglycemic cardiac arrest status epilepticus, perinatal asphyxia, anorexia, such as from drowning, pulmonary surgery and cerebral trauma [23,24].

## 2. Materials and Methods

**General:**

Melting points were determined with an Electrothermal melting point apparatus and are uncorrected. $^{1}$H NMR spectra were recorded on a Bruker AC-250 MHz spectrometer in $CDCl_3$ with TMS as an internal standard; coupling constants are reported in Hz. NMR data are listed in ppm and are reported relative to tetra-methylsilane ($^{1}$H, $^{13}$C); residual solvent peaks being used as internal standard. All reactions were followed by TLC. TLC analyses were carried out on 0.25 mm thick precoated silica gel plates (Merck FertigplattenKieselgel 60F254) and spots were visualised under UV light or by exposure to vaporised iodine. Mass spectra were recorded by electrospray on a micromassESl Platform II.

**Typical procedure:**

To a stirred solution of 2.86 mmol of *o*-phenylenediamine and 3.12 mmolof diisopropylethylamine in 10 mL of dry acetone, 2.6 mmol of α-azido glycinatewere added. The mixture was stirred at room temperature and the reaction was followed by TLC (Kiesegel Merck 60F254). The solvent was evaporated under reduced pressure. The residue was quenched with saturated aqueous solution of ammonium chloride (20 mL) and extracted with dichloromethane (20 mL × 3). The organic phase was dried in sodium sulfate ($Na_2SO_4$) and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel using ether as eluant.

**N-benzoylated methyl a-azidoglycinate1:**Yield = 92% (white solid); m.p = 80–82 °C. $^{1}$H-NMR (DMSO, $\delta_H$ppm): 3.74 (s, 3H, -$OCH_3$); 5.82 (d, 1H, N-CH-$N_3$, J = 7.80Hz); 7.49–7.91 (m, 5H, 5$H_{arom}$); 9.83 (d, 1H, NHBz, J = 7.80Hz). $^{13}$C-NMR (DMSO, $\delta_C$ ppm): 53.41 (C, -$OCH_3$); 65.62 (1C, N-CH-$N_3$); 128.03, 129.04, 132.76 and 132.87 (6C, $C_{arom}$); 167.18 and 167.67 (2C, CO). MS ESI m/z (%) = 235.

**N-(3-Oxo-2,4-dihydro-1H-quinoxalin-2 yl)benzamide2:**$^{1}$H NMR ( DMSOd6 ): δ: 4.91 (br s, 1H, NH), 5.82 (1H, m, Hα); 6.9-7.2 (3H, m, Harom); 7.4-7.9 (6H, m, Harom); 9.1 (1H, d, J = 8.2 Hz, NHamide); 10.8 (1H, s, NHamide). $^{13}$C NMR (DMSOd6): δ: 63.91 (-CH-); 117.32, 118.86, 123.67, 126.64, 127.35, 127.76(2C), 128.80 (2C), 132.85, 133.91, 136.42 ($C_6H_5$ aromatic carbons); 166.70, 169.85 (2CO).MS. (electrospray): [M+] = 267.2; [M+H+] = 268.2; [M+Na+] = 307.2; [2M+Na+] = 556.4; $C_{15}H_{13}N_3O_2$.

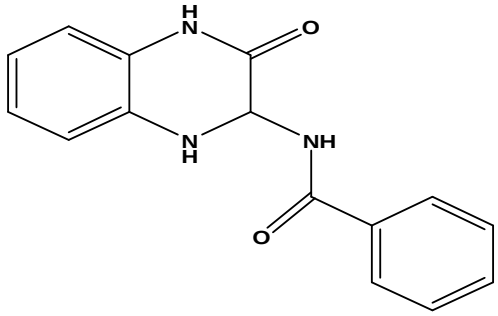
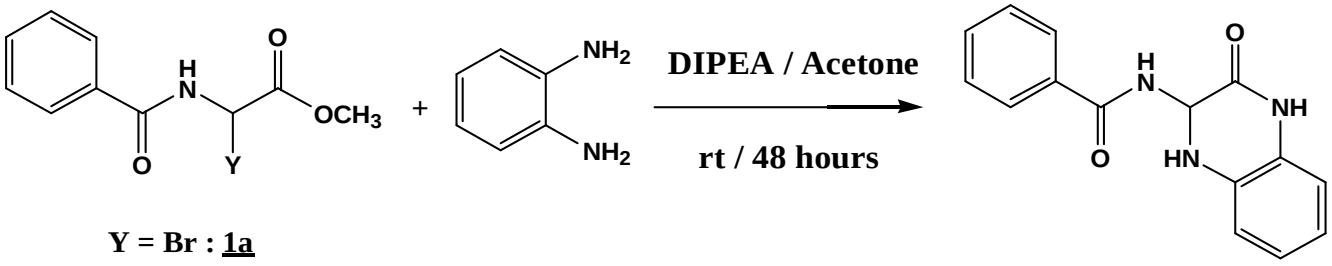


**Figure 1**

## 3. Results and Discussions

Continued our investigations on the useof organic azides[25] in heterocyclic synthesis, we reported in this paper another part of our investigations concerning the synthesisof new heterocyclic carboxylic compounds.Our strategy is based on a double *N*-alkylation of *o*-phenylenediamine with methyl 2-bromo-2-benzamidoacetate **1a** or methyl α-azido glycinate**1b** (scheme 1). Methyl α-azido glycinate**1b** was obtained by the reaction of sodium azide with the methyl α-bromoglycinate. The title compound is stable and can be stored for an unlimited time without any signs of decomposition. The azide**1b** is used especially for its stability. As shown in Scheme 1, the reaction of *o*-phenylenediamine with methyl α-bromoglycinate**1a** or methyl α-azido glycinate**1b**were performed in presence of diisopropylethylamine (DIEPA) in acetone at room temperature for 48 hours. Results are summarized in Table 1.




**Y = Br : 1a**

**Y = $N_3$ : 1b**

**Scheme 1:** Double *N*-alkylation of *o*-phenylenediaminewith methyl α-bromoglycinate**1a** and methyl α-azido glycinate**1b**

**Table 1:** Synthesis of*N*-(3-Oxo-2,4-dihydro-1*H*-quinoxalin-2-yl)benzamide **2**

| Nu-H | Entry | Product | Reaction Time (h) | DIPEA Acetone |
|---|---|---|---|---|
| | | | | Yield (%) |
| o-phenylenediamine | **1a** | *N*-(3-Oxo-2,4-dihydro-1*H*-quinoxalin-2-yl)benzamide**2** | 48 | 78 |
| | **1b** | | 24 | 90 |

The product **2** was obtained in high yieldfrom **1a**and **1b** and was analyzed by MS, $^{13}$C NMR and$^{1}$HNMR.

## 4. Conclusion

In order to study their biological activities, we considered it interesting to synthesize new compounds of *N*-(3-Oxo-2,4-dihydro-1*H*-quinoxalin-2-yl)benzamideand its derivatives. The nucleophilic substitution of α-azido glycinate and α-bromoglycinate with o-phenylenediamine occurred under very mild conditions and led after about 48 h to the desired productwith satisfactory yields. This method provides general and convenient access to a wide range of the heterocyclic compounds.

## 5. Acknowledgement

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