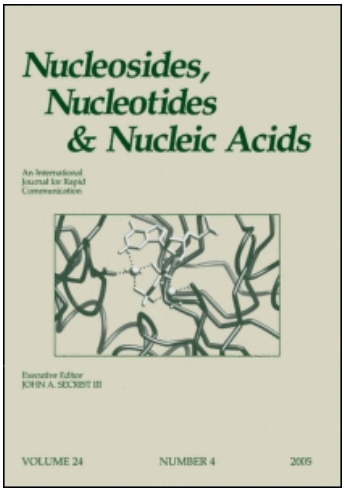

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SYNTHESIS AND ANTIVIRAL EVALUATION OF N-GLYCOSIDES DERIVED FROM 6-AMINO-3-ARYL-2-METHYL-4-(3H)-QUINAZOLINONES

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SYNTHESIS AND ANTIVIRAL EVALUATION OF N-GLYCOSIDES DERIVED FROM 6-AMINO-3-ARYL-2-METHYL-4-(3H)-QUINAZOLINONES

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ABSTRACT

Reaction of monosaccharides (D-glucose, D-galactose, D-xylose or L-arabinose) with 6-amino-3-aryl-2-methyl-4-(3H) quinazolinones (**1a–c**) in boiling methanol yielded the corresponding N-glycopyranosides **3a–c**, **4a–c**, **5a,b** and **6a,b**. The N-glycopyranosides **3a–c**, **4a–c**, **5a,b** and **6a,b** were acetylated with acetic anhydride and pyridine to give the corresponding acetate derivatives **7a–c**, **8a–c**, **9a,b** and **10a,b**. The structures of all these glycosides were assessed by elemental analysis, IR, NMR and mass spectra. Some of these products were tested for anti-cancer and anti-AIDS activity.

Key Words: 6-Amino-3-aryl-2-methyl-4-(3H)-quinazolinones; Glycosyl derivatives; Synthesis; Spectral analysis

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INTRODUCTION

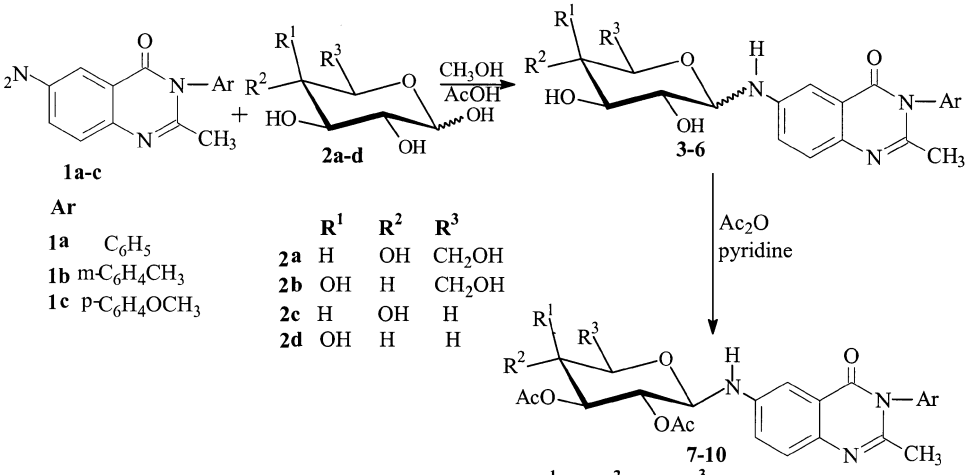
It is well known that quinazolinones in general possess wide medical application as: anti-inflammatory[1,2], vasodilator and antihypertensive[3,4], anticonvulsant[5,6], antibacterial[7,8], anthelmintic[9], CNS stimulance[10], anti-cancer[11], and HIV activity[12,13]. N-glycosides of substituted aniline have been reported to possess anticancer activity[14,15]. In continuation of our work on the synthesis of biologically active compounds[16–23], we report in this article the synthesis of new N-glycosides derived from 6-amino-3-aryl-2-methyl-4(3H)-quinazolinones as shown in Scheme 1, and their screening for these derivatives as anti-HIV activity.

RESULTS AND DISCUSSION

Glycosidation was carried out by the methods usually employed for the synthesis of N-glycosylarylamines[24]. 6-Amino-3-aryl-2-methyl-4-(3H)-quinazolinones[25,26] (**1a–c**) readily react with monosaccharides, namely D-glucose (**2a**), D-galactose (**2b**), D-xylose (**2c**) or L-arabinose (**2d**) in boiling methanol in the presence of glacial acetic acid as a catalyst to yield the corresponding N-glucosides **3a–c**, N-galactosides **4a–c**, N-xylosides **5a,b** or N-arabinosides **6a,b**, respectively, Scheme 1. The structures of glycosides **3–6** were assessed by elemental analysis, IR and NMR (see experimental section). In solution the glycosides **3–6** existed in the form of a mixture of anomers as has often been observed in several N-glycosides of arylamines[27].

Attempts to isolate the individual anomers from these mixtures were unsuccessful. The IR (KBr) spectra of compounds **3–6** showed strong absorption bands in the 3360–3430 cm^{-1} region due to the hydroxyl groups of the sugar residue and the *NH* group of the aglycon, in addition to the characteristic bands of quinazolinone nucleus[28] at 1620, 1570 and 1480 cm^{-1}. The configuration and confirmation of N-glycosides **3–6** were determined by ^1H NMR spectra (see experimental section). The N-glycosides **3a–c** were a mixtures of β- and α-anoers (approximately in a ratio 5:1) in the pyranose form and the $^4C_1$ (D) conformation. The ^1H NMR spectra of compounds **3a–c** in DMSO-d_6 were characterized by two triplets at δ 5.04–5.34 and δ 4.40–4.43. Upon deuterium exchange, the two triplets of the anomeric proton collapsed to two doublets and simultaneously the signal of the 1-*NH* disappeared. Coupling constants ($J_{1',2'}$) for the predominating anomers in compounds **3a–c** (8.1–8.6 Hz) correspond to the diaxial orientation of *H*-1′ and *H*-2′ which indicates the β-configuration and $^4C_1$ (D) conformation. The small value of $J_{1',2'}$ in the minor anomer (4.2–4.6 Hz) is consistent with its α-configuration in the same conformation. This conclusion was confirmed by ^{13}C NMR spectra. The signals at δ 84.9 and δ 81.1 of compound **3a** are attributed to the C-1′ atom of the β-and α-anomers, respectively.

Acetylation of compounds **3a–c**, **4a–c**, **5a,b** and **6a,b** with acetic anhydride in pyridine at room temperature proceed normally and gave 3-aryl-2-methyl-[6-(per-O-acetyl-glycopyranosyl)amino]-4-(3H)-quinazolinone derivatives **7a–c**, **8a–c**, **9a,b** and **10a,b** which were identified on the basis of elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy. The IR spectra of compounds **7–10** exhibited a very strong band at 1749 cm^{-1} assigned to the stretching vibration of the ester carbonyl group. The ^{1}H NMR spectra of compounds **7–9** indicated the β-configuration for these



Ar

1a C_6H_5
1b m-$C_6H_4CH_3$
1c p-$C_6H_4OCH_3$

	R^1	R^2	R^3
2a	H	OH	CH_2OH
2b	OH	H	CH_2OH
2c	H	OH	H
2d	OH	H	H

	Ar	R^1	R^2	R^3
3a	C_6H_5	H	OH	CH_2OH
3b	m-C6H_4CH_3	H	OH	CH_2OH
3c	p-$C_6H_4OCH_3$	H	OH	CH_2OH
4a	C_6H_5	OH	H	CH_2OH
4b	m-$C_6H_4CH_3$	OH	H	CH_2OH
4c	p-$C_6H_4OCH_3$	OH	H	CH_2OH
5a	C_6H_5	H	OH	H
5b	p-$C_6H_4OCH_3$	H	OH	H
6a	C_6H_5	OH	H	H
6b	p-$C_6H_4OCH_3$	OH	H	H
7a	C_6H_5	H	OAc	CH_2OAc
7b	m-$C_6H_4CH_3$	H	OAc	CH_2OAc
7c	p-$C_6H_4OCH_3$	H	OAc	CH_2OAc
8a	C_6H_5	OAc	H	CH_2OAc
8b	m-$C_6H_4CH_3$	OAc	H	CH_2OAc
8c	p-$C_6H_4OCH_3$	OAc	H	CH_2OAc
9a	C_6H_5	H	OAc	H
9b	p-$C_6H_4OCH_3$	H	OAc	H
10a	C_6H_5	OAc	H	H
10b	p-$C_6H_4OCH_3$	OAc	H	H

Scheme 1.

compounds and the $^4C_1$ (D) conformation and the α-configuration for compound **10** and $^4C_1$ (L) conformation.

The spectrum of compound **7a** displays one doublet for the anomeric proton at δ 4.88 ($J_{1',2'}$ 9.0 Hz) while in the spectrum of compound **8a** this doublet appears at δ 4.87 ($J_{1',2'}$ 9.6 Hz) (see Experimental Section). The ^1H NMR (DMSO-d_6) spectra of compounds **10a,b** showed the α-configuration and $^4C_1$(L) conformation, based upon the coupling constant values for **10a** ($J_{1',2'} = J_{2',3'}$ 8.6 Hz, $J_{3',4'}$ 3.0 Hz) which indicate the axial positions for the *H*-1′, *H*-2′ and *H*-3′ and equatorial positions for the proton *H*-4′ (see Experimental Section).

This conclusion was confirmed by ^{13}C NMR spectra. The ^{13}C NMR spectrum of compound **7a** was characterized by a signal at δ 84.0 corresponding to C-1′ of the β-anomer. Four signals attributed to the four acetoxy carbonyl carbons at δ 169.6, 170.0, 170.8 and 171.3 and signals at δ 20.6, 20.7, 20.8 and 20.9 corresponding to the four methyl carbons of the acetoxy groups. The signals at δ 71.1, 72.5, 66.5, 72.9 and 61.9 were assigned to C-2′, C-3′, C-4′, C-5′ and C-6′ of the glucosyl residue, respectively. The quinazolinone signals at δ 151.3, 161.3, 121.6, 108.1, 143.2, 123.2, 128.0, 130.2 can be attributed to the C-2, C-4, C-4a, C-5, C-6, C-7 C-8 and C-8a, respectively. Signals for the 3-phenyl group lie at δ 138.0, 124.7, 129.2 and 128.0, corresponding to the respective a, b, c and d aromatic carbon atoms.

The structures of acetylated compounds **7–10** were confirmed by mass spectrometry (see Experimental Section). In the mass spectrum of compound **7b**, the molecular ion was observed at m/z 595 (74%) and the loss of the sugar moiety produced m/z 308 (3%). Direct cleavage of the glycosidic bond produced m/z 265 (base+1) (12%) and 331 (sugar moiety (2%), such phenomena are common in reference mass spectra of N-glycosides[29].

Compounds **5b**, **7a**, **8c** and **8a** were tested as inhibitors of the L-1210 leukemia in mice and none of them showed significant anticancer activity. These compounds were but tested "*in vitro*" as inhibitors of the HIV virus, but none of these compounds showed anti-AIDS activity. These tests was carried out at the National Cancer Institute (NCI) according to the method reported in literature[30].

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded with a UNICAM SP. 1200 spectrophotometer using pellet technique KBr discs. Microanalyses were performed in Faculty of Science, Cairo University, Cairo, Egypt. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker AC spectrometer (400 MHz) in DMSO-d_6 and $CDCl_3$, shifts are expressed in δ values. The mass spectral data were obtained with micro mass spectrometer

model 7070F at of 70 ev and an inlet temperature of 90 °C. All analytical samples were tested by thin layer chromatography which was performed on EM silica gel 60 F_{254} sheets (0.2 mm). Compounds **1a–c** were prepared as reported in the literature[25,26].

General Procedure for the Synthesis of 3-Aryl-2-methyl-6- [(D-glucopyranosyl) amino]-4-(3H)-quinazolinone Derivatives (3a–c)

A mixture of compounds **1a–c** (0.01 mole) and D-glucose (**2a**, 0.01 mole) and glacial acetic acid (2.2 ml) in methanol (40 ml) was heated at reflux (TLC-monitored). Methanol was then evaporated under vacuum to one-third of its volume, kept at room temperature and the precipitate was then filtered off, dried and crystallized from methanol.

- **Compound 3a:** Yield, 65%, m.p. 128–30 °C, IR (KBr); 3360–3430 (*NH*, *OH*) and 1670 cm^{-1} (CO of quinazolinone); ^{1}H NMR (DMSO-d_6): δ 2.06 (s, 3*H*, 2-CH_3); 4.43 (t, 1*H*, β *H*-1′, $J_{1',2'}$ 8.5 Hz); 5.04 (t, 1*H*, α *H*-1′, $J_{1',2'}$ 4.2 Hz); 3.21–5.80 (m, 6*H*, *H*-2′, *H*-3′, *H*-4′, *H*-5′, *H*-6′, *H*-6″); 6.80 (s, 1H, *NH* disappeared with D_2O); 7.20–7.55 (m, 8*H*, Ar-H); ^{13}C NMR (DMSO-d_6) for aglycone: δ 150.7 (C-2); 159.8 (C-4); 121.5 (C-4a); 105.3 (C-5); 145.5 (C-6); 122.4 (C-7); 127.2 (C-8); 134.5 (C-8a); 138.8 (C-1 of Ph); 129.3 (2C, C-2,6 of Ph); 128.4 (2C, C-3,5 of Ph); 128.9 (C-4 of Ph); 21.4 (2-CH_3); for β-anomer: 84.9 (C-1′); 72.89 (C-2′); 77.22 (C-3′); 69.89 (C-4′); 77.50 (C-5′); 60.73 (C-6′); for α-anomer: 81.1 (C-1′); 70.9 (C-2′); 71.5 (C-3′); 70.1 (C-4′); 72.2 (C-5′); 60.6 (C-6′). Anal. Calcd for $C_{21}H_{23}O_6N_3$: C, 61.02; H, 5.61; N, 10.1. Found: C, 60.90; H, 5.47; N, 10.11.
- **Compound 3b:** Yield, 50%, m.p. 170–72 °C, IR (KBr): 3348–3405 (*NH*, *OH*) and 1664 cm^{-1} (CO of quinazolinone); ^{1}H NMR (DMSO-d_6): δ 2.53 (s, 3H, 2-CH_3); 2.57 (s, 3*H*, *m*-CH_3); 4.42 (t, β *H*-1′, $J_{1',2'}$ 8.1 Hz); 5.32 (t, 1*H*, α *H*-1′, $J_{1',2'}$ 4.6 Hz); 3.15–5.13 (m, 6*H*, *H*-2′, *H*-3′, *H*-4′, *H*-5′, *H*-6′, *H*-6″); 6.72 (s, 1H, *NH* disappeared with D_2O); 7.16–7.38 (m, 7H, Ar-H); ^{13}C NMR (DMSO-d_6): For aglycone: δ 149.3 (C-2); 161.7 (C-4); 121.0 (C-4a); 106.2 (C-5); 145.9 (C-6); 121.7 (C-7); 127.2 (C-8); 139.2 (C-8a); 138.2 (C-1 of Ph); 128.5 (C-2 of Ph); 139.5 (C-3 of Ph); 128.3 (C-4 of Ph); 127.1 (C-5 of Ph), 128.7 (C-6 of Ph); 23.4 (2-CH_3); 23.5 (*m*-CH_3), for β-anomer; 84.9 (C-1′); 73.0 (C-2′); 77.2 (C-3′); 70.0 (C-4′); 77.5 (C-5′); 60.7 (C-6′). For α-anomer: 80.8 (C-1′); 70.5 (C-2′); 71.8 (C-3′); 70.2 (C-4′); 72.2 (C-5′); 61.1 (C-6′). Anal. Calcd for $C_{22}H_{25}O_6N_3$: C, 61.86; H, 5.95; N, 9.84. Found: C, 61.63; H, 5.89; N, 9.73.
- **Compound 3c:** Yield 60% m.p. 105–07 °C. IR (KBr); 3270–3400 (*NH*, *OH*) and 1680 cm^{-1} (CO of quinazolinone); ^{1}H NMR (DMSO-d_6): δ 2.09 (s 3*H*, 2-CH_3); 3.80 (s, 3*H*, *p*-OCH_3); 4.40 (t, β *H*-1′, $J_{1',2'}$

8.6 Hz); 5.34 (t, 1*H*-1′, α *H*-1′, $J_{1',2'}$ 4.4 Hz); 3.05–5.42 (m, 6*H*-1′, *H*-2′, *H*-3′, *H*-4′, *H*-5′, *H*-6′, *H*-6″); 6.68 (s, 1*H*, *NH* disappeared with D_2O) 7.10–7.43 (m, 7H, Ar-H). Anal. Calcd for $C_{22}H_{24}O_7N_3$: C, 59.59; H, 5.64; N, 9.48. Found: C, 59.43; H, 5.52; N, 9.37.

3-Aryl-2-methyl-6-[(D-galactopyranosyl)amino]-4-(3H)-quinazolinone Derivatives (4a–c)

Compounds **4a–c** were prepared by the same method as compounds **3a–c** using (0.01 mole each) of compounds **1a–c** and D-galactose (**2b**).

- **Compound 4a:** Yield 70%; m.p. 180–82 °C: IR (KBr): 3365–3420 (*NH*, *OH*) and 1667 cm^{-1} (CO of quinazolinone); Anal. Calcd for $C_{21}H_{23}O_6N_3$: C, 61.02; H, 5.61; N, 10.17. Found: C, 60.82; H, 5.39; N, 10.09.
- **Compound 4b:** Yield, 65%; m.p. 169–70 °C: IR (KBr): 3340–3400 (*NH*, *OH*) and 1669 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{22}H_{25}O_6N_3$: C, 61.86; H, 5.95; N, 9.84. Found: C, 61.58; H, 5.68; N, 9.70.
- **Compound 4c:** Yield, 75%; m.p. 140–42 °C: IR (KBr): 3370–3405 (*NH*, *OH*) and 1669 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{22}H_{25}O_7N_3$: C, 59.59; H, 5.64; N, 9.48. Found: C, 59.33; H, 5.42; N, 9.27.

3-Aryl-2-methyl-6-[(D-xylopyranosyl)amino]-4-(3H)-quinazolinone Derivatives (5a,b)

Compounds **5a,b** were obtained as for **3a–c** using 0.01 mole each of **1a,c** and D-xylose (**2c**).

- **Compound 5a:** Yield 55%; m.p. 138–39 °C: IR (KBr): 3342–3390 (*NH*, *OH*) and 1660 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{20}H_{21}O_5N_3$: C, 62.66; H, 5.48; N, 10.79. Found: C, 62.38; H, 5.18; N, 10.28.
- **Compound 5b:** Yield, 53%; m.p. 95–97 °C: IR (KBr): 3340–3381 (*NH*, *OH*) and 1664 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{21}H_{23}O_6N_3$: C, 61.02; H, 5.57; N, 10.17. Found: C, 60.75; H, 5.29; N, 10.02.

3-Aryl-2-methyl-6-[(L-arabinopyranosyl)amino]-4-(3H)-quinazolinone Derivatives (6a,b)

Compounds **6a,b** was obtained similarly from compounds **1a,c** (0.01 mole each) and **L**-arabinose (**2d**).

- **Compound 6a:** Yield 60%; m.p. 216–17 °C: IR (KBr): 3340–3400 (*NH*, *OH*) and 1669 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{20}H_{21}O_5N_3$: C, 62.66; H, 5.48; N, 10.79. Found: C, 62.16; H, 5.10; N, 10.47.
- **Compound 6b:** Yield, 63%; m.p. 135–136 °C: IR (KBr): 3330–3420 (*NH*, *OH*) and 1668 cm^{-1} (CO of quinazolinone). Anal. Calcd for $C_{21}H_{23}O_6N_3$: C, 61.02; H, 5.57; N, 10.17. Found: C, 60.88; H, 5.11; N, 10.00.

General Procedure for the Synthesis of 3-aryl-2-methyl-6-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)amino]-4-(3H)-quinazolinones (7a–c)

To a solution of 0.003 mole of compounds **3a–c** in anhydrous pyridine (35 ml), redistill acetic anhydride (25 ml) was added. The reaction mixture was left at room temperature (TLC-monitoring). The solution was then poured on ice-water (600 ml) and the formed precipitate was filtered off, washed with water and dissolved in ethanol. The solvent was evaporated in vacuum and recrystallized from ethanol and water to give compounds **7a–c**.

- **Compound 7a:** Yield 70%; m.p. 145 °C: IR (KBr): 3350 (*NH*); 1748 (CO acetoxy) and 1680 cm^{-1} (CO of quinazolinone); ^{1}H NMR ($CDCl_3$): δ 2.04–2.07 (2s, 12*H*, 4 $COCH_3$); 2.25 (s, 3*H*, 2-CH_3); 4.88 (t, 1*H*, β *H*-1′ $J_{1',2'}$ 9.0 Hz); 5.08 (t, 1*H*, *H*-2′, $J_{2',3'}$ 9.2 Hz); 5.38 (t, 1*H*, *H*-3′, $J_{3',4'}$ 9.4 Hz); 5.14 (t, 1*H*, *H*-4′, $J_{4',5'}$ 10.2 Hz); 3.88 (m, 1*H*, *H*-5′, $J_{5',6'}$ 5.3 Hz); 4.17 (dd, 1*H*, *H*-6′); 4.28 (dd, 1*H*, *H*-6″); 5.10 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 8.8 Hz); 7.11–7.55 (m, 8*H*, Ar-H); ^{13}C NMR ($CDCl_3$): for aglycone: δ 151.3 (C-2); 161.3 (C-4); 121.6 (C-4a); 108.1 (C-5); 143.2 (C-6); 123.2 (C-7); 128.0 (C-8); 130.2 (C-8a); 138.0 (C-1 of Ph); 130.0 (2C, C- 2,6 of Ph); 128.0 (2C, C-3,5 of Ph); 129.2 (C-4 of Ph); 24.1 (2-CH_3); for sugar: 84.0 (β C-1′); 71.1 (C-2′); 72.5 (C-3′); 68.5 (C-4′); 72.9 (C-5′); 61.9 (C-6′); 20.6, 20.8 (4 $CO\underline{C}H_3$); 169.6, 170.0, 170.8, 171.3 ($\underline{C}OCH_3$). Mass spectrum: *m/z* 604 (6, M+Na), 582 (100, M+1), 581 (34, M^+), 250 (20, B^+), 2.61 (10, B+1), 331 (5, glucosyl moiety, S^+). Anal. Calcd for $C_{29}H_{31}O_{10}N_3$: C, 59.90, H, 5.33; N, 7.23. Found: C, 59.90; H, 5.07; N, 7.00.
- **Compound 7b:** Yield, 76%; m.p. 147 °C: IR (KBr): 3332 (*NH*); 1746 (CO acetoxy) and 1684 cm^{-1} (CO of quinazolinone) ^{1}H NMR ($CDCl_3$) δ 2.04–2.08 (2s, 12*H*, 4 $COCH_3$); 2.21 (s, 3*H*, 2-CH_3); 2.41 (s, 3*H*, *m*-CH_3); 4.87 (t, β *H*-1′, $J_{1',2'}$ 9.6 Hz); 5.09 (t, 1*H*, *H*-2′, $J_{2',3'}$ 9.3 Hz); 5.36 (t, 1*H*, *H*-3′, $J_{3',4'}$ 9.5 Hz); 5.16 (t, 1*H*, *H*-4′, $J_{4',5'}$ 10.1 Hz); 3.86 (m, 1*H*, *H*-5′, $J_{5',6'}$ 6.1 Hz); 4.16 (dd, 1*H*, *H*-6′, $J_{5',6''}$ 2.0 Hz); 4.29 (dd, 1*H*, *H*-6″); 5.12 (s, 1H, *NH* disappeared with D_2O,

$J_{1',NH}$ 8.9 Hz); 7.09–7.55 (m, 7*H*, Ar-H); ^{13}C NMR ($CDCl_3$): for aglycone: δ 151.4 (C-2); 161.2 (C-4); 121.6 (C-4a); 108.2 (C-5); 143.1 (C-6); 123.1 (C-7); 128.0 (C-8); 130.0 (C-8a); 137.9 (C-1 of Ph), 129.7 (C-2 of Ph); 141.3 (C-3 of Ph); 128.9 (C-4 of Ph); 128.5(C-5 of Ph); 123.1 (C-6 of Ph); 24.1(2-CH_3); 29.7 (*m*-CH_3); for sugar: 84.1 (β C-1′); 71.2 (C-2′); 72.6 (C-3′); 68.5 (C-4′); 72.9(C-5′); 61.9 (C-6′); 20.4, 20.6, 20.8 ($CO\underline{C}H_3$); 169.6, 170.0, 171.3 ($\underline{C}OCH_3$); Mass spectrum: *m/z* 618 (6, M+Na), 596 (100, M+1), 595 (33, M^+); 264 (11, B^+), 265 (6, B+1), 293 (21, B+26), 331 (5, glucosyl moiety, S^+). Anal. Calcd for $C_{30}H_{33}O_{10}N_3$: C, 60.50; H, 5.55; N, 7.06: Found: C, 60.20; H, 5.23; N, 6.74.

- **Compound 7c:** Yield, 80%; m.p. 180 °C: IR (KBr): 3309 (*NH*); 1752 CO acetoxy) and 1674 cm^{-1} (CO of quinazolinone); ^{1}H NMR ($CDCL_3$); δ 2.04–2.07 (4s, 12*H*, 4 $CO\underline{C}H_3$); 2.20 (s, 3*H*, 2-CH_3); 3.91 (s, 3*H*, p-OCH_3); 4.88 (t, β *H*-1′, $J_{1',2'}$ 9.2 Hz); 5.10 (t, 1*H*, *H*-2′); 5.37 (t, 1*H*, *H*-3′); 5.17 (t, 1*H*, *H*-4′); 3.88 (m, 1*H*, *H*-5′); 4.16 (dd, 1*H*, *H*-6′); 4.30 (dd, 1*H*, *H*-6″), 5.11 (s, 1*H*, *NH* disappeared with D_2O); 7.08–7.56 (m, 7*H*, Ar-H); Mass spectrum: *m/z* 612 (41, M+1). Anal. Calcd for $C_{30}H_{33}O_{11}N_3$: C, 58.92; H, 5.40; N, 7.87. Found: C, 58.38; H; 5.13; N, 7.29.

3-Aryl-2-methyl-6-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)amino]-4 (3H)-quinazolinones (8a–c):

Compound **8a–c** were prepared from compounds **4a–c** in the same manner as compounds **7a–c**.

- **Compound 8a:** Yield, 80% m.p. 130 °C: IR (KBr): 3352 (*NH*), 1749 (CO acetoxy) and 1658 cm^{-1} (CO of quinazolinone), ^{1}H NMR ($CDCl_3$): δ 2.05–2.10 (2s, 12*H*, 4$COCH_3$); 2.19 (s, 3*H*, 2-CH_3); 4.87 (t, 1*H*, β *H*-1′, $J_{1',2'}$ 8.7 Hz); 5.72 (t, 1*H*, *H*-2′, $J_{2',3'}$ 9.2 Hz); 5.20 (t, 1*H*, *H*-3′, $J_{3',4'}$ 3.5 Hz); 5.47 (t, 1*H*, *H*-4′, $J_{4',5'}$ 2.6 Hz); 4.08 (m, 1*H*, *H*-5′, $J_{5',6'}$ 6.4 Hz); 4.15 (dd, 1*H*, *H*-6′, $J_{5',6''}$ 6.4 Hz); 4.13 (dd, 1*H*, *H*-6″), 5.22 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 8.8 Hz); 7.13–7.50 (m, 8*H*, Ar-H); ^{13}C NMR ($CDCl_3$): for aglycone: δ 151.2 (C-2); 162.1 (C-4); 121.6 (C-4a); 108.3 (C-5); 143.3 (C-6); 122.9 (C-7); 128.0 (C-8); 141.2 (C-8a); 138.0 (C-1 of Ph); 129.9 (2C, C-2,6 of Ph); 128.0 (2C, C-3,5 of Ph); 129.2 (C-4 of Ph);); 24.1 (2-CH_3); for sugar: 84.3 (β C-1′); 68.7 (C-2′); 71.0 (C-3′); 67.3 (C-4′); 71.4 (C-5′); 61.4 (C-6′); 20.6, 20.6; 20.9 ($CO\underline{C}H_3$); 169.9, 170.2, 170.5, 171.5 ($\underline{C}OCH_3$). Mass spectrum: *m/z* 582(100, M +1); 581 (70, M^+), 251 (17, B+1), 331 (7, galactosyl moiety S^+), 271 (1.2, 331-AcOH), 229 (1, 271-CH_2CO), 187 (2, 229 - Ac^+), 127 (7, 187-AcOH). Anal. Calcd for

$C_{29}H_{31}O_{10}N_3$: C, 59.82; H, 5.33; N; 7.23. Found: C, 59.28; H, 5.19; N, 6.80.

- **Compound 8b:** Yield, 86% m.p. 160 °C: IR (KBr): 3330 (*NH*), 1752 (CO acetoxy) and 1680 cm^{-1} (CO of quinazolinone), Mass spectrum *m/z* 596 (27, M+1). Anal. Calcd for $C_{30}H_{33}O_{10}N_3$: C, 60.50; H, 5.55; N, 7.06. Found: C, 60.19; H, 5.19; N; 6.80.
- **Compound 8c:** Yield, 89% m.p. 145 °C: IR (KBr): 3310 (*NH*), 1736 (CO acetoxy) and 1671 cm^{-1} (CO of quinazolinone), Mass spectrum *m/z* 612 (27, M+1). Anal. Calcd for $C_{30}H_{33}O_{11}N_3$: C, 58.92; H, 5.40; N, 6.87. Found: C, 58.49; H, 5.05; N, 6.38.

3-Aryl-2-methyl-6-[(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)amino]-4 (3H)-quinazolinones (9a–c)

Compounds **9a–c** were prepared from **5a,b** in the same manner as for **7a–c**.

- **Compound 9a:** Yield, 70% m.p. 140 °C: IR (KBr): 3330 (*NH*), 1752 (CO acetoxy) and 1673 cm^{-1} (CO of quinazolinone), ^{1}H NMR ($CDCl_3$): δ 2.04–2.06 (3s, 9*H*, $3COCH_3$); 2.19 (, 3*H*, 2-CH_3); 4.82 (t, 1*H*, β *H*-1′, $J_{1',2'}$ 8.8 Hz); 5.07 (t, 1*H*, *H*-2′, $J_{2',3'}$ 9.1 Hz), 5.35 (t, 1*H*, *H*-3′, $J_{3',4'}$ 9.5 Hz); 5.09 (q, 1*H*, *H*-4′, $J_{4',5a}$ 9.6 Hz); 4.09 (t, 1*H*, *H*-5a, $J_{4',5e}$ 5.7 Hz); 3.47 (t, 1*H*, *H*-5e, $J_{5a,5e}$ 11.6 Hz); 5.00 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 8.1 Hz), 7.11–7.55 (m, 8*H*, Ar-H); ^{13}C-NMR ($CDCl_3$): for aglycone: δ 151.1 (C-2); 162.3 (C-4); 122.8 (C-4a); 108.1 (C-5); 143.4 (C-6); 130.0 (C-7); 128.0 (C-8); 137.97 (C-8); 141.2 (C-8a); 137.8 (C-1 of Ph); 129.7 (2C, C-2,6 of Ph); 128.5 (2C, C-3,5 of Ph); 128.8 (C-4 of Ph);); 24.1(2-CH_3); for sugar: 84.3 (β C-1′); 69.1 (C-2′); 68.2 (C-3′); 70.7(C-4′); 64.6 (C-5′); 20.8, 20.7; 20.7 ($CO\underline{C}H_3$); 169.2, 170.0, 171.2, ($3\underline{C}OCH_3$). Mass spectrum: *m/z* 509 (100, M+1); 508 (58, M^+), 251 (7, B+1), 279 (32, B+29), 293 (8, B+43), 259 (3, xylosyl moiety, S^+). Anal. Calcd for $C_{26}H_{27}O_8N_3$: C, 61.95; H, 5.54; N, 8.25. Found: C, 61.49; H, 5.19; N, 8.09.
- **Compound 9b:** Yield, 74% m.p. 165 °C: IR (KBr): 3338 (*NH*), 1748 (CO acetoxy) and 1679 cm^{-1} (CO of quinazolinone), ^{1}H NMR ($CDCl_3$): δ 2.04–2.05 (3s, 9*H*, $3COCH_3$); 2.21 (s, 3*H*, 2-CH_3); 4.81 (t, 1*H*, β*H*-1′, $J_{1',2'}$ 8.8 Hz); 5.03, (q, 1*H*, *H*-2′, $J_{2',3'}$ 9.2 Hz); 5.35 (t, 1*H*, *H*-3′, $J_{3',4'}$ 9.5 Hz); 5.06 (q, 1*H*, *H*-4′, $J_{4',5a}$ 9.8 Hz); 4.08 (t, 1*H*, *H*-5′a, $J_{4',5e}$ 5.6 Hz); 3.46 (t, 1*H*, *H*-5′e); 5.05 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 8.4 Hz), 7.03–7.57 (m-7 *H*, Ar-H). Mass spectrum: *m/z* 540 (100, M+1); 539 (65, M^+), 281 (20, B+1); 309 (42, B+29), 323 (5, B+ CH_3, CO), 259 (5,

xylosyl moiety, S^+), 199 (7, 259-AcOH) 139 (4, 199-AcOH). Anal. Calcd for $C_{27}H_{29}O_8N_3$: C, 61.42; H, 5.43; N, 8.03. Found: C, 61.28; H, 5.19; N, 7.80.

3-Aryl-2-methyl-6-[(2,3,4-tri-O-acetyl-α-L-arabinopyranosyl)amino]-4 (3H)-quinazolinones (10a,b):

A mixture of compounds **6a,b** (0.003 mole) in anhydrous pyridine (32 ml) and acetic anhydride (22 ml) was treated as described for the preparation of compounds **7a,b**.

- **Compound 10a:** Yield 80%; m.p. 144 °C: IR (KBr): 3330 (*NH*); 1752 (CO acetoxy) and 1683 cm^{-1} (CO of quinazolinone); ^1H NMR ($CDCl_3$) δ 2.04–2.11 (3s, 9*H*, 3CO<u>C</u>H_3); 2.19 (s, 3*H*, 2-CH_3); 4.81 (t, 1*H*, α *H*-1′, $J_{1',2'}$ 8.6 Hz); 5.19 (q, 1*H*, *H*-2′, $J_{2',3'}$ 8.6 Hz); 5.38 (t, 1*H*, *H*-3′, $J_{3',4'}$ 3.0 Hz); 5.28 (q, 1*H*, *H*-4′); 4.01 (t, 1*H*, *H*-5′e); 3.79 (t, 1*H*, *H*-5′a); 5.13 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 7.5 Hz); 7.10–7.55 (m, 8*H*, Ar-H); ^{13}C NMR ($CDCl_3$): for aglycone: δ 151.1 (C-2); 162.2 (C-4); 121.6 (C-4a); 108.1 (C-5); 143.37 (C-6); 123.02 (C-7); 129.00 (C-8); 141.16 (C-8a); 137.9 (C-1 of Ph); 129.9 (2C, C-2,6 of Ph); 128.0 (2C, C-3,5 of Ph); 129.2 (C-4 of Ph);); 29.7 (2-CH_3); for sugar: 84.5 (α C-1′); 69.0 (C-2′); 68.3 (C-3′); 70.7 (C-4′); 64.7 (C-5′); 20.9, 20.9, 20.7 (CO<u>C</u>H_3); 169.9, 170.3, 171.5, (3<u>C</u>OCH_3). Mass spectrum: *m/z* 509 (100, M+1). Anal. Calcd for $C_{26}H_{27}O_8N_3$: C, 61.30; H, 5.30; N, 8.25. Found: C, 61.09; H, 5.13; N, 8.18.
- **Compound 10b:** Yield 83%; m.p. 200 °C: IR (KBr): 3330 (*NH*); 1751 (CO acetoxy) and 1680 cm^{-1} (CO of quinazolinone); ^1H NMR ($CDCl_3$): δ 2.04–2.10 (3s, 9*H*, 3$COCH_3$); 2.21 (s, 3*H*, 2-CH_3); 4.83 (t, 1*H*, a *H*-1′, $J_{1',2}$ 8.4 Hz); 5.19 (d, 1*H*, *H*-2′, $J_{2',3'}$ 8.4 Hz); 5.38 (d, 1*H*, *H*-3′, $J_{3',4'}$ 3.0 Hz); 5.27 (t, 1*H*, *H*-4′); 4.00 (d, 1*H*, *H*-5′a); 3.79 (d, 1*H*, *H*-5′e); 5.14 (s, 1*H*, *NH* disappeared with D_2O, $J_{1',NH}$ 7.5 Hz); 7.03–7.55 (m, 7H, Ar-H). Mass spectrum: *m/z* 540 (100, M +1), 539 (58, M^+); 281 (25, B+1), 309 (54, B+29), 223 (7, B+CH_3CO), 25(13, arabinosyl moiety, S^+). Anal. Calcd for $C_{27}H_{29}O_8N_3$: C, 61.95; H, 5.54; N, 8.25. Found: C, 61.47; H, 5.11; N, 8.09.

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