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Quinazoline Based Synthesis of Some Novel Heterocyclic Schiff Bases

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ABSTRACT

3-Amino-2-methyl-3H-quinazolin-4-one on condensation with different substituted acetophenones in presence of acetic acid under classical procedure to affords novel series of Schiff bases containing quanzoline moiety. The newly synthesized imines are confirmed on the basis of spectral technique, ^{1}H NMR, IR and mass spectroscopy.

1. Introduction

Quinazoline is a compound made up of two fused six-membered simple aromatic rings, structure compound containing benzene fused to pyrimidine. Medicinally it has been used in various areas as an analgesic and anti-inflammatory [1-4], antihypertensive [5, 6], antimicrobial [7-9], antibacterial [10], anticonvulsant [11-13], anticancer [14, 15], antimalarial [16] and antidepressant activities [17].

Schiff bases (imines) are well known for their wide applications and are useful intermediates in organic synthesis [18]. These compounds have intrinsic biological activities including anticancer [19], antitumour [20], antitubercular [21], antibacterial [22], antioxidant [18], and antiproliferative [23] activities. Moreover, Schiff bases also exhibit fluorescence [24], photoluminescence [25], and aggregation [26] properties. In view of these observations, we plan to synthesize some novel quinazoline based imines **3a-i** by a condensation reaction of a substituted acetophenones with 3-amino-2-methyl-3H-quinazolin-4-one in presence of acetic acid using classical procedure (Fig. 1).

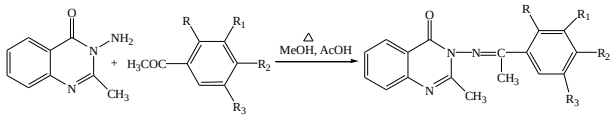
2. Experimental Methods

2.1 Chemistry

Melting points were determined in open capillary tubes and are uncorrected. FT-IR spectra were recorded in KBr pellets on a Perkin-Elmer [8201] spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHz instrument in DMSO-d_6 as the solvent and TMS was used as an internal standard. The mass spectra were recorded on SHIMADZU (GCMS-QP 1000 EX) GC-EI-MS spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 CHN elemental analyser. Purification of the compound was indicated using TLC (ethyl acetate / cyclohexane (0.25 mL: 0.25 mL, v/v) as the mobile phase).

2.1.1 Preparation of Schiff bases

In 50 mL of round bottom flask, mixture of 3-amino-2-methyl-3H-quinazolin-4-one **1** (0.01mole) and substituted acetophenones **2a-i** (0.01 mole) was dissolved in methyl alcohol (15 mL). To this reaction mixture acetic acid (0.001 mole) was added and resultant reaction mixture was refluxed for 2 to 3 hrs. On completion of reaction as monitored by TLC (ethyl acetate: cyclohexane, 0.25 mL: 0.25 mL, v/v as the mobile phase) the reaction mixture was work-up using cold water to obtained crud solid product. The separated solid was filtered and recrystallised from ethanol to yield pure Schiff's bases **3a-i**. Analytical and physical data are given in table 1.



1 2a-i 3a-i

3a: R, Cl; R_1, Cl; R_2, Cl; R_3, H
3b: R, OH; R_1, Br; R_2, OH; R_3, Br
3c: R, H; R_1, Cl; R_2, Cl; R_3, H
3d: R, Cl; R_1, H; R_2, Cl; R_3, H
3e: R, OH; R_1, H; R_2, CH_3; R_3, Cl
3f: R, OH; R_1, Br; R_2, H; R_3, Cl
3g: R, OH; R_1, Br; R_2, H; R_3, CH_3
3h: R, H; R_1, H; R_2, OCH_3; R_3, H
3i: R, H; R_1, H; R_2, Cl; R_3, H

Fig. 1 Synthesis of some novel heterocyclic Schiff bases

2-Methyl-3-[1-(2,3,4-trichloro-phenyl)-ethylideneamino]-3H-quinazolin-4-one (3a)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3228, 3066, 2945, 1788, 1618, 1547, 1454, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.72-8.32 (m, 6H, ArH), 2.60 (s, 3H, CH_3), 2.71 (s, 3H, CH_3). (MS (EI), *m/z* (%): 380.5 (M+, 62%).

3-[1-(3,5-Dibromo-2,4-dihydroxy-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3b)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3225, 3087, 2950, 1786, 1620, 1542, 1450, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.1 (s, 2H, OH), 6.69-8.29 (m, 5H, ArH), 2.61 (s, 3H, CH_3), 2.73 (s, 3H, CH_3). (MS (EI), *m/z* (%): 467 (M+, 68%).

3-[1-(3,4-Dichloro-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3c)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3229, 3090, 2953, 1784, 1620, 1558, 1457, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.70-8.26 (m, 7H, ArH), 2.60 (s, 3H, CH_3), 2.72 (s, 3H, CH_3). (MS (EI), *m/z* (%): 346 (M+, 70%).

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3-[1-(2,4-Dichloro-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3d)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3235, 3087, 2960, 1786, 1620, 1562, 1450, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.73-8.29 (m, 7H, ArH), 2.60 (s, 3H, CH_3), 2.73 (s, 3H, CH_3). (MS (EI), *m/z* (%): 346.5 (M+, 50%).

3-[1-(5-Chloro-2-hydroxy-4-methyl-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3e)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3230, 3082, 2937, 1785, 1620, 1550, 1431, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.10 (s, 1H, OH), 6.78-8.25 (m, 6H, ArH), 2.31 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.73 (s, 3H, CH_3). (MS (EI), *m/z* (%): 341.5 (M+, 43%).

3-[1-(3-Bromo-5-chloro-2-hydroxy-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3f)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3234, 3067, 2981, 1788, 1620, 1527, 1447, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.10 (s, 1H, OH), 6.74-8.28 (m, 6H, ArH), 2.60 (s, 3H, CH_3), 2.72 (s, 3H, CH_3). (MS (EI), *m/z* (%): 406.5 (M+, 75%).

3-[1-(3-Bromo-2-hydroxy-5-methyl-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3g)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3230, 3047, 2970, 1787, 1620, 1530, 1450, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.10 (s, 1H, OH), 6.68-8.23 (m, 6H, ArH), 2.31 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 2.73 (s, 3H, CH_3). (MS (EI), *m/z* (%): 386 (M+, 65%).

3-[1-(4-Methoxy-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3h)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3228, 3061, 2923, 1786, 1620, 1568, 1416, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.70-8.26 (m, 8H, ArH), 3.83 (s, 3H, OCH_3), 2.61 (s, 3H, CH_3), 2.73 (s, 3H, CH_3). (MS (EI), *m/z* (%): 307 (M+, 40%).

3-[1-(4-Chloro-phenyl)-ethylideneamino]-2-methyl-3H-quinazolin-4-one (3i)

Appearance: Light Yellow Solid, FT-IR (KBr, ν, cm^{-1}): 3230, 3042, 2938, 1786, 1620, 1554, 1422, 810, 650. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.74-8.29 (m, 8H, ArH), 2.62 (s, 3H, CH_3), 2.72 (s, 3H, CH_3). (MS (EI), *m/z* (%): 311.5 (M+, 80%).

Table 1 Analytical and physical data of compounds (3a – i)

Entry	Mol. Formula	Yield	M.P.	Elemental Analysis found [calculated]			
			^{0}C	C	H	X=Cl, Br,I	N
3a	$C_{17}H_{12}ON_3Cl_3$	76	64	53.43 [53.61]	3.25 [3.15]	27.70 [27.98]	11.25 [11.03]
3b	$C_{17}H_{13}O_3N_3Br_2$	69	179	43.59 [43.68]	2.84 [2.78]	34.33 [34.26]	8.89 [8.99]
3c	$C_{17}H_{13}ON_3Cl_2$	78	70	58.77 [58.95]	3.60 [3.75]	20.45 [20.52]	12.50 [12.13]
3d	$C_{17}H_{13}ON_3Cl_2$	75	142	58.77 [58.95]	3.80 [3.75]	20.58 [20.52]	12.16 [12.13]
3e	$C_{18}H_{16}O_2ClN_3$	68	110	63.11 [63.25]	4.60 [4.68]	10.82 [10.76]	12.34 [12.29]
3f	$C_{17}H_{13}O_2N_3BrCl$	72	172	50.35 [50.18]	3.33 [3.19]	10.92 [10.33]	8.82 [8.73]
3g	$C_{18}H_{16}O_2N_3Br$	70	190	55.60 [55.95]	4.17 [4.14]	10.60 [10.88]	20.61 [20.72]
3h	$C_{18}H_{17}O_2N_3$	60	210	70.15 [70.35]	5.15 [5.53]	-	13.2 [13.6]
3i	$C_{17}H_{14}ON_3Cl$	76	185	65.11 [65.48]	4.41 [4.49]	13.52 [13.48]	11.15 [11.39]

3. Result and Discussion

In view of the biological and medicinal importance of imines (Schiff bases), the present studies describe synthesis of novel quinazoline based synthesis of Schiff bases **3a-i**. The starting 3-amino-2-methyl-3H-quinazolin-4-one **1** were prepared by the action of 2-amino benzoic acid with acetic anhydride to yield 2-Methyl-benzo[d][1,3]oxazin-4-one, which on further condensation with hydrazine hydrate to give 3-amino-2-methyl-3H-quinazolin-4-one (Fig. 2). The obtained **1** on condensation with substituted acetophenones in presence of acetic acid using classical route to obtained imines **3a-i**. The use classical procedure for synthesis of imines is found to efficient in term of short reaction time, operationally being simple better yield of products and reactions were take place smoothly without any typical catalyst and modified apparatus.

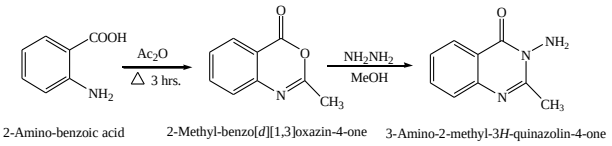

Fig. 2 Synthesis of 3-amino-2-methyl-3H-quinazolin-4-one

The structures of newly synthesized imines **3a-i** were confirmed on the basis of spectral analysis. In IR spectra of condensed product display the disappearance absorption band due C=O stretch and appearance of band near 1620 cm^{-1} due to C=N stretch of azomethine. The absorption band observed near 3230 cm^{-1} is due to presence of OH stretch. In ^{1}H NMR spectrum of imines display near δ 2.73 ppm due to singlet of CH_3 of quinazolines nucleus and at δ 2.60 ppm due to CH_3 of imines. The singlet of hydroxy proton apperas near δ 12.1 ppm. Therefore all synthesized compounds exhibited satisfactory spectral data consistent with their structures.

4. Conclusion

In summary, we have synthesized novel series of quinazolines based Schiff bases using classical procedure under slightly acidic conditions.

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