Synthesis and Antimicrobial Evaluation of 6-Chloroquinolinylhydrazones and Acyclonucleosides of 7-Chloro-1,2,4-triazolo [4,3-a] quinolines

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(Received 26th March, 2007, revised 24thJuly 2007)

Summary: Condensation of 6-chloro-2-hydrazinoquinoline (1) with monosaccharides 2a-e gave the corresponding sugar hydrazones 3a-e which upon acetylation gave the corresponding acetates 4f-j. Cyclization of 3a-e using iron (III) chloride afforded the acyclic nucleosides of triazoloquinolines 5a-e which were also acetylated to give 6f-j. Compound 1 was also condensed with aldehydes and isatin to give the corresponding hydrazones 7-10. Reactions of 1 with ethylchloroformate, phthalic anhydride, acetyl acetone and tosyl chloride were also investigated. All compounds were screened for their antimicrobial activity against gram positive and gram negative bacteria.

Introduction

Quinoline nucleus is present in a large number of natural products and drugs [1-5]. The quinoline derivatives exhibit a broad spectrum of biological activities [6-8] such as antimalarial, [9] antimicrobial, antibacterial and antifungal activities [10-16]. A large number of 1,2,4-triazolo[4,3-a]quinolines were synthesized as agricultural bactericides and fungicides and have been found to be active against *Piricularia oryzae* [17].

In continuation of our studies on the synthesis and biological activities of quinolines [18-20], sugar hydrazones [21-24] and acyclonucleosides [25-29] we report herein the synthesis and antimicrobial activity of the title compounds.

Results and Discussion

A number of sugar hydrazones 3a-e were prepared by condensation of 6-chloro-2-hydrazinoquinoline (1) with equimolar amounts of aldohexoses and aldopentoses namely: D-glucose (2a), D-galactose (2b), D-mannose (2c), D-xylose (2d) and D-arabinose (2e), respectively in boiling ethanol in presence of drops of acetic acid as catalyst. Their IR spectra showed characteristic absorption bands at 3459-3135 cm^{-1} corresponding to the OH and NH groups. Acetylation of the sugar hydrazones 3a-e with acetic anhydride in pyridine at room temperature afforded the corresponding per-acetyl derivatives 4f-j, whose IR spectra showed the disappearance of the OH groups and appearance of absorption bands in the carbonyl frequency region at 1711-1725 cm^{-1} and 1673-1692 cm^{-1} due to (OAc) and (NAc) groups, respectively. Their ^{1}H NMR spectra showed signals corresponding to *O*-acetyl groups in addition to the NAc groups; whereas no signals could be found for NH groups confirming that per-*O*- and *N*-acetylation had taken place. The spectra also confirmed the presence of the HC=N proton as a doublet at low field at δ 6.55-6.74 ppm in addition to the rest of the alditol-1-yl side chain (experimental part).

The elemental analysis and the mass spectral data of 4j showed a molecular ion peak at *m/z* 535 and 537 that agreed with the molecular formula $C_{24}H_{26}ClN_3O_9$. The spectrum also showed ions at *m/z* 204 and 206 which could be attributed to the loss of sugar residue from the molecular ion. Moreover, the fragment at *m/z* 163 and 165 was assigned to the quinoline ring (Scheme 2). The isotopes of chlorine were apparent in the assigned fragments and the ratio of their signal agreed with the isotopic ratio.

Subjecting the sugar hydrazones 3a-e to oxidative cyclization with iron (III) chloride in ethanolic solution afforded the triazolo [4, 3-a]

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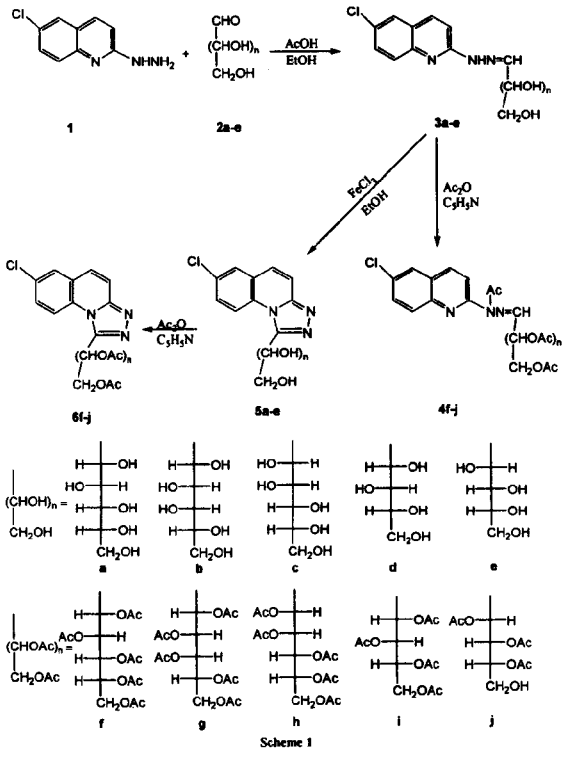
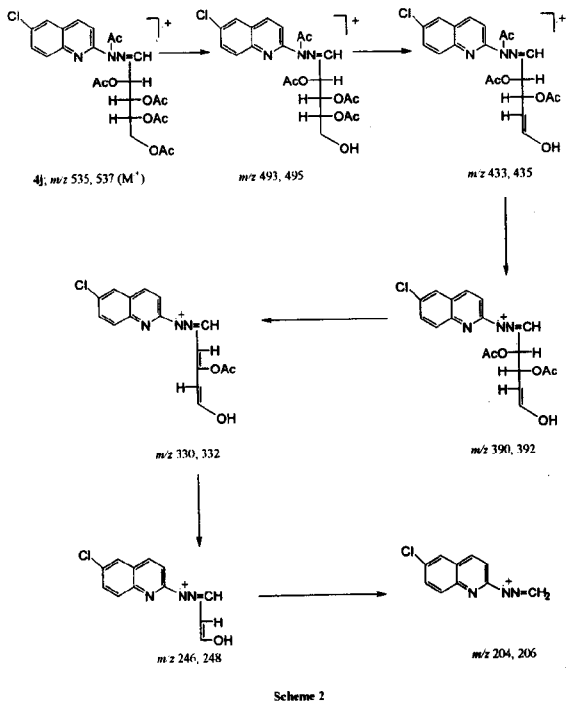
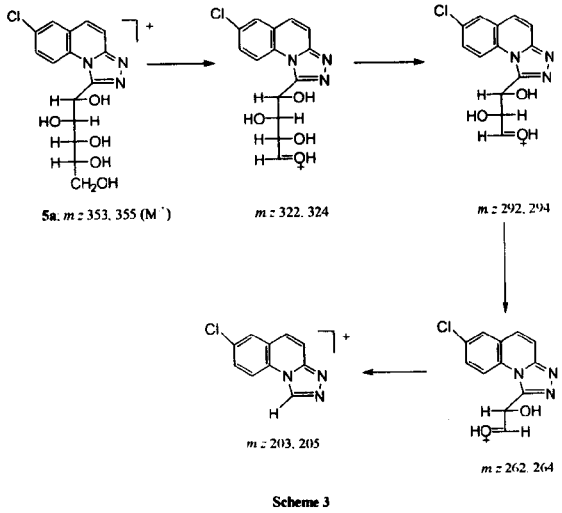


Scheme 1



Scheme 2

quinoline derivatives 5a-e. This oxidation may take place by the electrophilic attack of the hard acid site of iron III chloride [21] on the hardest basic site of the sugar hydrazones 3a-e, followed by the elimination of hydrogen chloride and formation of possibly a nitrilimine that undergoes a 1,5-electrocyclization to give 5a-e. Their IR spectra showed bands at 3240-3488 cm^{-1} (OH). The mass spectral data of 5a showed a molecular ion peak at *m/z* 353 and 355, in addition to ion peak at *m/z* 203 and 205 presumably attributed to the triazoloquinoline ring (Scheme 3)



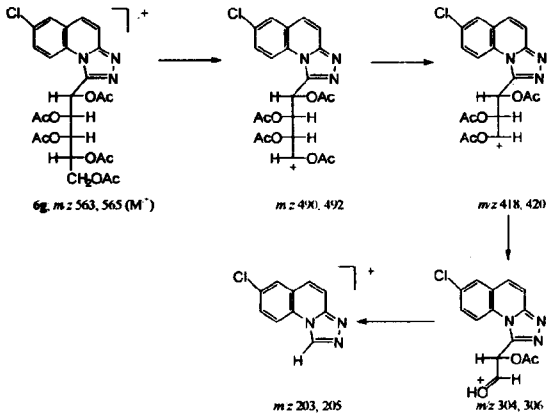
Scheme 3

The ^1H NMR spectrum of compound 5b showed a doublet at low field at δ 5.22 ppm which was assigned to H-1, followed by the rest of the aldito-1-yl side chain at higher field. The spectra of 5c-e showed a similar pattern.

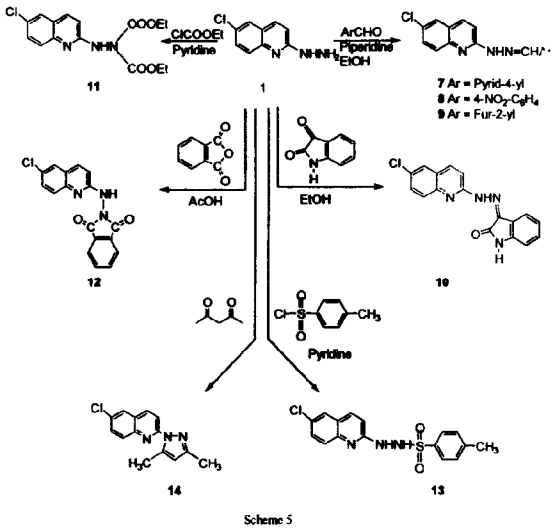
Acetylation of 5a-e with acetic anhydride in pyridine at room temperature afforded the polyacetoxyalkyl derivatives 6f-j, whose IR spectra showed the presence of only one absorption band in the carbonyl frequency region (OAc) (experimental part). The ^1H NMR spectra confirmed the presence of the OAc groups. The doublets at δ 5.74-6.02 were attributed to H-1. The mass spectra of 6g and 6i showed molecular ion peaks at *m/z* 563, 565 and 491, 493 which when combined with the elemental analysis led to the assignment of the molecular formulas $C_{25}H_{26}ClN_3O_{10}$ and $C_{22}H_{22}ClN_3O_{8_1}$ respectively. Moreover, they showed a characteristic

fragment at *m/z* 203 and 237 attributed to the triazoloquinoline ring.

Condensation of 1 with pyrid-4-yl carboxaldehyde, 4-nitrobenzaldehyde, fur-2-yl carboxaldehyde and isatin in boiling ethanol and in presence of catalytic amount of piperidine gave the corresponding hydrazones [7-10]. Their structures were confirmed by their elemental and spectral data. The elemental analysis and mass spectrum of 7 agreed with the molecular formula $C_{15}H_{11}ClN_4$. Its molecular ion peak appeared at *m/z* 282 and 284. Loss of the pyridyl ring was also observed to give ion at m/z 204 and 206. Moreover, other expected signals also appeared in the spectrum as shown in Scheme 6.



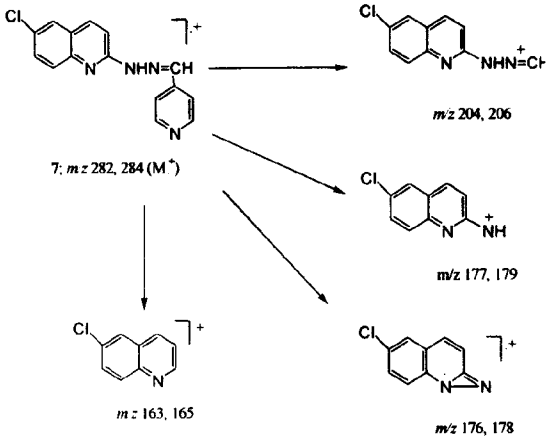
Scheme 4



Scheme 5

The ^{1}H NMR spectra of compound 8 and 9 showed signals at δ 6.12 and 6.13, respectively, confirming the presence of N=CH group. The ^{1}H NMR spectrum of 10 showed two singlets at δ 10.15 and 9.60 due to the NH proton of the hydrazone moiety and indole ring, respectively.

Treatment of 1 with ethylchloroformate in refluxing pyridine afforded bis (ethoxycarbomyl) hydrazine 11. Its IR spectrum showed the appearance of characteristic absorption band at 1250 cm^{-1} and 1731 for (C-O) and (C=O) groups, respectively. Its ^{1}H NMR spectrum indicated the presence of two quartets at δ 4.15-4.25 ppm due to methylene protons and triplet at δ 1.25 ppm due to methyl protons.



Scheme 6

Dehydrative condensation of 1 with phthalic anhydride in refluxing acetic acid gave 12. Its IR spectrum showed the presence of amidic carbonyl band at 1710 cm^{-1}. Its mass spectrum showed molecular ion peak at *m/z* 323 and 325 which when combined with the elemental analysis led to the assignment of the molecular formula $C_{17}H_{10}ClN_3O_2$.

Reaction of *p*-toluenesulphonyl chloride with hydrazinoquinoline 1 in pyridine gave 6-chloro-2-[2-(*p*-methylphenylsulphonyl) hydrazino]-quinoline (13). Its ^{1}H NMR spectrum confirmed the presence of one methyl group (δ 2.15 ppm). The reaction of (1) with acetyl acetone under acidic conditions afforded 6-chloro-2-(3,5-dimethyl-

pyrazol-1-yl) quinoline (14). Its ^{1}H NMR showed the presence of two singlets at δ 2.3 and 2.8 ppm due to the two methyl protons.

Antimicrobial Activity

All compounds were screened for their antimicrobial activity against gram-positive bacteria *Staphylococcus aureus, Streptobacillus moniliformis* and *Bacillus subtillis* and gram-negative bacteria *Escherishia coli, Streptobacillus moniliformis* and *Pseudomonas acruginosa* species applying the agar plate diffusion technique. The screening results (Table-1) indicated that all the compounds exhibited antimicrobial activities against one or more type of bacteria. Almost all triazoloquinoline derivatives 5a-e, 6f-j showed more inhibition against gram positive bacteria specially *Streptobacillus* than the gram negative one. Compounds 10 showed the highest inhibitory effect against all the gram-negative tested organism.

Table-1: Antimicrobial activity.

Compd. No	Gram-positive Bacteria			Gram-negative Bacteria		
	Staphy-lococcus sp	*Strepto-bacillus sp.*	*Bacillus-subtillis sp.*	*E. coli sp.*	*Streptoba-cillus sp.*	*Pseudo-monas sp.*
3a	-	+	-	-	-	-
3b	-	+	-	-	-	-
3c	-	+	+	-	-	-
3d	-	+	-	-	-	-
3e	-	+	-	-	-	-
4f	-	+	+	-	+	-
4g	-	+	+	+	-	-
4h	-	+	+	-	-	+
4i	-	+	-	+	-	-
4j	-	+	+	+	-	+
5a	-	+	+	+	-	-
5b	-	+	+	+	+	+
5c	-	++	++	+	+	+
5d	+	+++	++	+	-	-
5e	+	+	+	+	-	-
6f	-	+++	++	+	+	+
6g	-	++	+	+	-	-
6h	-	++	+	+	-	-
6i	+	+	+	+	-	-
6j	-	++	+	+	-	-
7	-	-	-	+	-	-
8	-	+	+	++	+	+
9	-	-	-	+	-	+
10	-	-	-	+++	++	+++
11	-	+	-	+	-	-
12	-	-	-	++	-	-
13	-	+	+	+	-	-
14	++	-	-	++	-	+

Experimental

Melting points 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. 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 microanalyses units at Cairo and Ain-Shams Universities.

General Method for the Synthesis of Sugar (6-chloroquinolin-2-yl)-hydrazones (3a-e)

To a solution of 6-chloro-2-hydrazino-quinoline (1) (0.1 mol) in ethanol (50 ml) was added the respective sugar 2a-e (0.1 Mol) and acetic acid (0.1 mL). The mixture was heated under reflux on a water bath for 1-1.5 h. The solid that separated on cooling was filtered, washed with EtOH and crystallized from the appropriate solvent.

D-Glucose (6-chloroquinolin-2-yl)-hydrazone (3a)

Yield: 62 % (from ethanol); m.p. 200 °C; Analysis (% calc/ found): for $C_{15}H_{18}ClN_3O_5$ C: 50.63/ 51.00, H: 5.06/ 5.46, N: 11.81/ 11.60; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3225-3417 (OH, NH), 1615 (C=N), 1502 (C=C).

D-Galactose(6-chloroquinolin-2-yl)-hydrazone (3b)

Yield: 90 % yield (from DMF/ EtOH); m.p. 180-182 °C; Analysis (% calc/ found): for $C_{15}H_{18}ClN_3O_5$ C: 50.63/ 51.05, H: 5.06/ 5.44, N: 11.81/ 11.50; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3135-3391 (OH, NH), 1615 (C=N), 1506 (C=C).

D-Mannose (6-chloroquinolin-2-yl)-hydrazone (3c)

Yield: 77 % (from DMF/ EtOH); m.p. 213-215 °C; Analysis (% calc/ found): for $C_{15}H_{18}ClN_3O_5$ C: 50.63/ 51.00, H: 5.06/ 5.48, N: 11.81/ 11.50; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3232-3459 (OH, NH), 1618 (C=N), 1504 (C=C).

D-Xylose (6-chloroquinolin-2-yl)-hydrazone (3d)

Yield: 59 % (from DMF/ EtOH); m.p. 207-209 °C; Analysis (% calc/ found): for $C_{14}H_{16}ClN_3O_4$ C: 51.61/ 51.60, H: 4.91/ 4.80, N: 12.90/ 12.90; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3210-3439 (OH, NH), 1616 (C=N), 1502 (C=C).

D-Arabinose(6-chloroquinolin-2-yl)-hydrazone (3e)

Yield 63 % (from EtOH); m.p. 179 °C; Analysis (% calc/ found): for $C_{14}H_{16}ClN_3O_4$ C: 51.61/ 51.73, H: 4.91/ 5.23, N: 12.90/ 12.94.IR (KBr) ($\nu_{max.}$ cm^{-1}): 3230-3414 (OH, NH), 1613 (C=N), 1500 (C=C).

General Method for the Synthesis of per-O-Acetyl-Sugar [1-acetyl-1-(6-chlroquinolin-2-yl)] hydrazones (4f-j)

A cold solution of 3a-e (0.02 Mol) in dry pyridine (50 mL) was treated with Ac_2O (50 ml). The mixture was kept overnight at room temprature with occasional shaking. The mixture was poured onto crushed ice, and the product was collected by filtration, washed repeatedly with water, dried and recrystallized from EtOH.

2,3,4,5,6-Penta-O-acetyl-D-glucose [1-acetyl-1-(6-chloroquinolin-2-yl)]hydrazone (4f)

Yield: 58 % yield; m.p. 60-61 °C; Analysis (% calc/ found): for $C_{27}H_{30}ClN_3O_{11}$ C, 53.33/ 53.10, H, 4.93/ 4.70; N, 6.91/ 6.60; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1718 (OAc), 1608 (C=N), 1673 (NAc), 1517 (C=C); ^{1}H NMR (DMSO-d_6) δ 2.02, 2.04, 2.10 (3s, 15H, 5 OAc), 2.50 (s, 3H, NAc), 4.15 (dd, 1H, H-6`), 4.26 (dd, 1H, H-6), 5.02-5.10 (m, 1H, H-5), 5.44-5.55 (m, 2H, H-4, H-3), 5.62 (dd, 1H, H-2), 6.74 (d, 1H, H-1), 7.30-8.24 (m, 5H, Ar-H).

2,3,4,5,6-Penta-O-acetyl-D-galactose [1-acetyl-1 (6-chloroquinolin-2-yl)] hydrazone (4g)

Yield: 80 % yield; m.p. 160-163 °C; Analysis (% calc/ found): for $C_{27}H_{30}ClN_3O_{11}$ C: 53.33/ 53.20, H: 4.93/ 4.80, N: 6.91/ 6.60; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1722 (OAc), 1692 (NAc), 1633 (C=N), 1518 (C=C); ^{1}H NMR (DMSO-d_6) δ 1.96, 1.99, 2.03, 2.08, 2.09 (5s, 15H, 5 OAc), 2.47 (s, 3H, NAc), 3.88 (dd, 1H, H-6`), 4.28 (dd, 1H, H-6), 5.38-5.88 (m, 4H, H-5, H-4, H-3, H-2), 6.55 (d, 1H, H-1), 7.30-8.23 (m, 5H, Ar-H).

2,3,4,5,6-Penta-O-acetyl-D-mannose [1-acetyl-1-(6-chloroquinolin-2-yl)] hydrazone (4h)

Yield: 63 %; m.p. 58-60 °C; Analysis (% calc/ found): for $C_{27}H_{30}ClN_3O_{11}$ C: 53.33/ 53.71, H: 4.93/ 4.82, N:6.91/ 6.85; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1711 (OAc), 1682 (NAc), 1615 (C=N), 1508 (C=C); ^{1}H NMR (DMSO-d_6) δ 2.05, 2.06, 2.10 (3s, 15H, 5 OAc), 2.52 (s, 3H, NAc), 4.14 (dd, 1H, H-6`), 4.28 (dd, 1H, H-6), 5.22-5.40 (m, 1H, H-5), 5.42 (d, 1H, H-4), 5.54 (dd, 1H, H-3), 5.66 (dd, 1H, H-2), 6.68 (d, 1H, H-1), 7.32-8.28 (m, 5H, Ar-H).

2,3,4,5-Tetra-O-acetyl-D-xylose [1-acetyl-1-(6-chloroquinolin-2-yl)] hydrazone (4i)

Yield: 52 % yield; m.p. 95 °C; Analysis (% calc/ found): for $C_{24}H_{26}ClN_3O_9$ C: 53.78/ 53.70, H: 4.85/ 4.70, N:7.84/ 7.69; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1725 (OAc), 1682 (NAc), 1619 (C=N), 1510 (C=C); ^{1}H NMR (DMSO-d_6) δ 1.91, 1.94, 2.00, 2.19 (4s, 12H, 4 OAc), 2.51 (s, 3H, NAc), 4.22 (dd,1H, H-5), 4.39 (dd, 1H, H-5), 5.38-5.40 (m, 1H, H-4), 5.78 (dd, 1H, H-3), 6.01 (dd, 1H, H-2), 6.59 (d, 1H, H-1), 7.23-8.40 (m, 5H, Ar-H).

2,3,4,5-Tetra-O-acetyl-D-arabinose [1-acetyl-1-(6-chloroquinolin-2-yl)] hydrazone (4j)

Yield 67 %; m.p. 110-113 °C; Analysis (% calc/ found): for $C_{24}H_{26}ClN_3O_9$ C: 53.78/ 53.60, H: 4.85/ 4.71, N: 7.84/ 7.90; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1715 (OAc), 1682 (NAc), 1516 (C=C), 1610 (C=N); ms: *m/z* (M^+) 535 (42.9), 537 (14.3); 493 (10.5), 495 (3.4); 433 (25.0), 435 (8.2); 390 (13.3), 392 (4.4); 330 (17.6); 332 (5.8); 246 (40.5), 248 (13.4); 204 (100), 206 (33.3); 176 (16.2), 178 (5.3); 163 (2.8); 165 (0.9); 63 (0.6).

General Procedure for the Synthesis of 1-(Alditol-1-yl)-7-chloro-1,2,4-triazolo [4,3-a] quinolines (5a-e)

A 2 M solution of iron (III) chloride in EtOH (2 mL) was added dropwise to a boiling solution of 3a-e (0.01 Mol) in EtOH (50 mL). Heating was continued for 10 min and the mixture was then kept overnight at room temperature. The

product was filtered, washed repeatedly with water, dried and recrystallized from EtOH to give the title compounds.

7-Chloro-1-(D-gluco-pentitol-1-yl)-1,2,4-triazolo [4,3-a] quinoline (5a)

Yield: 89 %; m.p. 85 °C; Analysis (% calc/ found): for $C_{15}H_{16}ClN_3O_5$ C: 50.91/ 50.82, H: 4.52/ 4.51, N:11.88/ 11.78; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3240-3454 (OH), 1613 (C=N), 1508 (C=C); ms: *m/z* (M^+) 353 (14.4), 355 (4.8); 322 (0.3), 324 (0.1); 292 (0.6), 294 (0.2); 262 (0.6), 264 (0.2); 203 (100), 205 (33.4); 176 (59.8), 178 (19.6); 163 (6.2); 165 (2.1); 63 (29.9).

7-Chloro-1-(D-galacto-pentitol-1-yl)-1,2,4-triazolo [4,3-a]quinoline (5b):

Yield: 85 %; m.p. 80 °C; Analysis (% calc/ found): for $C_{15}H_{16}ClN_3O_5$ C: 50.91/ 50.90; H: 4.52/ 4.44, N: 11.88/ 11.65; IR (KBr) (v, cm^{-1}): 3340-3450 (OH), 1619 (C=N), 1500 (C=C).

7-Chloro-1-(D-manno-pentitol-1-yl)-1,2,4-triazolo [4,3-a]quinoline (5c)

Yield: This 73 %; m.p. 105 °C; Analysis (% calc/ found): for $C_{15}H_{16}ClN_3O_5$ C: 50.91/ 50.93, H: 4.52/ 4.48, N: 11.88/ 11.71; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3290-3466 (br OH), 1615 (C=N), 1500 (C=C); ^{1}H NMR (DMSO-d_6+D_2O) δ 3.97-4.20 (m, 2H, H-5`, H-5), 4.40 (dd, 1H, H-4), 4.62 (dd, 1H, H-3), 5.03 (t, 1H, H-2), 5.22 (s, 1 H, H-1), 7.29-7.90 (m, 5H, Ar-H).

1-(D-Xylo-pentitol-1-yl)-7-chloro-1,2,4-triazolo [4,3-a] quinoline (5d)

Yield: 65 %; m.p. 125 °C; Analysis (% calc/ found): for $C_{14}H_{14}ClN_3O_4$ C: 51.93/ 51.89, H: 4.32/ 4.44, N: 12.98/ 12.91; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3310-3444 (OH), 1623 (C=N), 1505 (C=C); ms: *m/z* (M^+) 323 (21.1), 325 (7.0); 292 (3.5), 324 (1.1); 262 (0.6), 264 (0.2); 203 (9.9), 205 (3.2); 176 (100), 178 (33.2); 163 (0.3); 165 (0.1); 63 (25.2).

1-(D-Arabino-pentitol-1-yl)-7-chloro-1,2,4-triazolo [4,3-a]quinoline (5e)

Yield: 63 % yield; m.p. 92 °C; Analysis (% calc/ found): for $C_{14}H_{14}ClN_3O_4$ C: 51.93/ 51.85, H: 4.32/ 4.40, N: 12.98/ 12.88; IR (KBr) ($\nu_{max.}$ cm^{-1}) 3320-3480 (OH), 1619 (C=N), 1500 (C=C); ^{1}H NMR (DMSO-d_6+D_2O) δ 3.49-3.75 (m, 2H, H-4`, H-4), 4.18-4.39 (m, 2H, H-3, H-2), 5.03 (s, 1H, H-1), 7.40-8.05 (m, 5 H, Ar-H).

General Procedure 7-Chloro-1-(penta-O-acetyl-sugar-1-yl)-1,2,4-triazolo [4,3-a] quinoline (6f-j)

A cold solution of 5a-e (1.5 mMol) in dry pyridine (3mL) was treated with Ac_2O (3ml), and the mixture was kept overnight at room temperature with occasional shaking. It was poured onto crushed ice, and the product was filtered, washed with water and dried. It was crystallized from EtOH.

7-Chloro-1-(1,2,3,4,5-penta-O-acetyl-D-gluco-pentitol-1-yl)- 1,2,4-triazolo[4,3-a]quinoline (6f)

Yield: 75 %; m.p. 69 °C; Analysis (% calc/ found): for $C_{25}H_{26}ClN_3O_{10}$ C: 53.23/ 53.30, H: 4.61/ 4.59, N: 7.45/ 7.51; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1725 (OAc), 1650 (C=N), 1510 (C=C); ^{1}H NMR (DMSO-d_6) δ 1.99, 2.01, 2.03 (3 s, 12H, 4 OAc), 3.98 (dd, 1H, H-5`), 4.30 (dd, 1H, H-5), 5.30-5.52 (m, 3H, H-4, H-3, H-2), 5.86 (d, 1 H, H-1), 7.26-8.30 (m, 5H, Ar-H).

7-Chloro-1-(1,2,3,4,5-penta-O-acetyl-D-galacto-pentitol-1-yl)-1,2,4-triazolo [4,3-a]-quinoline (6g):

Yield: 80 % yield; m.p. 63 °C; Analysis (% calc/ found): for $C_{25}H_{26}ClN_3O_{10}$ C: 53.23/ 53.33, H: 4.61/ 4.58, N: 7.45/ 7.55; (KBr) ($\nu_{max.}$ cm^{-1}): 1719 (OAc), 1619 (C=N), 1512 (C=C); ms: *m/z* (M^+) 563 (19.3), 565 (6.3); 490 (27.4), 492 (9.1); 418 (31.7), 420 (10.5); 304 (9.5), 306 (3.2); 203 (100), 205 (33.3); 176 (59.8), 178 (19.9); 163 (3.3); 165 (1.1); 63 (29.9).

1-(1,2,3,4,5-penta-O-acetyl-D-mannopentitol-1-yl)-7-chloro-1,2,4-triazolo [4,3-a]quinoline (6h):

Yield: 60 %; m.p. 71 °C; Analysis (% calc/ found): for $C_{25}H_{26}ClN_3O_{10}$ C: 53.23/ 53.35, H: 4.61/ 4.51, N: 7.45/ 7.59; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1745 (OAc), 1639 (C=N), 1517 (C=C); ^{1}H NMR (DMSO-d_6) δ 1.96, 1.99, 2.03, 2.08 (4 s, 12H, 4 OAc), 3.90 (dd, 1H, H-5`), 4.32 (dd, 1H, H-5), 5.30-5.53 (m, 3H, H-4, H-3, H-2), 5.76 (d, 1H, H-1), 7.28-8.23 (m, 5H, Ar-H).

1-(1,2,3,4-Tetra-O-acetyl-D-xylopentitol-1-yl)-7-chloro-1,2,4-triazolo[4,3-a]quinoline (6i)

Yield: 55 %; m.p. 68 °C; Analysis (% calc/ found): for $C_{22}H_{22}ClN_3O_8$ C: 53.71/ 53.8, H: 4.47/ 4.50, N: 8.54/ 8.61; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1731 (C=O), 1629 (C=N), 1514 (C=C); ^1H NMR (DMSO-d_6) δ 2.03, 2.06, 2.08 (3 s, 12H, 4OAc), 4.05 (dd, 2H, H-4`, H-4), 4.35-4.55 (m, 1H, H-3), 5.56 (dd, 1H, H-2), 5.74 (d, 1H, H-1), 7.29-7.90 (m, 5H, Ar-H); ms: *m/z* (M^+) 491 (21.3), 493 (7.1); 419 (17.6), 421 (5.8); 347 (21.4), 349 (7.1); 275 (16.9), 277 (5.6); 203 (39.4), 205 (13.1); 176 (100), 178 (33.2); 163 (8.4); 165 (2.8); 63 (2.8).

7-Chloro-1-(1,2,3,4-tetra-O-acetyl-D-arabino-pentitol-1-yl)-1,2,4-triazolo[4,3-a]-quinoline (6j):

Yield: 65 %; m.p. 93 °C; Analysis (% calc/ found): for $C_{22}H_{22}ClN_3O_8$ C: 53.71/ 53.75, H: 4.47/ 4.51, N: 8.54/ 8.48; IR (KBr) ($\nu_{max.}$ cm^{-1}): 1720 (OAc), 1618 (C=N), 1502 (C=C); ^1H NMR (DMSO-d_6): δ 1.81, 1.86, 1.91, 2.19 (4 s, 12H, 4OAc), 4.22 (dd, 2H, H-4`, H-4), 5.36-5.41 (m, 1H, H-3), 5.76 (dd, 1H, H-2), 6.02 (d, 1H, H-1), 7.29-8.42 (m, 5H, Ar-H).

General Method for the Synthesis of 1-(6-Chloroquinolin-2-yl)-2-arylidenehydrazones (7-9)

A mixture of 1 (0.01 Mol, 1.93 g) and aromatic aldehydes (0.025 Mol) in absolute ethanol (20 ml) and few drops of piperidine as catalyst was heated under reflux for 8 h. After cooling the precipitate was collected by filtration and recrystallized from the appropriate solvent.

2-(Pyrid-4-yl) carboxaldehyde-1-(6-chloroquinolin-2-yl)-hydrazone (7)

Yield: 71 % (from EtOH); m.p. 275 °C; Analysis (% calc/ found): for $C_{15}H_{11}ClN_4$: C: 63.71/ 63.88, H: 3.89/ 3.66, N: 19.82/ 19.52; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3380 (NH), 1628 (C=N), 1505 (C=C); ms: *m/z* (M^+) 282 (21.8), 284 (7.3); 204 (100), 206 (33.4); 177 (54.0), 179 (17.6); 176 (2.3), 178 (0.8); 163 (4.1); 165 (1.7); 63 (9.7).

2-(4-Nitrophen-1-yl)-carboxaldehyde-1-(6-chloro-quinolin-2-yl) hydrazone (8)

Yield: 85 % yield (from EtOH/ DMF); m.p. 255 °C; Analysis (% calc/ found): for $C_{16}H_{11}ClN_4O_2$ C: 61.90/ 58.87, H: 3.54/ 3.75, N: 18.06/ 17.55; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3378 (NH), 1615 (C=N), 1500 (C=C); ^1H NMR (DMSO-d_6) δ 6.12 (s, 1H, N=CH), 7.55-8.45 (m, 9H, Ar-H), 10.45 (s, 1H, NH).

2-(Fur-2-yl) carboxaldehyde-1-(6-chloroquinoline-2-yl)-hydrazone (9)

Yield: 86 % yield (from EtOH); m.p 178 °C; Analysis (% calc/ found): for $C_{14}H_{10}ClN_3O$ C: 61.87/ 61.85, H: 3.68/ 3.71, N: 15.46/ 15.26; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3298 (NH), 1619 (C=N), 1510 (C=C); ^1H NMR (DMSO-d_6) δ 6.13 (s, 1H, N=CH), 6.56-7.35 (m, 3H, furyl-H), 7.55-8.15 (m, 5H, Ar-H), 10.75 (s, 1H, NH).

Isatin [1-(6-chloroquinolin-2-yl)] hydrazone (10)

A mixture of 1 (02 Mol, 3.86 g), isatin (0.02 Mol) in ethanol (20 ml) was heated under reflux for 6 h. After cooling the precipitate was filtered off and crystallized from EtOH to give 10: Yield: 79 %; m.p. 290°C; Analysis (% calc/ found): for $C_{17}H_{11}ClN_4O$ C: 63.25/ 63.45, H: 3.41/ 3.71, N, 17.36/ 17.17; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3339 (NH), 1614 (C=N), 1512 (C=C); ^1H NMR (DMSO-d_6) δ 7.45-8.56 (m, 9H, Ar-H), 10.15 (2 s, 2H, NH indole).

1-(6-Chloroquinolin-2-yl)-2-bis (ethoxycarbomyl)-hydrazine (11)

A mixture of 1 (0.01 mol) and ethylchloroformate (0.02 Mol) in dry pyridine (20 ml) was heated at boiling water bath for 4 h. The solvent was evaporated under vacuum, the residue was cooled and recrystallized from EtOH to give 11. Yield: 48 % yield; m.p. 120 °C; Analysis (% calc/ found): for $C_{15}H_{16}ClN_3O_4$ C: 53.33/ 53.55, H: 4.74/ 4.81, N: 12.44/ 12.63; IR (KBr) ($\nu_{max.}$ cm^{-1}): 2986 (C-H), 1731 (C=O), 1622 (C=N), 1529 (C=C), 1250 (C-O); ^1H NMR (DMSO-d_6) δ 1.25 (t, 6H, 2 CH_3), 4.15-4.25 (2 q, 4H, 2 CH_2), 7.45-8.25 (m, 5H, Ar-H), 10.05 (s, 1H, NH).

6-Chloro-2-(2-N-phthaloyl)-hydrazino-quinoline (12)

A mixture of 1 (0.02 Mol) and phthalic anhydride (0.02 mol) in glacial acetic acid (25 ml) was heated under reflux for 4 h. After cooling, the precipitate was filtered off, and crystallized from

ethanol to give 12. Yield: 58 %; mp. 168 °C; Analysis (% calc/ found): for $C_{17}H_{10}ClN_3O_2$ C: 63.06/ 63.16, H: 3.09/ 3.12, N: 12.98/ 12.88; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3396 (NH), 1710 (C=O), 1619 (C=N), 1505 (C=C); ms: *m/z* (M^+) 323 (5.5), 325 (1.8); 204 (20.0), 206 (6.7); 177 (10.3), 179 (3.4); 163 (17.1); 165 (5.7); 63 (100).

6-Chloro-2-[2-(tolylsulphonyl)hydrazino]-quinoline (13)

A mixture of 1 (0.02 Mol), Tosyl chloride (0.02 Mol) in pyridine (20 ml) was heated under reflux for 20 h. After cooling, the mixture was poured onto (20 ml) of cold water with stirring. The precipitate was filtered off and crystallized from benzene to give 13. Yield: 79 %; mp. 130 °C; Analysis (% calc/ found): for $C_{16}H_{14}ClN_3SO_2$ C: 55.25/ 55.5, H: 4.02/ 4.41, N: 12.08/ 12.28; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3329 (NH), 1620 (C=N), 1519 (C=C); ^{1}H NMR (DMSO-d_6) δ 2.15 (s, 3H, CH_3), 7.60-8.35 (m, 9H, Ar-H).

6-Chloro-2-(3,5-dimethylpyrazol-1-yl)-quinoline (14)

A mixture of 1 (0.02 Mol), acetyl acetone (0.02 Mol) and acetic acid (1 ml) in ethanol (20 mL) was heated on a boiling water bath for 6 h. After cooling, the precipitate was filtered and crystallized from EtOH to give 13. Yield: 85 %; m.p. 116°C; Analysis (% calc/ found): for $C_{14}H_{12}ClN_3$ C: 65.24/ 65.33, H: 4.66/ 4.50, N: 16.31/ 16.09; IR (KBr) ($\nu_{max.}$ cm^{-1}): 3075 (C-H Ar), 1680 (C=N), 1630 (C=C); ^{1}H NMR ($CDCl_3$) δ (ppm) 2.3 (s, 3H, CH_3), δ 2.8 (s, 3H, CH_3), 6.15 (s, 1H, =CH), 7.60-8.20 (m, 5H, Ar-H).

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