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SYNTHYSES, REACTIONAND CHARACTRIZATION OF QUINOLINE DERIVATIVES

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ABSTRACT

Starting with 4, 7-dichloroquinoline and on treatment with hydrazine hydrate we obtained the hydrazine derivative **1**. Compound **1** reacted with dithioacetal to give compounds **2a, b,** respectively. Compound **2a** reacted with formamide and formic acid to give compounds **3** and **4**. The imidoformate derivative **5** obtained through the reaction of compound **2a** with trimethyl orthoformate in presence of acetic anhydride. The imino derivatives **6a-c** was obtained upon reacting of **5** with hydrazine hydrate and appropriate primary amines. The chloroquinoline derivative **7** was subjected to react with glycine, anthranilic acid, hydrazine hydrate and appropriate primary amines affording compounds **8**, **9, 10a-d**, respectively Also compound **10a** was allowed to react sodium azide and acetohydrazid affording fused quinolone derivatives **11**and **12**. Compounds **2a** and **2b** were allowed to react with aryl sulfonylchloride, namely benzene sulfonylchloride, p-toluene sulfonylchloride *p*-chlorosulfonylchloride and *p*-bromo benzene sulfonylchloride to give the corresponding **13a-d**, **14a-d** derivatives, respectively. All structures of the newly synthesized compounds were elucidated by their correct values in elemental analysis and spectral data.

Keywords: quinoline derivatives, acetylhydrazide, dithioacetal.

INTRODUCTION

Quinoline is a heterocyclic scaffold of paramount importance to human race. The utility of quinoline derivatives in the areas of medicine, food, catalyst, dye, materials, refineries and electronics is well established. [1]

Quinolines and their derivatives are important constituents of several pharmacologically active synthetic compounds [2-4] including biological activities such as DNA binding capability [5] antitumor [6, 7] and DNA-intercalating carrier. [8]

The development of general methods for the synthesis and biological evaluation of new agents retaining the 'core' quinoline moiety is the subject of considerable synthetic effort. [9]

EXPERIMENTAL

All melting points are uncorrected and were determined in capillary tubes, elemental analysis was carried out in National Research Centre. The IR spectra were recorded in potassium bromide on a Backman Infrared Spectrometer Model PU 9712 using KBr discs (υ cm^{-1}). The ^{1}H-NMR spectra were obtained on Joel EX 270 MHz and on a Varian-Gemini-300 MHz Spectrometer using TMS as an internal standard. The Mass spectra (MS) were recorded on Finnigan Mat SSQ 7000 Mass Spectrometer at 70 eV. All the reactions were followed up and checked by T.L.C using chloroform/methanol (3:1) and spots were examined by U.V lamp. The purity of the synthesized compounds was tested by thin layer chromatography (TLC) on Merck Silica gel F245 plates (0.2mm)

using chloroform/methanol (3/1, v/v) and visualization under UV lamp.

A mixture of 4, 7-dichloroquinoline (0.5g, 10mmole), hydrazine hydrate (0.75g, 15mmole) in absolute ethanol was refluxed for 8 h. The reaction mixture was cooled then the solid formed was collected by filtration and crystallized from the proper solvent to afford **1**.

5-amino-1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-1*H*-pyrazole-4-carbonitrile 2a: An equimolecular amounts of **1** and ketene dithioacetal a, b, and 2-4 drops of triethylamine in 25ml methanol was heated for 8hr. the reaction mixture was cooled and was poured onto ice-water. The solid was formed was collected by filtration, was dried and was crystallized from ethanol absolute to give 2a, b respectively.

2a: 75 % yield m.p.295-7^{O}C, Anal. Calc. for $C_{14}H_{10}ClN_5$ S (315.78) IR (cm^{-1}) : 3547,3425 (NH_2,NH), 3030, 3019 (C-H aromatic), 2218(CN); ^{1}H-NMR (DMSO-d_6) δ (ppm) ; 6.91-8.26 (5H,m, aromatic), 9.1 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 315.5 (10%), 317.5 (3.4 %).

Methyl-5-amino-1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-1*H*-pyrazole-4-car -boxylate 2b: **2b**: 75 % yield m.p. ›300 OC, Anal. Calc. for $C_{15}H_{13}ClN_4O_2S$ (348.81; IR (υcm^{-1}) : 3320 (NH), 3060, 3027 (C-H aromatic), 1637 (CO) ; ^{1}H NMR (DMSO-d_6) δ (ppm) :1.8, 2.9 (8H,m, 4CH_2), 2.5(3H,s,CH_3),6.54 (1H,s, of pyrimidine),7.32-8.2 (7H,m, aromatic), 9.11 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 348.5 (9%), 350.5 (3%).

1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-amine 3:
4, 1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyri-midin-4-one 4.

General procedure: A solution of **1** (3.12g) in formamide or formic acid (20ml) was heated under reflux for 8hrs. The reaction mixture was cooled then the solid was formed was collected by filtration and was crystallized from methanol to afford **3** and **4** respectively.

3: 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{15}H_{11}ClN_6S$ (342.81) : ; IR (υcm^{-1}) : 3410-3210 (NH_2), 3030, 3019 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) (δppm) : 2.81 (3H,s, CH_3), 4.25 (2H,s, NH_2 ,exchangeable with D_2O), 6.53 (1H,s, of pyrimidine), 7.13,7.32 (d, 2H, *j*=8.51 Hz , Ar-H),8.22,8.35 (d, 2H, *j*=8.51 Hz , Ar-H), 8.75 (1H,m, Ar-H), MS: (m/z) M^+ at m/z = 342 (15%).

4: 70 % yield m.p. ›300 ^{O}C, Anal. Calc. for $C_{15}H_{10}ClN_5OS$ (343.79),IR (υcm^{-1}) : 3425 (NH), 3030, 3019 (C-H aromatic), 1675 (CO) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.65(3H,s,CH_3),6.5 (1H,s, of pyrimidine), 7.13,7.32 (d, 2H, *j*=8.51 Hz , Ar-H),8.22-8.35 (3H,m, Ar-H),, 9.1 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 342 (8%).

methyl [1-(7-chloroquinolin-4-yl)-4-cyano-3-(methylsulfanyl)-1*H*-pyrazol-5-yl] imidoformate 5: A mixture of **2a** (0.003mol), trimethylorthoformate and acetic anhydride (1:1) was heated under reflux for 8hr. The reaction mixture was cooled then the solid was formed was collected by filtration and was crystallized from methanol to afford **5**.

5: Yield 78% crystallization from ethanol, m.p. 272-4ºC,for. $C_{16}H_{12}ClN_5OS$ (357.82) ; IR (KBr, cm^{-1}) 3220 (NH), 3090 (C=N), 2209 (CN) ; ^{1}H.NMR (DMSO-d6, δ ppm) : 2.40 (3H,s, S-CH_3), 3.71 (3H,s, OCH_3), 6.34 (1H,s, CH=N), 6.59- 7.80 (5H, m, aromatic); MS (m/z%): 357.5 (16%).

1-(7-chloroquinolin-4-yl)-4-imino-3-(methylsulfanyl)-1,4-dihydro-5*H*-pyrazolo[3, 4-*d*]pyrimidin-5-amine 6a: A mixture of compound **14** (2.86 g, 10 mmole), hydrazine hydrate (0.75 g, 15 mmole) in ethanol (25 ml) was stirred at 0ºC for 4 hr. The reaction mixture was poured onto water and the deposited solid was filtered off, washed with water several times to afford compound of type **6a**.

6a: Yield 78% crystallization from ethanol, m.p. ›300ºC, mol. for. $C_{16}H_{14}ClN_7S$ (357.82) ; IR (KBr, υ cm^{-1}) 3460-3380 (NH_2), 3220 (NH); ^{1}H.NMR (DMSO-d6, δ ppm), 2.32 (3H,s, S-CH_3), 6.45-7.78 (5H, m, aromatic), 8.24 (1H, s, pyrimidine), 4.22,6.60 (3H,s, NH_2, =NH exchangeable with D_2O), MS (m/z%): 357 (20%).

1-(7-chloroquinolin-4-yl)-4-imino-*N*-methyl-3-(methylsulfanyl)-1,4-dihydro-5*H*-pyrazolo[3,4-*d*]pyrimidin-5-amine 6b: and 5-(4-chlorophenyl)-1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-imine 6c:
General procedure: A mixture of equimolecular amounts of compound **5,** methylhydrazine hydrateor *p*-chloroaniline in ethanol (25 ml) was stirred for 8 hr. and leave overnight. The reaction mixture was poured onto water and the deposited solid was

filtered off, washed with water several times, then crystallized from methanol to afford compounds **6b,c**.

6b, Yield 78% crystallization from ethanol, m.p.295-7ºC, mol. for. $C_{16}H_{14}ClN_7S$ (371.85) ; IR (KBr, υ cm^{-1}), 3220,3090 (NH); ^{1}H-.NMR (DMSO-d_6, δ ppm) 2.40 (3H,s, S-CH_3), 3.73 (3H,s, N-CH_3), 6.50-7.82 (5H, m, aromatic), 8.40 (H, s, pyrimidine), 4.25,6.60 (2H,s, =NH, NH exchangeable with D_2O, NH), MS (m/z%): 371 (11%).

6c, Yield 78% crystallization from ethanol, m.p .›300ºC, for. $C_{21}H_{14}Cl_2NS$ (453.35) ; IR (KBr,υ cm^{-1}) 3460-3380 (NH_2), 3220 (NH); ^{1}H.NMR (DMSO-d6, δ ppm) 2.65 (3H,s, S-CH_3), 6.74-8.10 (9H, m, aromatic), 8.32 (1H, s, pyrimidine), 6.65 (1H,s, =NH exchangeable with D_2O), MS (m/z%): 453 (9%), 455 (3%).

7-chloro-4-[4-chloro-3-(methylsulfanyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl]quinoline 7: Compound **4(** 10 gm)was heated with $POCl_3$ (40 mL)and PCl_5 (5g) on water bath for 10 hr, then cooled and poured drop wise on ice /water, the produced chloro derivative **5** was filtered off, dried under vacuum and used as a crude for subsequent work.

7 : 75 % yield m.p. 240-2 ^{O}C, Anal. Calc. for $C_{15}H_9Cl_2N_5S$ (362.23) : IR (υcm^{-1}) : 3030, 3019 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.72 (3H, s, SCH_3),6.3 (1H,s, pyrimidine),7.1-8.0 (5H,m, aromatic), MS: (m/z) M^+ at m/z = 342 (15%).

7-(7-chloroquinolin-4-yl)-9-(methylsulfanyl)-2,7-dihydro-3*H*-imidazo[1,2-*c*]pyra- zolo [4,3-*e*]pyrimidin-3-one 8: A solution of **5** (0.01 mol) and glycine (0.01 mol) in (30 ml) n-butanol was heated under reflux for 6hr. The solid separated on cooling was refluxed with Ac_2O for 7hr. The product obtained after cooling was crystallized from methanol.

8: 75 % yield m.p. ›300 Anal. Calc. for $C_{17}H_{11}ClN_6OS$ (382.83) : IR (υ cm^{-1}) : 3030, 3019 (C-H aromatic), 1695 (CO) : ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.64 (3H,s,SCH_3),4.22 (2H,s, CH_2), 6.61 (1H,s, of pyrimidine),7.3-8.2 (5H,m, aromatic), 9.15 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 382 (11%).

8-[(7-Chloroquinolin)-1-methylsulfanyl-3H-2,3,4,5a,11-pentaaza-cyclopena[a]anthr- acen-6-one 9: A solution of **5** (0.01 mol) and anthranilic acid (0.015 mol) in (30ml) n-butanol was heated under reflux for 14hr. The product obtained after cooling was filtered off, dried and crystallized from methanol.

9: 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{22}H_{13}ClN_6OS$ (444.89 ; IR (υ cm^{-1}) : 3120, 3025 (C-H aromatic), 1689 (CO) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.4(3H,s, SCH_3),6.2 (1H,s, of pyrimidine),6.9-7.8 (9H,m, aromatic) : MS (m/z) M^+ at m/z = 444 (11%), 446 (5%).

7-chloro-4-[4-hydrazinyl-3-(methylsulfanyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl] -quinoline 10a: A solution of compounds **5** (0.01 mole) and hydrazine hydrate (0.02 mole) in 30 mL methanol was heated under reflux for 7 hr, then cooled, stirred for 24hr. then the solution was poured into ice / water containing few drops of HCl, the produced precipitate was filtered off, dried under suction and crystallized from ethanol to give compound **10a**.

10: 75 % yield m.p. ›300 ^{O}C, Anal. Calc. for $C_{15}H_{12}ClN_7S$ (357.82) : IR (υcm^{-1}) : 3410-3210, 3110 (NH_2, NH), 3030, 3019 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ (ppm) : 2.65 (3H,s,SCH_3),6.55 (1H,s, of pyrimidine),7.32-8.24 (5H,m, aromatic), 9.12,4.52 (3H,s, NH, NH_2 exchangeable with D_2O) MS: (m/z) M^+ at m/z = 357 (15%).

1-(7-chloroquinolin-5-yl)-3-(methylthio)-*N*-(4-aryl)-1*H*-pyrazolo[3,4-*d*]- pyrimidin-4-amine 10 b-d : A solution of **5** (0.01 mol) and the primary amine namely 4-bromoaniline, 4-chloroaniline and 4-nitroaniline (0.02 mol) in (30 ml)n- butanol was heated under reflux for 6-9 hr. The solid obtained after cooling was filtered off, dried and crystallized from methanol.

10b: 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{21}H_{14}BrClN_6S$ (497.80) IR (υ cm^{-1}) : 3215 (NH), 3050, 3014 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ (ppm) : 2.39 (3H, s, SCH_3),6.58 (1H,s, pyrimidine),7.36-8.48 (9H, m, aromatic), 9.25 (1H,s, NH exchangeable with D_2O). MS: (m/z) M^+ at m/z = 497 (15%), 499 (5%).

10c: 75 % yield m.p ›300^{O}C, Anal. Calc. for $C_{21}H_{14}Cl_2N_6S$ (453.35) : IR (υcm^{-1}) : 3312 (NH), 3125, 3017 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.65 (3H,s, SCH_3),6.15 (1H,s, pyrimidine), 7.1-8.0 (9H,m, aromatic), 9.6 (1H,s, NH exchangeable with D_2O). MS: (m/z) M^+ at m/z = 453.5 (13%).

10d: 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{21}H_{14}ClN_7O_2S$ (463.90) IR (υcm^{-1}) : 3210 (NH), 3130, 3019 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) δ

(ppm) : 2.65 (3H,s, SCH_3),6.23 (1H,s, pyrimidine), 7.29-8.20 (9H,m, aromatic), 9.23 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 463 (13.5%), 465 (4.5%).

7-(7-chloroquinolin-4-yl)-9-(methylsulfanyl)-7*H*-pyrazolo[4,3-*e*]tetrazolo[1,5-*c*]–pyrimidine 11: A mixture of compound **5** (0.01 mol) and sodium azide (0.05 mol) in (30 ml) glacial acetic acid was refluxed for 5 hr. The product obtained after cooling was filtered off, dried and crystallized from acetic acid.

11: 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{15}H_9ClN_8$ S (368.81IR (υ cm^{-1}) : 3125, 3020 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ(ppm) : 2.36 (3H,s, SCH_3),6.25 (1H,s, pyrimidine),7.15-8.37 (5H,m, aromatic) : MS: (m/z) M^+ at m/z = 368 (9%).

7-(7-chloroquinolin-4-yl)-3-methyl-9-(methylsulfanyl)-7*H*-pyrazolo[4,3-*e*][1,2,4] -triazolo[4,3-*c*]pyrimidine 12: A mixture of **5** (0.01 mol) and acetohydrazine (0.01 mol) in (30ml) n-butanol was heated under reflux for 48 hr. The product obtained after cooling was filtered off, dried and crystallized from methanol.

12 : 75 % yield m.p. ›300^{O}C, Anal. Calc. for $C_{17}H_{12}ClN_7$ S (381.84) IR (υ cm^{-1}) : 3030, 3019 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ (ppm) : 1.69 (3H,s ,CH_3), 2.75 (3H,s, SCH_3), 6.49 (1H,s, pyrimidine), 7.00-8.25 (5H,m, aromatic) : MS (m/z) M^+ at m/z = 381 (12%).

***N*-[1-(7-chloroquinolin-5-yl)-4-cyano-3-(methylsulfanyl)-1*H*-pyrazol-5-yl] benze – nesulfonamide 13a:**
13a: 75 % yield m.p. 220-2^{O}C, Anal. Calc. for $C_{20}H_{14}ClN_5O_2S_2$ (455.94) : IR (υcm^{-1}) : 3335 (NH), 3030, 3019 (C-H aromatic), 2216 (CN) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.59 (3H,s, SCH_3), 7.22-8.19 (10H,m, aromatic), 9.13 (1H,s, NH exchangeable with D_2O) MS : (m/z) M^+ at m/z = 455 (11.6%).

4-bromo-*N*-[1-(7-chloroquinolin-5-yl)-4-cyano-3-(methylsulfanyl)-1*H*-pyrazol-5-yl]benzenesulfonamide 13b : 13b: 75 % yield m.p.240-42^{O}C, Anal. Calc. for $C_{20}H_{13}BrClN_5O_2S_2$ (534.84) IR (υcm^{-1}) : 3353 (NH), 3140, 3050 (C-H aromatic), 2215 (CN) : ^{1}H- NMR (DMSO-d_6) δ (ppm) : 2.35 (3H, s, SCH_3), 7.13-8.40 (9H,m, aromatic), 9.19 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 534.5 (12%).

***N*-[1-(7-chloroquinolin-5-yl)-4-cyano-3-(methylsulfanyl)-1*H*-pyrazol-5-yl]-4-meth – yl benzene sulfonamide 13d : 13d**: 75 % yield m.p.262-4^{O}C, Anal. Calc. for $C_{21}H_{16}ClN_5O_2S_2$ (469.97) : IR (υ cm^{-1}) : 3410 (NH), 3030, 3019 (C-H aromatic), 2213(CN) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 2.30 (3H,s,CH_3), 2.35 (3H,s, SCH_3), 7.31-8.10 (9H,m, aromatic), 9.35 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 469 (8.3%).

Methyl 1-(7-chloroquinolin-4-yl)-3-(methylsulfanyl)-5-[(phenylsulfonyl)amino]-1 *H*-pyrazole-4-carboxylate 14a: 14a: 75 % yield m.p. 243-5^{O}C, Anal. Calc. for $C_{21}H_{17}ClN_4O_4S_2$ (488.97) ; IR (υ cm^{-1}) : 3350 (NH), 3030, 3020 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ (ppm) : 1.03(3H, t, *j*= 4.21Hz, CH_3), 2.42 (3H,s,SCH_3), 3.71 (2H,s, CH_2), 7.20-8.40 (9H,m, aromatic), 9.21 (1H,s, NH exchangeable with D_2O) : MS: (m/z) M^+ at m/z = 488 (11%) 490 (3.6%).

5-{[(4-Bromophenyl)sulfonyl]amino}-1-(7-chloroquinolin-4-yl)-3-(methyl-sulfanyl)-1*H*-pyrazole-4-carboxylate 14b: 14c: 75 % yield m.p.250-52^{O}C, Anal. Calc. for $C_{21}H_{16}BrClN_4O_4S_2$ (567.86); IR (υ cm^{-1}) : 3328 (NH), 3030, 3019 (C-H aromatic) ; ^{1}H-NMR (DMSO-d_6) δ (ppm) : 1.55(3H, t, *j*= 4.22Hz, CH_3),2.45 (3H,s, SCH_3), 3.60 (2H,s, CH_2), 7.12-8.30 (8H,m, aromatic), 9.71 (1H,s, NH exchangeable with D_2O) MS : (m/z) M^+ at m/z = 567 (10%).

5-{[(4-Chlorophenyl)sulfonyl]amino}-1-(7-chloroquinolin-4-yl)-3-(methyl-sulfanyl)-1*H*-pyrazole-4-carboxylate 14c: 14c: 75 % yield m.p.230-32^{O}C, Anal. Calc. for $C_{21}H_{16}Cl_2N_4O_4S_2$ (523.41 ; IR (υ cm^{-1}) : 3325 (NH), 3130, 3065 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) δ (ppm) :1.23(3H,t, *j*= 3.54Hz, CH_3), 2.63 (3H,s, SCH_3), 3.72 (2H,m, CH_2), 7.40-8.51 (8H,m, aromatic), 9.51 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 523 (13%).

Methyl 5-{[(4-methylphenyl)sulfonyl]amino}-1-(7-chloroquinolin-4-yl)-3-(methyl -sulfanyl)-1*H*-pyrazole-4-carboxylate 14d: 14d: 75 % yield m.p.260-63^{O}C, Anal. Calc. for $C_{22}H_{19}ClN_4O_4S_2$ (502.10) ; IR (υ cm^{-1}) : 3410 (NH), 3140, 3045 (C-H aromatic) ; ^{1}H NMR (DMSO-d_6) δ (ppm) : 1.32(3H, , t, *j*= 4.21Hz, CH_3), 2.26 (3H,s,CH_3), 2.50 (3H,s, SCH_3), 3.82 (3H,s, OCH_3), 7.37-8.20 (8H,m, aromatic), 9.16 (1H,s, NH exchangeable with D_2O) MS: (m/z) M^+ at m/z = 502 (9%) 504 (3%).

RESULTS AND DISCUSSION

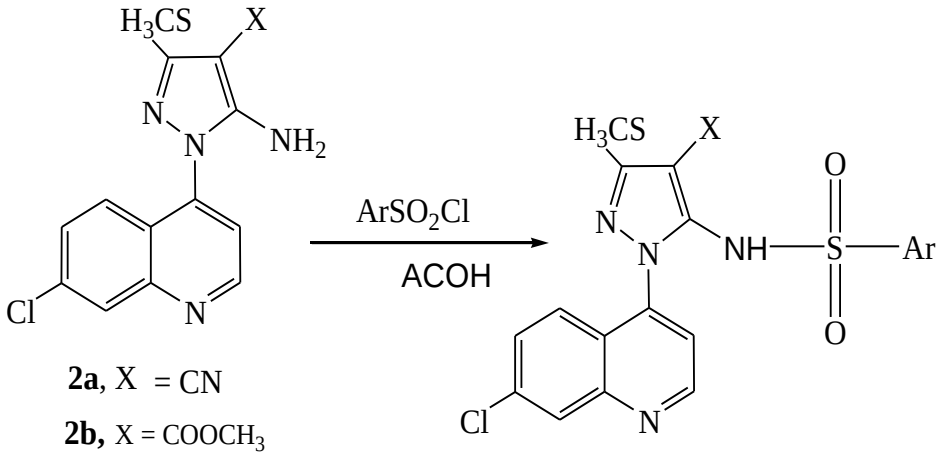
In continuation of our work dealing with the synthesis of new heterocyclic compounds [13-16] ,

therefore, our goal is to develop new general and convenient procedures for the preparation of quinoline derivatives starting with 4, 7-dichloroquinoline derivatives. Thus, the interaction of 4, 7-dichloroquinoline with hydrazine hydrate gave 4-chloro, 7-hydrazioquinoline **1**. Thus, the interaction of compound **1** with dithioacetal derivatives gave pyrazole derivatives **2a, b,** respectively following Afred Kreutzberger et al [17, 18] procedure. The structure of the obtained products was confirmed from their correct values in their elemental analysis, agreeable spectral data in addition to chemical conformational reaction.

Thus obtained product **2a** reacted with formamide to give compound **3** and when **2a** treated with formic acid afforded the compound of type **4**.The structure of the obtained products were confirmed from their agreeable elemental and spectral data (Scheme 1, exp.). The structure of the formed products confirmed from the correct values in elemental analysis and agreeable spectral features. ^{1}H-NMR (DMSO-d_6) showed characteristic signals at δ (ppm) 6.53, 6.54 and (1H, s, of pyrimidine). Upon treatment of the compound **2a** with trimethyl orthoformate afforded the corresponding imidoformate of quinoline derivative **5** which upon its cyclization using hydrazine hydrate gave the aminoimino of quinoline derivatives **6a-c** (Scheme 1, exp.).

The chloro pyrazolopyrimidine derivative **7** was prepared upon heating of compound **4** with $POCl_3$. The structure of chloro derivative **7** was confirmed chemically upon its reaction with glycine and anthranilic acid in n-butanol affording the imidazopyrazolopyrimidine **8** and pentaaza-cyclopena[a]anthr- acen-6-one **9.** ^{1}H-NMR (DMSO-d_6) for compound **8** showed characteristic signal at δ (ppm) at 4.22 (S, 2H, CH_2, imidazole).

The mass spectra for 9 showed M^+ at m/z = 444 (11%), 446 (5%) (Scheme 2, exp.). Nucleophilic displacement of chloro derivative **7** with hydrazine hydrate and appropriate primary amines, namely 4-bromoaniline , 4-chloroaniline and 4-nitroaniline afforded compounds **10a-d** . On the other hand treatment of compounds **2a, b** with aryl chlorosulfonyl derivatives namely benzene sulfonyl chloride, *p*-bromobenzene sulfonyl chloride, *p*-chlorobenzene sulfonyl chloride and *p*-toluene sulfonyl chloride afforded the corresponding sulfonamide derivatives **13a-d** and **14a-d** respectively.



2a, X = CN

2b, X = $COOCH_3$

13 a-d

14 a-d

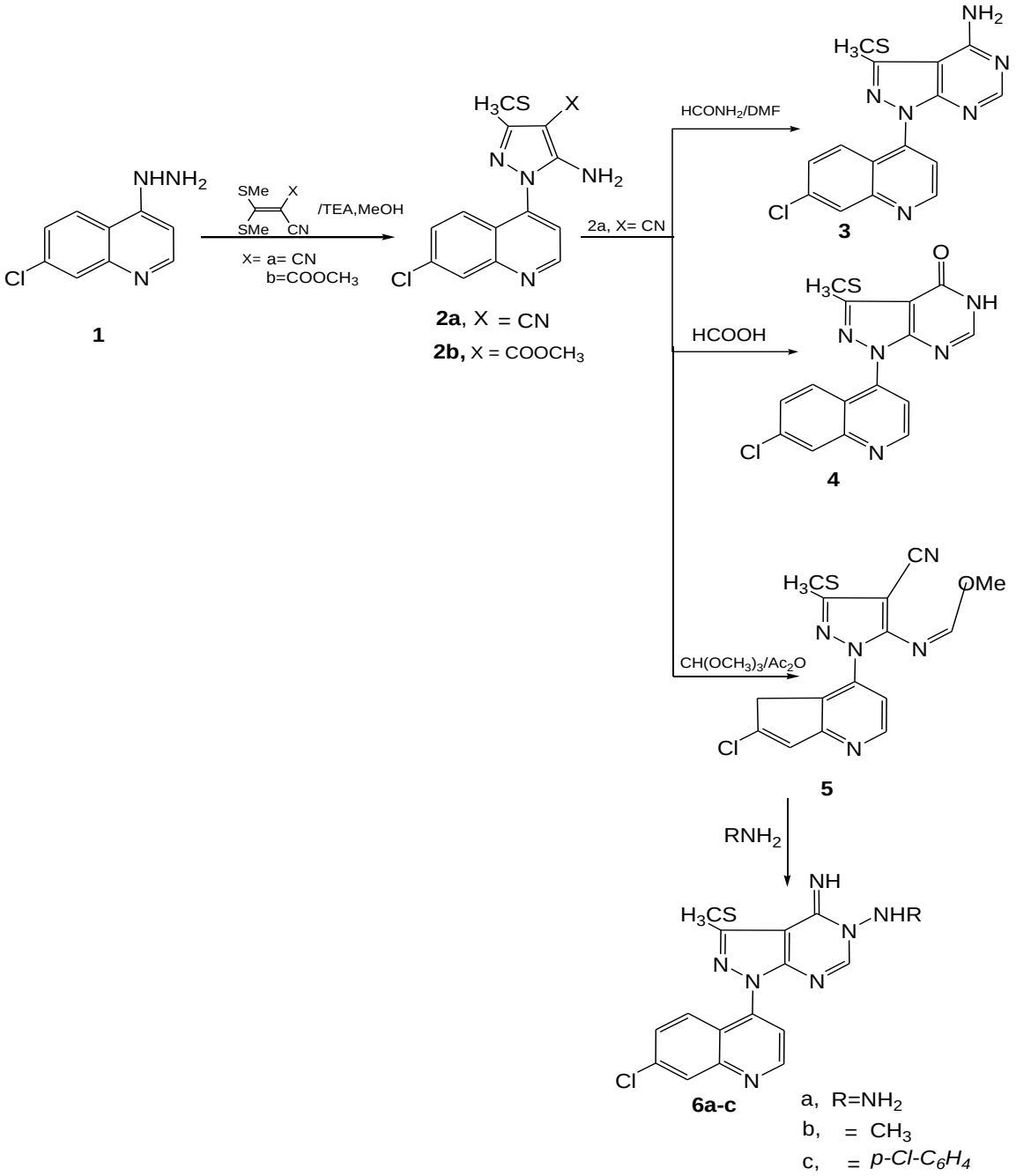
13,14, Ar= C_6H_5

= *p-Br-*C_6H_4

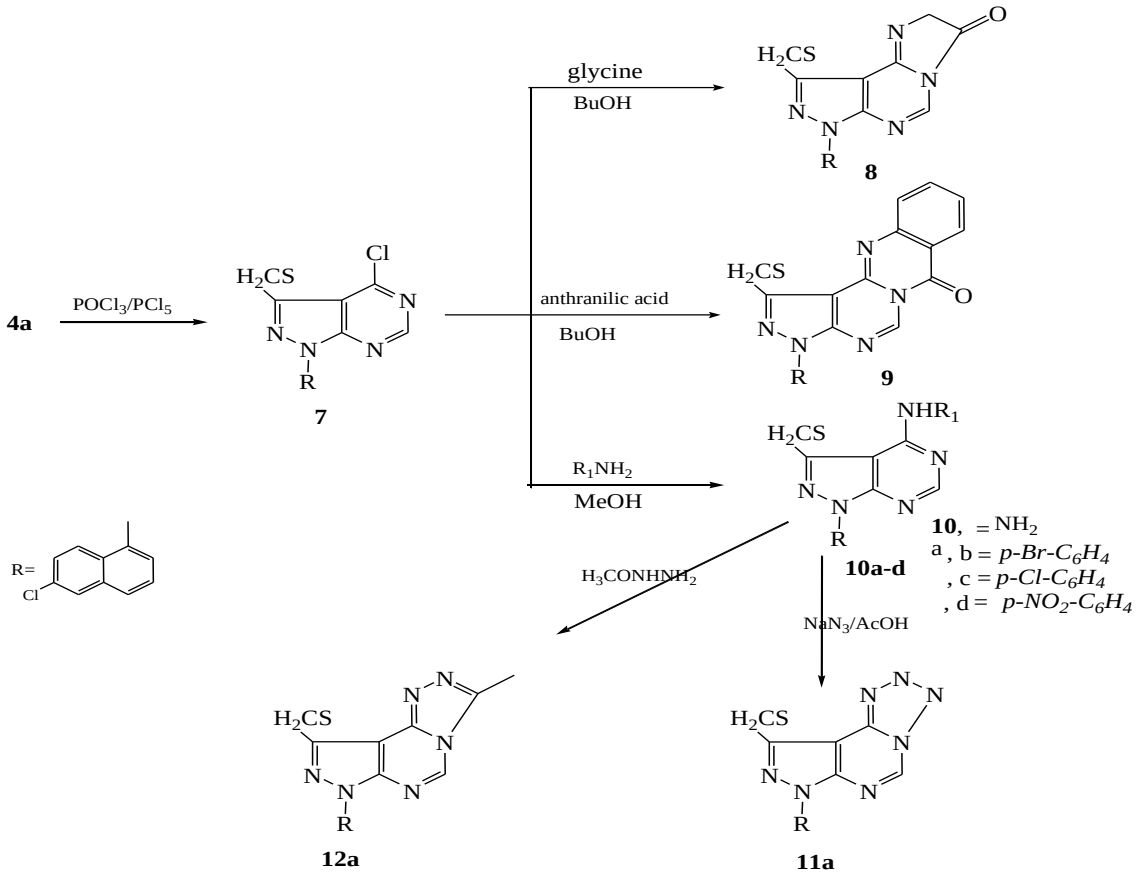
= *p-Cl-*C_6H_4

= *P-*OCH_3*-*C_6H_4

Scheme 3


NHNH2
Cl
N
1
SMe
X
SMe
CN
/TEA,MeOH
X= a= CN
b=COOCH3
H3CS
X
N
N
NH2
Cl
N
2a, X = CN
2b, X = COOCH3
2a, X= CN
HCONH2/DMF
NH2
H3CS
N
N
N
N
Cl
N
3
HCOOH
O
H3CS
NH
N
N
N
Cl
N
4
CH(OCH3)3/Ac2O
CN
H3CS
OMe
N
N
N
Cl
N
5
RNH2
NH
H3CS
NHR
N
N
N
N
Cl
N
6a-c
a, R=NH2
b, = CH3
c, = p-Cl-C6H4

Scheme 1



Scheme 2

REFERENCES

1. Sudharshan Madapa, Zehra Tusi *and* Sanjay Batra, Curr Org Chem, 2008; 12 (13): 1116-83.
2. El-Subbagh HI, Abu-Zaid SM, Mahran MA, Badria FA, Alofaid AM. J Med Chem, 2000; 43: 2915.
3. Watson AA, Fleet GWJ, Asano N, Molyneux RJ, Nugh R. J Phytochem, 2001; *56:* 265.
4. Jerom BR, Spencer KH. Eur Pat Appl, 1988; 277794.
5. Atwell GJ, Baguley BC, Denny WA. J Med Chem, 1989; *32:* 396.
6. Kuo SC, et al. J. Med. Chem, 1993; *36:* 1146.
7. Xia Y, et al. J. Med. Chem, 1998; *41*: 1155.
8. Chen YL, Chen IL, Tzeng CC, Wang TC. Helv Chim Acta, 2000; *83:* 989.
9. Silverman RB. "Organic Chemistry of Drug Design and Drug Action" Academic Press, San Diego,; Thompson (1992).
10. Ellman, JA. Chem. Rev. 1996; 96: 555.
11. Tominaga Y, HakowaY, Hera M, Hosomi A. *J Heterocyclic Chem*, 1990; 27: 775.
12. Kolb M. *Synthesis*, 1990; 171.
13. Fathala OA, Zaki MEA. *Indian J Chem*, 1998; 37B: 484- 90.
14. SA. Swelam, OA. Fathalla, MEA Zaki. Afindad, 2008; 53: 65.
15. ME AZaki, OA Fathalla, SA Swelam, HF Aly. Acta Poloniae Pharma -ceutica- Drug Res, 2004; 61(1), 55-64.
16. Fathalla OA, Zaki MEA, Swelam SA, El-Eraky WI. *Acta Polonia Pharm Drug Resh*, 2003; 60 (1): 51-60.
17. Kreutzberger A, Burgwitz K. *J Heterocyclic Chem*, 1980; 17: 265.
18. Tominaga Y, Matsuda Y. J Heterocyclic Chem, 1985; 22: 937.