INTERNATIONAL JOURNAL OF RESEARCHES IN BIOSCIENCES, AGRICULTURE & TECHNOLOGY
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www.vmsindia.org

Synthesis and Characterization of Phenolic Schiff's Bases Bearing Quinoline Moiety

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Abstract:
Phenolic Schiff's bases bearing quinoline moiety (3a-d) were synthesized from substituted carbohydrazide derivatives (2a-c) derived from substituted methyl salicylates and quinoline aldehydes (1a-b). The synthetic root of quinolines involves the reaction between substituted acetanilide with Vilsmayer-Heack reagent (POCl3 and DMF). The structures of synthesized compounds have been established on the basis of IR, 1H NMR, Mass spectra and element analysis.

Keywords: Schiff's base, quinoline, hydrazine hydrate, carbohydrazides

Introduction

Schiff base are the compound containing azomethine group (-HC=N-). A Schiff base is a nitrogen analogue of an aldehyde or ketone in which the C=O group is replaced by C=N-R group. Metal complex Schiff bases have also been used in oxidation reaction [1]. Schiff bases that contain aryl substituents are substantially more stable and more readily synthesized, than alkyl substituents which are relatively unstable. Schiff's bases are well known intermediates for the preparation of azetidinones, thiazolidinone, formazane, arylacetamide and many other entities of pharamaceutical potential. Over the past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis.

Different methods for the preparation of azomethine derivatives are documented in literature [2-10]. Quinoline or 1-aza-napthalene or benzo [b] pyridine is nitrogen containing heterocyclic aromatic compound. Quinoline is readily degradable by certain microorganisms, such as *Rhodococcus* species Strain Q1, which was isolated from soil and paper mill sludge[11]. Although there has been tremendous development for obtaining several quinoline derivatives, different synthetic routes have been highlighted to suffer from various problems harsh conditions, multistep and a large amount of promoters such as base expensive and or harmful metals, the oxidants for the aromatization and other additives. Chemistry of quinoline and its derivatives continues to attract interest due to their importance as synthetic intermediates [12-13] well recognized by synthetic and biological chemists and as the key structural element found in a large array of natural products and pharmaceuticals [14-15]. Studies have discovered that these compounds exhibit diverse medicinal functions such as anti-inflammatory[16], antimalarial[17], antibacterial[18], antiproliferative[19], anticancer[20], antiparasitic[21], antidepressive[22], antidiabetic[23], analgesic, antipsychotic, cardiovascular, antileishmanial[24], antiplatelet [25], antiviral and fungicide[26].

It is evident from the literature assimilated that the synthesis of quinoline nucleus is a subject of great interest for several research groups. As a result impressive spectrum of novel strategies have evolved providing the opportunity to construct Schiff's bases bearing quinoline moiety derivatives decorated with choicest of substitutions. This has assisted the discovery of new properties in quinoline based compounds in particular the biological activities associated with them. Although the work towards synthesis of Schiff's bases bearing quinoline moiety systems has come a long way, we believe this area of research will continue to evolve with discovery of newer applications of new catalysts and reagents. Encouraged by the literature survey we planned to prepare Schiff's bases incorporating the quinoline moiety and characterize them by spectral analysis.

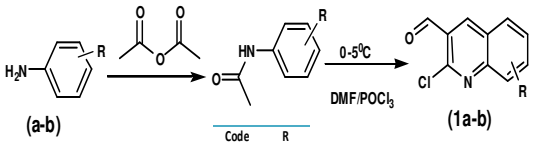
Experimental:

The preparation of starting material includes following two steps.

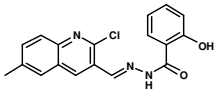
1. Preparation of substituted quinoline aldehydes (1a-b): p-Toludine **(a)** and p-chloro aniline **(b)** were acetylated to obtain corresponding anilides, which were then treated with DMF and $POCl_3$ at 0-5˚C according to Vilsmeier-Haeck reaction to afford

substituted quinoline aldehyde **(1a-b)** (Scheme **1**).

Reaction Scheme : 1



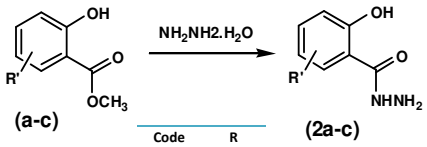
Code	R
a	4-CH_3
b	4-Cl



f substituted 2-

ides (2a-c): Substituted 0 mmol) and hydrazine ere taken in ethanol (20mL) and the reaction mixture was refluxed for 2h. Later the reaction mixture was poured in crushed ice, the precipitate so obtained was filtered and washed with water and recrystallized from ethanol to get **2a** (Scheme **2**).

Reaction Scheme: 2

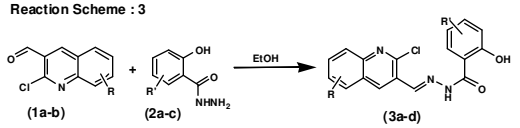


Code	R
a	4- H
b	4- Cl
c	4- Br

Similarly, **2b-c** were synthesised from substituted methyl salicylates **b-c** by extending the same procedure followed for **2a.**

General procedure for the synthesis of *N*'-[(*E*)-(2-chloro-6-substituted quinolin-3-yl)methylidene]-2-hydroxybenzohydrazides (3a-d): Quinoline aldehyde **(1a,** 10 mmol), substituted 2-hydroxybenzohydrazide (**2a**, 10 mmol), ethanol (10 mL) and 5-6 drop of acetic acid as a catalyst were taken in a clean round bottom flask. The reaction mixture was refluxed for 2h, cooled, filtered and recrystallized from ethanol to get **3a** (Scheme **3**).

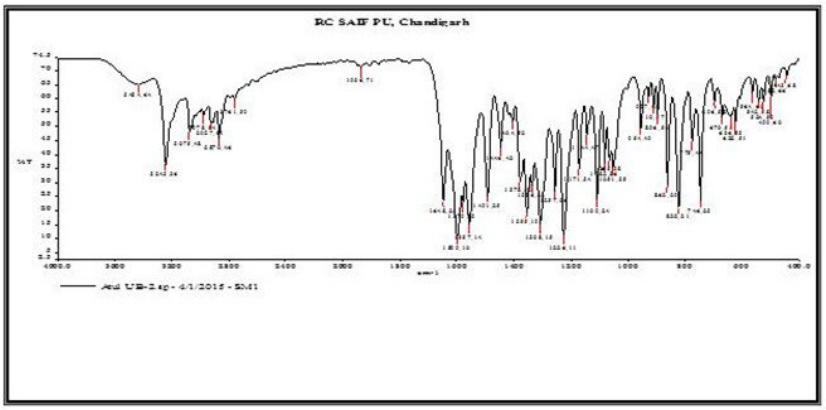
Reaction Scheme : 3



Code	R	R'
a	4-CH_3	4- H
b	4-CH_3	4- Br
c	4-CH_3	4- Cl
d	4- Cl	4- H

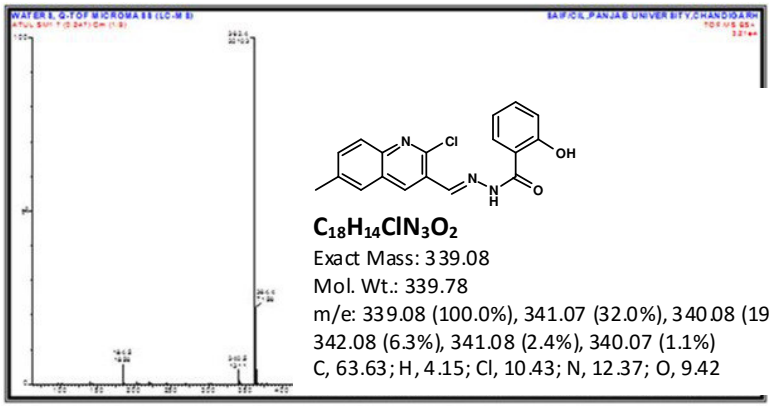
***N*'-[(*E*)-(2-chloro-6-methylquinolin-3-yl)methylidene]-2-hydroxybenzohydrazide (3a):** M.P.,210-215°C, Yield: 79%, Yellowish crystals, Recrystallizing solvent: Ethanol, MF: $C_{18}H_{14}N_3O_2Cl$. IR: 3434 cm^{-1} (-OH), 3243 cm^{-1} (N-H), 3075-2978 cm^{-1} (ArH), 2870, 2927 (CH_3, CH_2), 1648 (C=O), 1557, 1491 (C=C), 1599 (C=N). ^1H NMR: 2.5292 (s, 3H, -CH_3), 12.2289 (b, 2H, -OH and NH), 6.9525-8.914 1 (m, 9H, ArH) MS: 340 $[M]^+$, 362 $[M+ Na]^+$ Calculated: C, 63.71; H, 4.12; N, 12.38 Found: C, 61.019; H, 4.692; N, 10.616.

IR Spectra : 3a



^{1}HNMR Spectra : 3a

Mass Spectra : 3a



$C_{18}H_{14}ClN_3O_2$
Exact Mass: 339.08
Mol. Wt.: 339.78
m/e: 339.08 (100.0%), 341.07 (32.0%), 340.08 (19.7%), 342.08 (6.3%), 341.08 (2.4%), 340.07 (1.1%)
C, 63.63; H, 4.15; Cl, 10.43; N, 12.37; O, 9.42

Similarly, **3b-d** were synthesised from **2a-c** by extending the same procedure followed for **3a.**

4-bromo-*N*'-[(*E*)-(2-chloro-6-methylquinolin-3-yl)methylidene]-2-hydroxybenzo hydrazide (3b): M.P., 215-218°C, Yield: 68%, White crystals, Recrystallizing solvent: Ethanol, MF: $C_{18}H_{13}N_3O_2ClBr$. ^{1}H NMR : 2.5384 (s, 3H, -CH_3), 12.2358 (b, 2H, -OH and NH), 6.9613-8.8214 (m, 8H, ArH) MS : 419 $[M+H]^+$, 441[M+ Na]$^+$ Calculated: C, 51.64; H, 3.13; N, 10.04 Found: C, 51.70; H, 3.01; N, 10.00.

4-chloro-*N*'-[(*E*)-(2-chloro-6-methylquinolin-3-yl)methylidene]-2-hydroxybenzo hydrazide (3c): M.P., 195-200°C, Yield:73%, White crystals Recrystallizing solvent: Ethanol, MF: $C_{18}H_{13}N_3O_2Cl_2$. ^{1}H NMR: 2.4992 (s, 3H, -CH_3), 12.2471 (b, 2H, -OH and NH), 6.9424-8.9243 (m, 8H, ArH). MS: 375 $[M+H]^+$ Calculated: C, 57.77; H, 3.50; N, 11.23 Found: C, 57.91; H, 3.39; N, 11.01.

***N*'-[(*E*)-(2,6-dichloroquinolin-3-yl)methylidene]-2-hydroxybenzohydrazide (3d):** M.P., 210-212°C, Yield:70%, Yellowish crystals, Recrystallizing solvent: Ethanol, MF: $C_{17}H_{11}N_3O_2Cl_2$. ^{1}H NMR: 12.3105 (b, 2H, -OH and NH), 6.9122-8.9452 (m, 9H, ArH). MS: 360 $[M]^+$, 361 $[M+H]^+$ Calculated: C, 56.69; H, 3.08; N, 11.67 Found: C, 57.00; H, 3.00; N, 11.57.

Results and Discussion:

The synthesis of the novel compounds **(3a-d)** is described in reaction schemes. The identities of the newly synthesized compounds have been established on the basis of their elemental analysis and spectral data such as IR, ^{1}H NMR and Mass spectral studies [27]. The presence of bromo, chloro at different position of benzene ring of the carbohydrazide and the use of substituted quinoline aldehyde resulted in synthesis of new phenolic Schiff's bases bearing quinoline moiety derivatives with significantly high yield.

Some new phenolic Schiff's bases bearing quinoline moiety **(3a-d)** were synthesized by refluxing substituted quinoline aldehyde **(1a-b)** and carbohydrazide derivatives **(2a-c)**.

The IR spectra of **3a** showed stretching bands at 3434 cm^{-1} for -OH group, 3243 cm^{-1} for –NH, 2978 cm^{-1} for CH_3, 1648 cm^{-1} for C=O and 1599 cm^{-1} for C=N. The ^{1}H NMR spectra of **3a** showed a singlet at δ 2.5292 ppm due to three -CH_3 protons, a broad singlet at δ 12.2289 ppm due to each proton of –OH and –NH similarly, a multiplet at δ 6.9525-8.914 1 ppm due to nine aromatic protons proves its formation, which is further confirmed by its mass spectra, peaks obtained at 340 $[M]^+$ and

362 [M+Na] confirms its formation having the molecular formula $C_{18}H_{14}O_2N_3Cl$ (Scheme **3)**.

Conclusion:

In conclusion, we have synthesised phenolic Schiff's bases **(3a-d)**, in the good yields by refluxing substituted 2-hydroxy benzocarbohydrazides with substituted quinolone aldehyde and their structures were confirmed on the basis of spectral and the elemental analysis data.

Acknowledgments:

The authors are thankful to the Director, Institute of Science, Nagpur, Head, Department of Chemistry, Principal, Government Science College, Gadchiroli, Mr. R. D. Nasre and Mr. S. M. Pathan, for their support and cooperation. The authors are also thankful to the Director, SAIF, Punjab University, Chandigarh for providing CHN analysis, IR, ^{1}H-NMR and Mass Spectra.

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