Chapter

Quinazoline Based Synthesis of some Heterocyclic Schiff Bases

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Abstract

3-amino-2-methylquinolin-4(3H)-one on condensation with different substituted naphthanones in presence of acetic acid under classical procedure to affords novel series of Schiff bases containing quinazoline moiety. The procedure is simple and easy to obtain the resultant quinazoline Schiff bases in good yields. The product **2a–d** is purified by crystallization in pure 94% ethanol and characterized by thin layer chromatography. The newly synthesized imines (Schiff bases) are confirmed on the basis of spectral techniques, ^{1}H NMR, IR, and mass spectroscopy.

Keywords: synthesis, quinazolines, heterocyclic Schiff bases, naphthnones

1. Introduction

Quinazoline and quinazolinones are the compounds made up of two fused six-membered simple aromatic rings, structure compound containing benzene fused to pyrimidine. This quinazoline ring system consist a structural fragments of about 150–160 natural alkaloids. The first derivative of quinazoline was prepared in 1869 by Griess as 2-cyano-3,4-dihydro-4-oxoquinazoline. This compound bicyclic called as bicyanoamido benzoyl and obtained by the reaction of cyanogens with anthranilic acid [1].

Many of these derivatives possess broad range of biological properties such as antimalarial, antimicrobial, diuretic, anticancer, antiviral, antifungal, anti-protozoal, anti-inflammatory, muscle relaxant, antitubercular, antidepressant, anticonvulsant, weedicide and many others [2–20]. Quinazoline and quinazolinone compounds are also useful nucleus in preparation of various functional materials for synthetic chemistry and also present in various drugs molecules (**Figure 1**).

Schiff bases (imines) are well known for their application and are useful intermediates in organic synthesis. These compounds have intrinsic biological activities including anticancer, antitumour, antitubercular, antioxidant and antiproliferative activity. The combination of quinazoline nucleus with imines further may increase the pharmacological activity, in view of these studies I plan to synthesize four new Schiff bases containing quinazoline (**Figure 2**).

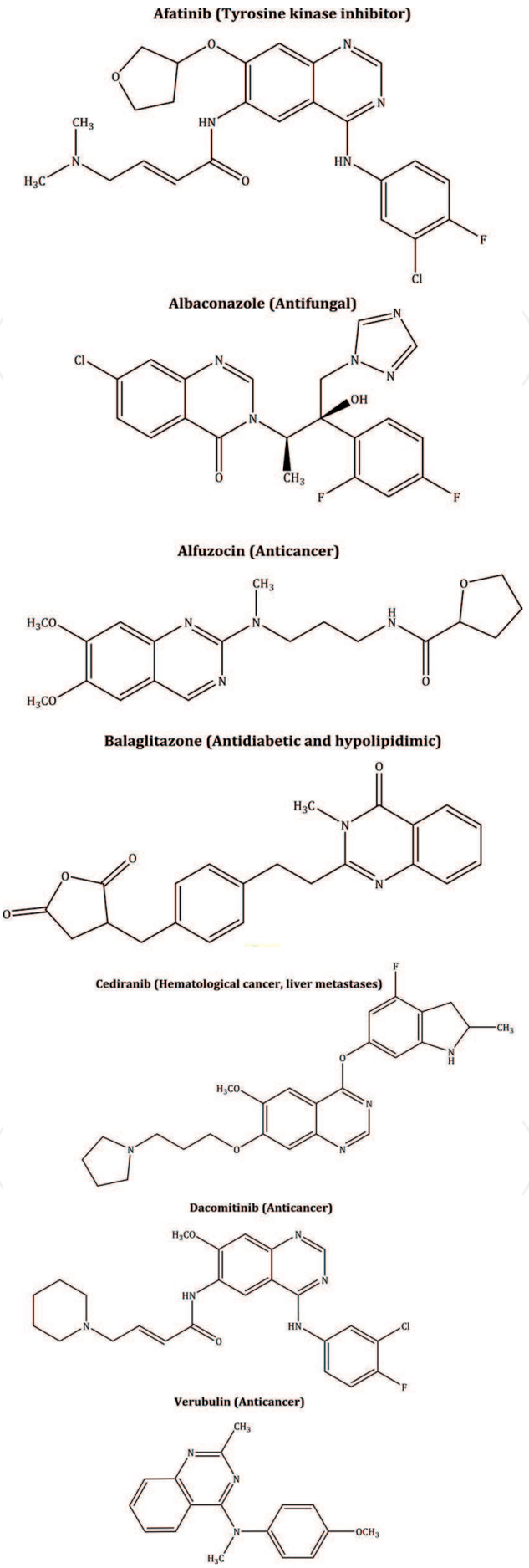

Figure 1.
Biological active drugs containing quinazoline and quinazolinone.

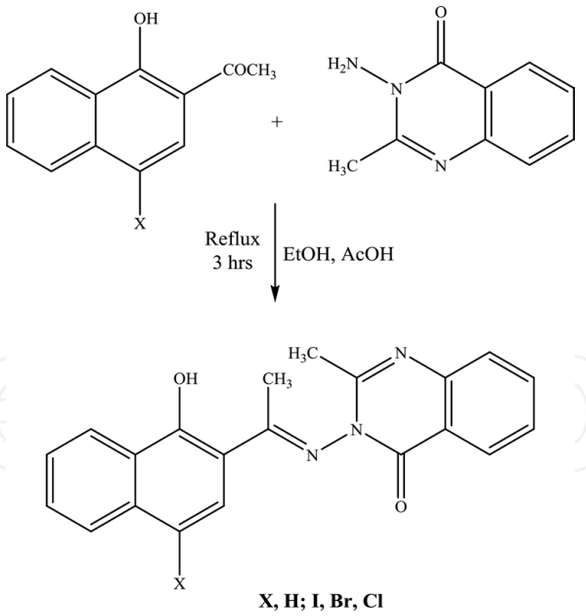

Figure 2.
Synthesis of heterocyclic Schiff bases ***2a–d****.*

2. Chemistry

The chemistry of quinazolines was reviewed by a scientist, Williamson in 1957 and then by Lindquist in 1959 and brought up to date by Armarego in 1963. Quinazolines is stable in cold dilute acid and alkaline solutions, but it is destroyed when these solutions are boiled. *O*-Amino benzaldehyde, ammonia, and formic acid are formed when quinazoline is boiled with hydrochloric acid.

2.1 Experimental methods quinazoline based Schiff bases

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. 1H NMR spectra were recorded on a Gemini 300-MHz instrument in DMSO-d6 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 analyzer. Purification of the compound was indicated using TLC (ethyl acetate/cyclohexane (0.25 mL:0.25 mL, v/v) as the mobile phase).

2.2 Procedure for preparation of quinazoline based Schiff bases

In 50 mL of round bottom flask, mixture of 3-amino-2-methyl-3H-quinazolin-4-one (0.01 M) and substituted acteonaphthanones (0.01 M) was dissolved in ethyl alcohol (15 mL). To this reaction mixture acetic acid (0.001 M) was added and resultant reaction mixture was refluxed for 2–3 h. 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 recrystallized from ethanol to yield pure Schiff's bases.

- (E)-3-((1-(1-hydroxy-4-iodonaphthalen-2-yl)ethylidene)amino)-2-ethylquinazolin-4(3H)-one.

Appearance: light yellow solid, FT-IR (KBr, ν, cm^{-1}): 3237, 3065, 2925, 1775, 1628, 1547, 1465, 815, 668. ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.5 (s, 2H, OH), 6.69–8.29 (m, 9H, ArH), 3.26 (s, 3H, CH_3)2.61 (s, 3H, CH_3). (MS, EI) *m/z* (%): 453 (M+, 57%).

- (E)-3-((1-(4-bromo-1-hydroxynaphthalen-2-yl)ethylidene)amino)-2-methylquinazolin-4(3H)-one.

Appearance: light yellow solid, FT-IR (KBr, ν, cm^{-1}): 3242, 3068, 2933, 1772, 1630, 1549, 1460, 818, 663. ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.5 (s, 2H, OH), 6.67–8.29 (m, 9H, ArH), 3.26 (s, 3H, CH_3)2.61 (s, 3H, CH_3). (MS, EI) *m/z* (%): 406 (M+, 69%).

- (E)-3-((1-(4-chloro-1-hydroxynaphthalen-2-yl)ethylidene)amino)-2-methylquinazolin-4(3H)-one.

Appearance: light yellow solid, FT-IR (KBr, ν, cm^{-1}): 3247, 3063, 2935, 1774, 1632, 1544, 1462, 816, 665. ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.5 (s, 2H, OH), 6.68–8.29 (m, 9H, ArH), 3.27 (s, 3H, CH_3)2.61 (s, 3H, CH_3). (MS, EI) *m/z* (%): 361.5 (M+, 65%).

- (E)-3-((1-(1-hydroxynaphthalen-2-yl)ethylidene)amino)-2-methylquinazolin-4(3H)-one.

Appearance: light yellow solid, FT-IR (KBr, ν, cm^{-1}): 3242, 3067, 2937, 1773, 1635, 1546, 1465, 818, 667. ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 12.5 (s, 2H, OH), 6.68–8.29 (m, 10H, ArH), 3.25 (s, 3H, CH_3)2.62 (s, 3H, CH_3). (MS, EI) *m/z* (%): 327(M+, 64%).

3. Conclusion

The author has reported the synthesis of novel series of quinazolines based Schiff bases from hydroxynaphthanones and 3-amino-2-methyl-3H-quinazolin-4-one using classical procedure under slightly acidic conditions.

4. Result and discussion

Quinazoline derivatives are further classified into the following main five categories. This classification is on the basis of their substitution patterns present in the ring system [3]. These are 2-substituted-4(3*H*)-quinazolinones, 3-substituted-4(3*H*)-quinazolinones, 4-substituted-quinazolines, 2,3-disubstituted-4(3*H*)-quinazolinones, and 2,4-disubstituted-4(3*H*)-quinazolinones. In view of the importance of quinazoline derivatives, the present study describes the synthesis of some important quinazoline based imines. The mixture of corresponding 3-amino-2-methyl-3*H*-quinazolin-4-one and substituted naphthnones treated in presence slightly acidic condition under reflux for 3 h to give formation imines (**Figure 2**). The formation of imines confirmed on the basis of spectral data, the IR spectra reveals the stretching band around 1630 cm^{-1} is due to imines C=N. The NMR reveals the absence of $–NH_2$ protons around δ 5.2 confirms the condensation reaction carried successfully. The mass spectrum of compounds **2a–d** gives molecular ion which is corresponding to molecular weight of products.

Conflict of interest

The authors confirm that this article content has no conflict of interest.

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