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DESIGN, SYNTHESIS AND CHARACTERISATION OF SOME SEMICARBAZONE
AND THIOSEMICARBAZONE DERIVED FROM 3-PHENYLQUINAZOLINE-2, 4(1H,
3H)-DIONE

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ABSTRACT

This paper presents the synthesis and characterizations of some semicarbazone and thiosemicarbazone derivatives of 3-phenylquinazoline-2,4(1H,3H)-dione. All compounds reported here had been characterised by ¹H NMR and IR spectral studies and elemental analysis. semicarbazone and thiosemicarbazone derivatives of 3-phenylquinazoline-2,4(1H,3H)-dione were prepared by treating mixture of phenyl isocyanates and anthranilic acid in ethanol to get 3-phenylquinazoline-2,4(1H,3H)-dione which will then condense with substituted 4-chloro/bromo/iodoacetophenones in ethanol to form the chalcones. These chalcones were treated with semicarbazide and thiosemicarbazide in ethanol to get semicarbazone and thiosemicarbazone derivatives of 3-phenylquinazoline-2,4(1H,3H)-dione to explore the biological activities and importance as ligands for various transition metal complexes.

Keywords: Schiff's base, Semicarbazone, Thiosemicarbazone, 3-phenylquinazoline-2,4(1H,3H)-dione

I. INTRODUCTION

Many quinazoline derivatives possessing wide range of biological activities are reported in the literature [1]. The antimalarial activity of febrifuge spurred the synthesis and testing of a number of quinazolines derivatives and this resulted in the claim of patents for potent anti-malarial materials. Valentini [2] observed anti-malarial activity with less toxicity in 4-alkylamino quinazolines and this leads to synthesis of several such compounds [3-6]. Several 2,3-disubstituted 4-keto quinazolines are found active against Plasmodium gallinaceum. Some quinazolines are known for their usefulness other than medicinal have also been reported. 2,4-dichloro and 2,4,6-trichloroquinazolines were used as dye fastening agents by Saftien [7]. Natural 4-quinazolones form a small but an important group of alkaloid and have been isolated from variety of plants. The prominent representatives of this group were erborine, febrifugine, evodiamine and rutacecrpine which contain a 4-keto quinazolin nucleus. Taking into consideration all above points and especially the importance of quinazoline moiety in the present investigation we have synthesized various semicarbazone and thiosemicarbazone derivatives of 3-phenylquinazoline-2,4(1H,3H)-dione in order to explore the biological activities and importance as ligands for various transition metal complexes.

II. EXPERIMENTAL

All chemicals used were of A.R. grade purchased from S.D Fine chemicals (Mumbai) and were used further purification. This experimental part divided into four parts,

- A) **Preparation of 3-phenylquinazoline-2,4(1H,3H)-dione (L₁):** In the three necked round bottom flask a mixture of anthranilic acid (0.1M) and Phenyl isocyanate (0.1M) in 50mL ethanol were taken and stirred for one hour and the reaction mass was refluxed on water bath for 2-3 hrs. After the reaction reached completion (monitored by TLC), the crude product obtained was recrystallized with ethanol.

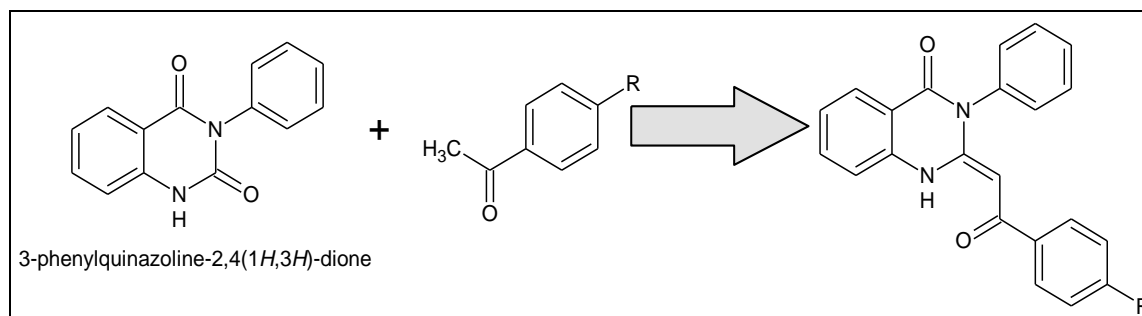
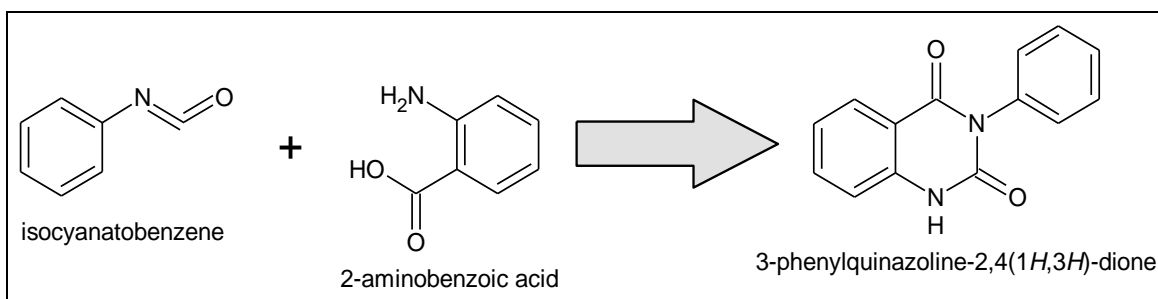
B) **Preparation of Chalcones of 3-phenylquinazoline-2,4(1H,3H)-dione(C-1toC-4) from substituted acetophenone:**

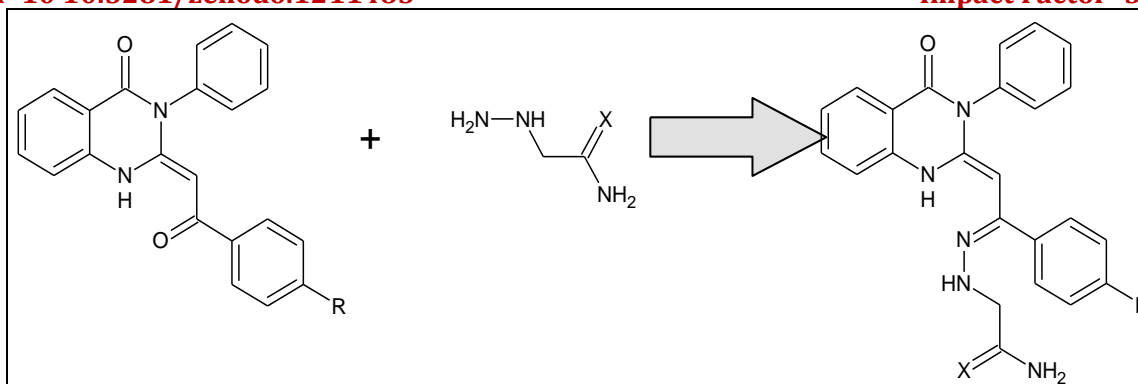
In the three necked round bottom flask a mixture of 3-phenylquinazoline-2,4(1H,3H)-dione[9-12] (0.1M) in 50mL ethanol were taken and stirred for one hour. Meanwhile the solution of 20% caustic soda solution (30ml) mix with and 4-chloro/bromo/iodoacetophenone(0.11M) was prepared, Above prepared solution was added slowly to ethanolic solution of 3-phenylquinazoline-2,4(1H,3H)-dione maintaining temp. 15-20°C, then the reaction mass was refluxed on water bath for 2-3 hrs. After the reaction reached completion (monitored by TLC), the mixture was cooled on ice salt bath. It was filtered and washed with water & Chalcones of 3-phenylquinazoline-2,4(1H,3H)-dione[C-1 to C-4] obtained was recrystallized with ethanol.

C) **Preparation of hydrazinecarbothiamide (L_1T) of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3,2,3-dihydroquinazoline-4(1H)-one** :The chalcones[C-1 to C-4] [13-14] (0.01mol) was added to 30 ml of THF & thiosemicarbazide (0.012mol) was added along with sodium acetate (5gm) reaction mixture was then refluxed on water bath for 2-3 hrs. After the reaction reached completion (monitored by TLC); the mixture was cooled on ice-salt mixture, it was then filtered and recrystallized with alcohol.

D) **Preparation of hydrazine-carboxamide (L_2C) of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3,2,3-dihydroquinazoline-4(1H)-one** :The mixture of chalcone[C-1 to C-4] (0.01mol) & semicarbazide hydrochloride (0.012mol) was added to 50ml THF. To that sodium acetate (5gm) was added. The reaction mixture was refluxed on water bath for 2-3 hrs. After completion of reaction (monitored by TLC); the reaction mixture was cooled, filtered & the product obtained was recrystallized by alcohol. The crystallized powder was further subjected to Silicagel column chromatography (2% EtoAc- Hexane) to get purified product.

Reaction Scheme





Scheme-3 Preparation of (2E)-2-[(4-substituted Phenyl)-2-oxoethylidene]-3,2-dihydroquinazoline-4(1H)-one(L₁T)& (L₁C)

Where R = H,Cl,Br,I and X=S,O

III. RESULT AND DISCUSSION

The compounds (L₁T & L₁C) : In the IR spectrum[15] of ligand (L₁T) bands corresponding to -NH₂ & -NH groups appeared at 3454 and 3260 cm⁻¹ respectively. The bands corresponding to ν(C=S) and ν(C=N) groups appeared at 814 & 1583 cm⁻¹. In (L₁C): the band corresponding ν(C=O) appeared at 1708 cm⁻¹. In the ¹H NMR spectrum of (L₁T & L₁C) the most common NMR multiplets for aromatic ring protons are found to be resonating around δ6.9-δ8.4 whereas the broad singlet for >NH & -NH₂ group protons appeared around δ3.3- δ3.6. A sharp singlet peak for olefinic protons (>C=C-H) group in are observed in the range of δ7.6- δ7.8 while >NH quinazoline ring singlet appears at δ9.8. The distinguishing singlet peak around δ10.2 (>C=N-group) azomethine protons singlet was shifted to downfield. The ¹H NMR and FTIR spectrums of synthesized compounds L₁, C-1, C-2, L₁T and L₁C were reported in Table -1&2

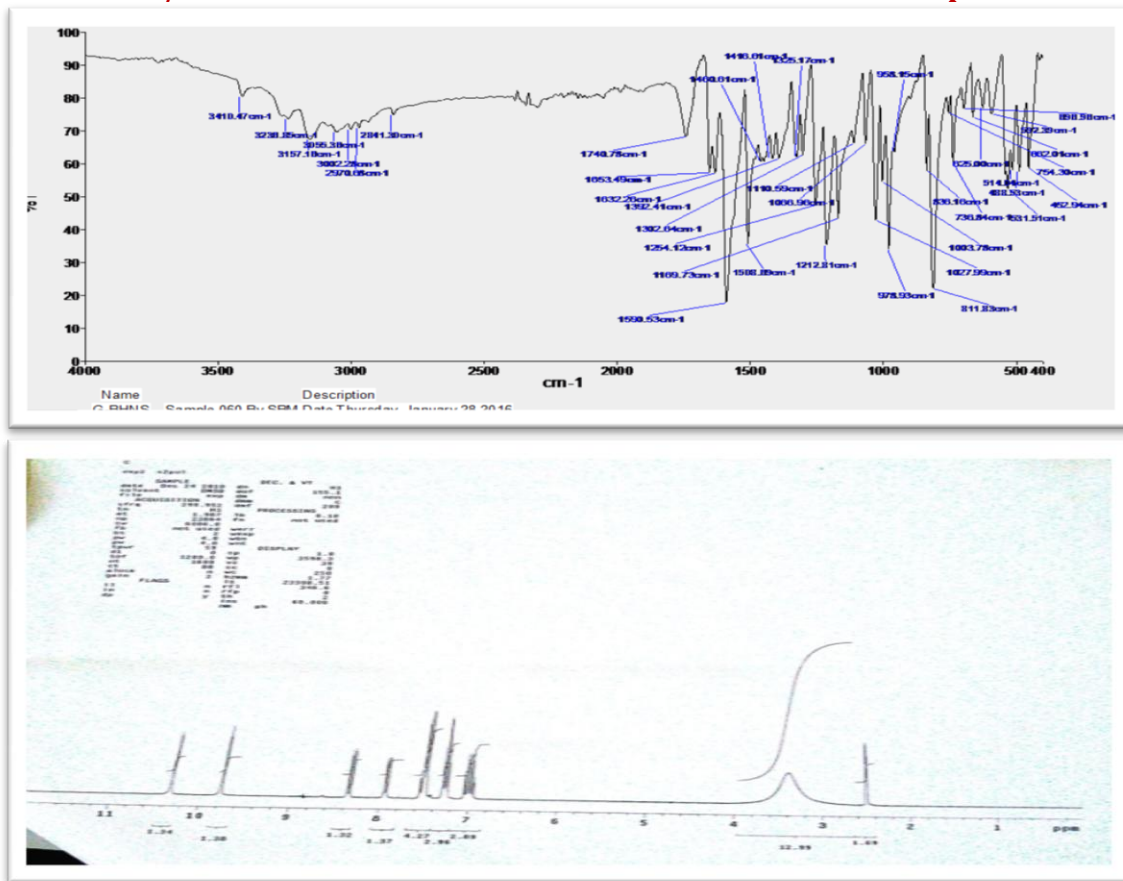


Figure:1 IR & NMR spectrum of (L₁T & L₁C)

Table-1: ¹HNMR (400 MHz, CDCl₃) δ_{ppm}:-

Sr. No	compounds	-NH2 δppm	>NH or >SH δppm	Olefinic Proton 1H singlet δppm	>NH quinazoline ring singlet δppm	Aromatic ring 8H Proton δppm
1	L1	--	--	--	---	7.0-7.9
2	C-1	---	--	7.8	9.8	6.9-7.7
3	C-2	--	---	7.6	9.8	7.0-8.1
4	L1T	3.6	10.4	7.7	9.8	7.7-8.2
5	L1C	3.6	10.4	7.6	9.8	7.0-7.8

Table-2: FTIR Spectrum(in KBr):

Sr. No	compounds	-NH ₂ ,>NH Stretching frequency incm-1	(>C=S) Stretching frequency incm-1	(>C=O) Stretching frequency incm-1	(>C=N) Stretching frequency incm-1	Aromatic ring Stretching frequency incm-1
1	L ₁	3400-3250	-----	1673	---	1603
2	C-1	3427-3279	----	1655	---	1591
3	C-2	3330-3185	-----	1680	---	1595
4	L ₁ T	3300-3195	811	1655	1580	1603
5	L ₁ C	3227-3161	----	1668	1558	1600

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