CONVENIENT SYNTHESIS OF NEW 7-METHYLTETRAZOLO[1,5-*a*]QUINOLINE-4-CARBALDEHYDE DERIVATIVES

Ibrahim Ali M. Radini[a]

Keywords: Tetrazolo[1,5-*a*]quinoline-4-carbaldehyde, hydrazonoyl chlorides, thiazole, chromene.

7-Methyltetrazolo[1,5-*a*]quinoline-4-carbaldehyde (**1**) was reacted with thiosemicarbazide to give the appropriate thiosemicarbazone (**2**). Compound (**2**) was reacted with different *α*-halocarbonyl compounds such as phenacyl bromide, hydrazonoyl chlorides and *α*-chloroacetic acid to afford thiazoles (**4**), aryldiazenylthiazoles (**6**), and thiazolidin-4-one (**8**), respectively. A series of 7-methyltetrazolo[1,5-*a*]quinoline derivatives, such as 2-imino-2*H*-chromene (**11**)**,** arylacrylohydrazides (**13**), (**15**) and (**17**) and (heteroarylethylidene) acrylohydrazides (**19**), (**21**) and (**23**) has been synthesized. The structures of the newly synthesized compounds have been confirmed by spectral and elemental analyses.

* Corresponding Authors
Phone: +966566444196
E-Mail: iradini44@gmail.com
[a] Chemistry Department, Faculty of Science, Jazan University, Jazan 2097, Saudi Arabia

Introduction

Quinoline derivatives are an important class of heterocyclic compounds.[1,3] Several quinoline derivatives have various biological activities, such as antimicrobial,[4,5] antiproliferative,[6] antimycobacterial,[7] antimalarial,[8] antitumor,[9] anti-inflammatory,[10-13] and antiparasitic,[14] anti-HIV,[15] insecticidal,[16] antidyslipidemic and antioxidant.[17]

The tetrazole group has been considered analogous to carboxylic group as a pharmacophore.[18] Several substituted tetrazoles show pronounced activities including antimicrobial, antimycobacterial, antiproliferative, anticancer and multi-drug resistance etc.[19] The most prominent pharmaceutical application of tetrazoles is as angiotensin II receptor antagonists for the treatment of high-blood pressure.[20] The fusion of quinoline to the tetrazole ring is known to increase the biological activity.[21] In particular, tetrazolo[1,5-*a*]quinoline-4-carbaldehyde serves as a key synthetic intermediate for the synthesis of novel medicinally valuable compounds.[22] Encouraged by these observations and in continuation of our previous work,[23-25] we have synthesized, by facile methods, newer quinoline derivatives, using 7-methyltetrazolo[1,5-*a*]quinoline-4-carbaldehyde as a synthon.

Experimental

Melting points were determined on digital Gallen-Kamp MFB-595 instrument using open capillary tubes and are uncorrected. IR spectra were recorded on Schimadzu FTIR 440 spectrometer using KBr pellets. Mass spectra were performed at 70 eV on an MS-50 Kratos (A.E.I.) spectrometer provided with a data system. ^{1}H NMR (500 MHz or 400 MHz) and ^{13}C NMR (125 MHz or 100 MHz) spectra were recorded on a Bruker model Ultra Shield NMR spectrometer in DMSO-d_6 using tetramethylsilane (TMS) as an internal standard, chemical shifts are reported as δ ppm units. The elemental analyses (% C, H, N) were done at the Microanalytical Center, Cairo University, Cairo, Egypt. Solvents were dried by standard techniques. The monitoring of the progress of all reactions and homogeneity of the synthesized compounds was carried out by TLC using aluminum sheets silica gel 60 F_{254} (Merck).

Synthesis of 2-((7-Methyltetrazolo[1,5-a]quinolin-4-yl)methylene)hydrazinecarbothioamide (2)

To a solution of 2-cyanoacetohydrazide (0.91 g, 10 mmol) in absolute ethanol (30 mL) containing two drops of glacial acetic acid, 7-methyltetrazolo[1,5-*a*]quinoline-4-carbaldehyde (**1**) (2.12 g, 10 mmol) was added. The reaction mixture was heated under reflux for 2 h then left to cool. The solid product obtained was collected by filtration and recrystallized from EtOH-DMF as green powder, m.p. >300 °C, Yield, 83 %; IR (KBr, cm^{-1}): *ν* = 3412 (NH), 3251, 3161(NH_2), 1598 (C=N) cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.68 (s, 3H, CH_3),7.43 (d, 1H, *J* = 8, quinoline-H), 7.56 (d, 1H, *J* = 8, quinoline-H), 7.62 (s, 1H, quinoline-H), 7.88 (s, D_2O exchangeable, 2H, NH_2), 8.24 (s, 1H, CH=N), 8.48 (s, 1H, quinoline-H), 10.92 (s, D_2O exchangeable, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 19.78 (CH_3), 121.85, 126.64, 128.12, 128.62, 131.12, 134.15, 136.38, 143.56, 147.17, 149.14, 175.11 (C=S). EI-Ms: m/z (%): 285 [M^+, 85]; Anal. Calcd. for $C_{12}H_{11}N_7S$ (285.32): C, 50.51; H, 3.89; N, 34.36 %; Found: C, 50.34; H, 3.90; N, 34.17 %.

General procedure for the preparation of compound (4)

To a suspension of thiosemicarbazone**2** (0.285g, 1 mmol) in EtOH (20 mL), the appropriate 1-aryl-2-bromoethanones (**3a** or **3b**) (0.01 mol) was added and heated under reflux for 4 h (TLC), then left to cool, the formed solid product was filtered off, washed with ethanol, dried, and crystallized from EtOH-DMF to afford (**4a**) or (**4b**).

4-(4-Bromophenyl)-2-(2-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)hydrazinyl)thiazole (4a)

Brown powder, m.p. 288 °C, Yield, 83 %; IR (KBr, cm^{-1}): ν = 3248 (NH), 1612, 1581 (C=N) cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.67 (s, 3H, CH_3),7.538 (s, 1H, thiazole-H), 7.618-7.635 (dd, 4H, *J* = 7, *J* = 2, Ar-H), 7.803-7.848 (m, 3H, quinoline-H), 8.159 (s, D_2O exchangeable, H, NH), 8.476 (s, 1H, CH=N), 8.589 (s, 1H, quinoline-H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.87 (CH_3), 105.56, 116.29, 119.72, 120.62, 123.89, 127.54, 127.82, 129.32, 131.65, 132.76, 134.15, 138.18, 143.55, 145.86, 147.45, 148.14, 168.32. EI-Ms: m/z (%): 463 [M^+, 100], 465 [(M^+ + 2), 98]. Anal. Calcd. for $C_{20}H_{14}BrN_7S$ (464.34): C, 51.73; H, 3.04; N, 21.12 %; Found: C, 51.34; H, 2.89; N, 20.91 %.

3-(2-(2-((7-Methyltetrazolo[1,5-a]quinolin-4-yl)methylene)hydrazinyl)thiazol-4-yl)-2*H*-chromen-2-one (4b)

Yellow crystals, m.p. 279 °C, Yield, 81 %; IR (KBr, cm^{-1}): ν = 3194 (NH), 1707 (C=O), 1593 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6):2.69 (s, 3H, CH_3), 7.52-7.930 (m, 7H, coumarin-H and quinoline-H), 8.663 (s, 1H, thiazole-H), 8.013 (s, 1H, coumarin-H), 8.159 (s, D_2O exchangeable, H, NH), 8.526 (s, 1H, CH=N), 8.689 (s, 1H, quinoline-H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.70 (CH_3), 111.30, 112.31, 115.86, 118.96, 120.19, 124.93, 128.33, 128.41, 129.55, 129.61, 131.53, 131.65, 132.40, 138.07, 143.59, 145.37, 145.53, 146.07, 146.29, 152.20, 158.44, 163.54. EI-Ms: m/z (%): 453 [M^+, 5]. Anal. Calcd. for $C_{23}H_{15}N_7O_2S$ (453.47): C, 60.92; H, 3.33; N, 21.62 %; Found: C, 60.09; H, 3.15; N, 21.31 %.

General procedure for the preparation of compound (6)

Equimolar amounts of thiosemicarbazone (**2**) (0.285g, 1 mmol) and either oxo-*N*'-phenylpropanehydrazonoyl chloride (**5a**) or *N*'-(4-bromophenyl)-2-oxopropane hydrazonoyl chloride (**5b**) (1 mmol) in absolute ethanol (30 mL) in the presence of few drops of triethylamine as a catalyst was heated under reflux for 3 h (TLC), then left to cool. The solid formed was isolated by filtration, washed with ethanol, dried, and recrystallized from EtOH-DMF (2:1) to afford (**6a**) or (**6b**).

4-Methyl-2-(2-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)hydrazinyl)-5-(phenyldiazenyl)thiazole (6a)

Red crystals, m.p. >300 °C, Yield, 85 %; IR (KBr, cm^{-1}): *v* = 3251 (NH), 1558, 1539 (C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.75 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 7.018-7.665 (m, 8H, Ar-H), 8.570 (s, 1H, CH=N), 8.790 (s, 1H, quinoline-H), 11.56 (s, D_2O exchangeable, H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 15.40, 21.70, 106.36, 121.49, 123.45, 124.77, 127.80, 128.43, 129.55, 131.30, 131.68, 133.38, 145.23, 145.49, 146.06, 149.11, 150.33, 154,43, 164.42. EI-Ms: m/z (%): 427 [M^+, 30]. Anal. Calcd for $C_{21}H_{17}N_9S$ (427.48): C, 59.00; H, 4.01; N, 29.49 %; Found: C, 58.77; H, 3.97; N, 29.05 %.

5-((4-Bromophenyl)diazenyl)-4-methyl-2-(-2-((7-methyl tetrazolo[1,5-*a*]quinolin-4-yl)methylene)hydrazinyl)thiazole (6b)

Red crystals, m.p. 285 °C, Yield 85 %; IR (KBr, cm^{-1}): *v* 3251 (NH), 1556, 1544 (C=N) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.73 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 7.60-7.937 (m, 7H, Ar-H), 8.60 (s, 1H, CH=N), 8.91 (s, 1H, quinoline-H), 11.98 (s, D_2O exchangeable, H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ =15.40, 21.70, 116.15, 119.66, 124.01, 128.04, 129.10, 133.04, 134.25, 136.40, 138.26, 145.23, 145.49, 146.06, 149.11, 150.33, 154.43, 164.01, 178.61. EI-Ms: m/z (%): 505 [M^+, 33], 507 [M^++ 2, 31]. Anal. Calcd for $C_{21}H_{16}BrN_9S$ (506.38): C, 49.81; H, 3.18; N, 24.89 %; Found: C, 49.37; H, 2.97; N, 24.46 %.

Synthesis of 2-((7-methyltetrazolo[1,5-*a*]quinolin-4-yl)methylene)hydrazono)thiazolidin-4-one (8)

A mixture of thiosemicarbazone (**2**) (0.285g, 1 mmol) and chloroacetic acid (**7**) (0.1 g, 1 mmol) in glacial acetic acid (30 mL) containing anhydrous sodium acetate (0.33 g, 4 mmol) was heated under reflux for 6 h (TLC). The reaction mixture was cooled; the formed solid product was filtered off, washed with ethanol, dried, and recrystallized from AcOH to afford (**8**). Brown, m.p. 290 °C (charing), yield, 89 %; IR (KBr, cm^{-1}): *v* = 3222 (NH), 1648 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.65 (s, 3H, CH_3),3.97 (s, 2H, CH_2), 7.85 (d, 1H, *J* = 8.5, quinoline-H), 8.16 (s, 1H, quinoline-H), 8.53 (d, 1H, *J* = 8.5, quinoline-H), 8.59 (s, 1H, CH=N), 8.84 (s, 1H, quinoline-H), 11.20 (s, D_2O exchangeable, H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.73, 33.6, 123.50, 126.26, 128.33, 128.76, 131.31, 135.26, 136.68, 147.49, 149.21, 164.42, 173. EI-Ms: m/z (%): 325 [M^+, 73]. Anal. Calcd for $C_{14}H_{11}N_7OS$ (325.34): C, 51.68; H, 3.41; N, 30.14 %; Found: C, 51.36; H, 3.21; N, 29.85 %.

Synthesis of 2-cyano-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)acetohydrazide (9)

To a solution of 2-cyanoacetohydrazide (0.99 g, 10 mmol) in absolute ethanol (30 mL), (**1**) (2.12 g, 10 mmol) was added in the presenceof two drops of glacial acetic acid. The reaction mixture was heated under reflux for 1-2 h then left to cool. The solid product formed was collected by filtration and recrystallized from MeOH-DMF (1:1).Yellowish green, m.p. 272-274 °C, Yield, 85 %; IR (KBr, cm^{-1}): ν = 3284 (NH), 2260 (CN), 1691 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6) δ = 2.68 (s, 3H, CH_3), 3.98 (s, 2H, CH_2), 7.28-7.92 (m, 4H, Ar-H), 8.90 (s, 1H, CH=N), 11.88 (s, 1H, NH, D_2O exchangeable). EI-Ms: m/z (%): 293 (M^+, 42). Anal. Calcd. for $C_{14}H_{11}N_7O$ (293.28): C, 57.33; H, 3.78; N, 33.43 %; Found: C, 57.04; H, 3.47; N, 33.05 %.

Synthesis of Compounds (11), (13), (15) and (17)

Equimolecular mixture of **9** (0.293 g, 1 mmol) and appropriate aldehyde (1 mmol), [2,4-dihydroxy benzaldehyde (**10**) in case of (**11**), 4-(dimethylamino) benzaldehyde (**12**) in case of (**13**), 2-chloroquinoline-3-car-

baldehyde (**14**) in case of (**15**) and 7-methyltetrazolo[1,5-a]quinoline-4-carbaldehyde (**16**) in case **17**] in anhydrous methanol (20 mL) containing piperidine (0.50 mL) was heated under reflux for 3-5 h (TLC). The formed solid was collected by filtration and recrystallized from methanol to gave compounds (**11**), (**13**), (**15**) and (**17**).

7-Hydroxy-2-imino-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)-methylene)-2H-chromene-3-carbohydrazide (11)

Brown powder, m.p. >300 °C, Yield, 85 %; IR (KBr, cm^{-1}): *v*3396.6 (OH), 3284 (NH), 1678 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.69 (s, 3H, CH_3),4.37 (s, H, NH, D_2O exchangeable), 6.53-8.57 (m, 8H, Ar-H), 8.51 (s, 1H, CH=N), 9.04 (s, 1H, OH, D_2O exchangeable), 11.98 (s, H, NH, D_2O exchangeable); EI-Ms: m/z (%): 413 [M^+, 25]. Anal. Calcd. for $C_{21}H_{15}N_7O_3$ (413.12): C, 61.01; H, 3.66; N, 23.72 %; Found: C, 60.87; H, 3.49; N, 23.32 %.

2-Cyano-3-(4-(dimethylamino)phenyl)-N'-((7-methyltetrazolo-[1,5-a]quinolin-4-yl)methylene)acrylohydrazide (13)

Orange crystals, m.p. 290-291 °C, Yield, 87%; IR (KBr, cm^{-1}): *v* 3205 (NH), 2202 (CN), 1660 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.73 (s, 3H, CH_3), 3.10 (s, 6H, $2CH_3$), 6.87-855 (m, 8H,Ar-H), 8.65 (s, 1H, CH=C), 9.09 (s, 1H, CH=N), 12.16 (s, 1H, NH, D_2Oexchangeable) ppm; EI-Ms: m/z (%): 424 [M^+, 33]. Anal. Calcd. for $C_{23}H_{20}N_8O$ (424.17): C, 65.08; H, 4.75; N, 26.40; Found C, 64.87; H, 4.59; N, 26.05.

3-(2-Chloroquinolin-3-yl)-2-cyano-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)acrylohydrazide (15)

Yellow crystals, m.p. 290-292 °C, Yield, 89%; IR (KBr, cm^{-1}): *v* 3234 (NH), 2202 (CN), 1660 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 2.68 (s, 3H, CH_3), 6.96-8.22 (m, 9H,Ar-H), 8.47 (s, 1H, CH=C), 8.68 (s, 1H, CH=N), 12.08 (s, 1H, NH, D_2Oexchangeable) ppm; EI-Ms: m/z (%): 466 [M^+, 33], 468 [M^+ +2, 11]. Anal. Calcd. for $C_{24}H_{15}ClN_8O$ (466.88): C, 61.74; H, 3.24; N, 24.00; Found C, 61.11; H, 2.99; N, 23.78.

2-Cyano-3-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)acrylohydrazide (17)

Yellow crystals, m.p. 266-267 °C, Yield, 85 %; IR (KBr, cm^{-1}): *v* = 3237 (NH), 2214 (CN), 1667 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.83 (s, 6H, $2CH_3$), 6.99-8.28 (m, 8H, Ar-H), 8.51 (s, 1H, CH=C), 8.72 (s, 1H, CH=N), 12.05 (s, 1H, NH, D_2O exchangeable); EI-Ms: m/z (%): 487 [M^+, 16]. Anal. Calcd. for $C_{25}H_{17}N_{11}O$ (487.47): C, 61.60; H, 3.52; N, 31.61 %; Found: C, 61.34; H, 3.43; N, 31.22 %.

Synthesis of compounds (19) and (21)

Equimolecular mixture of (**1**) (0.221 g, 1 mmol) and appropriate hydrazones (**18**) and (**20**) (1 mmol) in anhydrous methanol (20 mL) containing piperidine (0.5 mL) was heated under reflux for 3-5 h (TLC). The formed solid was collected by filtration and recrystallized from methanol to gave compound (**19**) and (**21**).

2-Cyano-3-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-N'-(1-(thien-2-yl)ethylidene)acrylohydrazide (19)

Brown powder, m.p. >300 °C, Yield, 81 %; IR (KBr, cm^{-1}): *v* = 3197 (NH), 2205 (CN), 1619 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.33 (s, 3H, CH_3), 2.90 (s, 3H,CH_3), 7.16-8.50 (m, 7H, Ar-H), 8.64 (s, 1H, CH=C-), 11.33 (s, 1H, NH, D_2O exchangeable); EI-Ms: m/z (%): 401 [M^+, 43]. Anal. Calcd. for $C_{20}H_{15}N_7OS$ (401.44): C, 59.84; H, 3.77; N, 24.42 %; Found: C, 59.51; H, 3.47; N, 24.13 %.

2-Cyano-N'-(1-(fur-2-yl)ethylidene)-3-(7-methyltetrazolo[1,5-a]quinolin-4-yl)acrylohydrazide (21)

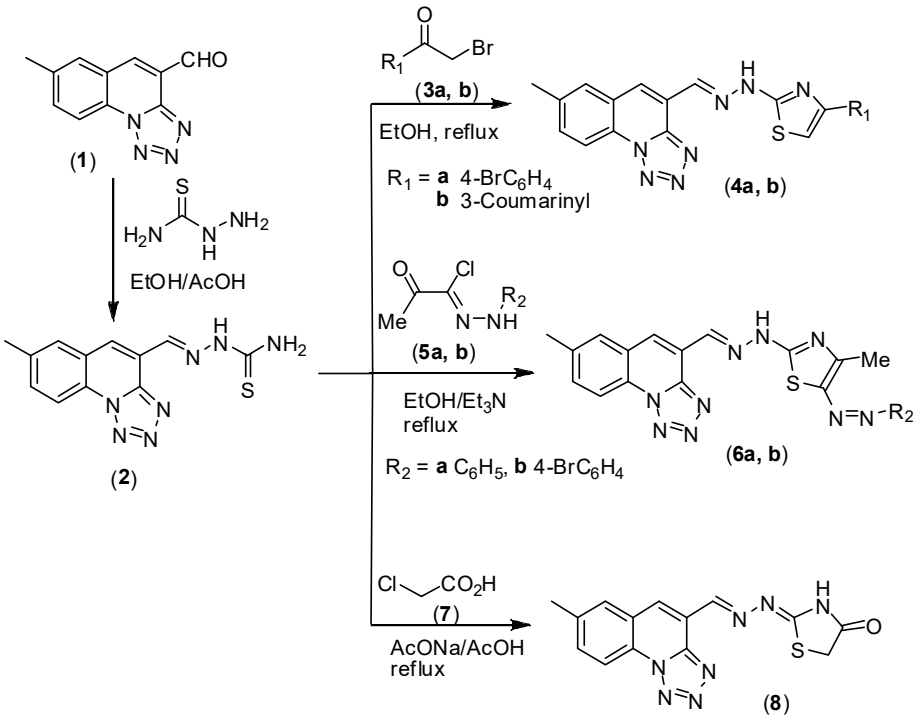
Yellow crystals, m.p. 296 °C, Yield 79 %; IR (KBr, cm^{-1}): *v* = 3124 (NH), 2200 (CN), 1610 (C=O) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.29 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 6.49-7.15 (m, 3H, furan-H), 7.65-8.60, (m, 4H, quinoline-H), 8.76 (s, 1H, CH=C-), 11.60 (s, 1H, NH, D_2O exchangeable); EI-Ms: m/z (%): 385 [M^+, 43]. Anal. Calcd. for $C_{20}H_{15}N_7O_2$ (385.37): C, 62.33; H, 3.92; N, 25.44 %; Found: C, 62.03; H, 3.61; N, 25.16 %.

Results and Discussion

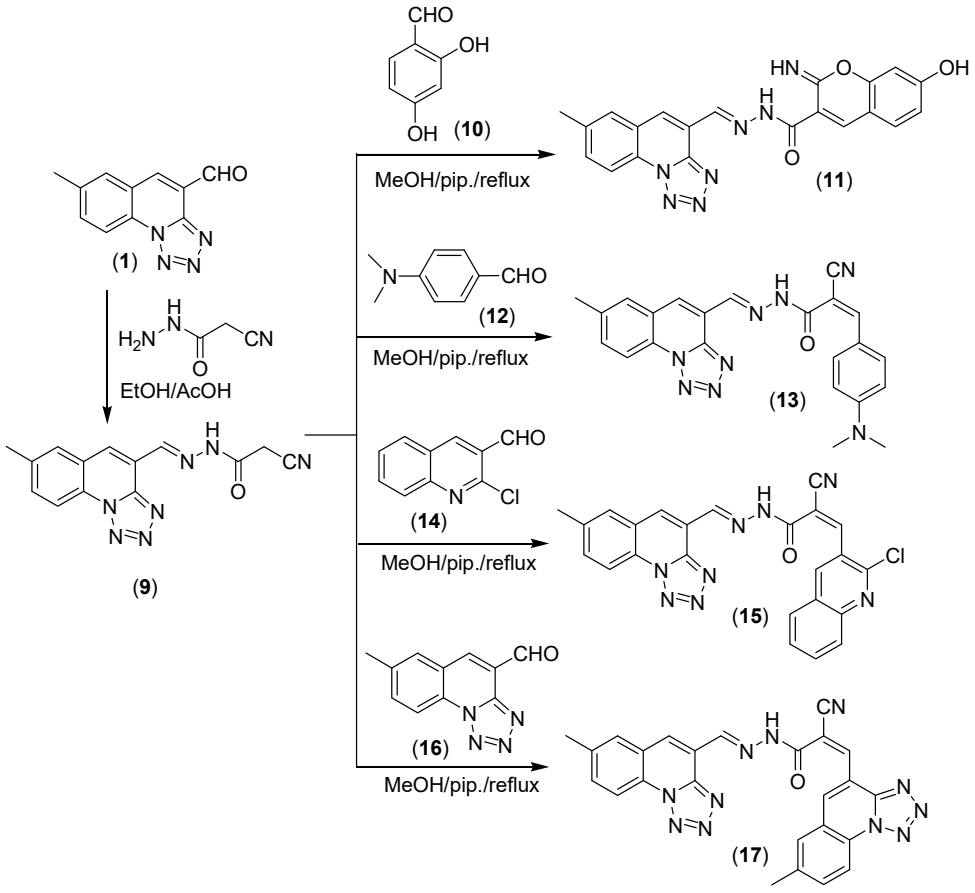
The synthetic procedures adopted to obtain the target compounds are depicted in Schemes 1-3. The starting material (**1**) was prepared according the literature procedures.[14]

Reaction of (**1**) with molar amount of thiosemicarbazide in boiling absolute ethanol containing few drops of acetic acid for 2 h, afforded 2-((7-methyltetrazolo[1,5-*a*]quinolin-4-yl)methylene) hydrazinecarbothioamide (**2**) in a good yield.

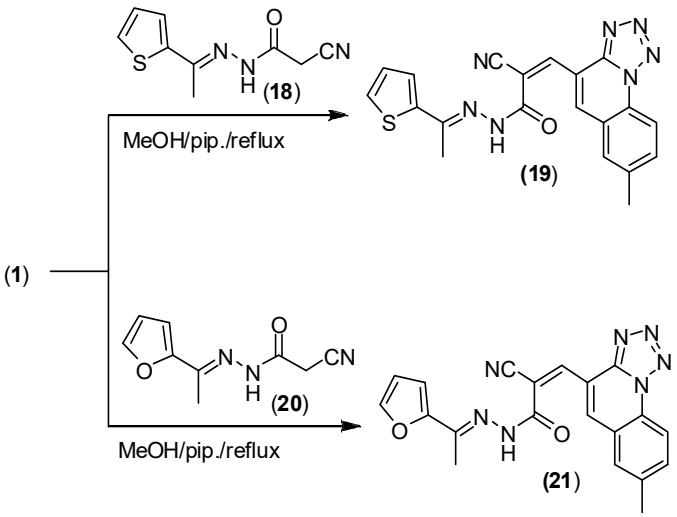
The reaction of compound (**2**) with equivalent amount of *α*-haloketones, for example, 4-bromophenacyl bromide (**3a**) and 3-bromoacetylcoumarin (**3b**), was performed in refluxing ethanol to yield (**4a**) and (**b**) in good yields. Also, (**2**) was reacted with hydrazonoyl chlorides, e.g. (**5a**) and (**5b**), in boiling ethanol in the presence of catalytic amount of triethyl amine to give thiazoles (**6a**) and (**6b**) in good yields.



Scheme 1. Synthesis of compounds (**4**), (**6**) and (**8**).



Scheme 2. Synthesis of compounds (**11**), (**13**), (**15**) and (**17**).



Scheme 3. Synthesis of compounds (**19**), and (**21**).

Similarly, 2-((7-methyltetrazolo[1,5-*a*]quinolin-4-yl)methylene)hydrazono) thiazolidin-4-one (**8**) was obtained from the reaction of (**2**) with chloroacetic acid in acetic acid in the presence of sodium acetate at reflux temperature.

Spectroscopic data (IR, ^{1}H NMR, and MS) and elemental analysis of compounds (**4**), (**6**), and (**8**) confirmed their structures. The IR spectra of compounds (**4**), (**6**), and (**8**) revealed the absence of absorption bands of NH2 and C=S functions. In addition ^{1}H NMR of these compounds indicates the disappearance of NH_2 signal. Also, C=S signals was disappeared in ^{13}C NMR spectrum. Thus clearly indicating the carbothioamide moiety was involved in cyclization reaction to afford thiazole ring. The mass spectra of compounds (**4**), (**6**), and (**8**) was showed the molecular ion peaks which were in an agreement with the calculated masses (c.f. experimental section).

Reaction of compound (**1**), with molar amount of 2-cyanoacetohydrazide in boiling absolute ethanol containing few drops of acetic acid for 2 h, afforded 2-cyano-N'-((7-methyltetrazolo[1,5-*a*]quinolin-4-yl)methylene)acetohydrazide (**9**) in a good yield. Condensation of (**9**) with equimolar amounts of different aldehydes, namely 2,4-dihydroxybenzaldehyde (**10**), 4-(dimethylamino)-benzaldehyde (**12**), 2-chloroquinoline-3-carbaldehyde (**14**), and 7-methyltetrazolo[1,5-*a*]quinoline-4-carbaldehyde (**16**) in methanol in the presence of few drops of piperidine at reflux temperature gave 7-hydroxy-2-imino-N'-((7-methyltetrazolo[1,5-*a*]quinolin-4-yl)methylene)-2H-chromene-3-carbohydrazide (**11**), 2-cyano-3-(4-(dimethylamino)-phenyl)-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)acrylohydrazide (**13**), 3-(2-chloroquinolin-3-yl)-2-cyano-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)methylene)acrylohydrazide (**15**), 2-cyano-3-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-N'-((7-methyltetrazolo[1,5-a]quinolin-4-yl)-methylene)acrylohydrazide, respectively (Scheme 2). The formation of (**11**) probably takes place through condensation of the aldehydic group with the active methylene function followed by nucleophilic attack of the hydroxyl group on the neighboring nitrile residue eventually giving the target compound.

The structures suggested for compounds (**9**), (**11**), (**13**), (**15**), and (**17**) are in a good agreement with their analytical and spectroscopic data. The ^{1}H-NMR spectrum of (**9**) indicated the presence of a singlet signal at δ = 3.98 ppm, assignable for the active methylene group (-$COCH_2$-CN). The IR spectrum of (**11**) revealed the absence of the nitrile group this confirmed the cyclization process. Also, mass spectrum of (**11**) contains a molecular ion peak at m/z 413, which supports the structure of compound (**11**).

On the other hand, Knoevenagel condensation reaction of (**1**) with 2-cyano-N'-(1-(thien-2-yl)ethylidene)aceto-hydrazide (**18**) and 2-cyano-N'-(1-(fur-2-yl)ethy-lidene)acetohydrazide (**20**) in refluxed methanol containing few drops of piperidine afforded 2-cyano-3-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-N'-(1-(heteroaryl)ethy-lidene)acrylohydrazide (**19**) and (**21**), respectively. The structures of compounds (**19**) and (**21**) are in a good agreement with their analytical and spectroscopic data (c.f. experimental section).

References

[1]Elderfield, R. C., Kremer, C. B., Kupchan, S. M., Birstein, , Cortes, G., *J. Am. Chem Soc.*, **1947**, *69*, 1258-1260.

[2]Meth-Cohn, O., Narine, B., *Tetrahedron Lett.*, **1978**, *19*, 2045-2048.

[3]Ali, M. M., Rajanna, K. C., Prakash, P. K. S., *Synlett.*, **2001**, 51-253.

[4]Shah, N. K., Shah, N. M., Patel,M. P., Patel, R. G., *Chin. Chem. Lett.,* **2012**, *23*, 454-457.

[5]Khidre, R. E., Abu-Hashem, A. A., El-Shazly, M., *Eur. J. Med. Chem.*, **2011**, *46*, 5057-5064.

[6]Zieba, A., Sochanik, A., Szurko, A., Rams, M., Mrozek, A., Cmoch, P., *Eur. J. Med. Chem.*, **2010**, *45*, 4733-4739.

[7]Carta, A., Palomba, M., Briguglio, I., Corona, P., Piras, S., Jabes, D., Guglierame, P., Molicotti, P., Zanetti, S. *Eur. J. Med. Chem.*, **2011**, *46*, 320-326.

[8]Dominguez, J. N., Gamboa, N., Rodrigues, J. R., Angel, J. E., *Lett. Drug Design Discov.*, **2007**, *4*, 49-54.

[9]Abdou,W. M., Khidre R. E., Kamel, A. A., *Arch. Pharm. Chem. Life Sci.*, **2012**, *345*, 123–136

[10]Chen, Y.-L., Chen, I-L., Lu, C.-M., Tzeng, C.-C., Tsao, L.-T., Wang, J.-P., *Bioorg. Med. Chem.,* **2004**, *12*, 387-392.

[11]Bawa, S., Kumar, S., *Indian J. Chem.*, **2009**, *48B*, 142-145.

[12]Khidre, R. E., Abdel-Wahab, B. F., Badria, F. A.-R., *Lett. Drug Design Discov.*, **2011**, *8*, 640-648.

[13]Abdou, W. M., Khidre, R. E., Shaddy, A. A., *J. Heterocycl. Chem.,* **2013**, *50*, 33-41.

[14]Kouznetsov, V. V., Méndez, L. Y. V., Leal, S. M., Cruz, U. M., Coronado, C. A., Gómez, C. M. M., Bohórquez, A. R. R., Rivero, P. E., *Lett. Drug Design Discov.,* **2007**, *4*, 293-296.

[15]Luo, Z. G., Zeng, C. C., Yang, L. F., He, H. Q., Wang, C. X., Hu, L. M., *Chin. Chem. Lett.*, **2009**, *20*, 789-792.

[16]Wu, Q. L., Li, Y. Q., Yang, X. L., Ling, Y. *Chin. J. Org. Chem.*, **2012**, *32*, 747-754.

[17]Sashidhara, K.V., Kumar, A., Bhatia, G., Khan, M. M., Khanna, A. K., Saxena, J. K., *Eur. J. Med. Chem.*, **2009**, *44*, 1813-1818.

[18]Lei, P., Yuchuan, L., Yuzhang, Y., Wei, L., Xuejiao, Z., Siping. P., *Chin. J. Org. Chem.*, **2012**, *32*, 667-676.

[19]Adamec, J., Beckert, R., Weib, D., Waisser, K. , Möllmann, U. , Kaustová, J. , Buchta, V., *Bioorg. Med. Chem.*, **2007**, *15*, 2898-2906.

[20]Wexler, R. R., Greenlee, W. J., Irvin, J. D., Goldberg, M. R., Prendergast, K., Smith, R. D., Timmermans, P. B. M. W. M., *J. Med. Chem.*, **1996**, *39*, 625-656.

[21]Mukharjee, A., Akhater, M. S., Sharma, V. L., Seth, M., Bhaduri, A., P.,Agnihotri, A., Mehrotra, P. K., Kamboj, V. P., *J. Med. Chem.*, **1989**, *32*, 2297-2300.

[22]Bekhit, A. A., El-Sayed, O. A.,Aboulmagd, E., Park, J. Y., *Eur. J. Med. Chem.*, **2004**, *39*, 249-255.

[23]Radini, I. A. M., Elsheikh, T. M. Y., El-Telbani, E. M., Khidre, R. E., *Molecules*, **2016**, *21*, 909-921.

[24]Radini, I. A. M., Abdel-Wahab, B. F., Khidre, R. E., *Phosphorus Sulfur Silicon Relat.Elem.*, *2016*, 191, 844-856

[25]Radini, I. A. M., Abd El-Wahab, A. H. F., *Eur. J. Chem*., **2016**, *7*, 230-237.

Received: 16.07.2016
Accepted: 07.08.2016.