SYNTHESIS OF FUNCTIONALIZED 7-CHLORO-1,2,4-TRIAZOLO [4,3-a]QUINOLINE

J. A. Hassanin[a], E. S. I. Ibrahim [a], M. A. Zein[a], M. R. Aouad[b] and E. S. H. El Ashry[b,*]
[a]*Chemistry Department, Faculty of Science, Suez Canal University, Suez*
[b]*Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt*
E-mail adress: eelashry60@hotmail.com

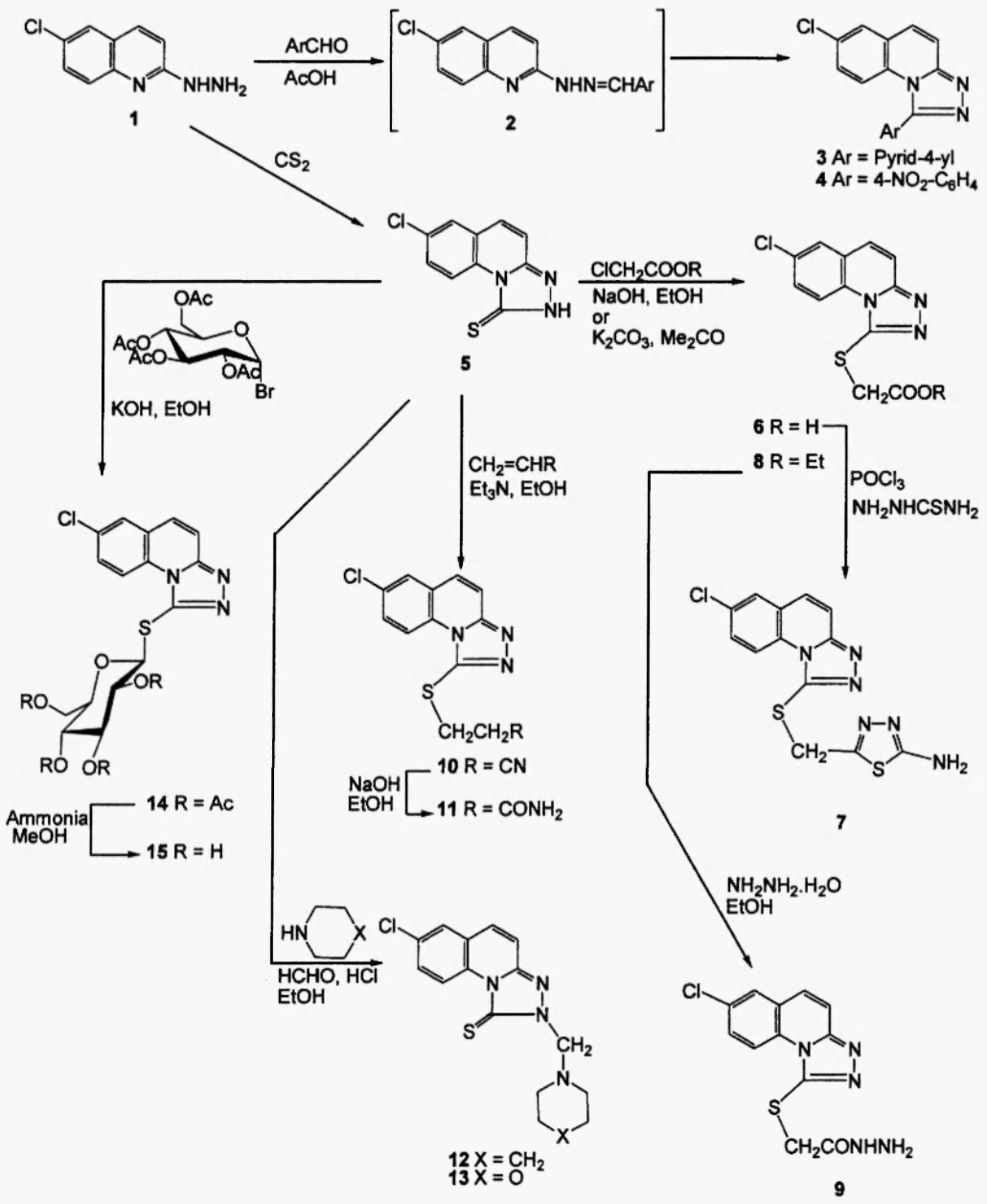
Abstract : One carbon inserting agents transformed 6-chloro-2-hydrazinoquinoline (**1**) into the 2-functionalized 1,2,4-triazolo[4,3-a]quinoline skeleton. The 1-aryl and 1-pyridyl derivatives were prepared via condensation with aldehydes and then dehydrogenative ring closure. The 1-thiol group in **5** was introduced by reaction of **1** with carbon disulfide. Carboxy- and carboethoxy-methylation of **5** afforded the respective mercaptoacetic acid derivatives **6** and **8**. Chlorination of **6** followed by dehydrative cyclization through its reaction with thiosemicarbazide afforded the respective amino thiadiazole derivative **7**. Hydrazinolysis of **8** gave the corresponding hydrazide derivative **9**. Compound **5** was reacted with acrylonitrile and acrylamide to give the corresponding cyano and carboxamido methylated derivatives **10** and **11**. Under Mannich conditions, reaction of **5** with piperidine and morpholine afforded the respective Mannich bases **12** and **13**. Reaction of **5** with acetobromoglucose gave the respective thioglucoside **14** which was deacetylated to **15**. All compounds were screened for their antimicrobial activity against gram-positive and gram-negative bacteria.
Keywords: quinoline, alkylation, tautomerism, AM1 semiemperical calculation.

Introduction

Quinoline nucleus was found in many drug structures.[1-4] Moreover, heterocycles that incorporate the quinoline ring exhibit a wide variety of biological activities including antimicrobial, antibacterial, antifungal agents.[4-13] 1,2,4-Triazolo[4,3-a]quinolines have activity against *Piricularia oryzae*[14] and are used as agricultural bactericides and fungicides. Some show a remarkable potent activity as antitumor,[15] antineoplastic,[16] anthelmintic and antihypertensive,[17,18] agents. In continuing our work on the synthesis of quinoline derivatives,[4,19-21] we report here the synthesis and biological properties of new fused heterocycles incorporating the 1,2,4-triazolo[4,3-a]quinolines prepared via the insertion of one carbon reagents in 6-chloro-2-hydrazinoquinoline (**1**).

Results and Discussions

Reaction of 6-chloro-2-hydrazinoquinoline (**1**) with *p*-nitrobenzaldehyde and 4-pyridyl carboxaldehyde in refluxing acetic acid gave 7-chloro-1-pyrid-4-yl-(*p*-nitrophenyl)-1,2,4-triazolo[4,3-a]quinolines **3** and **4**, respectively rather than **2**. Their structures were confirmed by their elemental and spectral analysis. Thus, the ^{1}H NMR spectrum of **3** showed the absence of signals corresponding to the NH protons.



Scheme-1

The fragments in mass spectrum of **4** confirmed that the anticipated condensation of **1** with aldehydes to give the hydrazones **2** proceeded with dehydrogenative processes to give **3** or **4** which can be attributed to be as a consequence of the thermal conditions used during the reaction. Thus, it showed molecular ion peak at m/z 324 and 326. Loss of the nitro phenyl ring was also observed to give ion at m/z 203 and 205. Moreover, other expected signals also appeared in the spectrum as shown in figure-1. The isotopes of chlorine were apparent in the assigned fragments and the ratio of their signals agreed with the isotopic ratio.

Electrophilic attack of CS_2 on the hydrazine **1** gave via further intramolecular cyclization and elimination of H_2S 7-chloro-1,2,4-triazolo-1-mercapto-[4,3-a]quinoline (**5**) which exhibits a thione-thiol equilibrium. The IR spectrum of **5** showed bands at 1620 and 3200 cm^{-1} for the C=N and NH groups, respectively. The elemental analysis and the mass spectral data of which showed a molecular ion peak at m/z 235 and 237 that led to assign its molecular formula as $C_{10}H_6ClN_3S$.

The spectrum also showed ion at m/z 176 and 178 which could be attributed to the loss of HS-C=N residue from the molecular ion. Moreover, the fragment at m/z 163 and 165 was assigned to the quinoline ring. Carboxymethylation of **5** with chloroacetic acid in ethanol afforded 7-chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thioglycolic acid (**6**). Chlorination of 6 with $POCl_3$ followed by condensative cyclization with thiosemicarbazide gave 1-[(2-amino-1,3,4-thiadiazol-5-yl)methylthio]-7-chloro-1,2,4-triazolo[4,3-a]quinoline (**7**). The structure of compounds **6** and 7 were deduced from their spectral and elemental analysis. The IR spectrum of **6** showed characteristic absorption bands due to C=O (1720 cm^{-1}) and OH (3400 cm^{-1}), whereas that of **7** showed the disappearance of these absorption bands and appearance of band due to NH_2 (3250 cm^{-1}). Moreover, the ^1H NMR spectrum of compound **6** showed a singlet at δ_H 8.8 ppm characteristic for the COOH group which disappeared in the spectrum of compound **7** and showed instead a signal at δ_H 10.8 due to the NH_2 group.

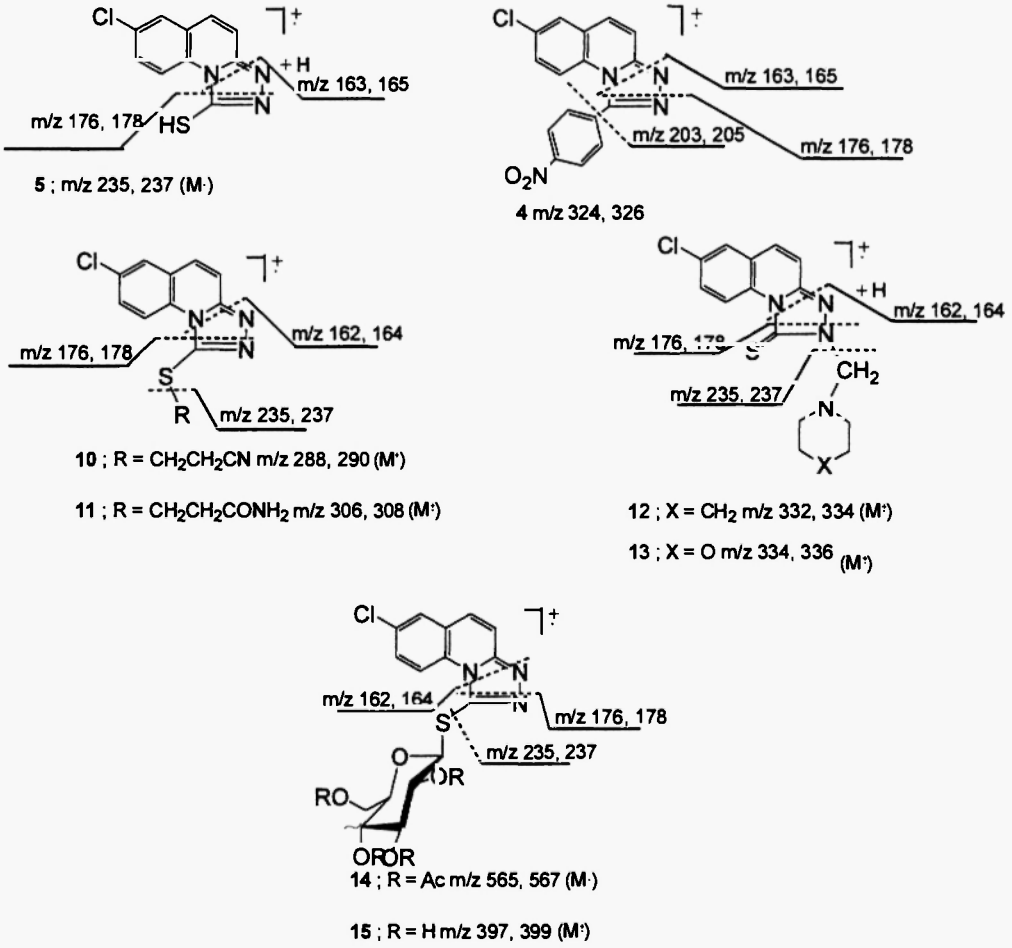
Carboethoxy-methylation of **5** with ethyl chloroacetate afforded 7-chloro-1-(ethoxycarbonylmethylthio)-1,2,4-triazolo[4,3-a]quinoline (8) which upon reflux with hydrazine hydrate gave the corresponding hydrazide derivative 9. The IR spectrum of **9** showed a band at 1690 cm^{-1} for the amide carbonyl group whereas that of 8 showed an ester band at 1730 cm^{-1}. ^1H NMR spectrum of 9 indicated the presence of two characteristic singlets at δ_H 9.2 and 10.7 ppm corresponding to hydrazine group whereas that of 8 showed signals due to ethyl-ester group.

Treatment of **5** with acrylonitrile and acrylamide in presence of triethylamine under reflux afforded 7-chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thiomethylcyanide (**10**) and 7-chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thiomethylcarboxamide (**11**). Alternatively, compound **11** was also obtained by partial hydrolysis of **10**. The IR spectra of compounds **10** and **11** showed characteristic absorption bands due to CN (2250 cm^{-1}) and CO (1661 cm^{-1}).

The mass spectra of **10** and **11** showed molecular ion peaks at m/z 288, 290 and 306, 308 which when combined with the elemental analysis led to the assignment of the molecular formula $C_{13}H_9ClN_4S$ and $C_{13}H_{11}ClN_4SO$, respectively. Moreover, they showed a characteristic fragment at m/z 235 and 237 attributed to the triazoloquinoline ring.

Reaction of **1** with either piperidine or morpholine afforded 7-chloro-2-(N-piperidyl-methyl)-1,2,4-triazolo[4,3-a]quinoline-1-thione (**12**) or 7-chloro-2-(N-morpholinyl-methyl)-1,2,4-triazolo[4,3-a]quinoline-1-thione (**13**), respectively. Their spectral data agreed with the structures.

The glycosylation of nitrogen heterocyclic thiols may lead to thioglycosides or nucleosides. Both of which are important classes in the carbohydrate field as biologically important targets[22-30] or as glycosyl donors.[30-32] Glycosylation of **1** with acetobromoglucose gave the corresponding thioglucoside **14** which upon treatment with ammonia gave the deacetylated product **15**. The structure of compounds **14** and **15** were deduced from elemental and spectral data. The IR spectrum of **14** showed bands at 1720 cm^{-1} for C=O groups, which disappeared in the spectrum of **15**. The ^1H NMR spectrum of **14** showed four signals in the upfield region corresponding to the methyl of acetoxy groups. The anomeric proton appeared at δ_H 6.20 ppm as doublet, whereas H-2, H-3 and H-4 appeared at δ_H 4.89, 5.15 and 6.54 ppm, respectively. The mass spectral data of **14** showed a molecular ion peak at m/z 565 and 567, in addition to ion at m/z 203 and 205 presumably attributed to the loss of thio-sugar moiety. The spectrum of **15** showed molecular ion peak at m/z 397 and 399 agreeing with the molecular formula $C_{16}H_{16}ClN_3SO_5$. The spectrum also showed similar ion to that resulting from **14** at m/z 203 and 205.



5 ; m/z 235, 237 (M·)

4 m/z 324, 326

10 ; R = CH_2CH_2CN m/z 288, 290 (M·)

11 ; R = $CH_2CH_2CONH_2$ m/z 306, 308 (M·)

12 ; X = CH_2 m/z 332, 334 (M·)

13 ; X = O m/z 334, 336 (M·)

14 ; R = Ac m/z 565, 567 (M·)

15 ; R = H m/z 397, 399 (M·)

Figure-1

In order to assign the site of alkylation and glycosylation, we have attempted to study the tautomerism in 7-chloro-1-mercapto-1,2,4-triazolo-[4,3-a]quinoline (**5**), which may exist in thiol-thione equilibrium due to the mobility of the NH proton where the C-2 flanked between the two nitrogen atoms.

This was performed by considering a theoretical approach by means of semiemperical AM1 method for reactants and transition state tautomers **5**a-d carried out with MOPAC7 program package.[33] Thus, the heat of formation, dipole moment, the highest occupied molecular orbital energies E_{HOMO}, the lowest unoccupied molecular orbital energies E_{LUMO}, the charge density on triazole heteroatoms as well as relative stability have been calculated (Table-1).

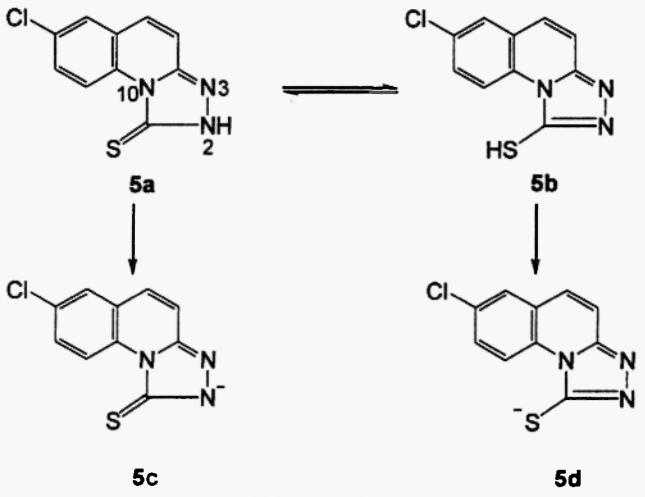
The relative stability (RS) calculations from gas phase AM1 method for the triazoloquinoline favored the predominance of the thiol form **5**b over the thione form **5**a with relative stability energy (7.090 kcal.mol^{-1}).

Charge density measurements for the reactant tautomers **5**a,b and their anionic forms **5**c,d generated by proton-abstraction from the SH and NH groups, respectively showed that the negative charge density was more localized on sulfur atom than that on nitrogen atoms. These results explained the higher reactivity of the sulfur than nitrogen atoms towards the electrophilic attack presumably due to the higher nucleophilic properties and the lower electronegativity of the sulfur atom [**34**]. Accordingly the theoretical calculations agreed with the experimental results, where the alkylation and the glycosylation have occurred on the sulfur atom.

Table-1: Calculated (AM1) Heat of Formation (Kcal.mol^{-1}), Dipole Moments (μ, Debye), HOMO Orbital Energies (E_{HOMO}, eV), LUMO Orbital Energies (E_{LUMO}, eV), Charge Density on triazole heteroatoms and Relative Stability (Kcal.mol^{-1}) for the reactant tautomers.

Tautomer No	Heat of Formation (ΔH_f) Kcal.mol^{-1}	Dipole moment Debye	E_{HOMO} eV	E_{LUMO} eV	Charge Density on imidazole heteroatoms	Relative Stability (RS) Kcal.mol^{-1}
5a	124.817	3.498	-8.484	-1.122	(S) -0.196 (N2) -0.049 (N3) -0.228 (N10) -0.159	**(5a-5b) = 7.090**
5b	117.727	3.368	-8.532	-1.030	(S) 0.215 (N2) -0.053 (N3) -0.079 (N10) -0.075	
5c	80.962	10.404	-3.583	2.755	(S) -0.449 (N2) -0.169 (N3) -0.071 (N10) -0.146	**(5c-5d) = 8.483**
5d	71.479	11.802	-3.755	2.522	(S) -0.456 (N2) -0.063 (N3) -0.148 (N10) -0.167	

RS = ΔH_f(thione) – ΔH_f (thiol); minus sign indicates that thione is more stable and vise versa.



Scheme-2

Antimicrobial Activity

All compounds were screened for their antimicrobial activity against gram-positive bacteria *Staphylococcus, Streptobacillus* and *Bacillus Subtillis* and gram-negative bacteria *Escherishia Coli, Streptobacillus* and *Pseudomonas* species applying the agar plate diffusion technique. The screening results are given in Table 2 which indicated that all the compounds except compound 3 exhibited antimicrobial activities against one or more type of bacteria. Almost all compounds showed more inhibition against gram-negative bacteria especially Escherishia *Coli* than the gram-positive one. Compounds **5** and 11 showed the highest inhibitory effect against all the gram-negative tested organism.

Table-2: Antimicrobial activity

Compd. No	Gram-positive Bacteria			Gram-negative Bacteria		
	Staphylococcus sp.	*Streptobacillus sp.*	*Bacillussubtillis Sp.*	*E. coli sp.*	*Streptobacillus sp.*	*Pseudomonas sp.*
3	-	-	-	-	-	-
4	-	+	+	++	-	+
5	-	+	+	+++	+++	+++
6	-	+	-	++	-	-
7	-	+	++	+++	-	-
8	-	-	+	+++	+	+++
9	-	++	+	++	-	+++
10	-	-	-	++	+	+
11	-	+	+	+++	+++	+++
12	-	-	+	+++	++	+
13	-	-	-	+++	+	+
14	-	+	+	-	+	-
15	-	+	+	-	-	-

Experimental

General Procedures. Mps were determined with a Melt-Temp apparatus and are uncorrected. IR spectra were recorded with Perkin-Elmer 1430 spectrometer. ^{1}H NMR spectra were recorded on Varian Gemini (200 MHz) spectrometer, Cairo University. Chemical shifts δ are given in ppm relative to the signal for TMS as internal standard. Mass spectra were recorded on GC Ms-QP 1000 EX (SHIMADZU) Mass spectrometer and on Varian MAT 711 spectrometer. The elemental analyses were performed at microanalysis unit in the Faculty of Science, Cairo and Ain-Shams Universities.

1-Aryl-7-chloro-1,2,4-triazolo[4,3-a]quinolines (3, 4)

A mixture of 1 (0.01 mol) and aromatic aldehydes (0.025 mol) was heated under reflux in glacial acetic for 6 hours. After cooling the precipitate was filtered and crystallized from ethanol.

7-Chloro-1-(4-pyridyl)-1,2,4-triazolo[4,3-a]quinoline (3)

This compound was obtained in 53 % yield; mp 271 °C; IR: 1630 (C=C), 1650 (C=N), 3085 (C-H Ar) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ (ppm) 7.6-8.3 (m, 9H, Ar-H). Anal. Calcd. for $C_{15}H_9ClN_4$: C, 64.17; H, 3.20; N, 19.96. Found: C, 64.21; H, 3.43; N, 19.99.

7-Chloro-1-(p-nitrophenyl)-1,2,4-triazolo[4,3-a]quinoline (4)

This compound was obtained in 72 % yield; mp 255 °C; IR: 1350, 1490 (NO_2), 1650 (C=C), 1690 (C=N), 3050 (C-H Ar) cm^{-1}; ms: *m/z* (M^{+}) 324 (13.4), 326 (4.3); 278 (1.0), 280 (0.3); 203 (58.5), 205 (19.8); 176 (100), 178 (30.3); 163 (8.2), 165 (2.7); 151 (24.1); 142 (14.8). Anal. Calcd. for $C_{16}H_9ClN_4O_2$: C, 59.16; H, 2.77; N, 17.25. Found: C, 59.22; H, 2.53; N, 17.41.

7-Chloro-1-mercapto-1,2,4-triazolo[4,3-a]quinoline (5)

62 on of **1** (0.1 mol) in carbon disulfide (40 ml) was heated under reflux for 16 hr. After cooling the precipitate was filtered, dried and crystallized from benzene to give **5** (84 % yield); mp 235 °C; IR: 1336 (C=S), 1620 (C=N), 3274 (NH) cm^{-1}; MS: *m/z* (M^{+}) 235 (100), 237 (33.5); 176 (45.3), 178 (14.5); 163 (83.4), 165 (27.6); 142 (75.1); 127 (48.7); 63 (40.8). Anal. Calcd. for $C_{10}H_6ClN_3S$: C, 50.95; H, 2.54; N, 17.83. Found: C, 50.77; H, 2.81; N, 17.94.

7-Chloro-1-(1,2,4-triazolo[4,3-a]quinoiin-1-yl)thioglycolic acid (6)

To a solution of **5** (0.03 mol) in alcoholic sodium hydroxide (5 %, 6 ml), chloroacetic acid (0.04 mol) was added with stirring. The mixture was heated under reflux for 5 hr and then cooled, acidified with dil. HCl. The product was crystallized from ethanol to give 6 (72 % yield); mp 155 °C; IR: 1620 (C=N), 1720 (C=O), 2950 (CH_2) 3400 (OH) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 3.4 (s, 2H, SCH_2), 7.7-8.3 (m, 5H, Ar-H), 8.8 (s, 1H, D_2O exchangeable, OH). Anal. Calcd. for $C_{12}H_8ClN_3SO_2$: C, 49.06; H, 2.72; N, 14.31. Found: C, 49.16; H, 2.82; N, 14.41.

1-[(2-Amino-1,3,4-thiadiazol-5-yl)methylthio]-7-chloro-1,2,4-triazolo[4,3-a]quinoline (7)

A mixture of **6** (0.01 mol) and phosphorous oxychloride (5 ml) was heated on a boiling water-bath, then thiosemicarbazide (0.01 mol) was added and heating was continued for 3 hr. The mixture was allowed to cool, ice water (10 ml) was added and the precipitate was filtered and crystallized form ethanol to give **7** (42 % yield); mp 218 °C; IR: 1650 (C=N), 2950 (CH_2), 3120 (C-H Ar.), 3250 (NH_2) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 3.3 (s, 2H, SCH_2), 7.6-8.3 (m, 5H, Ar-H), 10.8 (s, 2H, D_2O exchangeable, NH_2). Anal. Calcd. for $C_{13}H_9ClN_6S_2$: C, 44.76; H, 2.58; N, 24.10. Found: C, 44.82; H, 2.62; N, 24.42.

7-Chloro-1-(ethoxycarbonylmethylthio)-1,2,4-triazolo[4,3-a]quinoline (8)

A mixture of **5** (0.01 mol), ethyl chloroacetate (2 ml, 0.01 mol) and anhydrous potassium carbonate (0.01 mol) in dry acetone was heated under reflux for 30 hr. The hot mixture was filtered to remove the inorganic materials. After cooling, the precipitate was filtered, washed with water and crystallized from ethanol to give **8** (66 % yield), mp 190 °C; IR: 1690 (C=N), 1730 (C=O), 2950 (C-H), 3050 (C-H Ar.) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 1.2 (t, 3H, CH_3), 2.1 (q, 2H, CH_2), 3.4 (s, 2H, SCH_2), 7.6-8.3 (m, 5H, Ar-H). Anal. Calcd. for $C_{14}H_{12}ClN_3SO_2$: C, 52.25; H, 3.73; N, 13.06;. Found: C, 52.35; H, 3.88; N, 13.12.

7-Chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thioglycolic acid hydrazide (9)

A mixture of 8 (0.01 mol) and hydrazine hydrate 98 % (3 ml, 0.04 mol) in ethanol (25 ml) was heated under reflux for 6 hr. After cooling, the residue was filtered and crystallized from ethanol to give 9 (63 %); mp 113 °C; IR: 1620 (C=N), 1690 (C=O), 2950 (CH_2), 3050 (C-H Ar), 3200-3400 (NH, NH_2) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 3.35 (s, 2H, SCH_2), 7.6-8.3 (m, 5H, Ar-H), 9.2 (s, 1H, D_2O exchangeable, NH), 10.7 (S, 2H, D_2O exchangeable, NH_2). Anal. Calcd. for $C_{12}H_{10}ClN_5SO$: C, 46,82; H, 3.25; N, 22.76. Found: C, 46.87; H, 3.51; N, 22.46.

7-Chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thiomethylcyanide (10)

A mixture of **5** (0.01 mol), drops of triethylamine and acrylonitrile (0.015 mol) in ethanol (15 ml) was heated under reflux for 6 hr. After cooling, the precipitate was filtered, washed with water and crystallized from ethanol to give **10** (40 % yield); mp 227 °C; IR: 1650 (C=N), 2250 (CN), 2950 (CH_2), 3100 (C-H Ar) cm^{-1}; MS: *m/z* (M^{+}) 288 (34.3), 290 (10.5); 235 (100), 237 (33.6); 176 (1.2), 178 (0.4); 162 (44.1), 164 (14.3); 142 (35.5); 127 (26.2); 63 (6.4). Anal. Calcd. for $C_{13}H_9ClN_4S$: C, 54.07; H, 3.11; N, 19.41. Found: C, 54.23; H, 3.34; 19.60.

7-Chloro-1-(1,2,4-triazolo[4,3-a]quinolin-1-yl)thiomethylcarboxamide (11)

Method A: A mixture of **5** (0.01 mol), drops of triethylamine and acrylamide (0.015 mol) in ethanol (15 ml) was processed as above to give **11** (78 % yield).

Method B: A mixture of **10** (0.01 mol) and sodium hydroxide (10 %, 5 ml) in ethanol (20 ml) was heated under reflux for 5 hr. After cooling, the precipitate was filtered and crystallized from ethanol to give **11** (35 %); mp 193 °C; IR: 1640 (C=N), 1661 (C=O), 2959 (CH_2), 3072 (C-H Ar), 3275 (NH_2)cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 3.1 (t, 2H, SCH_2), 3.8 (t, 2H,

CH_2CO), 7.1-7.9 (m, 5H, Ar-H), 11.85 (s, 2H, D_2O exchangeable, NH_2); MS: *m/z* (M^+) 306 (17.6), 308 (5.8); 235 (100), 237 (33.7); 176 (20.2), 178 (6.6); 162 (35.6), 164 (10.1); 142 (24.3); 127 (15.2); 63 (8.1). Anal. Calcd. for $C_{13}H_{11}ClN_4SO$: C, 50.89; H, 3.58; N, 18.27. Found: C, 50.91; H, 3.60; 18.33.

General Procedure for the preparation of Mannich Bases (12,13)

A mixture of **5** (0.01 mol), formaldehyde (40 %, 5 ml), con. HCl (2 ml) and secondary amines (0.01 mol) in ethanol (50 ml) was stirred for 3 hr at room temperature. The precipitate was filtered, washed with ethanol and recrystallized from ethanol.

7-Chloro-2-(N-piperidyl-methyl)-1,2,4-triazolo[4,3-a]quinoline-1-thione (12)

This compound was obtained in 38 % yield; mp 181 °C; IR: 1576 (C=C), 1625 (C=N), 2850-2950 (CH_2), 3055 (C-H Ar) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 1.86-2.13 (m, 6H, $CH_2CH_2CH_2$), 3.06 (t, 4H, NCH_2), 4.22 (s, 2H, NCH_2N), 7.29-8.39 (m, 5H, Ar-H); MS: *m/z* (M^+) 332 (0.03), 334 (0.01); 249 (0.08), 251 (0.03); 235 (100), 237 (32.6); 203 (15.6), 205 (5.2); 162 (37.9), 164 (12.2); 142 (37.5); 127 (15.6); 63 (5.8). Anal. Calcd. for $C_{16}H_{17}ClN_4S$: C, 57.74; H, 5.11; N, 16.84. Found: C, 57.82; H, 5.29; 16.82.

7-chloro-2-(N-morpholinyl-methyl)-1,2,4-triazolo[4,3-a]quinoline-1-thione (13)

This compound was obtained in 50 % yield; mp 220 °C; IR: 1070 (C-O-C), 1600 (C=C), 1652 (C=N), 2900-2972 (CH_2) and 3030 (C-H Ar) cm^{-1}; MS: *m/z* (M^+) 334 (0.03), 336 (0.01); 235 (0.12), 237 (0.04); 176 (0.09), 178 (0.03); 162 (0.06), 164 (0.02); 142 (0.05); 100 (100); 63 (0.01). Anal. Calcd. for $C_{15}H_{15}ClN_4SO$: C, 53.81; H, 4.48; N, 16.74. Found: C, 53.87; H, 4.52; 16.82.

7-Chloro-1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thio-1,2,4-triazolo[4,3-a]quinoline (14)

A mixture of **5** (0.01 mol), potassium hydroxide (0.01mol) and 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (0.015 mol) in ethanol (15 ml) was heated under reflux for 2 hr. After cooling, the precipitate was filtered and crystallized from ethanol to give **14** (58 % yield); mp 93-95 °C; IR : 1600 (C=C), 1650 (C=N), 1720 (C=O), 2920 (CH_3), 3100 (C-H Ar) cm^{-1}; ^1H NMR (DMSO-d_6) δ (ppm) 1.80, 1.85, 1.97, 2.01 (4s, 12H, 4OAc), 3.83-3.86 (m, 1H, H-5'), 4.29-4.37 (m, 2H, H-6', H-6"), 4.89 (dd, 1H, H-4'), 5.15 (t, 1H, H-2'), 6.20 (d, 1H, H-1', *J* = 9.9 Hz), 6.54 (t, 1H, H-3'), 7.29-8.38 (m, 5H, Ar-H). MS: *m/z* (M^+) 565 (26.2), 567 (7.4); 537 (54.1), 539 (16.7); 435 (29.1), 437 (8.3); 204 (100), 206 (33.6); 162 (1.5), 164 (0.05); 63 (26.8). Anal. Calcd. for $C_{24}H_{24}ClN_3SO_9$: C, 50.92; H, 4.24, N, 7.42. Found: C, 50.95; H, 4.31; N, 7.46.

7-Chloro-1-(β-D-glucopyranosyl)thio-1,2,4-triazolo-[4,3-a]quinoline (15)

To a mixture of **14** (0.01 mol) in methanol (30 ml), methanolic ammonia was added dropwise with stirring and the mixture was kept at 0 °C for 24 hr. The solvent was removed under vacuum at 40 °C and the residue was collected and crystallized from methanol to give **15** (68 % yield); mp 170 °C; IR: 1620 (C=N), 2950 (CH_2), 3200-3420 (OH) cm^{-1}; MS: *m/z* (M^+) 397 (22.6), 399 (7.2); 235 (2.5), 237 (0.8); 179 (100); 176 (1.3), 178 (0.4); 162 (14.6), 164 (4.8); 63 (8.1). Anal. Calcd. for $C_{16}H_{16}ClN_3SO_5$: C, 48.30; H, 4.02; N, 10.56. Found: C, 48.67; H, 4.11; N, 10.46.

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