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Research Article

One-Pot Three Component Synthesis of some 8-Benzeloxy-5-{2-[N-(2-Chloro-Quinolin-3yl -Methelene)-Hydrazino]-Thiazole-4-yl}c-1H-Quinoline 2-Ones

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Abstract—Synthesis of a new series of 8-Benzeloxy-5-{2-[N-(2-chloro-quinolin-3ylmethelene)-hydrazino] is investigated in this work. One-pot multicomponent synthesis of -thiazole-4-yl-1H-quinoline-2-one was achieved by condensation of substituted 2. Chloroquinoline thiosemicarbazide, -3-carbaldehydes, and 8-benzyloxy-5-(2-bromo-acetyl)-1H-quinolin-2-one.

Keywords—Multicomponent synthesis, quinoline, thiazole,maxium yields, room temperature conditions.

1. Introduction

The majority of pharmacologically active substances are heterocyclic molecules with several heterocyclic rings [1]. These various compounds are essential to the creation of new drugs because of their many heteroatoms and range of ring sizes [2]. Among these, quinoline is a special scaffold that is essential for creating innovative drugs with therapeutic potential. Many bioactivities, such as anti-microbial, anti-cancer, anti-convulsant, anti-tumor, anti-obesity, anti-fungal, antiprozoal, antimalarial, antiviral, antibacterial, and anti-inflammatory properties, are displayed by its derivatives [3-12]. In a similar vein, alpha bromocarbonyl molecules are necessary organic synthesis intermediates.

Heterocyclic molecules with several heterocyclic rings are the main constituents of pharmacologically active drugs [1]. These heteroatom-rich compounds with a range of ring diameters are essential to the creation of new drugs [2]. Quinidine is one of them that stands out as a special scaffold that is essential to creating cutting-edge medications with therapeutic value. The compounds derived from it demonstrate a wide range of biological activities, such as antimicrobial, anti-tumor, anti-cancer, anti-convulsant, anti-obesity, anti-fungal, antiprozoal, antimalarial, antiviral, antibacterial, and anti-inflammatory properties [3–12]. Similar to this, alpha bromocarbonyl substances are necessary organic synthesis intermediates.

Another major class of heterocyclic chemicals is thiazoles, which are used as effective pesticides in agriculture and medicine. They are also commercially significant. The pharmacological effects of thiazoles and their derivatives include anti-inflammatory, anti-diabetic, anti-tumor, anti-tumor, analgesic, antifilarial, antifungal, antibacterial, anaesthetic, sedative, anti-helmintic, and anticonvulsant qualities [13–22]. Quinolones have a bicyclic aromatic core and a variety of pharmacological properties, such as antitubercular, anti-HIV, antimalarial, and cytotoxic effects on cancer cell lines [23–26]. Their derivatives are used as building blocks for naturally occurring goods and medicinally effective substances [27].

Since quinoline and thizaole scaffolds have a wide range of therapeutic uses [3-22], we have developed a one-pot synthesis technique for a novel series of 8-Benzyloxy-5-{2-[N'-(2-chloro-quinolin-3-ylmethylene)-hydrazino] here.-thiazol-4-yl}using the condensation of substituted 2-chloro-quinoline in the -1H-quinolin-2-one methodthiosemicarbazid 2, -3-carbaldehyde derivatives 1, and 8-benzyloxy-5-(2-bromo-acetyl)1H-quinolin-2-one 3 at 80 ^{0}C in ethanol as the reaction media. In 3.4-5 hours, the products were obtained with a yield of 75-93%.

2. Material and methods

All of the chemicals and solvent used for present study were used of AR grade and used without further purification. The melting points were determined in open capillary tubes with no corrections. Formation of the compounds were checked by thin-layer chromatography (TLC) on aluminum sheets with silica gel 60 F254 plates 0.5 mm thick. Infrared (IR) spectra were recorded on a Shimadzu FT-IR-8400 instrument using the KBr pellet method. 1H NMR and 13C NMR were

recorded in DMSO-d_6 solvent on a BrukerAvance Neo 500-MHz spectrometer.

3. Experimental section

Typical procedure for one pot synthesis of thiazole derivatives *4a–d*

An equimolar mixture of 2-Chloro-quinoline-3-carbaldehyde 1a-d and thiosemicarbazide 2 (1 mmol) was added in a 50 ml round bottom flask in 5 ml of ethanol. To this catalytic amount of 20 mol % acetic acid was added. The reaction mass was stirred at RT for 30 minutes to obtain a clear solution, then 8-benzyloxy-5-(2-bromo-acetyl)-1H-quinolin-2-one 3 (1 mmol) was added to the above reaction mass and stirred at 80^0 C. The reaction was monitored by thin layer chromatography. After completing the reaction, the solid separated out and was filtered, washed by water and dried.

Spectral data

8-Benzyloxy-5-{2-[N'-(2-chloro-6-fluoro-quinolin-3-ylmethylene)-hydrazino]-thiazol-4-yl}-1H-quinolin-2-one (4a): melting point 172–175^0C, ^{1}H NMR (500 MHz, DMSO-d_6): δ at 5.36 (s, 2H, -OCH_2), 8.45(d,1H, Ar-H, quinoline), 8.47(d, 1H, Ar-H, quinoline), 8.81(s,1H,Ar-H, quinoline),6.58(d,1H,J=9.9Hz Ar-H quinoline), 8.06 (d, 1H, J= 2.8Hz,quinoline),7.13(s,1H, Ar-H, thiazole), 12.69(s, 1H, N-H),10.74 (s,1H,N-H,amide),7.25(s,1H, Ar-H, quinoline),7.30-7.42(m,6H, Ar-H), 7.76(s, 1H,C=H, hydrazide) , 7.27(d,1H,J=8.45Hz, Ar-H, quinoline). **^{13}C-NMR($CDCl_3$) spectrum** recorded at 69.79 (-O CH_2), 107.42, 111.70, 111.88, 112.14, 116,97, 122,01, 122.36, 126.94, 127.70, 127.81, 128.25, 129.53, 130.46, 133.74, 136.45, 138.54,143.73, 143.92, 147.41, 159.16, 160.84, 161.12 (C=O), 167.19 (C=N).**FTIR(KBr-cm-1)** 3790.72(N-H), 3058.70(CH=CH, Aromatic), 1251.14(O-Ar), 680.85(C-Cl), 1068.41(C-f), 825(C-S), 1663.08(C=O), 1251.14 (C-N). **Mass: [ES]+**: Calculated: 555.13, Found: 556.68.

8-Benzyloxy-5-{2-[N'-(2-chloro-6-ethyl-quinolin-3-ylmethylene)-hydrazino]-thiazol-4-yl}-1H-quinolin-2-one (4b): melting point 165 – 168^0C.**^{1}H NMR(500 MHz, DMSO-d_6)**: δ at 1.5 (s,3H, CH_3), 3.45 (s, 2H, CH_2), 7.20 (d, 1H, Ar-H, quinoline), 7.40 (d,1H, Ar-H), 7.60 (s, 1H, C=H, hydrazid), 10.74 (s,1H, N-H, hydrazid), 7.06 (s,1H, Ar-H, thiazole), 8.74 (s,1H,Ar-H, quinoline),7.29 (s, 1H,Ar-H, quinoline), 8.80 (s, 1H, N-H, amide), 6.56(d,1H, Ar-H,quinoline),7.60(d,1H, Ar-H, quinoline),7.12(d,1H, Ar-H, quinoline), 7.42(d1H, Ar-H, quinoline), 5.21 (s, 2H, O-CH_2, ethelene),7.33-7.46 (m, 5H, Ar-H). **^{13}C-NMR(500 MHz, DMSO-d_6):** spectrum recorded at14.30(-CH_3),aliphatic, 18.07 (- CH_2) aliphatic, 69.77 (-O CH_2), 105.70, 106.71, 112.12, 116.97, 121,83, 122,21, 122.26, 125.86, 127.69, 127.80, 128.24, 129.46, 136.46, 138.69, 142.28, 143.77, 160.85 (C=O), 168.08 (C=N). **IR(KBr-cm-1)** 3388.43(N-H), 3055.91 (CH=CH Aromatic), 1648.48 (C=O), 680.97 (C-Cl), 1251.12(O-Ar), 1583.66 (C=N), 1452.76 (- CH3), 827.07 (C-S).Mass: [ES]+: Calculated – 565.13, Found – 566.2.

8-Benzyloxy-5-{2-[N'-(2-chloro-6-methoxy-quinolin-3-ylmethylene)-hydrazino]-thiazol-4-yl}-1H-quinolin-2-one (4c): melting point 162 – 164^0C.^{1}H NMR (500 MHz, DMSO-d_6): δ at 3.91(s,3H, O-CH3), 5.36 (s, 2H, O-CH_2), 9.20(s,1H,Ar-H, quinoline), 7.26(s,1H, Ar-H, thiazole), 8.72(s,1H,C=N), 7.32(s,1H, Ar-H,quinoline), 7.39(d,1H,J=1.95Hz,Ar-H, quinoline),7.62(d,1H,Ar-H,quinoline), 6.55(d,1H, Ar-H,quinoline), 7.87(d,1H, J=9.2Hz, Ar-H, quinoline), 8.22(s,1H, N-H amide), 11.80(s, 1H, N-H), 7.31-7.90(m,7H,Ar-H). **^{13}C-NMR($CDCl_3$)** spectrum recorded at 55.48(O-CH3), 69,77(-O CH_2), 105.0, 105.74, 121.5, 121.7, 122.7, 123.95, 124.7, 126.13, 126.3, 127.1, 127.71, 127.82, 128.11, 128.26, 129.12, 134.63, 136.73, 139.5, 142.95, 143.3, 145.76, 147.8, 150.5, 152.6, 157.87(C=O), 178.32(C=N). **FTIR (KBr-cm-1)** 3560(N-H), 3054(CH=CH, Aromatic), 1695(C=O), 1070.24(C-O), 643.85(C-Cl), 682(C-S), 1245.14 (C-N), 1201.14(O-Ar).

8-Benzyloxy-5-{2-[N'-(2,6-dichloro-quinolin-3-ylmethylene)-hydrazino]-thiazol-4-yl}-1H-quinolin-2-one (4d):melting point 147 – 150^0C. ^{1}H NMR (500 MHz, DMSO-d_6): δ at 5.34 (s, 2H, O-CH_2), 11.62(s,1H,Ar-H, quinoline),12.71 (s, 1H, N-H),10,70 (s, 1H, N-H, amide), 8.81(s, 1H,C=H, hydrazide), 6.58 (d, 1H, J=16.5Hz, Ar-H, quinoline), 8.47(d, 1H, Ar-H, quinoline), 6.96 (s, 1H, Ar-H, quinoline), 7.83 (s, 1H, Ar-H, Thiazole), 7.13-7.8 (m, 9H, Ar-H). **^{13}C-NMR($CDCl_3$)** spectrum recorded at 69.77 (-O CH_2), 105.7, 106.71, 112.12, 116.97, 121.83, 122.21, 122.26, 125.86, 127.69, 127.80, 128.24, 129.46, 136.46, 138.69, 142.28, 143,77, 160.85 (C=O), 168.08 (C=N).**FTIR(KBr-cm-1)** 3410 (N-H), 3084(CH=CH, Aromatic), 1713(C=O), 643.85(C-Cl), 695(C-S), 1285.14 (C-N), 1251.14(O-Ar). **Mass: [ES]+**: Calculated – 571.064, Found – 572.68.

4. Results and discussion

The synthesis of 2-Chloro-quinoline-3-carbaldehyde derivatives 1a–d was carried out using the well-known Vilsmeier-Hack formulation. 5-(2-bromo-acetyl)-8-benzyloxyOne method of producing -1H-quinolin-2-one 3 is bromination of a derivative of the acetyl quinoline molecule. Finally, the one-pot synthesis of thiazole derivatives 4a–d was completed using 1 mmol of compounds 1a–d, 1 thiosemicarbazide 2, and benzyloxyquinoline 3.

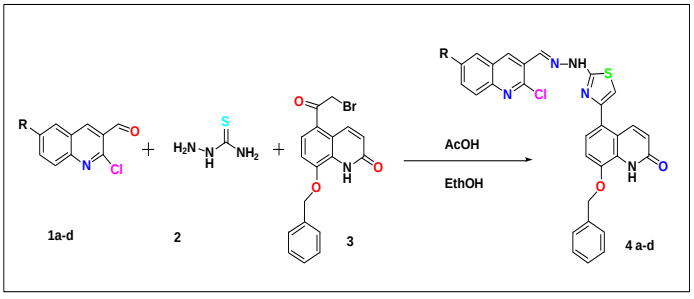

Figure: 1. Synthesis of New QuinolineThiazole Derivatives

The synthesis of the intermediate thiosemicarbazone between the aldehydes and the amine functional group was identified using thin layer chromatography (TLC). Next, we introduced 8-benzyloxy-5-(2-bromo-acetyl) in an equimolarquantity.To obtain the desired, use -1H-quinolin-2-one 3. [N-(2-chloro-

quinolin-3ylmethelene)-hydrazino]-8-Benzeloxy-5-{2-[(thiazole-4-yl)Distilled -1H-quinoline-2-ones 4a–d (Figure 1).

Table 1: One pot synthesis of new Quinoline derivatives

Entry	R	Time(hr)	Yield(%)[a]	M.P, ^oC
4a	6-F	3.3	90	172 - 175
4b	6- C_2H_5	3.	93	165 - 168
4c	6-OCH_3	4	85	162 - 164
4d	6-Cl	4.55	75	147 - 150

[a]Isolated yield

Nuclear magnetic resonance (NMR) spectrum data analysis methods, infrared spectroscopy (IR), and mass spectrometry were utilised to clarify the structures of the synthesised compounds (4a-d). The protons of the benzyloxy group (Ar-OCH2), the thiazole ring, (-NH, hydrazine), -NH amide, quinoline proton, C=H proton, and hydrazide are represented by singlet signals in the 1H-NMR spectrum of compound 4a at 5.36 ppm, 8.81 ppm, 7.13 ppm, 12.69 ppm, 10.74 ppm, 7.25 ppm, and 7.76 ppm, respectively. However, at values ranging from 7.30 to 8.47 ppm, additional protons emerge, resulting in the observation of doublet and multiplet signals of aromatic hydrogen.

This also applies to compound 4d. Compound 4b, on the other hand, displayed two new singlet signals at 1.5 ppm and 3.45 ppm, which are caused by the quinoline rings' position six ethyl group. In contrast, Compound 4c exhibits a novel singlet signal at 3.91 ppm, which is caused by the presence of a methoxy group on the quinoline ring's sixth position.

5. Conclusion

To summarise, we have effectively developed a handy, effortless, straightforward, and efficient technique for creating several novel 8-Benzeloxy-5-{2-[N-(2-chloro-quinolin-3ylmethelene)-hydrazino](thiazole-4-yl)-1H-quinoline 2-one derivatives by 8-Benzyloxy-5-(2-bromo-acetyl) cyclocondensationOne-pot multicomponents technique was used to synthesise -1H-quinolin-2-one, substituted 2-chloro-quinoline-3-carbaldehyde, and thiosemicarbazid under ambient conditions

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