Chemical Bulletin of "Politehnica" University of Timisoara, ROMANIA
Series of Chemistry and Environmental Engineering
Chem. Bull. "POLITEHNICA" Univ. (Timisoara) *Volume 59(73), 1, 2014*

Synthesis and Antimicrobial Evaluation of Quinoline Linked Benzazoles Possessing Azetidin-2-One / Thiazolidin-4-One / Tetrazole Moieties

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Abstract: The aim of this work is to synthesize, characterize and evaluate the biological activity of a series of quinoline linked benzimidazoles (5a-c), benzothiazole (6a-c) and benzoxazoles (7a-c) bearing azetidin-2-one / thiazolidin-4-one / tetrazole nuclei. The newly synthesized compounds were characterized by elemental analysis and IR, ^{1}H-NMR, ^{13}C NMR and mass spectral data. The antimicrobial activity of the novel compounds was screened by the agar disc diffusion method. Quinoline linked benzimidazoles and benzothiazoles with thiazolidin-4-one nucleus has shown good antibacterial and antifungal activity than other compounds of the series.

Keywords: Quinoline, benzimidazole, benzoxazole, benzothiazole, azetidin-2one, thiazolidin-4-one, tetrazole.

1. Introduction

Among the fused heterocyclic compounds, benzazoles have become important synthons for the development new therapeutic agents. Compounds with benzimidazole, benzoxazole, benzothiazole moiety were found to possess broad spectrum of biological activities individually including antimicrobial [1], anti-inflammatory [2], anticytotoxic [3], antiviral [4], antiulcer [5], insecticidal [6], antitumor [7], antihistaminic, antiparasitic, herbicidal, antiallergic, antihelmintic [8], COX-2 inhibitory [9], antituberculosis, antibacterial, anticancer, antifungal, anticonvulsant [10], diarrhoea-predominant irritable bowel syndrome [11], hypoglycaemic [12], HIV-1 reverse transcriptase inhibitor [13], anti-diabetic [17], anticancer [18-20] activities. It was expected the benzazoles containing quinoline moiety along with azetidinones / thiazolidinones / tetrazoles may enhance the drug activity of compounds up to some extent or might posses some of the above mentioned biological activities. Hence it was thought of our interest to synthesise the compounds containing quinoline, benzimidazole / benzoxazole / benzthiazoles and azetidinone / thiazolidinone / tetrazole.

2. Experimental

2.1. Materials

Melting points were determined on open capillaries using a cintex melting point apparatus. T.L.C analyses were performed on precoated silicagel (E-Merck Kieselgel $60F_{254}$) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. IR Spectra were recorded in KBr on Perkin-Elmer Spectrum BX series FT-IR spectrometer. ^{1}H-NMR spectrum were recorded on DRX 300MHz Bruker spectrometers using TMS as internal standard (chemical shifts in δ ppm). ^{13}C-NMR Spectra were recorded on a Bruker 75MHz spectrometer. Mass spectra were scanned on a Varian MATCH-7 at 70ev. Elemental analyses were carried out on a Carlo Erba 106 and Perkin-Elmer Analyser. All the chemicals used in the present investigation were purchased from Sigma-aldrich, India.

2.2. Procedures for Synthesis of (2a, 2b, 2c)

3-chloro-1-(8-hydroxyquinolin-5-yl)-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (2a)

5-((4-trifluoromethyl)benzylidene)amino)quinolin-8-ol (1) was synthesized by reported procedure [22]. Monochloroacetyl chloride (0.01 mol) was added drop wise to Schiff's base (1) (0.01 mol) and triethyl amine (0.02 mol) in dioxane (25 mL) at room temperature. The mixture was stirred for 8h and left at room temperature for 3 days. The contents were poured on crushed ice. The product thus formed was filtered and washed with sodium bicarbonate solution. The dried product was recrystalized with absolute alcohol.

3-(8-hydroxyquinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one(2b)

A mixture of Schiff's base (0.01 mol) and mercaptoacetic acid (0.01 mol) dissolved in diaoxane (20 mL), anhydrous zinc chloride (0.5 mg) was added and refluxed for 8 hrs. The reaction was cooled and the resulting solid was washed with sodium bicarbonate solution and recrystallized from absolute alcohol.

5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-ol (2c)

Schiff base (0.004 mol) and PCl_5 (0.004 mol) was heated at 100^{0}c for 1h. When the evolution of fumes of HCl ceased, excess of PCl_3 was removed under reduced

pressure and the residual imidoyl chloride was treated with an ice-cold solution of sodium azide (0.0075 mol) and excess of sodium acetate in water (25 mL) and acetone (30ml) with stirring. Stirring was continued for overnight, thereafter acetone was removed under reduced pressure. The remaining aqueous portion was extracted with chloroform was dried.

2.3. General Procedure for the Synthesis of (3a-c)

A mixture of 3-chloro-1-(8-hydroxyquinolin-5-yl)-4-(4-(trifluoromethyl) phenyl) azetidin-2-one (2a) / 3-(8-hydroxyquinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (2b) / 5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-ol (2c) (0.02 M) anhydrous K_2CO_3 (0.03 M) chloro ethyl acetate (0.02 M) and Dimethylformamide was stirred at room temperature for 8 hours. The progress of the reaction was monitored by TLC with acetone : ethyl acetate (7:3) as eluent. The reaction mixture was diluted with ice-cold water. The separated solid was identified as ethyl-2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl)quinolin-8-yl)oxy)acetate(3a) / Ethyl-2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetate(3b) / Ethyl-2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetate (3c) respectively. This was collected by filtration and recrystallized from ethanol.

2.4. General procedure for the synthesis of acids by esters hydrolysis (4a-c)

To a solution of one equivalent ethyl-2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl) azetidin-1-yl)quinolin-8-yl)oxy)acetate (3a) / 2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl) thiazolidin-3-yl)quinolin-8-yl)oxy)acetate(3b)/ethyl-2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetate (3c) in tetrahydrofuran / MeOH / H_2O(1:1:1) solvent mixture, aqueous NaOH (2 N) was added and refluxed for 6h. The progress of the reaction was monitored by TLC. After completion, solvent was evaporated under vaccum to give a crude residue. The residue was washed with ethyl acetate to remove the impurities. The residue was acidified with 1N HCl up to pH-2 to give solid suspension, which was filtered under vacuum to give crude solid. The crude was purified by column chromatography (60-120 mesh- silca gel, eluent: 70% ethyl acetate-petroleum ether) to afford acid compound 2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl)quinolin-8-yl)oxy)acetic acid (4a) / 2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetic acid (4b) / 2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetic acid (4c)**.**

2.5. Synthesis of benzimidazole systems (5a, 6a, 7a)

A mixture of 2-((5-(3-chloro-2-oxo-4-phenylazetidin-1-yl)quinolin-8-yl)oxy)acetic acid (4a) / 2-((5-(4-oxo-2-(4-(trifluoromethyl) phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetic acid (4b) / 2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetic acid (4c) and ortho phenylene diamine in 1:1 equivalent ration was refluxed for 3-3.5h at 100^0C in presence of 6N HCl. The progress of the reaction was monitored by TLC using acetone:ethyl acetate (6:4) as eluent. After completion of the reaction, The reaction mixture was neutralized by $NaHCO_3$. The crude product 1-(8-((1H-benzo[d]imidazol-2-yl)methoxy)quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (5a) / 3-(8-((1H-benzo[d]imidazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin - 4-one (6a) / 8-((1H-benzo[d]imidazol-2-yl)methoxy)-5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl) quinoline (7a) was purified by column chromatography and chloroform was used as eluent.

2.6. Synthesis of benzoxazole systems (5b, 6b, 7b)

A mixture of 2-((5-(3-chloro-2-oxo-4-phenylazetidin-1-yl)quinolin-8-yl)oxy)acetic acid (3a) / 2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetic acid (3b) / 2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetic acid (3c) (0.1 mol) and 2-aminophenol (0.07 mol) are refluxed for 2.5-3h at 150^0C in presence of trimethylsilyl polyphosphate ester (PPSE). The progress of the reaction was monitored by TLC using ethylacetate : acetone (4:6) as eluent. The reaction mixture was dissolved in dichloromethane and neutralized with aqueous NaOH (1 N). The organic layer was once again extracted with dichloromethane and dried over anhydrous Na_2SO_4. The excess of the solvent in organic layer was evaporated by rotary evaporator. The crude solid was purified by column chromatography using chloroform as eluent to get 1-(8-(benzo[d]oxazol-2-ylmethoxy) quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (5b) / 3-(8-(benzo[d] oxazol-2-ylmethoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6b) / 2-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl) benzo[d]oxazole (7b).

2.7. Synthesis of benzthiazole systems (5c, 6c, 7c)

A mixture of 2-((5-(3-chloro-2-oxo-4-phenylazetidin-1-yl)quinolin-8-yl)oxy)acetic acid (3a) / 2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetic acid (3b) / 2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetic acid (3c) (0.1 mol) and 2-aminobenzenethiol (0.07 mol) are refluxed for 3.5-4h at 150^0C in presence of trimethylsilyl polyphosphate ester (PPSE). The progress of the reaction was monitored byTLC using acetone:ethyl acetate(6:4) as eluent. The reaction mixture was dissolved in dichloromethane and neutralized with aqueous NaOH (1N). The organic layer was once again extracted with dichloromethane and dried over anhydrous Na_2SO_4. The excess of the solvent in organic layer was evaporated by rotary evaporator. The crude solid was purified by column

chromatography using chloroform as eluent and identified as 1-(8-(benzo[d]thiazol-2-ylmethoxy)quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl) phenyl)azetidin-2-one (5c) / 3-(8-(benzo[d]thiazol-2-ylmethoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6c) / 2-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl) benzo[d]thiazole(7c).

3. Results and Discussion

3.1. Physical and spectral data

3-chloro-1-(8-hydroxyquinolin-5-yl)-4-(4-(trifluoromethyl)phenyl) azetidin-2-one (2a)

148-9^{0}C with a yield of 58%. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s, 1H, -OH), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44 (d, 1H,-CH–Cl), 7.3-8.8 (m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 3048 (=C-H, aromatic), 1690 (-C=O), 677 (-C-Cl).

3-(8-hydroxyquinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one(2b)

The yield was 62% with MP: 162-3^{0}C. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s, 1H, -OH), 6.44(s, 1H, -CH-$C_6H_4CF_3$), 3.85(d, 1H, H_a), 3.97(d, 1H, H_b), 7.3-8.7(m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 1690 (-C==O) and 1156 (-C-S).

5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl) quinolin-8-ol (2c)

The yield was 55% with MP 174-5^{0}C. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6(s, 1H,-OH), 7.2-8.7(m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 2120 (-azide), 1157 (Tetrazole).

2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl)quinolin-8-yl)oxy) aceticacid(4a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.8 (s, 2H, -O-CH_2), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44 (d, 1H, -CH–Cl), 7.12-8.8 (m, 9H, Ar-H), 10.54 (s, 1H, -OH). IR (KBr) spectra cm^{-1}: 3100 (-O-H), 1690 (-C=O), 1620 (-C=N), 1320 (-C-O), 677 (-C-Cl).

2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl) oxy)aceticacid (4b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.85 (d, 1H, -H_a), 3.97 (d, 1H, -H_b), 4.58 (s, 2H, -O-CH_2), 6.44 (s, 1H, -CH-$C_6H_4CF_3$), 7.25-8.8 (m, 9H of C_6H_4 & C_9H_5 of quinoline), 10.10 (s, 1H, -OH). IR (KBr) spectra cm^{-1}: 3180 (-O-H), 1705 (-C=O), 1610 (-C=N), 1310 (-C-O), 1188 (C-S).

2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)aceticacid (4c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.58 (s, 2H,-O-CH_2), 7.25-8.8 (m, 9H, Ar-H), 10.15(s, 1H, -OH). IR (KBr) spectra cm^{-1}: 3160 (-O-H), 2107 (azide), 1698 (-C=O), 1620 (-C=N), 1310 (C-O), 1157 (tetrazole).

1-(8-((1H-benzo[d]imidazol-2-yl)methoxy)quinolin-5-yl) -3-chloro-4-(4-(trifluoromethyl) phenyl)azetidin-2-one(5a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s,1H, NH of imidazole), 5.0(s,2H,-O-CH_2), 5.16 (d,1H, -CH-C_6H_4), 5.44 (d,1H,-CH–Cl), 7.1-8.7(m,13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 129, 130, 133(ar-C), 126 (-CF_3), 139, 141 (imidazole-C), 146 (ar-C-O) 162 (-C=O). IR (KBr) spectra cm^{-1} 3210 (-N-H str), 3040 (ar-H str), 1692 (C=O), 1617 (-C=N) and 833(C-Cl). MS, m/z : (M^+, 522.34, M+2, 524.12).

1-(8-(benzo[d]oxazol-2-ylmethoxy)quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl)phenyl) azetidin-2-one (5b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.9 (s, 2H,-O-CH_2), 5.14 (d, 1H, -C-C_6H_4), 5.42 (d, 1H,-C-Cl), 7.1-8.8 (m,13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 73 (aliphatic C), 107, 110, 116, 119, 120, 126 (ar-C) 129 (-CF_3), 146 (ar-C-O) 162(-C=O), 139,150,152 (oxazole-C). IR (KBr) spectra cm^{-1} 3045(ar-H str), 1705 (C=O), 1622 (-C=N), 1158 (-C-O-C) and 819 (C-Cl). MS, m/z : (M^+, 523.42, M+2, 525.16).

1-(8-(benzo[d]thiazol-2-ylmethoxy)quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (5c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.8 (s, 2H, -O-CH_2), 5.15 (d, 1H, -CH-C_6H_4), 5.43 (d, 1H, -C–Cl), 7.3-8.7 (m, 13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 67, 69 (aliphatic C), 107, 116, 119, 121, 122, 129, 130, 133,139, (Ar-C), 126 (-CF_3), 146 (ar-C-O), 162(-C=O), 153,169, 135 (thiazole-C). IR (KBr) spectra cm^{-1} 3048 (ar-H str), 1715 (C=O), 1620 (-C=N), 1158 (-C-O-C), 1115 (C-S), and 833 (C-Cl). MS, m/z : (M^+, 539.26, M+2, 541.09).

3-(8-((1H-benzo[d]imidazol-2-yl)methoxy) quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.87 (d, 1H, -H_a), 3.99 (d, 1H, -H_b), 4.6 (s, 1H, -NH of imidazole), 4.9 (s, 2H, -O-CH_2), 6.44 (s, 1H, -CH-C_6H_4), 7.1-8.8 (m,13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 72, 75 (aliphatic-C), 107, 116, 120, 130, 133 (ar-C), 129 (-CF_3), 139,142 (imidazole-C), 146 (ar-C-O), 171 (-C=O). IR (KBr) spectra cm^{-1} 3190 (-NH-str), 3048 (ar-H str), 1698 (-C=O), 1613 (-C=N), 1188 (-C-S). MS, m/z : (M^+, 520.43).

3-(8-(benzo[d]oxazol-2-ylmethoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.85 (d, 1H,-H_a), 3.99 (d, 1H, -H_b), 4.8 (s, 2H,-O-CH_2), 6.44 (s, 1H, -CH-C_6H_4), 6.9-8.8 (m, 13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 72, 75 (aliphatic C), 107, 110, 116, 119, 120, 125 (ar-C) 126 (-CF_3), 146 (ar-C-O) 171(-C=O), 139, 150, 152 (oxazole-C). IR (KBr) spectra cm^{-1} 3040 (ar-H str), 1688 (-C=O), 1618 (-C=N), 1178 (-C-S), 1160 (C-O-C). MS, m/z : (M^+, 521.27).

3-(8-(benzo[d]thiazol-2-ylmethoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.80 (d, 1H, -H_a), 3.92 (d, 1H, -H_b), 4.9 (s, 2H,-O-CH_2), 6.44(s,1H, ,-CH-C_6H_4), 7.2-8.8(m, 13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 75, 67 (aliphatic C), 146, 107, 116, 119, 121, 122, 125, 129, 130, 133, 139 (ar-C), 142 (ar-C-O), 168, 152 (thiazole-C), 171 (-C=O). IR (KBr) spectra cm^{-1} 3045 (ar-H str), 1690 (-C=O), 1622 (-C=N), 1182 (-C-S). MS, m/z : (M^+, 537.07).

8-((1H-benzo[d]imidazol-2-yl)methoxy)-5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl) quinoline (7a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 5.1 (s, 2H,-O-CH_2), 4.8 (s, 1H, NH of imidazol), 7.1-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (O-CH_2), 107, 115, 116, 121, 123, 126 (Ar-C), 131(-CF_3), 138, 141 (imidazole -C), 163 (tetrazole-C), 155 (ar-C-O). IR (KBr) spectra cm^{-1} 3190 (-NH-str), 3045 (Ar-H str), 2115 (azide), 1694 (–C=O), 1618 (-C=N), 1158 (tetrazole). MS, m/z : (M^+, 487.47).

2-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl) benzo[d]oxazole (7b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 5.1 (s, 2H, -O-CH_2), 7.2-8.8 (m, 13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (O-CH_2), 107, 110, 116, 119, 121, 123, 125, 126, 131, 138,149, 134, 138,152 150 (oxazole-C), 155(ar-C-O), 163 (tetrazole-C). IR (KBr) spectra cm^{-1} 3050 (ar-H str), 2125 (azide), 1694 (–C=O), 1622 (-C=N), 1168 (tetrazole), 1150 (-C-O-C). MS, m/z : (M^+, 488.19).

2-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl) benzo[d]thiazole(7c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 5.12 (s, 2H, -O-CH_2), 7.15-8.82 (m, 13H, ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 67(O-CH_2), 107, 126, 116, 121, 131, 134,138, 149 (ar-C) 155 (ar-C-O), 163 (tetrazole-C), 168, 152 (thiazole-C). IR (KBr) spectra cm^{-1} 3050 (ar-H str), 2125 (azide), 1694 (–C=O), 1628 (-C=N), 1168 (tetrazole), 1152(-C-S-). MS, m/z : (M^+, 504.54).

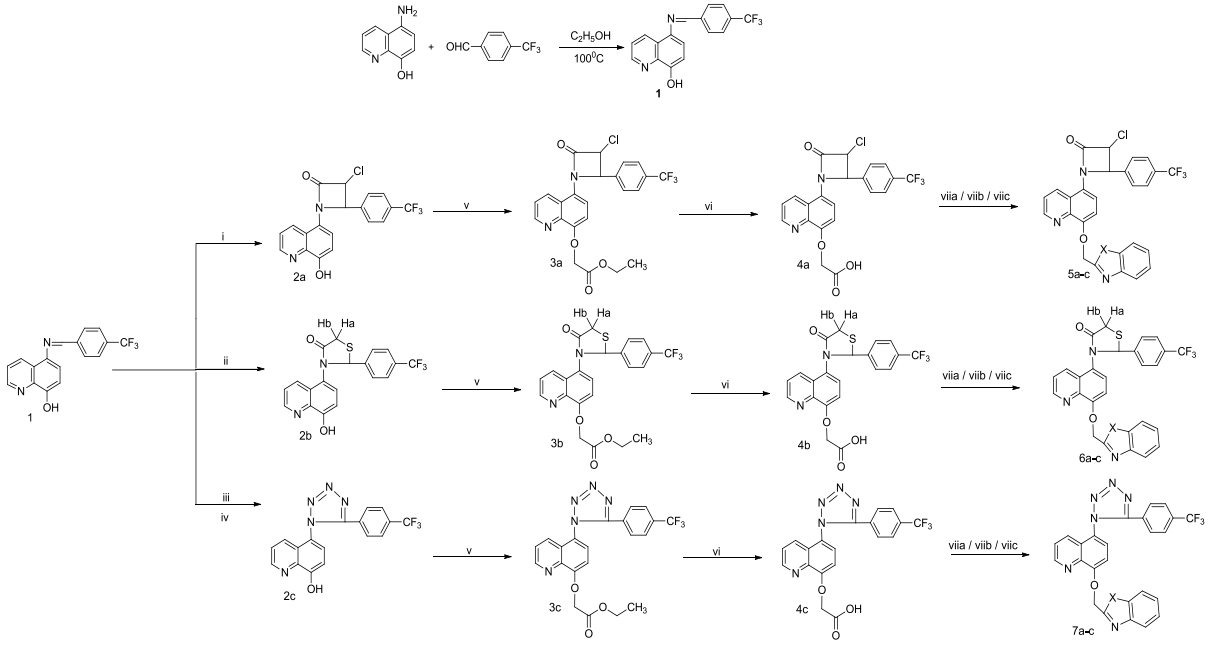
The target compounds were synthesized via the route as shown in Scheme below. The synthon required for the synthesis of the target molecules 5-amino-8-hydroxy quinoline was prepared by a reported method [21].

The quinoline containing azetidinones derivatives were prepared by the reaction of compound **1** with chloroacetyl chloride and the **1** on reaction with thioglycolicacid produce the thiazolidinone derivatives. Similarly, the compound **1** with sodium azide yields tetrazole derivatives.

The carboxylic acid intermediates 4a, 4b and 4c were converted into their corresponding benzimidazoles, benzoxazoles and benzthiazoles on treatment with orthophenylenediamine, 2-aminophenol & 2-aminobenzenethiol, respectively (Table 1).

TABLE 1. Physical and preparation data of the synthesized compounds (4a-c, 5a-c, 6a-c, 7a-c)

Comp	Yield (%)	Melting Point (^{0}C)	Elemental analysis data Calculated (%) Found (%)		
			C	H	N
4a	72	183-4	55.89 (55.95)	3.07 (3.13)	6.13 (6.21)
4b	61	162-3	56.18 (56.25)	3.29 (3.37)	6.18 (6.25)
4c	64	175-6	54.82 (54.95)	2.83 (2.91)	16.78 (16.86)
5a	64	154-5	61.94 (62.02)	3.36 (3.47)	6.69 (6.78)
5b	59	163-4	61.82 (61.90)	3.18 (3.27)	9.91 (8.02)
5c	49	134-5	59.98 (60.06)	3.11 (3.17)	7.72 (7.78)
6a	57	143-4	62.23 (62.30)	3.62 (3.68)	10.69 (10.76)
6b	54	158-9	62.07 (62.18)	3.39 (3.48)	7.95 (8.06)
6c	57	128-9	60.25 (60.32)	3.27 (3.37)	7.74 (7.82)
7a	52	157-8	61.49 (61.60)	3.25 (3.31)	20.04 (20.11)
7b	50	172-3	61.37 (61.48)	3.02 (3.10)	17.13 (17.21)
7c	42	147-8	59.43 (59.52)	2.94 (3.00)	16.58 (16.66)



X= -NH-, -O-, -S- for a,b,c respectively

Reagents & Conditions: (i) Chloroacetyl chloride, Triethyl amine, Dioxane, 8h. (ii) Thioglycolic acid, Zinc Chloride, Dioxane, 8h. (iii) PCl3, 100^0C, 1h. (iv) Sodium azide. (ice-cold), Zinc Chloride, Sodium acetate, acetone, water RT. (v) Chloroethylacetate, DMF, K2CO3, RT, 8h. (vi) THF / MeOH / H2O in 1:1:1 ratio, 2N NaOH, reflux, 6h, (viia) Orthophenylenediamine, 6N HCl, 3-3.5h. 100^0C (viib) 2-Aminophenol, trimethylsilyl polyphosphate ester (PPSE), 2.5-3h, 150^0C. (viic) 2-aminobenzenethiol, trimethylsilyl polyphosphate ester (PPSE), 3.5-4h, 160^0C.

The ^{1}H NMR (300MHz, DMSO-d_6) spectra of compounds (**6a-c**) shows doublets in the region of δ = 3.87 & 3.99 ppm due to the formation of two diastereomeric protons of thiazolidinone, labelled as H_a & H_b.

3.2. Antimicrobial Activities

Antibacterial Activity

The antibacterial activity of synthesised compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacteria screened were *Staphylococcus aureus* NCCS 2079 and *Bacillus cereus* NCCS 2106. The gram negative bacteria screened were *Escherichia coli* NCCS2065 and *Pseudomonas aeruginosa* NCCS2200.

The synthesised compounds were used at the concentration of 250 µg/mL and 500 µg/mL using DMSO as a solvent. The *Cefaclor* 10µg/disc was used as a standard. (Himedia Laboratories Ltd, Mumbai). The test results presented in the Table 2 suggest that 5a, 6a and 7c exhibit high activity against the tested bacteria, the rest of the compounds were found to be moderate active against the tested microorganisms.

Antifungal Activity

The antifungal activity of synthesised compounds were studied by disc diffusion method against the organisms of *Aspergillus niger* NCCS1196 and *Candida albicans* NCCS34471.

Compounds were treated at the concentrations of 100µg/mL, 250µg/mL, 500µg/mL and 1000µg/mL using DMSO as solvent. The standard used was *Clotrimazole* 50µg/mL against both microorganisms. The test results are presented in Table 3

TABLE 2. Antibacterial activity by the disc diffusion method of quinoline-benzazoles having azetidi-2-one(5a-c), thiazolidinone(6a-c) and tetrazole (7a-c)

Compound	Zone of Inhibition (mm)			
	Staphylococcus aureus	*Bacillus cereus*	*Escherichia coli*	*Pseudomonas aeruginosa*
5a	13	11	09	08
5b	10	08	06	06
5c	14	13	10	10
6a	15	13	12	10
6b	12	10	08	08
6c	17	15	14	13
7a	12	10	09	09
7b	09	06	06	07
7c	14	12	11	12
Cefaclor	19	22	19	20

TABLE 3. Antifungal activity by the disc diffusion method for quinoline-benzazoles having azetidi-2-one (5a-c), thiazolidinone (6a-c) and tetrazole (7a-c)

Compound	Zone of Inhibition (mm)	
	Asperigillus niger	*Candida albicans*
5a	16	12
5b	19	17
5c	17	11
6a	19	16
6b	18	17
6c	20	18
7a	19	20
7b	17	18
7c	14	16
Clotrimazole	25-30	25-30

4. Conclusions

The present investigation discovers a new class of biologically potent benzazoles possessing quinoline core unit bearing azetidin-2one / thiazolidin-4-one / tetrazole moieties in a single molecular frame work. These benzazoles exhibited promising antibacterial and antifungal activities. Hence, it can be concluded that, this new class of compounds certainly holds a greater consent in the design of new potent antibacterial and antifungal agents.

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Received: 14 February 2014
Accepted: 15 May 2014