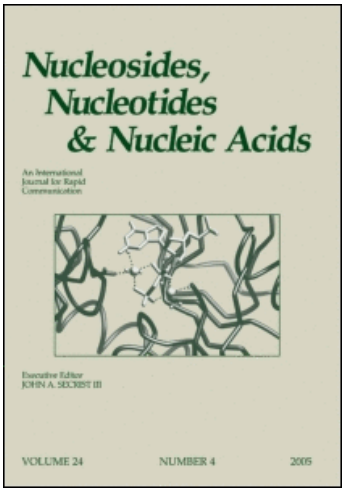

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Synthesis, Conformational and Configurational Studies of Some New Acetylated Glycosides of 2-Thio-3-aryl-4(3H)-quinazolinones, Their Thiono and 3,1-Benzothiazin-2,4-dithione

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NUCLEOSIDES & NUCLEOTIDES, 14(9&10), 1985-1996 (1995)

SYNTHESIS, CONFORMATIONAL AND CONFIGURATIONAL STUDIES OF SOME NEW ACETYLATED GLYCOSIDES OF 2-THIO-3-ARYL-4(3H)-QUINAZOLINONES, THEIR THIONO AND 3,1-BENZOTHIAZIN-2,4-DITHIONE.

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ABSTRACT

A series of some new acetylated S-glycosides of 2-thioxoquinazolin-4-ones, their thiono analogues and 3,1-benzothazin-2,4-dithione derivatives, including a D-glucose and a D-galactose derivatives and a D-xylose, and an L-arabinose derivatives have been synthesized. The conformation and configuration of these carbohydrate derivatives were determined by analysing their ^{1}H and ^{13}C NMR chemical shifts and coupling constants. The biological activity of these compounds has been studied.

Key words

4(3H)-Quinazolinone, 4(3H)-quinazolinethione, 3,1-benzothiazin-2,4-dithione, glycosyl derivatives.

INTRODUCTION

4-(3H)-Quinazolinones with a wide spectrum of biological activities are known.[1] Several derivatives are patented antihypertensive,[2] antifibrillatory,[2] choleretic,[2] antiphlogistic,[3] ammoebicidal,[4] antifungal[5] and bactericidal[6] agents. They have also been successfully tested as CNS depressants,[7] muscle relaxants[8] and antiinflammatory agents.[9] To the best of our knowledge, glycosyl derivatives of 2-thio-3-aryl-4(3H)-quinazolinones, their thiono analogues and 3,1-benzothiazin-2,4-dithione have not previously been described. We now report the synthesis of some new acetylated glycosides of 2-thio-3-aryl-4(3H)-quinazolinones and of 3,1-benzothiazin-2,4-dithione.

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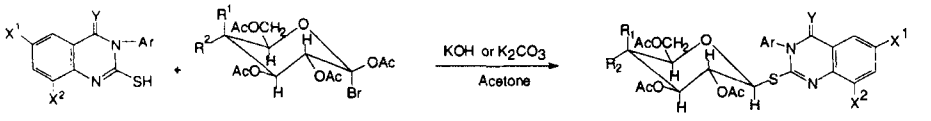
RESULTS AND DISCUSSION

6,8-Disubstituted 3-aryl-2-thio-4(3H)-quinazolinones[10] and quinazolinethione[10] (**1a-f**) readily react with tetra-O-acetyl-α-D-glucopyranosyl bromide (**2**) and with tetra O-acetyl-α-D-galactopyranosyl bromide (**3**) in the presence of potassium hydroxide or potassium carbonate in acetone to yield the corresponding S-glucosides **4a-f** and S-galactosides **5a-d**, respectively.



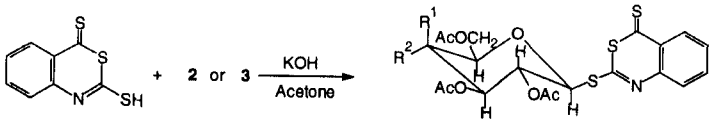
1a-f

2 R^1 = H R^2 = OAc
3 R^1 = OAc R^2 = H

	X^1	X^2	Y	Ar	R^1	R^2
4a	H	H	O	C_6H_5	H	OAc
4b	Br	H	O	C_6H_5	H	OAc
4c	H	H	O	$C_6H_4CH_3$-p	H	OAc
4d	Br	Br	O	C_6H_5	H	OAc
4e	H	H	S	C_6H_5	H	OAc
4f	Br	H	S	C_6H_5	H	OAc
5a	H	H	O	C_6H_5	OAc	H
5b	Br	H	O	C_6H_5	OAc	H
5c	H	H	O	$C_6H_4CH_3$-p	OAc	H
5d	H	H	S	C_6H_5	OAc	H

Scheme 1

Our interest also extended to the investigation of the reaction of 3,1-benzothiazin-2,4-dithione (**6**)[10,11] with **2** or **3** under the conditions described for **1a-e** and gave 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylthio)-3,1-benzothiazin-4-thione (**7a**) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosylthio)-3,1-benzothiazin-4-thione (**7b**) respectively.



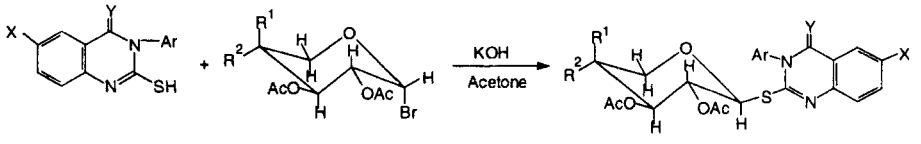
6

	R^1	R^2
7a	H	OAc
7b	OAc	H

Scheme 2

The last example is the reaction of 6-substituted 3-aryl-2-thio-4(3H)-quinazolinones (**1a-c**) and 2-thio-3-phenyl-4(3H)-quinazolinethione (**1e**) with freshly prepared 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide (**8**) or with 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide (**9**) in the presence of potassium hydroxide in acetone

which furnished the S-xyloside derivatives **10a-d** and the S-arabinoside derivatives **11a-c**, respectively.



1a-c,e

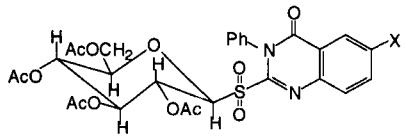
8 R^1 = H R^2 = OAc
9 R^1 = OAc R^2 = H

	X	Y	Ar	R^1	R^2
10a	H	O	C_6H_5	H	OAc
10b	Br	O	C_6H_5	H	OAc
10c	H	O	$C_6H_4CH_3$-p	H	OAc
10d	H	S	C_6H_5	H	OAc
11a	H	O	C_6H_5	OAc	H
11b	Br	O	C_6H_5	OAc	H
11c	H	S	C_6H_5	OAc	H

Scheme 3

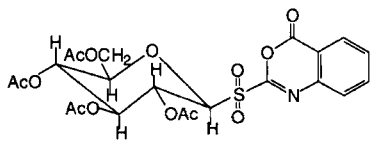
Thin layer chromatography in the system A or system B proves that a single unique compound was produced, the structure of which was demonstrated by elemental analysis, UV, IR and NMR spectroscopy.

Evidence for the attachment of the sugar moiety to the 2-position was obtained by oxidation of the thioglucosides **4a,b,e** with potassium permanganate[12] or with hydrogen peroxide in acetic acid which yielded the corresponding sulfones **12a,b**.



12a X = H
12b X = Br

Oxidation of **7a** under the same conditions gave **13**.



13

The structure of the compounds **12a,b** and **13** were confirmed from elemental analysis and IR spectra which shows three carbonyl bands at 1740-1765 cm^{-1} (acetate

C=O), 1640-1680 cm^{-1} (quinazolinone and benzoxazinone C=O) and band at 1225-1300 cm^{-1} due to ν_{SO_2} stretching vibrations.

The β-configuration in thioglucosides **12a,b** and **13** is predicted by Hudson's isorotation rules.[13] Unequivocal support in favor of the β-configuration was deduced from their 90 MHz N.M.R. spectra. The NMR spectra of these compounds were only partially resolved (see Table 2). The diaxial orientation of H-1'and H-2'in 12a,b and 13 was indicated by a large $J_{H^{1'},H^{2'}}$ coupling (8.50-10.00 Hz).

Additional evidence for the attachment of the sugar moiety to the 2-position was obtained by alkylation of **1a-e** with alkyl halides which yielded only S-alkyl derivatives.[14-16]

The UV spectra of **4a-e, 5a-d, 7a,b, 10a-d** and **11a-c** show λ_{max} at 286 nm in analogy to 2-methylthio-3-aryl-4(3H)-quinazolinones at λ_{max} 286 nm rather than to the corresponding N-methyl-3-aryl-2-thio-4(3H)-quinazolinone isomers at λ_{max} 300 n.

The IR spectra of **4a-e, 5a-d, 7a,b 10a-d** and **11a-c** are characterized by the absence of ν_{as} NH and ν_s SH at 3240-3300 cm^{-1} and by streching vibration frequencies of the acetate carbonyl in the 1780-1740 cm^{-1} region.

The ^1H NMR spectral data and their assignments are shown in Tables 1 and 2. All compounds synthesized, i.e. **4a-f, 5a-d, 7a,b, 10a-d,** and **11a-c** exist predominantly in a chair like configuration and conformation as shown in **Schemes 1-3**. In general the anomeric proton (H-1') of aldopyranosyl halides[17-19] and acetylated 1-thioaldopyranoses[20] resonate at relatively lower field than other sugar ring protons.

The structures of the synthesized acetylated S-glycopyranosyl derivatives were confirmed by ^1H NMR Spectra (250 MHz). The anomeric protons which appear as doublets with large coupling constants at C^1 and C^2 of the carbohydrate residue, corresponding to a diaxial orientation of the H-1' and H-2' protons which indicates the β-configuration in the $^4C_1(D)$ conformation of compounds **4a-d, 5a-d, 7a,b** and **10a-c** and the α-configuration in the $^4C_1(L)$ conformation of compounds **11a-c** (see Tables1 and 2).

The analysis of ^1H NMR spectrum of **4e** shows a mixture of the α- and β- anomer in the ratio 1:6 each of which contains a quinazolinethione and a carbohydrate residue. The coupling constant $J_{H^{1'},H^{2'}}$ for the predominating anomer ($J_{H^{1'},H^{2'}}$ = 10.70 Hz), corresponds to a diaxial orientation of H-1' and H-2' which indicates the β-configuration and $^4C_1(D)$ conformation for this anomer. The small value of $J_{H^{1'},H^{2'}}$ in the minor anomer (J ≈ 3.81 Hz) is consistent with an α-configuration in the same conformation (Table 1).

The structure of compounds **4a-e, 5a-d, 7a,b, 10a-c** and **11a-c** is also confirmed by the data of ^{13}C NMR spectra (see Tables 3 and 4).

The anticancer activites of the aglycones **1a-f** and their glycosides **4a-e, 5a-d, 7a,b, 10a-d** and **11a-c** against the precentage growth (PG) of a wide variety of cancer cells, including leukemia cancer cells, small and non-small cancer cells (brain), central nervous system (CNS), cancer cells melanoma cancer cell, overian cancer cells and renal cancer cells were investigated under different concentrations at the National Institute of cancer (Development therapeutic program) Maryland. USA.

Table 1: ^{1}H NMR spectra[A] of **4a-e, 5a-d**

Compound No.	Quinazolinone protons					Aryl-CH_3	Acetoxy protons	Carbohydrate protons				
	H-5	H-6	H-7	H-8	Ar. H			H-1' ($J_{1',2'}$)	H-2' ($J_{2',3'}$)	H-3' ($J_{3',4'}$)	H-4' ($J_{4',5'}$)	H-5', H-6, H-6' ($J_{5',6}$), ($J_{5',6'}$), ($J_{6,6'}$)
4a (β)	8.25 (d)	7.80 (t)	7.62	----------	7.20 (m)	----------	2.05, 2.00, 1.97, 1.96	5.85(d) (10.70)	5.06(t) (9.31)	5.35(t) (9.20)	5.12 (t) (9.20)	3.94 (m), 4.25 (q), 4.14(q) (4.80), (2.22), (-12.40)
4b (β)	8.30 (d)	----------	7.65	7.57 (d)	7.20 (m)	----------	2.04, 2.03, 2.00, 1.97	5.81 (d) (10.69)	5.05 (t) (10.30)	5.30 (t) (9.20)	5.13 (t) (9.11)	3.95 (m), 4.22 (q), 4.13 (q) (4.80), (2.28), (-12.50)
4c (β)	8.20	----------	----------	----------	7.07 (m)	2.42 (s)	2.04, 2.00, 1.98, 1.95	5.81 (d) (10.20)	5.04 (t) (9.52)	5.30 (t) (10.40)	5.10 (t) (9.12)	3.90 (m), 4.23 (q), 4.12 (q) (4.70), (2.30), (-12.40)
4d (β)	8.35	----------	----------	----------	7.18 (m)	----------	1.97-2.06	5.86 (d) (10.75)	5.06 (t) (9.60)	5.36 (t) (9.22)	5.12 (t) (9.12)	3.92 (m), 4.24 (q), 4.13 (q) (5.20), (2.15), (-12.48)
4e(β)	8.70 (d)	7.79 (t)	7.62	----------	7.15 (m)	----------	2.03, 1.99, 1.96	5.82 (d) (10.70)	5.05 (t) (9.62)	5.37 (t) (9.22)	5.12 (t) (9.13)	3.95 (m), 2.24 (q), 4.13 (q) ((5.14), (2.28), (-12.40)
4e(α)	8.47 (d)	C	C	C	C	----------	1.94 C	6.23 (d) (3.81)	C	C	C	C
5a (β)	8.26 (d)	7.77 (t)	7.54 (t)	7.63 (d)	7.47-7.22 (m)	----------	2.12, 2.02, 1.98, 1.94	5.86(d) (10.24)	5.30(t) (10.12)	5.20(q) (3.26)	5.48 (d) (3.10)	4.19-4.09 (m)
5b (β)	8.34	----------	7.86	----------	7.21 (m)	----------	2.12, 1.99, 1.98, 1.96	5.82 (d) (10.27)	5.31 (t) (10.16)	5.18 (q) (3.27)	5.47 (d) (3.17)	4.18-4.09 (m)
5c (β)	8.33	----------	----------	----------	7.15 (m)	2.15 (s)	2.09 -1..75	5.70 (d) (10.02)	5.45	---------	---------	4.03 (m)
5d (β)	8.73 (d)	7.79 (t)	7.65	----------	7.18 (m)	----------	2.13, 1.99, 1.98, 1.94	5.81 (d) (10.23)	5.30 (t) (10.14)	5.19 (q) (3.29)	5.48 (d) (2.89)	4.19-4.09 (m)

Notes:
A: Solvents deuterochloroform
B: Observed multiplicities: (d) doublet, (t) triplet, (q) quartet, (m) multiplet
C: Overlapping signals

Table 2: ^{1}H NMR spectra[A] of **7a,b, 10a-c, 11a-c, 12a,b** and **13**

Compound No.	Protons of benzothiazine, quinazolinone and benzoxazine					Aryl-CH_3	Acetoxy carbonyl carbon atoms	Carbohydrate protons					
	H-5	H-6	H-7	H-8	Ar. H			H-1' ($J_{1',2'}$)	H-2' ($J_{2',3'}$)	H-3' ($J_{3',4'}$)	H-4' ($J_{4',5'}$)	H-5'e	H-5'a (H-6')
7a (β)	8.59 (d)	7.82 (t)	7.50 (t)	7.63 (d)	----------	----------	2.07, 2.05, 2.00, 1.98	5.86 (d) (10.10)	5.15 (t) (9.62)	5.40 (t) (9.22)	5.25 (t) (9.30)	3.95 (m), 4.14 (q) (5.24),	4.26 (q), (2.66), (-12.40)
7b (β)	8.62 (d)	7.80 (t)	7.46 (t)	7.65 (d)	----------	----------	2.17, 2.07, 2.06, 2.04	5.83 (d) (10.30)	5.45	----------	----------	----------, 4.04 (q)	----------
10a (β)	8.25 (d)	8.10	----------	----------	6.94 (m)	----------	2.04, 1.99, 1.91	6.14 (d) (7.38)	4.96 (t) (7.30)	5.26 (t) (7.30)	4.85 (m) (4.53)	4.06 (q) (-11.97))	3.75 (q) (7.88)
10b (β)	8.33 (d)	----------	7.81 (d)	7.57	7.25 (m)	----------	2.089, 2.080, 1.900	6.17 (d) (6.23)	4.98 (t) (6.24)	5.16 (t) (6.34)	4.85 (m) (4.06)	4.23 (q) (-12.43)	3.70 (q) (6.25)
10c (β)	8.10 (d)	7.96	----------	----------	7.10 (m)	2.41	2.03, 2.02, 1.91	6.10 (d) (7.64)	4.96 (t) (7.50)	5.25 (t) (7.40)	4.84 (m) (4.52)	4.07 (q) (-11.89)	3.65 (q) (7.50)
11a (α)	8.33 (d)	7.90 (d)	7.70	----------	7.25 (m)	----------	2.00, 1.98, 1.88	6.16 (d) (10.5)	5.39 (d) (8.77)	5.20 (m) (3.12)	5.15 (m)	3.75 (q)	4.00 (q)
11b (α)	8.53 (s)	----------	7.85 (d)	7.60	7.30 (m)	----------	2.10, 2.05, 1.87	6.20 (d) (8.70)	5.30 (d) (8.70)	5.21 (m) (3.5)	5.18 (m)	4.02 (q)	3.82 (q)
11c (α)	8.70 (d)	8.52 (d)	7.82	----------	7.15 (m)	----------	2.15, 2.09, 1.90	6.22 (d) (9.50)	5.35 (d) (9.50)	5.18 (m) (2.95)	5.18 (m)	4.01 (q)	3.79 (q)
12a (β)	8.32	----------	----------	----------	7.25 (m)	----------	2.00-2.12	6.22 (10.00)	5.54	----------	5.29	4.49	3.49
12b (β)	8.34	----------	----------	----------	7.28	----------	2.02-2.14	6.47 (9.50)	5.60	----------	5.36	4.56	4.01
13 (β)	8.36	----------	----------	7.58	----------	----------	2.04-2.16	6.51 (8.50)	5.64	----------	5.42	4.63	4.05

Note:
A: Solvents deuterochloroform

Table 3: ^{13}C NMR spectra of **4a-e** and **5a-d**

Compound No.	quinazolinone moieties								Aryl at 3-positions				Aryl-CH_3	Carbohydrate moiety						C=O	CH_3
	C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	a	b	c	d		C-1'	C-2'	C-3'	C-4'	C-5'	C-6'		
4a (β)	154.3	162.0 162.0#	120.5 114.1#	130.8 127.5#	130.2 129.5#	135.1 135.0#	126.3 113.0#	147.8 139.8#	135.5 137.8#	129.7 129.5#	129.1 128.3#	127.7 128.8#	--------	82.76	69.21	74.56	68.61	76.75	62.30	170.9 170.5 169.7 169.5	20.98 20.90 20.85
4b (β)	155.1	160.7 162.0#	118.0 117.3#	130.8 130.5#	130.1 124.5#	135.1 138.0#	128.5 114.0#	146.5 138.2#	138.2 137.8#	130.2 129.5#	129.5 128.3#	128.9 128.8#	--------	82.23	68.63	73.98	67.92	76.23	61.81	170.4 170.0 169.2 169.0	20.63 20.50 20.45
4c (β)	154.4	161.6 162.0#	118.0 114.4#	130.3 127.5#	129.8 129.5#	134.6 135.0#	127.2 113.0#	147.3 139.8#	135.9 134.9#	130.4 129.4#	128.8 129.0#	136.6 137.7#	20.60	82.14	68.57	74.02	67.99	75.13	61.76	170.4 170.0 169.1 169.0	21.23 20.85 20.47 20.40
4d (β)	156.4	159.9 162.0#	119.2 116.4#	130.0 129.3#	128.9 125.7#	134.5 141.7#	122.2 108.2#	143.9 144.8#	134.5 137.8#	129.3 129.5#	128.8 128.3#	128.5 128.8#	--------	82.46	76.36	76.99	68.19	78.16	61.33	170.7 170.2 169.5 169.3	20.36 20.18 20.14 19.52
4e (β) **4e** (α)	153.3 153.3	189.8 189.8	114.8 114.8 114.4#	132.5 129.7 127.5#	129.4 128.3 129.5#	134.6 134.0 135.0#	127.3 125.4 113.0#	143.5 142.0 139.8#	139.3 135.1 137.8#	128.8 128.3 129.5#	128.2 127.9 128.3#	127.8 127.3 128.8#	--------	90.95 89.62	73.79 70.76	75.97 77.02	72.68 68.12	82.23 69.52	61.64 61.31	171.0 170.3 169.1 169.0	20.56 20.44 20.29 20.18
5a (β)	154.0	161.7 162.0#	126.5 114.1#	129.4 127.5#	128.8 129.5#	135.2 135.0#	127.3 113.0#	147.4 139.8#	134.8 137.8#	130.4 129.5#	129.9 128.3#	129.8 128.8#	--------	82.86	67.42	72.16	66.28	75.04	61.47	170.4 170.2 169.9 169.4	20.69 20.66 20.61
5b (β)	154.9	160.4 162.0#	121.5 117.3#	130.6 130.5#	129.9 124.5#	134.9 138.0#	119.6 114.0#	146.2 138.2#	137.9 137.8#	129.9 129.5#	129.7 128.3#	128.7 128.8#	--------	82.81	67.30	72.07	66.18	75.01	61.38	170.3 170.1 169.9 169.3	20.64 20.57 20.53
5c (β)	153.6	169.0 162.0#	119.5 114.3#	129.1 127.5#	128.8 129.5#	132.5 135.0#	128.4 113.0#	134.6 139.8#	134.6 134.9#	129.7 129.4#	128.0 129.0#	139.5 137.7#	20.77	81.79	67.37	70.87	66.01	74.01	61.18	169.5 169.0	20.77 20.56
5d (β)	153.7	190.2	127.1 114.4#	130.0 127.5#	129.2 129.5#	139.7 135.0#	128.4 113.0#	142.5 139.8#	135.0 137.8#	131.2 129.5#	130.5 128.3#	130.1 128.8#	--------	83.10	72.13	75.07	67.36	76.60	61.47	170.4 170.1 169.9 169.3	20.56

Note:
values are calculated

Table 4: ^{13}C NMR spectra of **7a,b, 10a-c** and **11a-c**

Compound No.	Benzothiazine and quinazolinone moieties								Aryl at 3-positions				Aryl-CH_3	Carbohydrate moiety						C=O	CH_3
	C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	a	b	c	d		C-1'	C-2'	C-3'	C-4'	C-5'	C-6'		
7a (β)	161.3	209.2	127.0	130.3	128.9	136.1	126.1	140.7	--------	--------	--------	--------	--------	80.78	68.81	73.63	68.01	76.26	61.81	160.4 169.9 196.2	20.54 20.47 20.43
7b (β)	170.7	202.6	126.0	130.4	129.0	136.2	126.2	140.9	--------	--------	--------	--------	--------	88.30	67.25	71.78	67.05	74.75	60.90	170.3 170.2 169.9 169.4	20.72 20.61 20.50
10a (β)	154.0	160.7 162.0#	119.8 114.1#	130.0 127.5#	128.9 129.5#	134.9 135.0#	128.8 113.0#	139.8 139.8#	138.7 137.8#	129.4 129.5#	128.5 128.3#	128.6 128.8#	--------	81.84	68.46	69.55	67.58	64.26	-------	169.64 169.13 169.09	20.73 20.67 20.47
10b (β)	154.8	160.4 162.0#	119.6 117.3#	130.3 130.5#	129.2 124.5#	135.2 138.0#	128.4 114.0#	146.2 138.2#	137.9 137.8#	129.9 129.5#	128.8 128.3#	129.0 128.8#	--------	81.55	68.12	69.67	67.46	63.96 1	-------	169.42 169.04 168.92	20.48 20.35 20.23
10c (β)	154.0	160.8 162.0#	119.8 114.3#	129.9 127.5#	129.1 129.5#	135.9 135.0#	128.6 113.0#	146.8 139.8#	134.8 134.9#	129.4 129.4#	129.0 129.0#	137.3 137.7#	20.76	81.63	68.19	69.98	67.56	64.15	-------	169.37 168.97 168.92	20.43 20.30 20.13
11a (α)	154.7	160.1 162.0#	119.3 114.1#	129.9 127.5#	128.9 129.5#	134.9 135.0#	128.8 113.0#	145.9 139.8#	137.5 137.8#	129.5 129.5#	128.1 128.3#	129.4 120.5#	--------	81.24	66.01	68.57	68.57	62.44	-------	169.41 168.8	20.67 20.35
11b (α)	154.8	160.4 162.0#	119.5 117.3#	130.0 130.5#	128.9 124.5#	135.1 138.0#	128.3 114.0#	146.4 138.2#	138.0 137.8#	129.6 129.5#	129.5 128.3#	129.1 128.8#	--------	81.27	66.02	68.61	68.61	63.00	-------	169.65 169.10 169.02	20.59 20.25
11c (α)	174.2	190.0	125.0 114.4#	130.0 127.5#	127.0 129.5#	135.0 135.0#	129.0 113.0#	144.0 139.8#	136.0 137.8#	129.0 129.5#	128.5 128.3#	131.4 128.8#	--------	81.30	65.95	68.20	68.20	63.60	-------	170.00 169.80 169.85	20.20 20.15

Note:
values are calculated

The compounds **4a-f**, **5a-c**, **7a**, **10a-d** and **11a-c** were found inactive against human immunodeficiency virus (HIV), The compounds **5d** and **7b** were slightly active on different types of tumor cell lines of cancer; e.g. leukemia, colon cancer, non-small cell lung leukemia, colon cancer, ovarain cancer, non-small cell lung cancer, small cell lung cancer, CNS cancer, renal cancer and melanoma.

EXPERIMENTAL

All melting points are uncorrected. They were performed by the open capillary method using a GallenKamp melting point apparatus. Microanalyses were performed by Microanalytical Laboratories, Faculty of Science, Cairo University.

IR spectra were recorded on a Perkin-Elmer 1420 spectrophotometer using the KBr wafer technique.

^{1}H NMR spectra were measured on Varian EM-390 90 MHz, Bruker and Matthews 250 MHz equipment.

^{13}C NMR spectra were recorded with a Bruker and Matthews 250 MHz spectrometer.

Specific rotations were measured on a polarimeter SR-6 at 25 ^{o}C in $CHCl_3$.

Biological evaluation studies were done by National Cancer Institute, Bethesda, Maryland 20892, USA. Anti-HIV tests was determined according to the reported method in literature .[21]

The UV spectra were recorded with a Shimadzu PR-1 spectrophotometer in spectroscopically pure solvents and a 1 cm matched silica cell.

All analytical samples were homogeneous by thin-layer chromatography, which was performed on Merck silica gel 60 F_{254} sheets (0.2 mm) with $C_6H_6/CHCl_3$ (2:5, v/v) and in $CHCl_3/CH_3COCH_3$ (5:2 v/v) as the developing eluents A and B. The spots were detected with a UV lamp model UVGL-58.

5-Bromoanthranilic acid and 3,5-dibromoanthranilic acid were prepared according to Wheeler and Oates.[22]

General procedure for the prepration of acetylated S-glycosides 4a-f, 5a-d, 7a,b, 10a-d and 11a-c.

Asolution of bromides **2, 3,8** or **9** (0.01 mole) in acetone (30-50 ml) was added to a solution of 2-thio-3-aryl-4(3H)-quinazolinone (**1a-d**), 2-thio-3-phenyl-4(3H)-quinazolinethiones (**1e,f**) or 2-thio-3,1-benzothiazin-4-thione (**6**) (0.01 mole) in water (6 ml) containing potassium hydroxide (0.6 g, 0.01 mole) [or in 8 ml water containg potassium carbonate (1.38 g, 0.01 mole)]. The reaction mixture was stirred at room temperature for 2-6 hours. Complete conversion of starting material to new product was indicated by T.L.C. in system A or system B. The solvent was evaporated under reduced pressure. The residue was washed with water to remove potassium bromide. The residue was stirred with chloroform (30-50 ml) and cooled, the mixture was filtered , the filtrate was evaporated to dryness. The residue was solidified by

Table 5 Analytical and other data for **4a-f, 5a-d, 7a,b, 10a-d, 11a-c, 12a,b** and **13**

Compound No	m. p. °C	yield %	$[\alpha]_D^{25}$ c1	Mol. formula (M. wt)	R_f in system		Analysis (Calculated/found)			
					A	B	C %	H %	N %	S %
4a	140-1 °C	51	+ 120	$C_{28}H_{28}N_2O_{10}S$ (548.596)	0.70	0.79	57.53 57.40	4.79 4.50	4.79 4.90	--------- ---------
4b	160-2 °C	80	+40	$C_{28}H_{27}BrN_2O_{10}S$ (663.492)	0.75	0.82	50.70 50.50	4.70 4.50	4.22 4.20	--------- ---------
4c	173-4 °C	86	+60	$C_{29}H_{30}N_2O_{10}S$ (598.623)	0.65	0.80	58.10 57.92	5.00 4.80	4.86 4.71	--------- ---------
4d	196-7 °C	43	+140	$C_{28}H_{26}Br_2N_2O_{10}S$ (742.388)	0.60	0.65	45.30 45.00	3.50 3.60	3.77 3.55	--------- ---------
4e	175-6 °C	32	+80	$C_{28}H_{28}N_2O_9S_2$ (600.657)	0.85	0.76	56.00 56.40	4.66 4.90	4.66 4.70	10.66 10.51
4f	206-7 °C	28	+20	$C_{28}H_{27}BrN_2O_9S_2$ (679.553)	0.60	.068	49.48 49.30	3.79 4.10	4.12 4.33	9.42 9.96
5a	145-7 °C	45	+60	$C_{28}H_{28}N_2O_{10}S$ (584.596)	0.55	0.63	57.53 57.10	4.79 5.01	4.79 4.88	--------- ---------
5b	180-2 °C	30	+25	$C_{28}H_{27}BrN_2O_{10}S$ (663.492)	0.70	0.76	50.70 50.90	4.70 4.50	4.22 3.92	--------- ---------
5c	179-81°C	65	+20	$C_{28}H_{30}N_2O_{10}S$ (598.623)	0.50	0.55	58.10 58.50	5.00 4.70	4.68 4.91	--------- ---------
5d	170-2 °C	60	+45	$C_{28}H_{28}N_2O_9S_2$ (600.657)	0.55	0.70	56.00 56.60	4.66 4.80	4.66 4.40	10.51 9.98
7a	182-3 °C	47	+20	$C_{22}H_{23}NO_9S_3$ (541.605)	0.44	0.60	48.75 48.90	4.28 4.30	2.58 2.45	17.74 17.92
7b	118-9 °C	35	+40	$C_{22}H_{23}N_2O_8S$ (541.605)	0.45	0.63	48.78 49.00	4.28 4.50	2.58 2.82	17.74 17.38
10a	188-9 °C	60	+60	$C_{25}H_{24}N_2O_8S$ (512.537)	0.70	0.79	58.58 58.24	4.71 4.75	5.46 5.52	--------- ---------
10b	236-7 °C	30	+75	$C_{25}H_{23}BrN_2O_8S$ ((591.433)	0.59	0.80	50.77 50.91	3.91 4.10	4.73 4.65	--------- ---------
10c	189-90°C	45	+30	$C_{26}H_{26}N_2O_8S$ (526.560)	0.55	0.60	59.30 60.10	4.98 4.80	5.32 5.40	--------- ---------
10d	197-8 °C	55	+60	$C_{25}H_{24}N_2O_7S$ (528.593)	0.50	0.60	56.80 56.70	4.57 4.70	5.30 5.50	12.13 12.60
11a	182-3 °C	25	+30	$C_{25}H_{24}N_2O_8S$ (512.537)	0.60	0.65	58.58 58.70	4.71 4.55	5.46 5.48	--------- ---------
11b	210-11°C	16	+50	$C_{25}H_{23}Br_2N_8S$ (591.433)	0.40	0.60	50.77 50.53	3.91 3.91	4.70 4.74	--------- ---------
11c	189-90°C	35	+45	$C_{25}H_{24}N_2O_7S_2$ (528.593)	0.54	0.59	56.80 57.00	4.57 4.42	5.30 5.39	12.13 11.90
12a	105-7 °C	50	+30	$C_{28}H_{28}N_2O_{12}S$ (616.567)	0.70	0.85	54.54 53.80	4.54 4.35	4.55 4.35	--------- --------
12b	139-40°C	53	+15	$C_{28}H_{27}BrN_2O_{12}S$ (695.463)	0.59	0.70	48.95 48.20	3.91 3.82	4.02 3.85	--------- ---------
13	145-6 °C	46	+26	$C_{22}H_{23}NO_{13}S$ (541.480)	0.45	0.60	48.79 48.55	2.40 2.21	2.59 2.42	--------- ---------

Recrystallization from ethanol.

trituration with diethyl ether or with water, filtered and recrystalized from ethanol to yield colourless needles of the thioglycosides **4a-f, 5a-d, 7a,b, 10a-d** and **11a-c**. Their yields, melting points and analytical data are recorded in Table 5.

Oxidation of 4a,b,e and 7a :-

a) By Potassium Permanganate:-

To a solution of substrate (0.002 mole) in glacial acetic acid (25 ml) a solution of potassium permanganate (0.6 g, 0.004 mole) in water (10 ml) was added gradually with stirring during 30 minutes and boiled for 5 minutes. The reaction mixture was cooled at room temperature, saturated solution of potassium bisulphite was added then poured into crushed ice water (200 ml) white crystal was separeted collected and filtered. Compounds **4a,e** yielded the same corresponding sulphone **12a** while **4b, 7a** yielded the corresponding sulphones **12b** and **13**, respectively.

b) By Hydrogen peroxide:-

To a solution of the S-glucosides **4a,b,e** (1.0 g) in glacial acetic acid (7.5 ml) added hydrogen peroxide 30 % (1.4 g) with stirring for about 12 hours at room temperature, poured into ice-water (200 ml). The separated solid was collected on filtration.The corresponding sulphones **12a,b** was obtained in good yield and high purity. Their yield, melting point and analytical data are recorded in Table 5.

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