

## A Facile Syntheses of 3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one

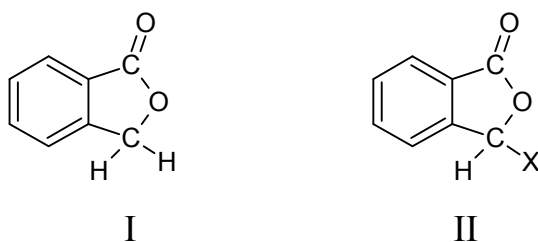
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### **Abstract :**

In this study, a simple one-pot reaction between 3-aminoquinoline and 2-formylbenzoic acid in methanol at 24<sup>0</sup>C affords the corresponding phthalide (3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one in high yields. The structure of the desired product was confirmed from their (NMR) and (IR) spectral data.

### Introduction:

The phthalide (Isobenzofuran-1(3H)-one ) ring system (I) and its derivatives(II) are of interest not only because it is present in some natural products<sup>1</sup> but also are known to possess biological activities as, antihemolytic<sup>2</sup>, antiallergic<sup>2</sup>, antirheumatic<sup>2</sup>, anti-inflammatory<sup>3</sup>, antihypertensives<sup>4</sup>, antiarrhythmias<sup>5</sup>, antiasthmatic<sup>6</sup>, anticonvulsant<sup>7</sup>, and vasorelaxant<sup>8</sup>, in addition some of them have industrial application<sup>9</sup>



X = NHR, OH, OR.

In previous Study<sup>10,11</sup>, we found that in the reaction of 2-formylbenzoic acid with secondary amines like N-methyl and N-phenylaniline afforded products, in which amination occurs at C-3 position while the reaction of diisopropyl amines as example of secondary aliphatic amines with 2-formylbenzoic acid afforded N,N-diisopropyl(o-formylbenzamide) this compound resulted from the nucleophilic addition reaction of the amine at C-1 of the phthalide, on the other hand, 2-formylbenzoic acid can react with primary heterocyclic amines and afford products, in which amination occurs at C-3 position.

In these study we thought of reacting 2-formylbenzoic acid (I) with 3-aminoquinoline as example of new polycyclic heterocyclic amines.

### **Experimental:**

All melting points were measured on electrothermal melting point apparatus (FP80), and were uncorrected. Infrared spectra (IR) were measured using FTIR Spectrophotometer. Proton nuclear magnetic resonance spectra ( $^1\text{H-NMR}$ ) were measured using a Bruker operating at 300 MHz Spectrometer, with tetramethylsilane (TMS) as standard and chemical shifts were recorded in ppm.

### **Reaction of 2-Formylbenzoic acid with 3-aminoquinoline:**

A mixture of 2-formylbenzoic acid (1.5g, 0.01mole) and equimolar amount of 3-aminoquinoline (1.4g, 0.01mole) in methanol (20ml) was refluxed for about 1 hr, and then cooled. The separated solid was collected.

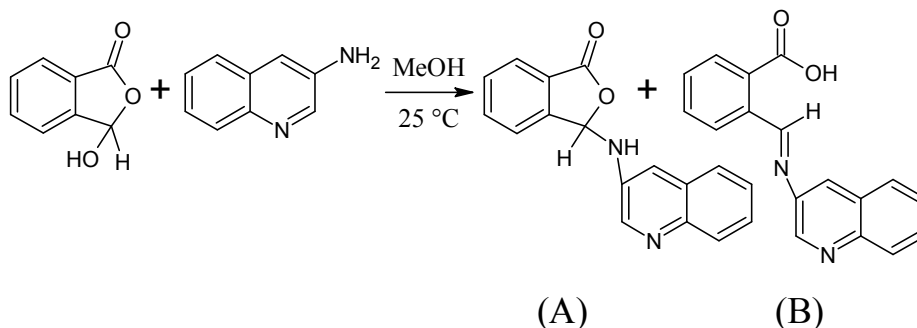
### **Results And Discussion:**

The condensation of 2-formylbenzoic acid with 3-aminoquinoline in refluxing methanol afforded a crystallisable solid product the analytical data of isolated phthalide given in Table-1. (TLC) of the crude product indicating the presence of one single component.

The IR spectra of isolated compound fig.(03) shows the presence of two strong absorption bands at ( $3310\text{ cm}^{-1}$ ) and at ( $1735\text{ cm}^{-1}$ ) . The former can be attributed to NH stretching, while the second is due to the presence of a lactonic group.

The  $^1\text{H-NMR}$  spectra ( $\text{CD}_3\text{OD}$ ) of the product (fig.01and 02) shows the presence of one proton singlet at  $\delta : 7.16$  due to phthalidyl proton (H-3) and a multiplet at  $\delta 7.50\text{-}7.93$  due to ten aromatic proton and at  $\delta 8.57$  a broad singlet exchange with  $\text{D}_2\text{O}$  due to NH proton

These results rule out the possibility of Schiff base formation of type (B) and clearly indicate the formation of N-(3-phthalidyl)-amine of type (A). These compounds can only arise if the 3-aminoquinoline reacts with the lactol form of the acid through  $\text{S}_{\text{N}}2$  nucleophilic substitution reaction on carbon No.3 The deshielding of H-3 in these compounds, compared with CH-N alkyl analogs can be attributed to the anisotropic effect caused by the hetero-aromatic ring.



The product of the closed form of the acid can be explained according to the following proposed mechanism.



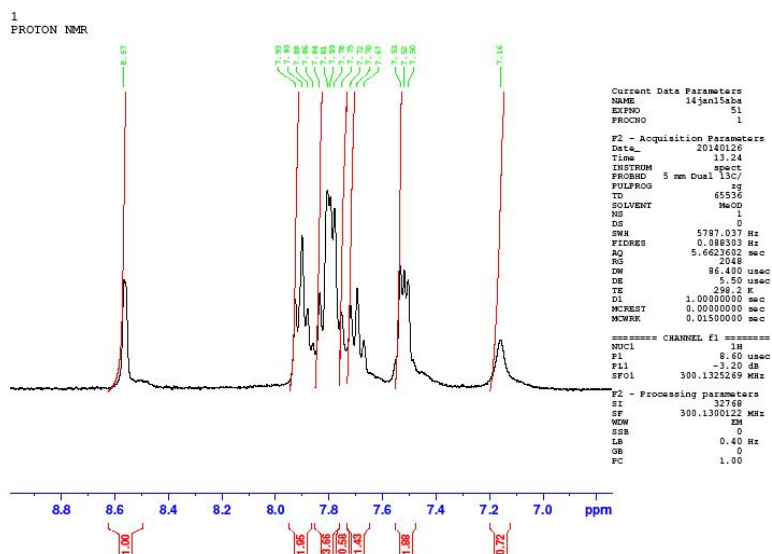


Fig. (02) The <sup>1</sup>H-NMR spectra of 3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one in (CD<sub>3</sub>OD), D<sub>2</sub>O added.

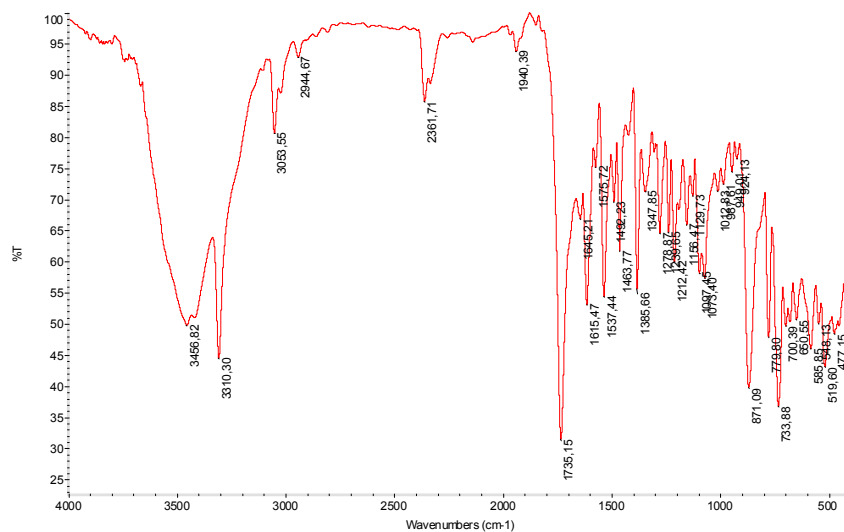


Fig. (03) The IR spectra of 3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one.

**Table (1) Analytical data of phthalide 3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one.**

phthalide	Molecular formula	Yield (%)	Melting point (°C)	Solvent for crystallization
3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one	C <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	89	184-185	Methanol

**Table (2) Spectral data of phthalide 3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one.**

phthalide	Infrared (cm <sup>-1</sup> )	H-3	<sup>1</sup> H-NMR (CD <sub>3</sub> OD, TMS, PPM) Aromatic protons
3-(quinolin-3-ylamino) isobenzofuran-1(3H)-one	(N-H) 3310 (C=O) 1735 (C=C) 1615	7.16	7,50-7.93 (m, 10H) 8.57(s, NH)

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