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Synthesis and Characterization of Schiff Bases Derived from 3-Aryl-2-Formyl-4(3*H*)-Quinazolinone

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ABSTRACT

Condensation of 3-aryl-4(3H)-quinazolinone-2-carbaldehydes with different substituted aniline under reflux conditions afforded a series of Schiff bases (imines) containing quinazoline moiety. The formed quinazoline Schiff bases were obtained in good yields. The structures of synthesized Schiff bases were confirmed based on their spectral data, ^{1}H NMR and IR spectroscopy.

Introduction

Quinazolinone analogues are versatile classes of nitrogen containing heterocycles that represent privileged scaffolds in synthetic chemistry and pharmacology. Many derivatives based on the quinazolinone system have attracted the great consideration of chemists and pharmacologists due to the wide range of biological activity of these compounds such as anticonvulsant [1, 2], antiinflammatory [3], antitubercular [4], anticancer [5] antibacterial [6], antifungal [7], antiallergic [8], antiHIV [9] antimalaria[10], and antivirus [11].

In addition, different types of Schiff bases have appealed to the chemists and biologists due to their biological activities. Compounds containing Schiff bases exhibited a broad-spectrum of pharmacological activities including antibacterial [12], antifungal [13], antiviral [14, 15], anticancer [16], analgesic [17], antiinflammatory [18], anticonvulsant [19], and antiprotozoal [20].

Schiff bases which have an azomethine (C=N) group, are formed simply from the condensation reaction between primary amine and carbonyl compound.

Due to the simplicity of synthesis coupled with their wide spectrum of biological, Schiff bases have brought in as one of the most widely investigated derivatives in coordination chemistry.

Some quinazolin-4(3H)-one derived Schiff bases and their complexes were synthesized via the condensation reaction of 3-amino-2-methylquinazolin-4(3H)-one with various aromatic aldehydes and characterized through spectral data. The synthesized Schiff bases have been screened for their antibacterial and antifungal activity. The results clearly showed that both Schiff bases and their complexes displayed moderate to good activity. The antimicrobial data indicated that the complexes are much more active compared to their free Schiff bases ligands [21].

Based on the above observations, herein series of Schiff bases based on 4(3H)-quinazolinone system have been synthesized.

Results and discussion

The synthesis of the starting aldehydic precursor used in the synthesis of the quinazoline Schiff bases, 3-arylquinazolin-4(3H)-one-2-carbaldehydes (2a-c), was carried out via the oxidation reaction of 3-aryl-2-methylquinazolin-4(3H)-ones (1a-c) with SeO_2 in dioxane. The Schiff bases (3a-o) were obtained via the condensation reaction of 3-arylquinazolin-4(3H)-one-2-carbaldehydes (2a-c) with different substituted anilines.

The synthetic route leading to the formation of Schiff bases (3a-o) is outlined in Schemes 1. The generality of this process is illustrated with respect to various aromatic amines and 3-arylquinazolin-4(3H)-one-2-carbaldehydes (2a-c) and the results are presented in Table 1.

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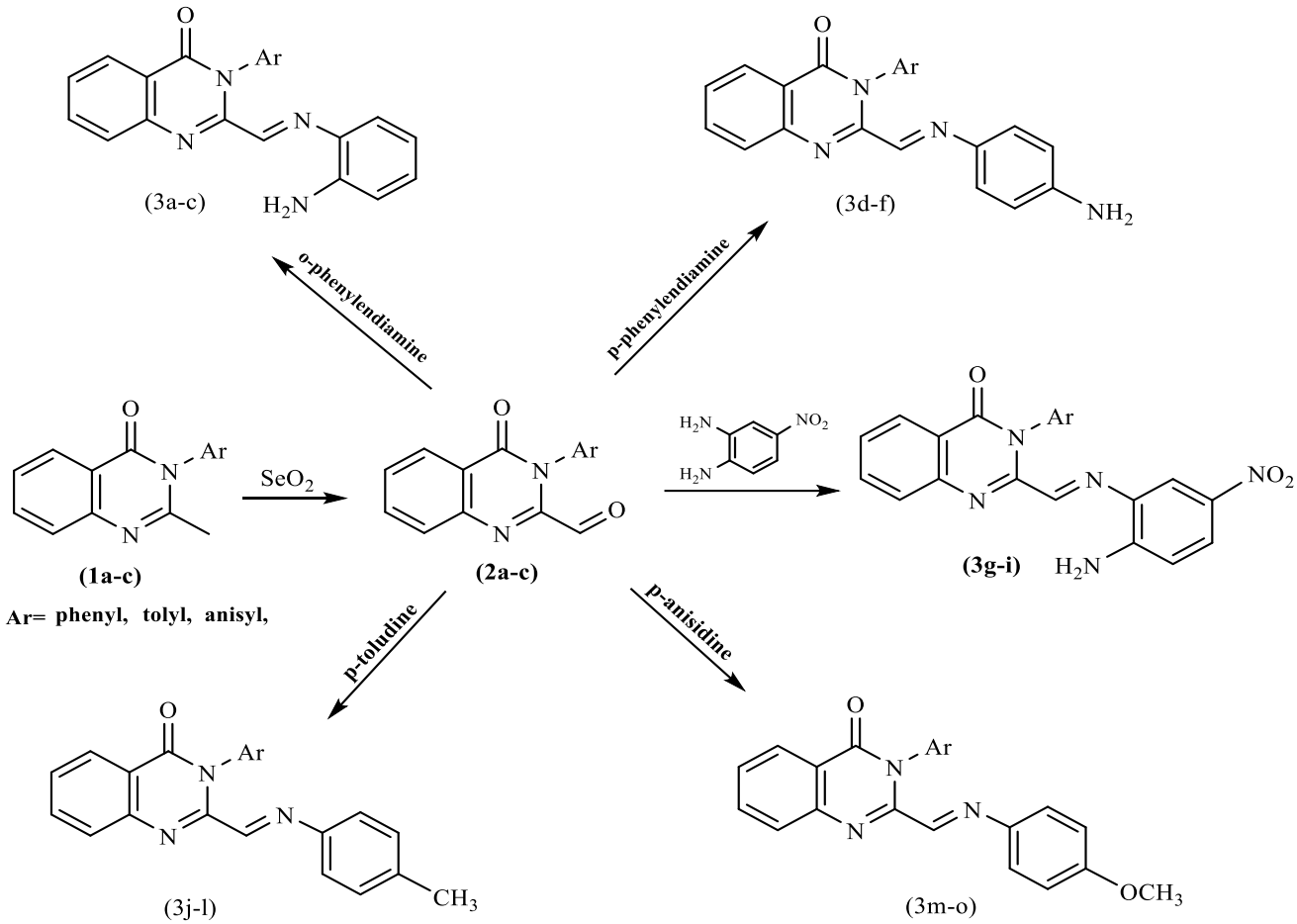
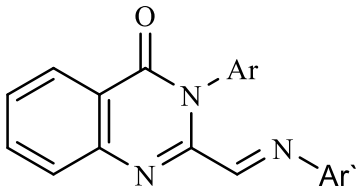


Scheme (1) synthesis of the target Shiff bases

Table 1. Various synthesized Schiff bases



Comp. No.	Ar	Ar`	Comp. No.	Ar	Ar`
3a	phenyl	2-aminophenyl	3j	phenyl	4-tolyl
3b	4-tolyl	2-aminophenyl	3k	4-tolyl	4-tolyl
3c	4-anisyl	2-aminophenyl	3l	4-anisyl	4-tolyl
3d	phenyl	4-aminophenyl	3m	phenyl	4-anisyl
3e	4-tolyl	4-aminophenyl	3n	4-tolyl	4-anisyl
3f	4-anisyl	4-aminophenyl	3o	4-anisyl	4-anisyl
3g	phenyl	2-amino-5-nitrophenyl			
3h	4-tolyl	2-amino-5-nitrophenyl			
3i	4-anisyl	2-amino-5-nitrophenyl			

The Infrared spectral data of compounds (**3a-o**) showed the presence of absorption bands at 1635–1686 cm^{-1} characteristic of the carbonyl function (C=O) of the quinazoline moiety. The stretching bands attributed to the azomethine group (C=N) were observed in the region 1583-1635 cm^{-1}. The spectra also showed the disappearance of the stretching bands characteristic to the (C=O) function of the formyl group, as showed in (Fig. 1).

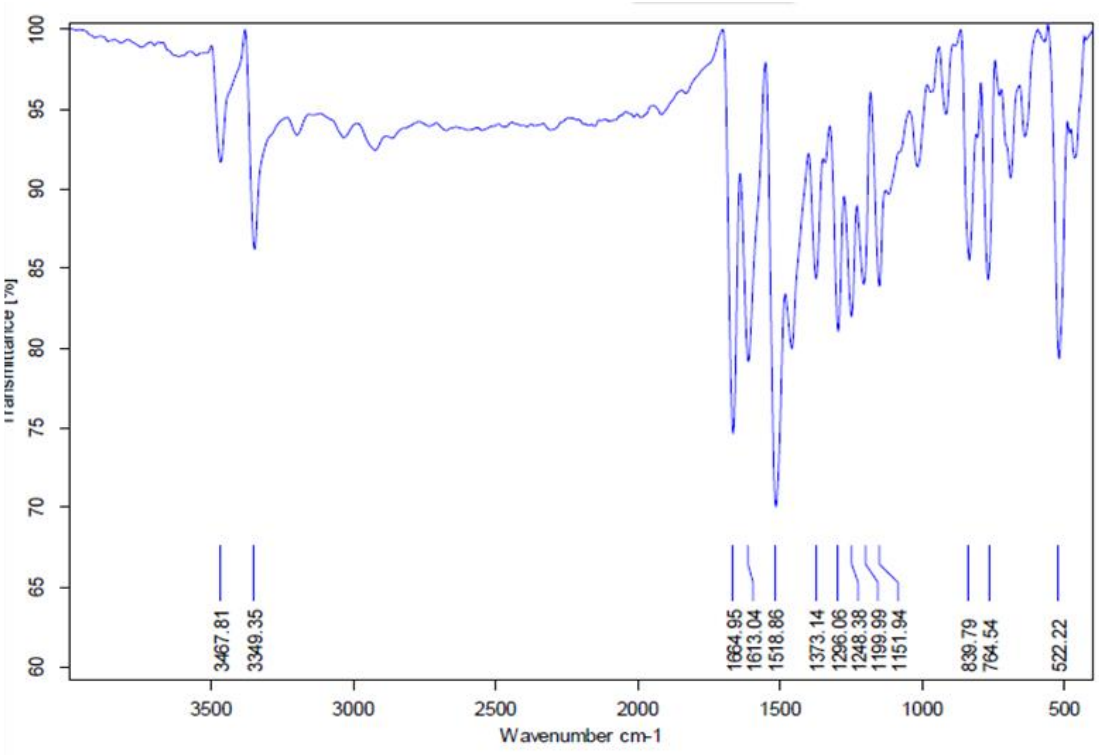


Fig. 1: IR spectrum of compound (**3e)**

The ^{1}H NMR spectra of some synthesized Schiff bases showed the presence of singlet signals at 8.74–7.97 ppm attributed to the protons of the imine groups (CH=N). The doublets observed in the spectra the in region of 8.72-8.33 ppm were attributed to the protons of (C-5) of the quinazoline moiety. The spectra also showed the presence of the signals characteristic of the methoxy, methyl, and aromatic protons in the expected regions.

The proton NMR spectrum of (**3j**), for example, exhibited the presence of signals at 8.37 ppm (doublet) and 7.99 ppm (singlet) corresponding to a proton of (C-5) of the quinazoline ring and the azomethine proton (CH=N) respectively. The spectrum showed also the presence of singlet signal at 2.28 ppm typical for the methyl protons (Fig 2).

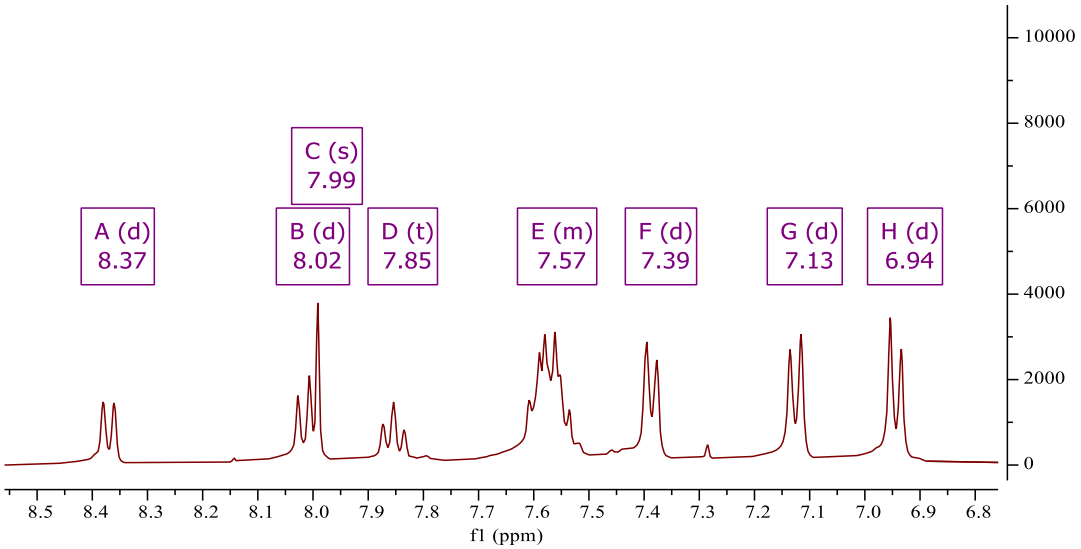


Fig. 2: Part of ^{1}H NMR spectrum of compound **(3j)**

Experiments

Melting points were measured on a Buuchi 510 melting point apparatus and were uncorrected. On Bruker (400 MHz), proton magnetic resonance spectra were measured using deuterated chloroform or deuterated dimethyl sulfoxide as the solvent with tetramethylsilane as internal standard. The infrared spectra were recorded on a Bruker ALPHA II FT-IR spectrophotometer using the ATR technique. 3-Aryl-2-methylquinazolin-4(3H)-ones (1a-c) were prepared from the reaction of 2-acetamidobenzoic acid with different anilines in refluxing toluene in the presence of phosphorus oxychloride [22]. Compounds (3a), (3b) and (3c) were prepared by us [23].

Synthesis of Schiff bases (3a-o)

A mixture of appropriate 3-arylquinazolin-4(3H)-one-2-carbaldehydes (2a-c) and the substituted anilines in equimolar amount (5 mmol each) in ethyl alcohol (20 ml), was refluxed for 4 h. The resulting product obtained after cooling, was filtered off, and crystallized from the suitable solvent to afford the corresponding Schiff base (3a-o).

2-((4-aminophenylimino)methyl)-3-phenylquinazolin-4(3H)-one (3d) orange (yield, 60%); m.p=257 °C, FTIR (cm^{-1}): 3313-3201 (NH_2), 1677 (C=O), 1629 (C=N); ^{1}H NMR ($CDCl_3$) δ ppm: 8.37 (d, *J*=7.9 Hz, 1H), 8.01 (d, *J*=8.1 Hz, 1H), 7.99 (s, 1H), 7.89–7.81 (m, 1H), 7.66–7.50 (m, 3H), 7.38 (d, *J*=6.6 Hz, 2H), 6.99 (d, *J*=8.6 Hz, 2H), 6.60 (d, *J*=8.7 Hz, 2H), 3.85–3.80 (m, 2H). Anal. Calcd. for $C_{21}H_{16}N_4O$ (340.38): C, 74.10; H, 4.74; N, 16.46; Found: C, 74.33; H, 4.81; N, 16.63.

2-((4-aminophenylimino)methyl)-3-(4-tolyl)quinazolin-4(3H)-one (3e) orange (yield, 60%); m.p=227 °C, FTIR (cm^{-1}): 3467-3349 (NH_2), 1664 (C=O), 1613 (C=N); ^{1}H NMR ($CDCl_3$) δ ppm: 8.33 (d, *J*=6.9 Hz, 1H), 7.99 (d, *J*=8.5 Hz, 1H), 7.97 (s, 1H), 7.81 (t, *J*=7.0 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J*=7.9 Hz, 2H), 7.23 (d, *J*=8.0 Hz, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.58 (d, *J*=8.6 Hz, 2H), 3.87 (s, 2H), 2.45 (s, 3H). Anal. Calcd. for $C_{22}H_{18}N_4O$ (354.40): C, 74.56; H, 5.12; N, 15.81; Found: C, 74.71; H, 4.95; N, 15.64.

*2-((4-aminophenylimino)*methyl*)-3-(4-anisyl)quinazolin-4(3H)-one* (3f) orange; (yield, 60%); m.p=247 °C, FTIR (cm^{-1}): 3437-3344 (NH_2), 1677- (C=O), 1610 (C=N). Anal. Calcd. for $C_{22}H_{18}N_4O_2$ (370.40): C, 71.34; H, 4.90; N, 15.13; Found: C, 71.62; H, 4.75; N, 15.38.

2-((2-amino-5-nitrophenylimino)methyl)-3-phenylquinazolin-4(3H)-one (3g) (yield, 60%); m.p=274 °C, FTIR (cm^{-1}): 3309 (NH_2), 1643 (C=O), 1591 (C=N). Anal. Calcd. for $C_{21}H_{15}N_5O_3$ (385.38): C, 65.45; H, 3.92; N, 18.17; Found: C, 65.59; H, 3.78; N, 18.34.

2-((2-amino-5-nitrophenylimino)methyl)-3-(4-tolyl)quinazolin-4(3H)-one (3h) Orange, (yield, 60%); m.p=250 °C, FTIR (cm^{-1}): 3262-3285 (NH_2), 1648 (C=O), 1594 (C=N); ^{1}H NMR (DMSO–d6) δ ppm: 8.74 (s, 1H), 8.61 (d, *J*=2.5 Hz, 1H), 8.53–8.36 (m, 1H), 8.33 (d, *J* = 2.6 Hz, 1H), 8.31 (d, *J*=2.6 Hz, 1H), 8.03 (d, *J*=8.7 Hz, 1H), 7.84 (d, *J*=7.8 Hz, 1H), 7.74 (d, *J*=9.2 Hz, 1H), 7.63 (t, *J*=7.8 Hz, 1H), 7.54 (t, *J*=7.6 Hz, 2H), 7.31 (t, *J*=7.3 Hz, 1H), 7.11 (d, *J*=8.2 Hz, 1H), 7.07 (d, *J*=8.2 Hz, 2H), 2.26 (s, 3H) Anal. Calcd. for $C_{22}H_{17}N_5O_3$ (399.40): C, 66.16; H, 4.29; N, 17.53; Found: C, 66.37; H, 4.42; N, 17.73.

2-((2-amino-5-nitrophenylimino)methyl)-3-(4-anisyl) quinazolin-4(3H)-one (3i) orange, (yield, 60%); m.p=240 °C, FTIR (cm^{-1}): 3315(NH_2), 1635 (C=O), 1592 (C= N). Anal. Calcd. for $C_{22}H_{17}N_5O_4$ (415.40): C, 63.61; H, 4.12; N, 16.86; Found: C, 63.45; H, 4.32; N, 16.67.

2-((4-tolylimino)methyl)-3-phenylquinazolin-4(3H)-one (3j) Yellow; (yield, 60%); m.p=203 °C, FTIR (cm^{-1}): 1681(C=O), 1553 (C=N); 1H NMR ($CDCl_3$) δ ppm: 8.37 (d, *J*=7.9 Hz, 1H), 8.02 (d, *J*=8.2 Hz, 1H), 7.99 (s, 1H), 7.85 (t, *J*=7.7 Hz, 1H), 7.63–7.49 (m, 4H), 7.39 (d, *J*=7.3 Hz, 2H), 7.13 (d, *J*=8.0 Hz, 2H), 6.94 (d, *J*=8.1 Hz, 2H), 2.34 (s, 3H). Anal. Calcd. for $C_{22}H_{17}N_3O$ (339.39): C, 77.86; H, 5.05; N, 12.38; Found: C, 77.61; H, 4.89; N, 12.55.

2-((4-tolylimino)methyl)-3-(4-tolyl)quinazolin-4(3H)-one (3k) Yellow; (yield, 60%); m.p=160 °C, FTIR (cm^{-1}): 1682 (C=O). Anal. Calcd. for $C_{23}H_{19}N_3O$ (*353.42*): C, 78.16; H, 5.42; N, 11.89; Found: C, 78.39; H, 5.62; N, 11.67.

2-((4-tolylimino)methyl)-3-(4-anisyl)quinazolin-4(3H)-one (3l) Off white; (yield, 60%); m.p=198 °C, FTIR (cm^{-1}): 1678 (C=O), 1607 (C=N) Anal. Calcd. for $C_{23}H_{19}N_3O_2$ (369.42): C, 74.78; H, 5.18; N, 11.37; Found: C, 74.91; H, 5.33; N, 11.62.

2-((4-anisylimino)methyl)-3-phenylquinazolin-4(3H)-one (3m) Yellow crystallized from ethanol (yield, 60%); m.p=181 °C, FTIR (cm^{-1}): 1675 (C=O), 1624 (C=N); ^{1}H NMR ($CDCl_3$) δ ppm: 8.36 (d, *J*=7.6 Hz, 1H), 8.01 (s, 1H), 7.99 (d, *J*=4.7 Hz, 1H), 7.90 – 7.80 (m, 1H), 7.57 (q, *J*=9.1, 7.6 Hz, 5H), 7.38 (d, *J*=6.8 Hz, 2H), 7.05 (d, *J*=8.3 Hz, 2H), 6.84 (d, *J*=8.4 Hz, 2H), 3.79 (s, 3H). Anal. Calcd. for $C_{22}H_{17}N_3O_2$ (355.39): C, 74.35; H, 4.82; N, 11.82; Found: C, 74.56; H, 4.72; N, 11.67.

2-((4-anisylimino)methyl)-3-(4-tolyl)quinazolin-4(3H)-one (3n)Yellow; (yield, 60%); m.p=143 °C, FTIR (cm^{-1}): 1685 (C=O), 1610 (C=N); ^{1}H NMR ($CDCl_3$) δ ppm: 8.33 (d, J=7.9 Hz, 1H), 8.00 (d, J=8.7 Hz, 1H), 7.82 (t, J=7.7 Hz, 1H), 7.55 (t, J=7.5 Hz, 1H), 7.36 (d, J=8.0 Hz, 2H), 7.25 (d, J=8.1 Hz, 2H), 7.08 (d, J=8.9 Hz, 2H), 6.84 (d, J=8.9 Hz, 2H), 3.78 (s, 3H), 2.45 (s, 3H). Anal. Calcd. for $C_{23}H_{19}N_3O_2$ (369.42): C, 74.78; H, 5.18; N, 11.37; Found: C, 74.63; H, 5.31; N, 11.49.

2-((4-anisylimino)methyl)-3-(4-anisyl)quinazolin-4(3H)-one (3o) yellow (yield, 60%); m.p=142 °C, FTIR (cm^{-1}): 1681 (C=O), 1613 (C=N). Anal. Calcd. for $C_{23}H_{19}N_3O_3$ (385.42): C, 71.67; H, 4.97; N, 10.90; Found: C, 71.52; H, 4.81; N, 10.76.

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