Synthesis of acyclo *C*-Nucleosides of H_1-antihistaminic 4-substituted [1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-ones

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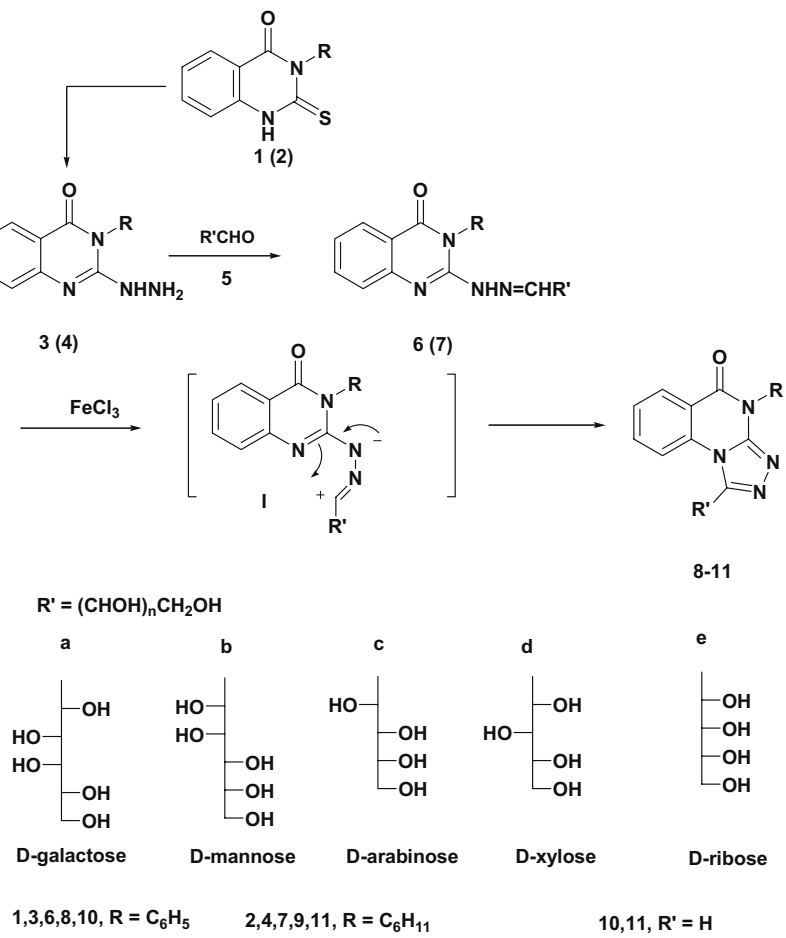
Two series of aldose N-(3-substituted-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazones were prepared by the reaction of each of the aldoses with the appropriate 2-hydrazino-3-substituted-quinazolin-4(3H)-ones. Oxidative cyclisation of these aldose hydrazones with ferric chloride in ethanol yielded the title acyclo *C*-nucleosides.

Keywords: aldoses, *C*-nucleosides, 1,5-electrocyclisation, nitrilimines

Recently, it was reported that various derivatives of 1,4-disubstituted[1,2,4]triazolo[4,3-*a*]quinazolin-5(4H)-ones exhibit promising antihistaminic activity against histamine-induced bronchospasm in a conscious guinea pigs *in vivo* model.[1-6] In addition, other derivatives of such a ring system were reported to exhibit antitoxoplasmosis effect.[7] Such findings attracted our attention towards the synthesis of their acyclo *C*-nucleoside analogues which have not been reported hitherto. This is because the sugar moieties of the target acyclo *C*-nucleosides are expected to enhance their penetration into living cells and therefore increase their biological activity. In continuation of our ongoing studies dealing with the chemistry of precursors of nitrilimines namely the hydrazonoyl halides[8-16] and hydrazones,[17-20] we report here the results of our study of tandem generation and 1,5-electrocyclisation of two new series of *C*-(alditol-1-yl) *N*-(4-oxo-3-substitutedquinazolin-2-yl)nitrilimines to give the respective 1-(alditol-1-yl)-4-substituted[1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-ones (Scheme 1).

Results and discussion

The required aldose *N*-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazones **6a–e** and their analogues aldose *N*-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazones **7a–e**, which have not been reported hitherto, were prepared by heating 2-hydrazino-3-phenylquinazolin-4(3*H*)-one **3** and 3-cyclohexyl-2-hydrazinoquinazolin-4(3*H*)-one **4** with equimolar amount of each of D-galactose, D-mannose, D-arabinose, D-xylose and D-ribose **5a–e**, respectively in ethanol for 2 h in the presence of catalytic amount of acetic acid (Scheme 1). The structures of the hydrazones **6a–e** and **7a–e** were confirmed by their elemental analyses and spectral



Scheme 1

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(MS, IR and ^{1}H NMR) data (see Experimental). Their IR spectra showed bands in the region 3433–3185 cm^{-1} due to OH and NH groups and at 1687–1649 cm^{-1} due to the C=O group of the quinazolinone ring residue. Their ^{1}H NMR in DMSO revealed, in each case, two common characteristic signals at δ 7.90 and 10.6 corresponding to the alditol-1-ylidene proton –N=CH– and hydrazone –NH–N=C protons, respectively, in addition to the signals due to the protons of the sugar and heterocyclic ring residues (see Experimental). The signals due to the hydrazone –NH–N=C– and the OH protons of the sugar residue disappeared upon addition of D_2O.

Treatment of each of the aldose hydrazones **6a–c** and **7a–c** with equivalent amount of iron(III) chloride in refluxing ethanol for 30 min and stirring the reaction mixture overnight at room temperature gave, in each case, one crystalline product as evidenced by tlc analysis. Elemental analyses and mass spectra of the products isolated from oxidation of **6a–c** and **7a–c** revealed that each has two hydrogens less than the respective hydrazone. Their ^{1}H NMR spectra, while they showed the aldose proton signals, they revealed the absence of the –N=CH– and hydrazone –NH–N=C proton signals. On the basis of these finding the isolated products were assigned the structure of 1,4-disubstituted[1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-ones **8a–c** and **9a–c**, respectively. To account for the conversion of **6** and **7** into **8** and **9**, respectively**,** it is suggested that the reaction starts with the formation of the respective nitrilimines **I** which undergo *in situ* 1,5-electrocyclisation to form **8** and **9** as end products. This suggested pathway for the studied reactions is reminiscent of other related oxidative cyclisation of aldehyde *N*-heteroarylhydrazones with iron(III) chloride to give the respective fused heterocycles.[21,22]

In contrast to the behaviour of **6a–c** and **7a–c**, when each of the hydrazones **6d** and **6e** was subjected to oxidative cyclisation following the same procedure above, both hydrazones were found to give, one and the same product whose IR spectrum showed the absence of the absorption band at 3500–3200 cm^{-1} due to NH and OH groups. Its ^{1}H NMR spectrum, while it revealed the absence of the signals of the alditol-1-ylidene protons in the region δ 3.3–4.1, it showed a singlet at δ 9.5 assignable to the triazolo proton N–CH=N. Its mass spectrum showed the molecular ion peak at *m/z* 262 (100%) and $M^+ + 2$ and $M^+ + 1$ peaks at *m/z* 264 (12%) and 263 (74%), respectively. Such spectral data indicate that the sugar residue has been eliminated during the reaction. On the basis of these data, the isolated product was assigned the structure of 4-phenyl[1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-one **10**. Similarly, oxidative cyclisation of the hydrazones **7d** and **7e** following the same procedure above gave also one and same compound that was identified on the basis of its elemental and spectral data (see Experimental) as 4-cyclohexyl [1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-one **11**.

The structures of the unexpected products **10** and **11** were further evidenced by comparison with authentic samples prepared by alteranate synthesis. Thus, refluxing each of 2-hydrazino-3-phenylquinazolin-4(3*H*)-one **3** and its 3-cyclohexyl analog **4** with ethyl orthoformate or formic acid, yielded products that proved identical in all respects with **10** and **11**, respectively obtained above. To account for the formation of the products **10** and **11** from oxidative cyclisation of the hydrazones **6c,d** and **7c,d**, respectively, it is suggested that the initially formed acyclo *C*-nucleosides **8c,d** and **9c,d** underwent *in situ* tandem oxidation and decarboxylation under the reaction conditions employed to give **10** and **11**, respectively.

In conclusion, the described synthesis offers an easy and efficient access to the title acyclo *C*-nucleosides. Since the latter acyclo *C*-nucleosides could be used as anti-histaminic drugs, further research in this field is in progress and the results will be reported later.

Experimental

All melting points were determined on an electrothermal Gallenkamp apparatus and are uncorrected. The IR spectra were measured on a Pye-Unicam SP300 instrument in potassium bromide discs. The ^{1}H NMR spectra were recorded in DMSO-d_6 using a Varian Mercury VXR-300 spectrometer. The mass spectra were recorded on a GCMS-Q1000-EX Shimadzu and GCMS 5988-A HP spectrometers, the ionising voltage was 70 eV. Elemental analyses were carried out by the Microanalytical Centre of Cairo University, Giza, Egypt. The starting 2-hydrazino-3-phenylquinazolin-4(3*H*)-one (**3**)[23] and its 3-cyclohexyl analog (**4**)[24] were prepared by hydrazinolysis of the respective 3-substituted-2-thioxo-1,2-dihydroquinazoline-4(3H)-ones **1** and **2** according to literature method.

Synthesis of aldose N-(3-substituted-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazones **6** and **7**: *General method*

To a mixture of 2-hydrazino-3-phenylquinazolin-4(3*H*)-one **3** (1.3 g, 5 mmole) and the appropriate aldose **5** (5 mmol) in ethanol (50 ml), few drops of acetic acid were added and the reaction mixture was refluxed for 2 h then cooled and poured onto ice-water. The precipitated solid was filtered off, washed with water then ethanol and finally crystallised from the appropriate solvent to give the corresponding hydrazone derivative **6**.

Use of 3-cyclohexyl-2-hydrazinoquinazoline **4** in place of **3** in the above procedure afforded the respective hydrazones **7**.

The various hydrazone derivatives **6a–e** and **7a–e** prepared are listed below together with their physical constants and spectral data.

D-Galactose N-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(6a):** White crystals (yield 80%), m.p. 202°C (ethanol). IR (KBr) ν 3613–3200 (NH + OH), 1700 (C=O), 1620 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.3–3.7 (5H, alditol protons congregated with DMSO solvent), 4.1–4.2 (m, 1H, alditol N=C–CH), 4.2–4.7 (m, 5H, 5OH, D_2O exchangable), 7.1–7.9 (m, 10 H, N=CH and 9H, ArH), 10.60 (s, 1H, NH, exchangable). Anal Calcd. for $C_{20}H_{22}N_4O_6$ (414.4): C, 58.0; H, 5.35; N, 13.5. Found: C, 57.8; H, 5.3; N, 13.8%.

D-Mannose N-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(6b):** White crystals (yield 85%), m.p. 228°C (ethanol). IR (KBr) ν 3650–3200 (NH + OH), 1700 (C=O), 1622 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.3–3.6 (5H, alditol protons congregated with DMSO solvent), 4.1–4.2 (m, 1H, alditol N=C–CH), 4.3–4.9 (m, 5H, 5OH, D_2O exchangable), 7.1–7.9 (m, 10 H, N=CH and 9H, ArH), 10.60 (s, 1H, NH, exchangable). Anal Calcd. for $C_{20}H_{22}N_4O_6$ (414.4): C, 58.0; H, 5.35; N, 13.5. Found: C, 57.8; H, 5.4; N, 13.6%.

D-Arabinose N-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(6c):** White crystals (yield 82%), m.p. 162°C (ethanol). IR (KBr) ν 3651–3200 (NH + OH), 1703 (C=O), 1621 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.3–3.6 (4H, alditol protons congregated with DMSO solvent), 4.3–4.8 (m, 4H, 4OH, D_2O exchangable). 4.4–4.5 (m, 1H, alditol N=C–CH), 7.0–7.9 (m, 10 H, N=CH and 9H, ArH), 10.60 (s, 1H, NH, exchangable). Anal Calcd. for $C_{19}H_{20}N_4O_5$ (384.4): C, 59.4; H, 5.2; N, 14.6. Found: C, 59.6; H, 5.3; N, 14.8%.

D-Xylose N-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl)-hydrazone **(6d):** White crystals (yield 84%), m.p. 206°C (ethanol-DMF). IR (KBr) ν 3651–3200 (NH + OH), 1703 (C=O), 1621 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.3–3.5 (4H, alditol protons congregated with DMSO solvent), 4.2–4.3 (m, 1H, alditol N=C–CH), 4.3–5.1 (m, 4H, 4OH, D_2O exchangable), 7.1–7.9 (m, 10 H, N=CH and 9H, ArH), 10.60 (s, 1H, NH, exchangable). MS *m/z* (%): 385 (M^+ + 1, 23), 384 (M^+, 26), 332 (12), 314 (7), 307 (19), 303 (19), 296 (5), 279 (10), 277 (36), 262 (12), 260 (19), 252 (14), 249 (17), 237 (100), 233 (8), 226 (13), 221 (79), 209 (21), 185 (13), 181 (9), 166 (13), 164 (17), 151 (12), 145 (16), 135 (9), 130 (17), 119 (10), 115 (15), 113 (12), 103 (40), 101(18), 91 (52), 90 (28), 88 (10), 82 (7), 76 (8). Anal Calcd. for $C_{19}H_{20}N_4O_5$ (384.4): C, 59.4; H, 5.2; N, 14.6. Found: C, 59.5; H, 5.05; N, 14.4%.

D-Ribose N-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazone (**6e**): White crystals (yield 84%), m.p. 212°C. (ethanol). IR (KBr) ν 3629–3200 (NH + OH), 1703 (C=O), 1621 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.3–3.7 (4H, alditol protons congregated with DMSO solvent), 4.3–4.4 (m, 1H, alditol N=C–CH), 4.3–5.0 (m, 4H, 4OH, D_2O exchangable), 7.1–7.9 (m, 10 H, N=CH and 9H, ArH), 10.60 (s, 1H, NH, exchangable). MS *m/z* (%): 385 (M^+ + 1, 3), 384 (M^+, 6), 360 (4), 358 (4), 293 (66), 276 (7), 263 (23), 236 (100), 208 (10), 206 (9), 178 (5), 145 (20), 118 (21), 92 (33), 77 (49). Anal Calcd. for $C_{19}H_{20}N_4O_5$ (384.4): C, 59.4; H, 5.2; N, 14.6. Found: C, 59.1; H, 5.5; N, 14.6%.

D-Galactose N-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(7a):** White crystals (yield 82%), m.p. 174°C (ethanol). IR (KBr) ν 3650–3200 (NH + OH), 1693 (C=O), 1620 (C=N), cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.1–1.8 (m, 10H, cyclohexyl protons).

3.3–3.7 (5H, alditol protons congregated with DMSO solvent), 4.5–4.6(m, 1H, alditol N=C–CH), 4.1–4.8 (m, 5H, 5OH, D_2O exchangable), 4.9–5.0 (m, 1H, –CH–N, cyclohexyl) 7.0–7.9 (m, 5 H, N=CH and 4H, ArH), 10.40 (s, 1H, NH, exchangable). MS *m/z* (%): 421 (M^+ + 1, 15), 420 (M^+, 22), 405 (7), 394 (8), 393 (15), 392 (47), 379 (13), 377 (11), 365 (9), 363 (13), 351 (22), 342 (10), 333 (11), 327 (19), 320 (23), 311 (13), 309 (25), 306 (13), 301 (6), 293 (11), 278 (7), 271 (16), 248 (11), 244 (15), 238 (12), 233 (11), 228 (22), 195 (6), 190 (11), 186 (25), 177 (9), 161 (100), 158 (8), 153 (6), 144 (8), 131 (10), 122 (6), 104 (5), 91 (14), 89 (10), 87 (5). Anal Calcd. for $C_{20}H_{28}N_4O_6$ (420.5): C, 57.1; H, 6.7; N, 13.3. Found: C, 57.1; H, 6.6; N, 13.5%.

D-Mannose N-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(7b):** White crystals (yield 85%), m.p. 208°C (ethanol-DMF). IR (KBr) ν 3651–3200 (NH + OH), 1671 (C=O), 1626 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.1–1.8 (m, 10H, cyclohexyl protons). 3.3–3.7 (5H, alditol protons congregated with DMSO solvent), 4.2–4.3 (m, 1H, alditol N=C–CH), 4.3–4.5 (m, 5H, 5OH, D_2O exchangable), 4.9–5.0 (m, 1H, –CH–N, cyclohexyl) 7.0–7.9 (m, 5 H, N=CH and 4H, ArH), 10.40 (s, 1H, NH, exchangable). MS *m/z* (%): 422 (M^+ + 2, 26), 421 (M^+ + 1, 42), 403 (12), 342 (8), 339 (15), 322 (13), 312 (17), 311 (32), 301 (13), 283 (14), 282 (21), 270 (10), 269 (39), 249 (10), 244 (100), 231 (14), 227 (8), 204 (8), 202 (29), 200 (10), 187 (22),184 (8), 169 (20), 163 (39), 160 (18), 130 (6), 123 (10), 112 (7), 103 (17), 100 (5), 80 (6), 78 (3). Anal Calcd. for $C_{20}H_{28}N_4O_6$ (420.5): C, 57.1; H, 6.7; N, 13.3. Found: C, 57.4; H, 7.0; N, 13.25%.

D-Arabinose N-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl)hydrazone **(7c)**: White crystals (yield 84%), m.p. 186°C (ethanol-ethyl acetate). IR (KBr) ν 3651–3200 (NH + OH), 1669 (C=O), 1620 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.1–1.8 (m, 10H, cyclohexyl protons). 3.3–3.6 (4H, alditol protons congregated with DMSO solvent), 4.5–4.6 (m, 1H, alditol N=C–CH), 4.3–5.0 (m, 4H, 4OH, D_2O exchangable), 4.9–5.0 (m, 1H, –CH–N, cyclohexyl), 7.1–7.8 (m, 5 H, N=CH and 4H, ArH), 10.50 (s, 1H, NH, exchangable). MS *m/z* (%): 392 (M^+ + 2, 2), 391 (M^+ + 1, 3), 390 (M^+, 2), 373 (3), 309 (16), 291 (6), 269 (17), 243 (15), 217 (20), 199 (6), 187 (63), 161 (100), 147 (10), 145 (31), 132 (9), 120 (15), 117 (8), 92 (10), 77 (4). Anal Calcd. for $C_{19}H_{26}N_4O_5$ (390.4): C, 58.45; H, 6.7; N, 14.35. Found: C, 58.6; H, 6.9; N, 14.3%.

D-Xylose N-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(7d):** White crystals (yield 82%), m.p. 176°C (ethanol). IR (KBr) ν 3651–3200 (NH + OH), 1692 (C=O), 1619 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.2–1.8 (m, 10H, cyclohexyl protons). 3.3–3.6 (4H, alditol protons congregated with DMSO solvent), 4.3–4.5 (m, 1H, alditol N=C–CH), 4.3–4.5 (m, 4H, 4OH, D_2O exchangable), 4.9–5.0 (m, 1H, –CH–N, cyclohexyl), 7.0–7.8 (m, 5 H, N=CH and 4H, ArH), 10.40 (s, 1H, NH, exchangable). Anal Calcd. for $C_{19}H_{26}N_4O_5$ (390.4): C, 58.45; H, 6.7; N, 14.35. Found: C, 58.3; H, 6.4; N, 14.6%.

D-Ribose N-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-2-yl) hydrazone **(7e):** White crystals (yield 87%), m.p. 157°C (ethanol-DMF). IR (KBr) ν 3651–3200 (NH + OH), 1692 (C=O), 1619 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.1–1.8 (m, 10H, cyclohexyl protons). 3.4–3.6 (4H, alditol protons congregated with DMSO solvent), 4.4–4.5 (m, 1H, alditol N=C–CH), 4.3–5.1 (m, 4H, 4OH, D_2O exchangable), 4.9–5.1 (m, 1H, –CH–N, cyclohexyl), 7.1–7.8 (m, 5 H, N=CH and 4H, ArH), 10.40 (s, 1H, NH, exchangable). MS *m/z* (%): 392 (M^+ + 2, 19), 391 (M^+ + 1, 14), 390 (M^+, 19), 373 (10), 311 (6), 309 (38), 291 (12), 269 (38), 259 (6), 247 (7), 242 (8), 231 (21), 217 (45), 215 (8), 213 (31), 203 (9), 200 (10), 187 (100), 177 (17), 162 (67), 147 (23), 145 (35), 140 (11), 134 (7), 119 (47), 92 (14), 90 (29), 81 (11), 77 (5). Anal Calcd. for $C_{19}H_{26}N_4O_5$ (390.4): C, 58.45; H, 6.7; N, 14.35. Found: C, 58.3; H, 6.7; N, 14.6%.

Oxidative cyclisation of aldose N-(3-substituted-4-oxo3,4-dihydro-quinazolin-2-yl)hydrazones **6** and **7:** *General procedure*

To a solution of each of the appropriate aldose hydrazones **6a–c** (2.5 mmole) in ethanol (50 ml) was added a solution of ferric chloride (2 M, 2 ml) and the mixture was refluxed for 30 min, then left overnight at room temperature, then water was added to it. The solid that precipitated was filtered off, washed with water, dried and finally recrystallised from appropriate sovent to give the respective 1-(D-alditol-1-yl)-4-phenyl[1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-ones **8a–c**.

When this procedure is repeated using aldose hydrazones **7a–c** in lieu of **6**, the corresponding 1-(D-alditol-1-yl)-4-cyclohexyl-1,2,4-triazolo[4,3-*a*]quinazolin-5(4*H*)-ones **9a–c**, respectively.

Repetition of the above procedure using **6d** and **6e** yielded one and the same compound identified as **10**. Similarly, when the same procedure was repeated using **7d** and **7e** gave also one product identified as **11**.

The various acyclo-*C*-nucleosides **8a–c**, **9a–c**, together with the two 4-substituted[1,2,4]triazolo[4,3-*a*]quinazolin-5(4H)-ones **10** and **11** prepared are listed below together with their physical constants and spectral data.

1-(D-galacto-*Pentitol-1-yl)-4-phenyl[1,2,4]triazolo*[*4,3-a*]*quinazolin-5(4H)-one* (**8a**): White crystals (yield 62%), m.p. 260°C (ethanol–DMF). IR (KBr) ν 3650–3200 (NH + OH), 1689 (C=O), 1608 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.3–4.2 (5H, alditol protons congregated with DMSO solvent), 4.2–5.8 (m, 5H, 5OH, D_2O exchangable),5.3–5.4 (m, 1H, alditol N=C–CH). 7.6–8.6 (m, 9 H, ArH). Anal Calcd. for $C_{20}H_{20}N_4O_6$ (412.4): C, 58.25; H, 4.9; N, 13.6. Found: C, 58.3; H, 4.7; N, 13.5%.

1-(D-manno-*Pentitol-1-yl)-4-phenyl[1,2,4]triazolo*[4,3-*a*]*quinazolin-5(4H)-one* (**8b**): White crystals (yield 60%), m.p. 264°C (ethanol–DMF). IR (KBr) ν 3623–3200 (NH + OH), 1694 (C=O), 1609 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.4–4.4 (5H, alditol protons congregated with DMSO solvent), 4.3–6.3 (m, 5H, 5OH, D_2O exchangable), 5.1–5.2 (m, 1H, alditol N=C–CH). 7.5–8.3 (m, 9 H, ArH). MS *m/z* (%): 412 (M^+, 1), 350 (3), 321 (6), 320 (7), 291 (65), 289 (7), 262 (25), 235 (49), 237 (8), 206 (9), 178 (5), 144 (21), 129 (10), 116 (15), 103 (53), 102 (54), 89 (43), 76(100). Anal Calcd. for $C_{20}H_{20}N_4O_6$ (412.4): C, 58.25; H, 4.9; N, 13.6. Found: C, 58.2; H, 4.8; N, 13.55%.

1-(D-arabino-*Tetritol-1-yl)-4-phenyl[1,2,4]triazolo*[4,3-*a*]*quinazolin-5(4H)-one* (**8c**): White crystals (yield 57%), m.p. 246°C (ethanol). IR (KBr) ν 3610–3200 (NH + OH), 1687(C=O), 1610 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.3–4.1 (4H, alditol protons congregated with DMSO solvent), 4.3–5.9 (m, 4H, 4OH, D_2O exchangable). 5.3 (m, 1H, alditol N=C–CH), 7.6–8.6 (m, 9 H, ArH). Anal Calcd. for $C_{19}H_{18}N_4O_5$ (382.4): C, 59.7; H, 4.7; N, 14.65. Found: C, 59.6; H, 4.7; N, 14.8%.

1-(D-galacto-*Pentitol-1-yl)-4-cyclohexyl[1,2,4]triazolo*[4,3-*a*] *quinazolin- 5(4H)-one* (**9a**): White crystals (yield 68%), m.p. 224°C (ethanol), IR (KBr) ν 3651–3200 (NH + OH), 1677 (C=O), 1611 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.4–1.9 (m, 10H, cyclohexyl protons). 3.3–4.2 (5H, alditol protons congregated with DMSO solvent), 4.2–5.8 (m, 5H, 5OH, D_2O exchangable), 5.3 (m, 1H, alditol N=C–CH), 5.0 (m, 1H, –CH–N, cyclohexyl) 7.6–8.5 (m, 4 H, ArH), MS *m/z* (%): 420 (M^+ + 2, 85), 419 (M^+ + 1, 21), 418 (M^+, 70), 387 (31), 357 (30), 340 (19), 320 (56), 299 (61), 277 (15), 275 (33), 267 (21), 244 (33), 239 (42), 225 (7), 213 (54), 189 (78), 175 (26), 172 (37), 170 (44), 159 (17), 139 (12), 133 (25), 129 (63), 118 (25), 93 (19), 89 (26), 85 (15), 83 (9). Anal Calcd. for $C_{20}H_{26}N_4O_6$ (418.45): C, 57.4; H, 6.3; N, 13.4. Found: C, 57.6; H, 6.5; N, 13.2%.

1-(D-manno-*Pentitol-1-yl)-4-cyclohexyl-1,2,4-triazolo*[4,3-*a*]*quina-zolin5(4H)-ones* (**9b**)*:* White crystals (yield 66%), m.p. 240°C (ethanol- DMF), IR (KBr) ν 3651–3200 (NH + OH), 1684 (C=O), 1613 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.4–1.9 (m, 10H, cyclohexyl protons). 3.3–4.4 (5H, alditol protons congregated with DMSO solvent), 4.3–6.2 (m, 5H, 5OH, D_2O exchangable), 5.1–5.2 (m, 1H, alditol N=C–CH), 5.0 (m, 1H, –CH–N, cyclohexyl) 7.6–8.5 (m, 4 H, ArH). Anal Calcd. for $C_{20}H_{26}N_4O_6$ (418.45): C, 57.4; H, 6.3; N, 13.4. Found: C, 57.2; H, 6.4; N, 13.2%.

1-(D-arabino-*Tetritol-1-yl)-4-cyclohexyl[1,2,4]triazolo*[4,3-*a*] *quinazolin-5(4H)-one* (**9c**)*:* White crystals (yield 65%), m.p. 244°C (ethanol-ethyl acetate), IR (KBr) ν 3651–3200 (NH + OH), 1690 (C=O), 1612 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.2–1.9 (m, 10H, cyclohexyl protons). 3.4–4.1 (4H, alditol protons congregated with DMSO solvent), 4.3–5.8 (m, 4H, 4OH, D_2O exchangable), 5.2–5.3 (m, 1H, alditol N=C–CH), 5.0 (m, 1H, –CH-N, cyclohexyl), 7.6–8.5 (m, 4 H, ArH). MS *m/z* (%): 390 (M^+ + 2, 11), 389 (M^+ + 1, 12), 388 (M^+, 5), 371 (4), 357 (3), 307 (58), 298 (19), 269 (7), 229 (13), 216 (42), 187 (100), 161 (15), 158 (7), 145 (13), 103 (7), 91 (5), 77 (5). Anal Calcd. for $C_{19}H_{24}N_4O_5$ (388.4): C, 58.75; H, 6.2; N, 14.4. Found: C, 58.75; H, 6.3; N, 14.1%.

4-Phenyl[1,2,4]triazolo[4,3-*a*]*quinazolin-5(4H)-one* **(10)**: White crystals (yield 65%), m.p. 338°C (ethanol). Lit. m.p. 332–334°C [1983BCSJ1227] IR (KBr) ν 1685 (C=O), 1601 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): 7.5–8.2 (m, 9 H, ArH), 9.5 (s, 1H, N–CH=N). MS *m/z* (%): 264 (M^+ + 2, 12), 263 (M^+ + 1, 74), 262 (M^+, 100), 261 (16), 235 (78), 234 (11), 206 (8), 130 (5), 104 (17), 90 (15), 77 (50). Anal Calcd. for $C_{15}H_{10}N_4O$ (262.3): C, 68.7; H, 3.8; N, 21.4. Found: C, 68.3; H, 4.0; N, 21.5%.

4-Cyclohexyl[1,2,4]triazolo[4,3-*a*]*quinazolin-5(4H)-one* (**11**)**:** Pale brown crystals (yield 63%), m.p. 215–217°C (ethanol-water), (Lit. m.p. 211–213°C [2007CBDD158]. IR (KBr) ν 1683 (C=O), 1615 (C=N), cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.1–1.9 (m, 10H, cyclohexyl protons). 4.9–5.0 (m, 1H, –CH–N, cyclohexyl), 7.5–8.2 (m, 4 H, ArH), 9.5 (s, 1H, –N–CH=N, triazol). MS *m/z* (%): 270 (M^+ + 2, 1), 269 (M^+ + 1, 1), 268 (M^+, 4), 188 (13), 187 (100), 158 (9), 133 (3), 131 (5), 118 (2), 103 (7), 90 (8), 77 (4). Anal Calcd. for $C_{15}H_{16}N_4O$ (268.3): C, 67.15; H, 6.0; N, 20.9. Found: C, 67.1; H, 6.2; N, 20.5%.

Alternate synthesis of **10** *and* **11**

The 3-phenyl-2-hydrazinoquinazolin-4(3*H*)-one **3** (1.52 g, 5 mmole) and formic acid (25 ml) was refluxed for 30 h and poured into ice water. The solid that precipitated was filtered off, washed with water, dried and crystallised from ethanol to give **10** in 85% yield, m.p. 338°C (ethanol), (Lit. m.p. 332–334°C).[25]

When the above procedure was repeated using the 3-cyclohexyl-2-hydrazinoquinazolin-4(3*H*)-one **4** in lieu of **3**, the 4-cyclohexyl[1,2,4]triazolo[4,3-*a*]quinazolin-5(4H)-one **11** was obtained in 82% yield, m.p. 215–217°C (ethanol-water) (Lit. m.p. 211–213°C).[3]

2',3',4',5',6'-Penta-O-acetyl-aldehydo-D-mannose[1-acetyl-1-(3-phenyl-4-oxo-quinazolin-2-yl]hydrazone (**11**):

A cold solution of aldose hydrazone (6) (1 mmol) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml). The reaction mixture was stirred for 48 h at room temperature. It was poured onto crushed ice, the product was filtered washed with water, dried and crystallised from ethanol-water**.**

Pale green solid (yield 65%), m.p. 103°C (ethanol-water), IR (KBr) ν 1750 (C=O, OAc), 1698 (C=O quinazoline), 1620 (C=N), cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.6–2.2 (6 s, 18H, NAc and 5OAc). 4.1–4.3 (m, 2H, H5', H6'), 5.1–5.2 (m, 1H, H4'), 5.5–5.6 (m, 2H, H2' and H3'), 5.8–5.9 (m, 1H, H1'), 7.3–8.1 (m, 9 H, ArH). MS *m/z* (%): 329 (8), 313 (12), 305 (20), 301 (9), 263 (100), 235 (29), 221 (14), 212 (5), 145 (7), 119 (7), 104 (11) 90 (20), 77 (28). Anal Calcd. for $C_{19}H_{26}N_4O_5$ (390.4): C, 58.45; H, 6.7; N, 14.35. Found: C, 58.3; H, 6.4; N, 14.6%.

4-Phenyl-1-(1',2',3',4',5'-penta-O-acetyl-D-manno-pentitol-1-yl)-1,2,4-triazolo[4,3-a]quiazolin-5(4H)-one(**12**):

A cold solution of triazolo quinazolinone (7) (1 mmol) in dry pyridine (7 ml) was treated with acetic anhydride (8 ml). The reaction mixture was stirred for 48 h at room temperature. It was poured onto crushed ice, the product was filtered washed with water, dried and crystallised from ethanol-water**.**

White solid (yield 78%), m.p. 194°C (ethanol–water). IR (KBr) ν 1750 (C=O, OAc), 1696 (C=O quinazoline), 1613 (C=N), cm^{-1}. ^1H NMR (DMSO): δ 1.7–2.2 (5 s, 15H, 5OAc). 4.0–4.3 (m, 2H, H5', H6'), 5.1–5.2 (m, 1H, H4'), 5.6–5.8 (m, 2H, H2' and H3'), 6.3–6.4 (m, 1H, H1'), 7.4–8.4 (m, 9 H, ArH). MS *m/z* (%): 624 (M^+ + 2, 4), 623 (M^+ + 1, 7), 622 (M^+, 4), 563 (24), 503 (10), 495 (5), 477 (6), 461 (35), 435 (7), 419 (8), 417 (12), 404 (6), 401 (8), 357 (8) 347 (9), 341 (16), 334(15), 317 (13), 305 (21), 291 (100), 279 (8), 221 (5), 145 (14), 132 (7). Anal Calcd. for $C_{19}H_{26}N_4O_5$ (390.4): C, 58.45; H, 6.7; N, 14.35. Found: C, 58.3; H, 6.4; N, 14.6%

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