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Synthesis of New Isolated Pyrazolo, Isoxazolo Derivatives Incorporating Pyrido[1,2]thiazinoquinoline

NADIA ALI AHMED ELKANZI^{1,2,*}

¹Chemistry Department, Faculty of Science, Aljouf University, Al Jouf 2014, Kingdom of Saudi Arabia

²Chemistry Department, Faculty of Science, Aswan University, Aswan 81528, Egypt

*Corresponding author: Fax: +966 4 6247183; Tel: +966 4 6242271; E-mail: nadiaelkanzi88@yahoo.com

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Acetylation of 7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (**1**) with acetic anhydride and glacial acetic acid gave 2,9-diacetyl-7,14-diamino-5,5a,6a,7,12,12a-hexahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (**2**). The one-pot reaction of compound (**2**) with the aromatic aldehydes (**3a-c**) in the presence of catalytic amount of piperidine gave the corresponding arylidene derivatives (**4a-c**). Reaction of the arylidene derivatives (**4a-c**) with an equimolar amount of hydrazine hydrate and/or phenylhydrazine in the presence of a base gave N-acetylpyrazolo-derivatives (**5a-c**) and N-phenylpyrazolo derivatives (**6a-c**). Similarly, the isoxazolo pyrimidine derivatives (**7a-c**) were obtained through the reaction of arylidene derivatives (**4a-c**) with an equimolar amount of hydroxylamine hydrochloride in ethanol in the presence of sodium hydroxide as a catalyst. The structures of the new compounds were elucidated by compatible analytical and spectroscopic measurements.

Keywords: Synthesis, N-acetylpyrazolo, N-phenylpyrazolo, Arylidene, Aromatic aldehydes.

INTRODUCTION

Pyrazoles are five member ring heterocyclic compounds, have some structural features with two nitrogen atoms in adjacent position and are also called as azoles¹. Recently, pyrazole derivatives have been found in nature¹, β -[1-pyrazolyl]-alanine was isolated from the seeds of water melons [citrullus lanatus]. The best described property of almost every group of pyrazoles is in the treatment of inflammation and inflammation associated disorders, such as arthritis². Pyrazole derivatives are the subject of many research studies due to their wide spread potential biological activities such as antimicrobial³, antiviral⁴, antitumor^{5,6}, antihistaminic⁷, antidepressant⁸, insecticides⁹ and fungicides⁹. Several pyrazole derivatives have been found to possess significant activities such as 5- α -reductase inhibitor¹⁰, antiproliferative¹¹, antiparasitic¹², herbicides¹³. A good number of pyrazoles have also been reported to have interesting biological activities like anti-inflammatory¹⁴ and antiprotozoal¹⁵⁻¹⁶ which render them valuable active ingredients of medicine and plant protecting agents. Further, current literature indicates 1,2-pyrazole derivatives to possess various biological activities¹⁷. Isoxazoles possess interesting medicinal¹⁸ properties and have some industrial utility¹⁹. Many biologically active isoxazoles and reduced isoxazole derivatives have been reported, viz., the naturally

occurring antituberculosis, antibiotic cycloserine, the monoamine oxidase inhibitor: isocarboxazid, useful in psychotherapy and isoxazole steroids show anabolic activity, e.g., denazole²⁰. The CNS active isoxazoles, ibotenic acid, muscimol and muscazone are isolated from amanita muscaria and other amanita species. Isoxazole derivatives were used as inhibitors for ulcers²¹, lipooxygenase²², acetylcholine esterase²³. 3-Substituted 5-methylthio isoxazoles were found to exhibit anthelmintic activity²⁴. Spiro isoxazolines²⁵ and benzofuroisoxazoles²⁶ were used as anti-convergents. 5-Amino-3-methyl-4-ureidoisoxazoles were found to exhibit antileukemic activity²⁷. Some new 2-isoxazole derivatives prepared from α,β -dibromochalcones showed mild antibacterial activity²⁸. A group of 4,5-diphenyl isoxazoles, 3,4-diphenyl-5-trifluoromethyl isoxazoles and 4,5-diphenyl-3-methyl sulfonamido isoxazole possessing a variety of substitutions (H, F, MeS, MeSO, MeSO₂) at the *para* position of one of the phenyl rings were used as analgesic and selective COX-2 inhibitory and anti-inflammatory agents²⁹. Isoxazolyl naphthoquinones act as potential trypanocidal and antibacterial agents³⁰. In the chemistry of polyfunctional heterocycles with enhanced biological potency, it is very interesting to synthesize new compounds which accommodate the biologically active quinoline, isolated pyrazole and/or isolated isoxazole moieties, in the same structure.

EXPERIMENTAL

All materials were obtained from commercial suppliers (Aldrich and Merck) and used without further purification. Melting points were uncorrected and recorded on Gallenkamp electro thermal melting point apparatus. The reactions were monitored and the purity of products was controlled by thin layer chromatography (TLC) using silica gel aluminum sheets 60F₂₅₄ (Merck, Germany). Elemental analytical data (in accordance with the calculated values) were calculated at the micro analytical unit of Cairo University. The IR spectra were obtained from KBr disks using Perkin Elmer 1650 ET-IR Spectrophotometer (USA). The ¹H-NMR and ¹³C-NMR spectra were recorded on an FT-NMR JNM-LA spectrometer (300 MHz) in CDCl₃ or DMSO-*d*₆ as solvent, using TMS as an internal standard.

Synthesis of 7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (1): This compound was prepared according to the reported method³¹.

2,9-Diacetyl-7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (2): A solution of compound **1** (4.30, 0.01 mol) in a mixture of acetic anhydride and acetic acid (1:1 molar ratio) was refluxed for about 9 h. The reaction mixture was filtered, dried and collected. On crystallization from the ethanol it gives compound **2**. This compound was obtained as brown crystals. m.p.: 296 °C, Yield: 68 % (EtOH). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3100 (NH, NH₂), 3048 (C-H, aromatic) 1685 (2CO), 1660-1640 (4CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.66 (s, 6H, 2CH₃), δ 6.76 (brs, 4H, 2NH₂), δ 7.01-8.01 (m, 6 Ar-H), δ 11.12 (brs, 2H, 2NH). ¹³C NMR δ (ppm): 169.08 (C=O of acetyl, group), 161.07 (C=O of 1,2-thiazino ring), 36.89 (CH₂ of 1,2-thiazino ring), 19.02 (CH₃ for acetyl group). MS (*m/z*, (%)): 502 (25) [M⁺]. Anal. (%) Calcd. for C₂₀H₁₈N₆O₆S₂ (502.52): C, 47.80; H, 3.61; N, 16.72; S, 12.76. Found: C, 47.79; H, 3.59; N, 16.71; S, 12.74.

Synthesis of arylidino derivatives (4a-c): A solution of compound **2** (5.14 g, 0.01 mol) and aromatic aldehydes (**3a-c**) (1.06, 1.22 and 1.51 g, 0.01 mol, respectively) in a mixture of ethanol and dimethyl formamide in presence of piperidine (0.5 mL) as catalyst was refluxed for 8-9 h. The mixture was concentrated and then left to cool and pour onto ice water acidified by concentrated hydrochloric acid. The solid product so formed was collected by filtration and recrystallized from the ethanol and dimethyl formamide to give arylidino derivatives (**4a-c**).

2-Acetyl-7,14-diamino-9-cinnamoyl-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (4a): This compound was obtained as reddish brown crystals. m.p.: >300 °C, Yield: 60 % (EtOH/DMF). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3150 (NH, NH₂), 3046 (C-H, aromatic) 1660 (2CO), 1658-1640 (4CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.66 (s, 3H, CH₃), δ 6.68 (brs, 4H, 2NH₂), 7.01-8.01 (m, 13 Ar), 10.48 (brs, 2H, 2NH). ¹³C NMR δ (ppm): 169.09 (C=O of acetyl group), 165.85 (C=O attached to chalcon), 118.02, 140.97 (CH=CH) 161.08 (C=O of 1,2-thiazino ring), 36.88 (CH₂ of 1,2-thiazino ring), 19.02 (CH₃ for acetyl group). MS

(*m/z*, (%)): 590 (20) [M⁺]. Anal. (%) Calcd. for C₂₇H₂₂N₆O₆S₂ (590.63): C, 54.91; H, 3.75; N, 14.23; S, 10.86. Found: C, 54.89; H, 3.73; N, 14.22; S, 10.85.

(E)-2-Acetyl-7,14-diamino-9-(3-(4-aminophenyl)acryloyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (4b): This compound was obtained as brown crystals. m.p.: >300 °C, Yield: 63 % (EtOH/DMF). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3150 (NH, NH₂), 3044 (C-H, aromatic), 1685 (2CO), 1675-1640 (4CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.16 (s, 3H, CH₃), δ 6.72 (brs, 4H, 2NH₂), 7.01-8.01 (m, 14Ar-H), 10.52 (brs, 2H, 2NH). MS (*m/z*, (%)): 605 (16) [M⁺]. Anal. (%) Calcd. for C₂₇H₂₃N₇O₆S₂ (605.64): C, 53.54; H, 3.83; N, 16.19; S, 10.59. Found: C, 53.53; H, 3.81; N, 16.18; S, 10.57.

(E)-2-Acetyl-7,14-diamino-9-(3-(4-hydroxyphenyl)acryloyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (4c): This compound was obtained as reddish violet crystals. m.p.: > 300 °C Yield: 62 % (EtOH/DMF). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3150 (NH, NH₂, OH), 3044 (C-H, aromatic), 1680 (2CO), 1670-1640 (4CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.09 (s, 3H, CH₃), δ 6.66 (brs, 4H, 2NH₂), 7.01-8.01 (m, 13H), 10.49 (brs, 2H, 2NH). MS (*m/z*, (%)): 606 (20) [M⁺]. Anal. (%) Calcd. for C₂₇H₂₂N₆O₇S₂ (606.63): C, 53.46; H, 3.66; N, 13.85; S, 10.57. Found: C, 53.45; H, 3.64; N, 13.84; S, 10.55.

Synthesis of N-acetyl pyrazolino derivatives (5a-c): To a solution of arylidino (**4a-c**) (6.02, 6.47 and 6.18 g, 0.01 mol, respectively) in ethanol (30 mL) as solvent, hydrazine hydrate (0.5 g, 0.01 mol) was added followed by glacial acetic acid (10 mL). The reaction mixture was refluxed for 11 h. The reaction mixture was concentrated and filtered. These materials were triturated with water and the precipitates were separated, filtered, washed several times with water, dried, collected and recrystallized from the ethanol solvent to give pyrazolino derivatives (**5a-c**).

2-Acetyl-9-(1-acetyl-4-phenyl-1H-pyrazole-3-carbonyl)-7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (5a): This compound was obtained as violet crystals. m.p.: >300 °C, Yield: 61 % (EtOH). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3100 (NH, NH₂), 1665 (2CO), 1660-1640 (4CO), 3044 (C-H, aromatic). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.02 (s, 3H, CH₃), δ 1.5 (s, 3H, CH₃), δ 6.54 (brs, 4H, 2NH₂), 7.01-8.01 (m, 12H), 10.39 (brs, 2H, 2NH). ¹³C NMR δ (ppm): 169.09 (C=O of acetyl group), 167.07 (C=O attached to pyrazole ring), 105.92, 139.89, 143.89 (carbon of pyrazole ring), 161.08 (C=O of 1,2-thiazino ring), 36.89 (CH₂ of 1,2-thiazino ring), 19.01 (CH₃ for acetyl group). MS (*m/z*, (%)): 672 (30) [M⁺]. Anal. (%) Calcd. for C₃₀H₂₄N₈O₇S₂ (672.12): C, 53.56; H, 3.60; N, 16.66; S, 9.53. Found: C, 53.55; H, 3.58; N, 16.65; S, 9.52.

2-Acetyl-9-[1-acetyl-4-(4-aminophenyl)-1H-pyrazole-3-carbonyl]-7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone(5b): This compound was obtained as deep violet crystals. m.p.: > 300 °C, Yield: 62 % (EtOH). IR (KBr, $\nu_{\max}$, cm⁻¹): 3400-3150 (NH, NH₂), 3044 (C-H, aromatic), 1688 (2CO), 1665-1640 (4CO).

¹H NMR (DMSO-*d*₆, δ ppm): δ 1.08 (s, 3H, CH₃), 1.54 (s, 3H, CH₃), δ 6.61 (brs, 4H, 2NH₂), 7.01-8.01 (m, 13H, Ar-H), 10.56 (brs, 2H, 2NH). MS (*m/z*, (%)): 687 (15) [M⁺]. Anal. (%) Calcd. for C₃₀H₂₅N₉O₇S₂ (687.71): C, 52.39; H, 3.66; N, 18.33; S, 9.33. Found: C, 52.38; H, 3.64; N, 18.31; S, 9.32.

2-Acetyl-9-[1-acetyl-4-(4-hydroxyphenyl)-1H-pyrazole-3-carbonyl]-7,14-diamino-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (5c): This compound was obtained as green violet crystals. m.p.: >300 °C, Yield: 63 % (EtOH). IR (KBr, ν_{max}, cm⁻¹): 3450-3100 (NH, NH₂, OH), 3042 (C-H, aromatic), 1670 (2CO), 1665-1640 (4CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.04 (s, 3H, CH₃), δ 1.52 (s, 3H, CH₃), δ 6.63 (brs, 4H, 2NH₂), 7.01-8.01 (m, 12H, Ar-H), 10.42 (brs, 2H, 2NH). MS (*m/z*, (%)): 688 (25) [M⁺]. Anal. (%) Calcd. for C₃₀H₂₄N₈O₈S₂ (688.69): C, 52.32; H, 3.51; N, 16.27; S, 9.31. Found: C, 52.31; H, 3.50; N, 16.25; S, 9.30.

Synthesis of N-phenyl pyrazolino derivatives (6a-c): To a solution of arylidino derivatives (4a-c) (6.02 g, 6.47 g, 6.18 g, 0.01 mol, respectively) in ethanol as solvent, added phenylhydrazine (1.08 g, 0.01 mol) in the presence of piperidine (0.5 mL) as catalyst. The reaction mixture was refluxed for 12 h. The reaction mixture was concentrated, cooled, poured onto ice water acidified by concentrated hydrochloric acid. The solid products were collected by filtration, washed with water for several times and crystallized from the ethanol solvent to yield the corresponding 6a-c.

2-Acetyl-7,14-diamino-9-(1,4-diphenyl-1H-pyrazole-3-carbonyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (6a): This compound was obtained as green violet crystals. m.p.: >300 °C, Yield: 63 % (EtOH). IR (KBr, ν_{max}, cm⁻¹): 3400-3100 (NH, NH₂), 3044 (C-H, aromatic), 1668 (2CO), 1660-1640 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.07 (s, 3H, CH₃), δ 6.65 (brs, 4H, 2NH₂), 7.01-8.01 (m, 17H, Ar-H), 10.46 (brs, 2H, 2NH). ¹³C NMR δ (ppm): 169.09 (C=O of acetyl group), 167.02 (C=O attached to phenyl pyrazole ring), 107.92, 141.99, 143.02 (carbon of pyrazole ring), 161.08 (C=O of 1,2-thiazino ring), 36.89 (CH₂ of 1,2-thiazino ring), 19.01 (CH₃ for acetyl group). MS (*m/z*, (%)): 706 (30) [M⁺]. Anal. (%) Calcd. for C₃₄H₂₆N₈O₈S₂ (706.14): C, 57.78; H, 3.71; N, 15.85; S, 9.07. Found: C, 57.77; H, 3.70; N, 15.84; S, 9.06.

2-Acetyl-7,14-diamino-9-[4-(4-aminophenyl)-1-phenyl-1H-pyrazole-3-carbonyl]-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (6b): This compound was obtained as blue violet crystals. m.p.: >300 °C, Yield: 57 % (EtOH). IR (KBr, ν_{max}, cm⁻¹): 3400-3150 (NH, NH₂), 3041 (C-H, aromatic), 1663 (2CO), 1657-1645 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.15 (s, 3H, CH₃), δ 6.69 (brs, 4H, 2NH₂), 7.01-8.01 (m, 18H, Ar-H), 10.44 (brs, 2H, 2NH). MS (*m/z*, (%)): 721 (25) [M⁺]. Anal. (%) Calcd. for C₃₄H₂₇O₆N₉S₂ (721.76): C, 56.58; H, 3.77; N, 17.47; S, 8.89. Found: C, 56.56; H, 3.75; N, 17.46; S, 8.88.

2-Acetyl-7,14-diamino-9-[4-(4-hydroxyphenyl)-1-phenyl-1H-pyrazole-3-carbonyl]-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (6c): This

compound was obtained as violet crystals. m.p.: >300 °C Yield 60 % (EtOH). IR (KBr, ν_{max}, cm⁻¹): 3400-3310 (NH, NH₂, OH), 3041 (C-H, aromatic), 1660 (2CO), 1655-1640 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.11 (s, 3H, CH₃), δ 6.67 (brs, 4H, 2NH₂), 7.01-8.01 (m, 17H, Ar-H), 10.40 (brs, 2H, 2NH). MS (*m/z*, (%)): 722 (15) [M⁺]. Anal. (%) Calcd. for C₃₄H₂₆N₈O₇S₂ (722.75): C, 56.50; H, 3.63; N, 15.50; S, 8.87. Found: C, 56.48; H, 3.61; N, 15.49; S, 8.86.

Synthesis of arylisooxazolo derivatives (7a-c): A solution of arylidino derivatives (4a-c) (6.20 g, 6.47 g, 6.18 g, 0.01 mol, respectively) was refluxed with hydroxylamine hydrochloride (0.69 g, 0.01 mol) in presence of sodium hydroxide as catalyst and ethanol as solvent for 9 h. The reaction mixture was filtered hot, the filtrate was concentrated and poured onto ice water where the products were separated, filtered, washed several times with water and crystallized from the methanol solvent to yield the corresponding 7a-c.

2-Acetyl-7,14-diamino-9-(4-phenylisoxazole-3-carbonyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (7a): This compound was obtained as reddish brown crystals. m.p.: >300 °C, Yield: 58 % (MeOH). IR (KBr, ν_{max}, cm⁻¹): 3400-3100 (NH, NH₂), 3044 (C-H, aromatic), 1670 (2CO), 1660-1640 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.06 (s, 3H, CH₃), δ 6.56 (brs, 4H, 2NH₂), 7.01-8.01 (m, 12H, Ar-H), 10.29 (brs, 2H, 2NH). ¹³C NMR δ (ppm): 169.09 (C=O of acetyl group), 166.87 (C=O attached to oxazole ring), 99.02, 149.87, 168.79 (carbon of oxazole ring), 161.08 (C=O of 1,2-thiazino ring), 36.89 (CH₂ of 1,2-thiazino ring), 19.01 (CH₃ for acetyl group). MS (*m/z*, (%)): 631 (20) [M⁺]. Anal. (%) Calcd. for C₂₈H₂₁N₇O₇S₂ (631.64): C, 53.24; H, 3.35; N, 15.52; S, 10.15. Found: C, 53.22; H, 3.32; N, 15.49; S, 10.13.

2-Acetyl-7,14-diamino-9-(4-(4-aminophenyl)isoxazole-3-carbonyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone (7b): This compound was obtained as brown crystals. m.p.: >300 °C, Yield: 57 % (MeOH). IR (KBr, ν_{max}, cm⁻¹): 3450-3100 (NH, NH₂), 3044 (C-H, aromatic), 1678 (2CO), 1665-1640 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.13 (s, 3H, CH₃), δ 6.60 (brs, 4H, 2NH₂), 7.01-8.01 (m, 13H, Ar-H), 10.34 (brs, 2H, 2NH). MS (*m/z*, (%)): 646 (18) [M⁺]. Anal. (%) Calcd. for C₂₈H₂₂N₈O₇S₂ (646.65): C, 52.01; H, 3.43; N, 17.33; S, 9.92. Found: C, 52; H, 3.41; N, 17.30; S, 9.90.

2-Acetyl-7,14-diamino-9-(4-(4-hydroxyphenyl)isoxazole-3-carbonyl)-5,5a,12,12a-tetrahydro-[1,2]thiazino[4',5':5,6]pyrido[2,3-g][1,2]thiazino[5,4-b]quinoline-1,6,8,13(2H,4H,9H,11H)-tetraone(7c): This compound was obtained as reddish violet crystals. m.p.: >300 °C, Yield 55 %. (MeOH). IR (KBr, ν_{max}, cm⁻¹): 3100-3450 (NH, NH₂, OH), 3044 (C-H, aromatic), 1673 (2CO), 1640-1660 (3CO). ¹H NMR (DMSO-*d*₆, δ ppm): δ 1.09 (s, 3H, CH₃), δ 6.58 (brs, 4H, 2NH₂), 7.01-8.01 (m, 12H, Ar-H), 10.36 (brs, 2H, 2NH). MS (*m/z*, (%)): 631 (15) [M⁺]. Anal. (%) Calcd. for C₂₈H₂₁N₇O₈S₂ (647.64): C, 51.93; H, 3.27; N, 15.14; S, 9.90. Found: C, 51.91; H, 3.26; N, 15.13; S, 9.87.

RESULTS AND DISCUSSION

Compound 2 was prepared by the reaction of compound 1³¹ with a mixture of acetic anhydride and glacial acetic acid

which was heated together under reflux for 12 h (**Scheme-I**). The IR spectra revealed the presence of band at 1685 (2CO) for two carbonyl groups of acetyl, ^1H NMR spectra revealed the presence of singlet at δ 1.66 (d, s, 6H, 2CH₃), for two methyl group. The structure of compound **2** was also confirmed by elemental analysis, IR spectra ^1H NMR, ^{13}C NMR and mass spectra as follow: (a) Compatible elementary and molecular weight determination (MS: m/z 502, 25 %) corresponded to C₂₀H₁₈N₆O₆S₂ (502.52); (b) Its IR spectrum (KBr, ν_{max} , cm⁻¹) showed strong absorption bands at 3048 (C-H, aromatic) 1685 (2CO), 1660-1640 (4CO); (c) The ^1H NMR spectrum (DMSO-*d*₆, δ ppm) showed singlet due to two methyl protons which appeared in the spectrum of compound **2** around 1.66 ppm, δ 1.66 (s, 6H, 2CH₃); (d) ^{13}C NMR δ (ppm): 169.08 (C=O of acetyl, group), 161.07 (C=O of 1,2-thiazino ring), 36.89 (CH₂ of 1,2-thiazino ring), 19.02 (CH₃ for acetyl group).

Reaction of compound **2** with the aromatic aldehydes (**3a-c**) in the presence of catalytic amount of piperidine gave the corresponding arylidene derivatives (**4a-c**). The reaction passed through the condensation of the methyl protons of compound **2** with the aldehydic carbonyl group of (**3a-c**).

Structural reasonings for **4a**, taken as a representative example are: (a) Compatible elementary and molecular weight determination (MS: m/z 590, 20 %) corresponded to C₂₇H₂₂N₆O₆S₂ (590.63); (b) Its IR spectrum (KBr, ν_{max} , cm⁻¹) showed strong absorption bands at 3046 (C-H, aromatic) 1660 (2CO), 1640-1658 (4CO); (c) The ^1H NMR spectrum (DMSO-*d*₆, δ ppm) showed one singlet due to methyl protons which appeared in the spectrum of compound **2** around 1.66 ppm; (d) ^{13}C NMR δ (ppm): 169.09 (C=O of one acetyl group), 165.85 (C=O attached to chalcon), 118.02, 140.97 (CH=CH) 161.08 (C=O of 1,2-thiazino ring), 36.88 (CH₂ of 1,2-thiazino ring), 19.02 (CH₃ for one acetyl group).

Moreover, reaction of the arylidene derivatives (**4a-c**) with an equimolar amount of hydrazine hydrate and/or phenylhydrazine in the presence of a base (**Scheme-II**) gave N-acetylpyrazolo derivatives **5a-c** and N-phenylpyrazolo derivatives (**6a-c**), respectively (**Scheme-III**).

Structural reasonings for **5a**, taken as a representative example for formation of acetyl pyrazole, are: (a) Compatible elementary and molecular weight determination (MS: m/z 672, 30 %) corresponded to C₃₀H₂₄N₈O₇S₂ (672.12); (b) IR (KBr,