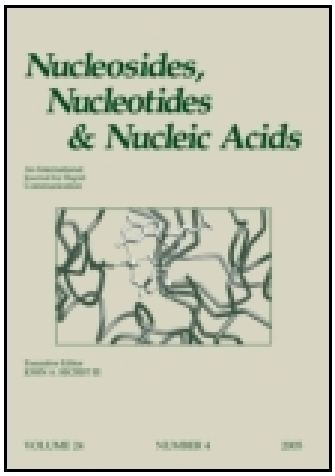


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn20

Selective Synthesis and Reactions of 6-Substituted-2-β-galactosyl-1,2,4-triazines of Potential Anticancer Activity

Abdel Kader Mansour [a c], Mohga M. Eid [a] & Nasser S. A. M. Khalil [b]
[a] Department of Chemistry, Faculty of Science , Cairo University , Giza, Egypt
[b] Central Laboratory for Food and Feed , Agricultural Research Centre , Giza, Egypt
[c] Department of Chemistry, Faculty of Science , Cairo University , Giza, Egypt
Published online: 07 Feb 2007.

To cite this article: Abdel Kader Mansour , Mohga M. Eid & Nasser S. A. M. Khalil (2003) Selective Synthesis and Reactions of 6-Substituted- 2-β-galactosyl-1,2,4-triazines of Potential Anticancer Activity, Nucleosides, Nucleotides and Nucleic Acids, 22:1, 21-44, DOI: 10.1081/NCN-120018621

To link to this article: http://dx.doi.org/10.1081/NCN-120018621

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, No. 1, pp. 21–44, 2003

Selective Synthesis and Reactions of 6-Substituted-2-β-galactosyl-1,2,4-triazines of Potential Anticancer Activity

Abdel Kader Mansour,[1,*] Mohga M. Eid,[1] and Nasser S. A. M. Khalil[2]

[1]Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt
[2]Central Laboratory for Food and Feed, Agricultural Research Centre, Giza, Egypt

ABSTRACT

Selective synthesis and reactions of different 6-substituted-2-β-D-galactosyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones using the developed amino or aryl protecting group strategy were investigated. Primary human anticancer screening of twelve selected compounds (in vitro) resulted in an active compound against both MCF7 (Breast) and SF-268(CNS) cell lines.

Key Words: Synthesis; 1,2,4-Triazines; Galactosides; Anticancer activity.

INTRODUCTION

During the last five decades, extensive chemical and biological studies of N-glycosides of 1,2,4-triazine-3,5-(2H, 4H)-diones (6-azauridine derivatives and their 3-thiones have been stimulated mainly by their cytotoxic, antiviral, enzyme inhibiting, immunosuppressive, antiphlogestic, antipsoriatic, therapeutic, bacteriostatic and

*Correspondence: Abdel Kader Mansour, Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt; E-mail: clff@intouch.com.

DOI: 10.1081/NCN-120018621
1525-7770 (Print); 1532-2335 (Online)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

antitumor activity.[1–7] Also, N-glycosyl derivatives of 3-substitiuted-1,2,4-triazin-5(2H)-ones were reported to be useful as floor and wall disinfectants.[8] Moreover, some glycosides of 6-vinyl-1,2,4-triazines were shown to exhibit antiviral activity.[9,10] All these facts prompted us to selectively synthesize some new 2-β-D-galactosyl derivatives of different 6-substituted-1,2,4-triazines of promising biological activity.

RESULTS AND DISCUSSION

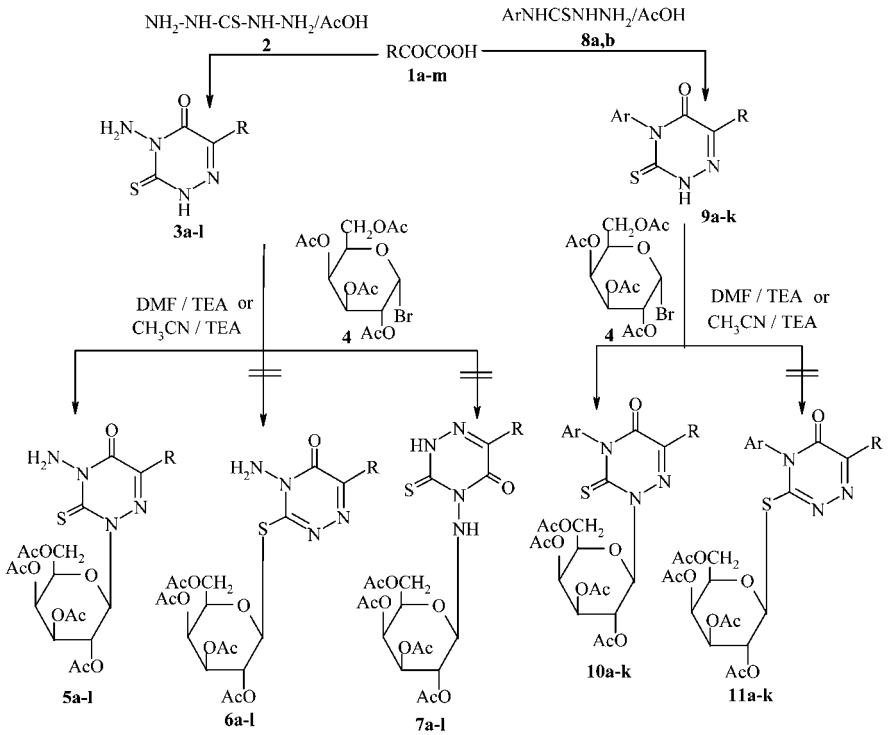
Direct glycosidation of 4-amino-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones followed by deamination was reported to offer a convenient selective synthesis of the 2-glycosyl derivatives.[11–13] Also, glycosidation of 4-aryl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones was reported to give the corresponding 2-glycosyl derivatives.[14] In the present investigation we applied these strategies to selectively synthesize some new 2-β-D-galactopyranosyl derivatives of 6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones. The starting 4-amino[15–17]/4-aryl[14,16]-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **3a–k**/**9a–h,k** were prepared as reported. The new 4-amino/4-aryl-6-β-(4-N,N-dimethylaminophenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones (**3l**/**9i,j**) are now synthesized using the same procedures starting with the appropriate α-ketocarboxylic acid **1l** and thiocarbohydrazide (**2**)/4-arylthiosemicarbazide **8a,b** (Sch. 1).

Galactosidation of the 4-amino-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **3a–l** with 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (**4**) in either N,N-dimethylformamide containing triethylamine or acetonitrile containing triethylamine afforded the corresponding 4-amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **5a–l**. Among the different possible monogalactosyl derivatives **5–7**, the structure of **5a–l** is clearly assigned by ^{1}H NMR spectral data which show the position of the anomeric proton at δ 6.7 ($J_{1'-2'} = 9$–9.4 Hz) and NH_2 protons at δ 6.4 (s, 2H, exchangeable) consistent with similar reported data.[11–13] Furthermore, the structure of **5a–l** was chemically established as will be seen later (Sch. 1).

Analogous glycosidation of the 4-aryl-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **9a–k** gave the corresponding 4-aryl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **10a–k**. Assignment of the structure of compounds **10a–k** rather than their isomeric S-galactosyl derivatives **11a–k** was established chemically and spectroscopically. Thus, the ^{1}H NMR spectral data of compounds **10a–k** revealed the position of the anomeric proton at δ 6.8–6.68 ($J_{1'-2'} = 8.4$–9.3 Hz) in agreement with that reported for analogous 4-aryl-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-6-substitutedbenzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones.[14] Also, the mass spectrum of **10a** showed the correct parent ion peak at m/z 625 (M^+, 16.13%) (Sch. 1).

Deamination of **5a–j** into the target 2-β-D-galactosyl derivatives **12a–j** was achieved in almost quantitative yields by the action of nitrous acid in acetic acid. The structure of compounds **12a–j** was inferred from their chemical and spectral evidences. Thus, the ^{1}H NMR spectra of compounds **12a–j** showed absence of NH_2 proton signal at δ 6.4 and appearance of NH proton signal at δ 10.3–9.4 (s, or brs, 1H, exchangeable) (Sch. 2).

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016



1,3,5-7	R
a	CH_3
b	Ph
c	$PhCH_2$
d	$4\text{-}MeC_6H_4CH_2$
e	$4\text{-}MeOC_6H_4CH_2$
f	$4\text{-}ClC_6H_4CH_2$
g	$3,4\text{-}(MeO)_2C_6H_3CH_2$
h	PhCH=CH
i	$4\text{-}MeC_6H_4CH=CH$
j	$4\text{-}MeOC_6H_4CH=CH$
k	$4\text{-}ClC_6H_4CH=CH$
l	$4\text{-}NMe_2C_6H_4CH=CH$
m	$4\text{-}NMe_2C_6H_4CH_2$

8	Ar
a	Ph
b	$4\text{-}MeC_6H_4CH_2$

9-11	R	Ar
a	$PhCH_2$	Ph
b	$PhCH_2$	$4\text{-}MeC_6H_4$
c	$4\text{-}MeC_6H_4CH_2$	Ph
d	$4\text{-}MeC_6H_4CH_2$	$4\text{-}MeC_6H_4$
e	$4\text{-}MeOC_6H_4CH_2$	Ph
f	$4\text{-}MeOC_6H_4CH_2$	$4\text{-}MeC_6H_4$
g	$4\text{-}ClC_6H_4CH_2$	Ph
h	$4\text{-}ClC_6H_4CH_2$	$4\text{-}MeC_6H_4$
i	$4\text{-}NMe_2C_6H_4CH_2$	Ph
j	$4\text{-}NMe_2C_6H_4CH_2$	$4\text{-}MeC_6H_4$
k	$4\text{-}ClC_6H_4CH=CH$	Ph

Scheme 1.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Methylation of compounds **12c,d,h–j** with methyl iodide in N,N-dimethylformamide containing either sodium carbonate or triethylamine gave a mixture of the 3-SCH_3 **13a–e**, 4-NCH_3 **14a–e,** and 5-OCH_3 **15a–e** derivatives. Identification of the products **13–15** and their ratios was achieved from their ^{1}H NMR spectral data. Thus, **13a–e** revealed 3-SCH_3 signal at δ 2.66–2.58, **14a–e** revealed 4-NCH_3 signal at δ 3.77–3.31, and **15a–e** revealed 5-OCH_3 signal at δ 3.4–3.29. The position of 3-SCH_3, 4-NCH_3, and 5-OCH_3 characteristic proton signals is consistent with that reported for similar methylation products of some 2-β-D-glucopyranosyl-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones.[11,13,18] Table 1 shows the action of methyl iodide on compounds **12c,d,h–j** (Sch. 2).

Glycosidation of the 4-arylideneamino-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **16a–h**[16,21] with compound **4** in acetonitrile containing triethylamine gave the corresponding 4-arylideneamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyra-nosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **17a–h**. The structure of compounds **17a–h** was established chemically and spectroscopically. Thus, compound **17f** was alternatively prepared via condensation of **5f** with benzaldehyde. Moreover, the ^{1}H NMR spectra of **17a–h** revealed the characteristic N=CH proton signal at δ 8.33–8.44 consistent with similar reported data[11–13] (Sch. 2).

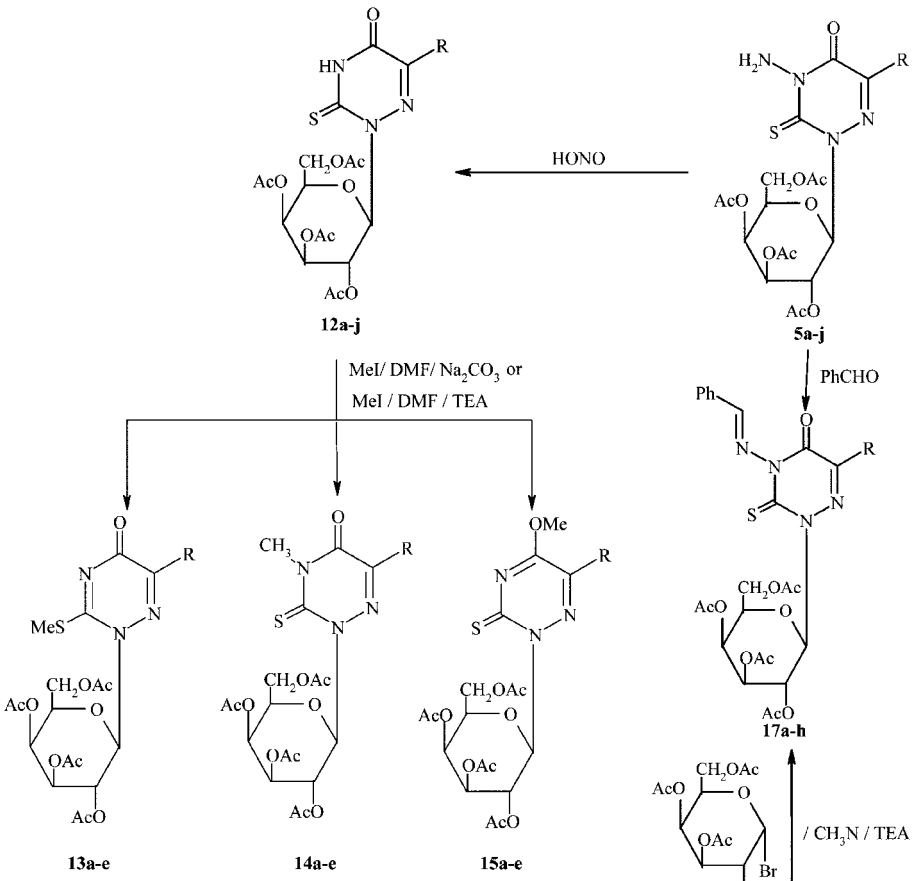
Thiation of compounds **10a,g**, and **12b–f,i** with phosphorous pentasulfide in pyridine afforded the corresponding 4-aryl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-1,2,4-triazine-3,5(2H,4H)-dithiones **18a,b**, and 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-1,2,4-triazine3,5(2H,4H)-dithiones **19a–f**, respectively. Structure assignment of compounds **18a,b** and **19a–f** was inferred from their correct analytical and spectral data. Thus, the IR spectra of these compounds showed the absence of the amide carbonyl function at 1715–1705 cm^{-1}. On the other hand, the mass spectrum of compound **19b** showed the correct parent ion peak at m/z 565 (M^+, 20.7%). Also, the ^{1}H NMR spectra of compounds **19a–f** revealed signals consistent with their structures (cf. experimental part). Moreover, the IR and ^{1}H NMR spectral data of compounds **19a–f** are in agreement with those reported for the analogous 2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-6-substituted-1,2,4-triazine-3,5(2H,4H)-dithiones[13] (Sch. 3).

Treatment of the appropriate acetyl derivatives **5i**, **10g**, and **12g,i** with methanolic ammonia led to the formation of the corresponding free glycosyl derivatives **20**, **21**, and **22a,b**, respectively (Sch. 3).

Table 1. Action of methyl iodide on compounds **12c,d,h–j**.

Compound	Reaction condition	Products (relative ratio %)
12c	MeI/DMF/TEA	**13a** (72.7), **14a** (9.1), **15a** (18.2)
12d	MeI/DMF/TEA	**13b** (38.5), **14b** (7.7), **15b** (53.8)
12h	MeI/DMF/Na_2CO_3	**13c** (27.3), **14c** (9.1), **15c** (63.6)
12i	MeI/DMF/TEA	**14d** (25.7), **15d** (74.3)
12i	MeI/DMF/Na_2CO_3	**13d** (18.1), **14d** (31.9), **15d** (50)
12j	MeI/DMF/Na_2CO_3	**13e** (51.6), **14e** (9.7), **15e** (38.7)

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016



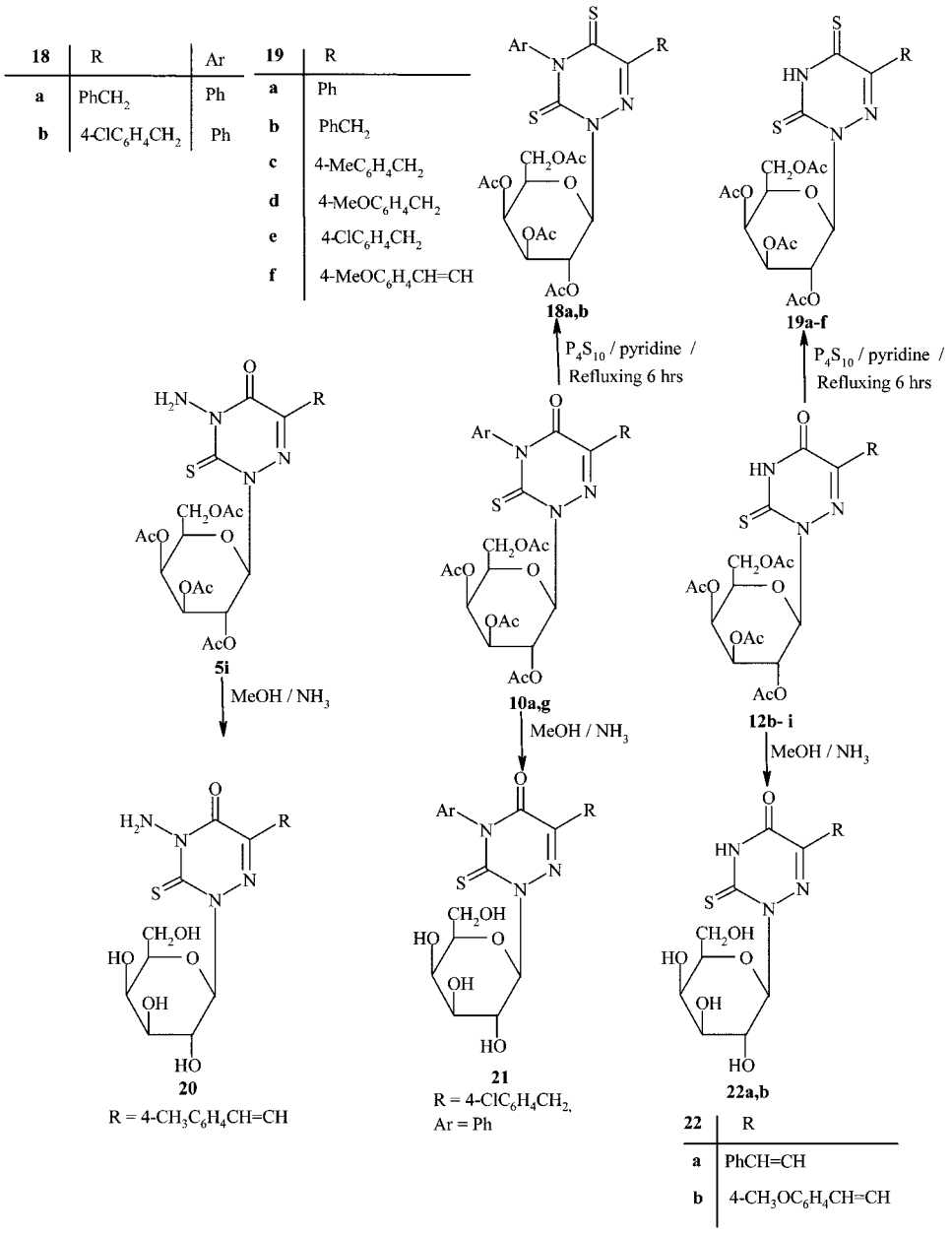
12	R
a	CH_3
b	Ph
c	$PhCH_2$
d	4-$MeC_6H_4CH_2$
e	4-$MeOC_6H_4CH_2$
f	4-$ClC_6H_4CH_2$
g	PhCH=CH
h	4-MeC_6H_4CH=CH
i	4-$MeOC_6H_4CH$=CH
j	4-ClC_6H_4CH=CH

13-15	R
a	$PhCH_2$
b	4-$MeC_6H_4CH_2$
c	4-MeC_6H_4CH=CH
d	4-$MeOC_6H_4CH$=CH
e	4-ClC_6H_4CH=CH

16,17	R
a	CH_3
b	Ph
c	$PhCH_2$
d	4-$MeC_6H_4CH_2$
e	4-$MeOC_6H_4CH_2$
f	4-$ClC_6H_4CH_2$
g	PhCH=CH
h	4-$MeOC_6H_4CH$=CH

Scheme 2.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016



Scheme 3.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

BIOLOGICAL EVALUATION

Compounds **5a–c,e,i,k**, **12a,b,j**, **19a,b**, and **22b** were tested for their human anticancer activity using an in vitro model through a 3-cell line, one dose primary anticancer assay consisting of MCF7 (Breast), NCI-H460 (lung) and SF-268 (CNS). Among the previously mentioned tested compounds, only compound **19b** was found to be active against both MCF7 (Breast) and SF-268 (CNS) in this 3-cell line, one dose primary human anticancer assay (Table 2).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 1430 spectrophotometer. ^{1}H NMR spectra were measured with a Varian GEMINI 200 spectrometer (200 MHz ^{1}H NMR). Mass spectra were recorded on a GCMS-QP 1000 EX (70 EV) spectrometer. Elemental analyses were carried out at the Microanalytical Centre, Cairo University. Anticancer screening of compounds **5a–c,e,i,k**, **12a,b,j**, **19a,b**, and **22b** was carried out at the National Cancer Institute – National Institutes of Health, Bethesda, Maryland, United States of America. The starting 4-amino/4-aryl-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **3a–k**,[15–17]/**9a–h,k**,[14,16] and 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (**4**)[20] were prepared as reported. The 4-arylideneamino-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones **16a–h** were prepared after the method described by Mansour[16] and Eid.[21]

4-Amino-6-β-(4-N,N-dimethylaminophenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (3l). To a mixture of pyruvic acid (7 mL, 0.1 mol), 4-N,N-dimethylaminobenzaldehyde (14.9 g, 0.1 mol), and methanol (10 mL), two thirds volume of a

Table 2. Human anticancer activity of compounds **5a–c,e,i,k, 12a,b,j, 19a,b and 22b**.

Compound	Concentration	Growth percentage (Lung) NCI-H460	(Breast) MCF7	(CNS) SF-268	Activity
5a	1.00E-04 M	117	92	89	Inactive
5b	1.00E-04 M	92	91	112	Inactive
5c	1.00E-04 M	95	92	95	Inactive
5e	5.00E-05 M	116	111	106	Inactive
5i	5.00E-05 M	90	93	79	Inactive
5k	1.00E-04 M	71	71	82	Inactive
12a	1.00E-04 M	104	96	86	Inactive
12b	1.00E-04 M	94	94	94	Inactive
12j	5.00E-05 M	67	36	54	Inactive
19a	1.00E-04 M	83	89	108	Inactive
19b	1.00E-04 M	42	−15	−38	Active
22b	1.00E-04 M	114	91	90	Inactive

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

solution of potassium hydroxide (10 g, 0.18 mol) in methanol (10 mL) was added at 0–5 °C while shaking over a fifteen minutes period. The last third volume of the previous methanolic potassium hydroxide solution was then added in one pot with constant shaking and the reaction mixture was allowed to stand at room temperature for one hour. The precipitate was then collected, washed with cold methanol, and dried at ambient temperature to give crude 4-N,N-dimethylaminobenzylidenepyruvic acid potassium salt (13.3 g, 51.7%). A boiling solution of thiocarbohydrazide (5.48 g, 0.05 mole) in water (50 mL) was added dropwise while shaking to a boiling mixture of 4-N,N-dimethylaminobenzylidene-pyruvic acid potassium salt (13.3 g, 0.05 mole), acetic acid (10 mL), and water (30 mL). The reaction mixture was then heated under reflux for six hours, cooled, and kept overnight at room temperature. After collection of the formed precipitate, it was washed several times with water, and recrystallized from N,N-dimethylformamide as brown crystals of **3l** (30.6%), mp. 220°C (decomp); IR (KBr) 3423 (NH), 3223, 3068 (NH_2), 1662 (C=O amide) cm^{-1}; ^1H NMR (DMDO-d_6) δ 9.38 (s, 1H, NH, exchangeable), 7.74, 6.85 (2d, 2H, $J = 16.3$ Hz, Hz, trans CH=CH), 7.45, 6.70 (2d, 4H, ArH's), 6.48 (s, 2H, NH_2, exchangeable), 3.02 (s, 6H, $N(CH_3)_2$).

Anal. For $C_{13}H_{15}N_5OS$ Calcd.: C, 53.96; H, 5.22; N, 24.20. Found: C, 54.0; H, 5.1;N, 24.3.

4-Aryl-6-(4-N,N-dimethylaminobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones 9i,j. General procedure: A solution of 4-(N,N-dimethylaminobenzylidene)-2-phenyl-oxazol-5-one (29.2 g, 0.1 mol) in potassium hydroxide (17.5 g, 0.31 mol, 1M aqueous solution) was refluxed for $6\frac{1}{2}$ h to give in situ the corresponding 4-N,N-dimethylaminophenylpyruvic acid **1m**. After acidification with acetic acid, the appropriate 4-arylthiosemicarbazide **8a,b** (0.1 mol) was added, and the reaction mixture was further refluxed for 8 h and left overnight at room temperature. The formed precipitate was collected and recrystallized from ethanol into yellow crystals of **9i,j**.

4-Phenyl-6-(4-N,N-dimethylaminobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (9i). Using the general procedure, **1m** gave **9i** (90%); mp. 165°C; IR (KBr) 3279 (NH), 1689 (C=O amide) cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.68 (s, 1H, NH, exchangeable), 8–6.42 (m, 9H, ArH's), 3.81 (s, 2H, 4-$NMe_2C_6H_4C\underline{H}_2$), 2.91 (s, 6H, $N(CH_3)_2$).

Anal. For $C_{18}H_{18}N_4OS$ Calcd.: C, 63.88; H, 5.36; N, 16.55. Found: C, 64.0; H, 5.4; N, 16.7.

4-(4-Methylphenyl)-6-(4-N,N-dimethylaminobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (9j). Using the general procedure, **1m** gave **9j** (95%); mp. 180°C; IR (KBr) 3275 (NH), 1691 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.95 (s, 1H, NH, exchangeable), 8–6.6 (m, 8H, ArH's), 3.81 (s, 2H, 4-$NMe_2C_6H_4C\underline{H}_2$), 2.99 (s, 6H, $N(CH_3)_2$), 2.34 (s, 3H, 4-$C\underline{H}_3C_6H_4N$).

Anal. For $C_{19}H_{20}N_4OS$ Calcd.: C, 64.75; H, 5.72; N, 15.9. Found: C, 64.6; H, 5.7; N, 15.8.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones 5a–l. General procedure: To a solution of each

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

of **3a–l** (10 mmol) in N,N-dimethylformamide or acetonitrile (5 mL) and triethylamine (2 mL, 14 mmol) was added 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (4.1 g, 10 mmol). The reaction mixture was shaken for 20 min and kept overnight at room temperature. The mixture was cooled, acidified with acetic acid (1 mL), and diluted with water. The precipitate was then collected, washed with water, and dried at room temperature. Compound **5b** was recrystallized from $EtOH/HCCl_3$. Compounds **5a,c–l** were extracted from ethyl acetate and purified by preparative TLC plates plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent. Compounds **5a,c–l** were then extracted from chloroform on a soxhlet extractor. The chloroform extracts were then concentrated, and diluted with petroleum ether (40–60°C). After collection of crude **5a,c–l** they were recrystallized from diethylether/petroleum ether (40–60°C) into colorless crystals of **5a,c,d,f** and yellow crystals of **5e,g–l**.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-methyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5a).[a] Using the general procedure, **3a** gave **5a** (39.2%); $R_f = 0.71$; mp. 115°C; IR (KBr), 3325, 3228 (NH_2), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.69 (d, 1H, $H^{1'}$, $J_{1'-2'} = 9$ Hz), 6.42 (s, 2H, NH_2, exchangeable), 5.89 (t, 1H, $H^{2'}$, $J = (J_{2'-1'} + J_{2'-3'})/2 = 8.6$ Hz), 5.49 (d, 1H, $H^{4'}$, $J_{4'-3'} = 2.8$ Hz), 5.24 (dd, 1H, $H^{3'}$, $J_{3'-4'} = 2.9$, $J_{3'-2'} = 10.3$ Hz), 4.22–4.1 (m, 3H, $H^{5'}$, $H^{6'}$), 2.39 (s, 3H, CH_3), 2.22, 2.06, 2.01, 1.95 (4s, 12H, CH_3CO).

Anal. For $C_{18}H_{24}N_4O_{10}S$ Calcd.: C, 44.26; H, 4.95; N, 11.47. Found: C, 44.3; H, 5.0; N, 11.3.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-phenyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5b). Using the general procedure, **3b** gave **5b** (42.9%); mp. 160°C; IR (KBr), 3319, 3225 (NH_2), 1761, 1751, 1736 (C=O acetate), 1707 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.18–7.48 (m, 5H, ArH's), 6.86 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.03 (t, 1H, $J = 9.4$ Hz, $H^{2'}$), 6.30 (s, 2H, NH_2, exchangeable), 5.51 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 9.4 Hz, $H^{3'}$), 4.2–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 2.21–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{23}H_{26}N_4O_{10}S$ Calcd.: C, 50.18; H, 4.76; N, 10.18. Found: C, 50.2; H, 4.8; N, 10.0.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5c). Using the general procedure, **3c** gave **5c** (74.0%); $R_f = 0.70$; mp. 85°C; IR (KBr), 3321, 3223 (NH_2), 1749 (C=O acetate), 1690 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37–7.23 (m, 5H, ArH's), 6.7 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.30 (s, 2H, NH_2, exchangeable), 5.97 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.4$, 10.2 Hz, $H^{3'}$), 4.23–3.92 (m, 5H, $H^{5'}$, $H^{6'}$, $C\underline{H}_2Ph$), 2.21, 2.04, 2.02, 1.9 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{28}N_4O_{10}S$ Calcd.: C, 51.06; H, 5.0; N, 9.92. Found: C, 51.1; H, 5.2; N, 10.1.

[a]Compound **5a** is an illustrative example that shows how *J* values including coupling protons assign different CH′ protons of the sugar moiety.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5d). Using the general procedure, **3d** gave **5d** (74.0%); $R_f = 0.72$; mp. 80°C; IR (KBr), 3319, 3223 (NH_2), 1751 (C=O acetate), 1693 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27, 7.2 (2d, 4H, ArH's), 6.70 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.30 (s, 2H, NH_2), 5.98 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.25–3.88 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$MeC_6H_4C\underline{H}_2$), 2.31 (s, 3H, CH_3), 2.21, 2.05, 2.03, 1.91 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{30}N_4O_{10}S$ Calcd.: C, 51.9; H, 5.22. Found: C, 52.0; H, 5.1.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5e). Using the general procedure, **3e** gave **5e** (76.9%); $R_f = 0.70$; mp. 86°C; IR (KBr), 3335, 3238 (NH_2), 1751 (C=O acetate), 1692 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31, 6.85 (2d, 4H, ArH's), 6.70 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.30 (s, 2H, NH_2), 5.98 (t, 1H, $J = 9.5$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.4$, 10.1 Hz, $H^{3'}$), 4.22–3.85 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$MeOC_6H_4C\underline{H}_2$), 3.78 (s, 3H, OCH_3), 2.22, 2.05, 2.03, 1.92 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{30}N_4O_{11}S$ Calcd.: C, 50.5; H, 5.08. Found: C, 50.5; H, 5.1.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5f). Using the general procedure, **3f** gave **5f** (77.0%); $R_f = 0.74$; mp. 104°C (decomp.); IR (KBr), 3319, 3223 (NH_2), 1751 (C=O acetate), 1693 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36–7.25 (2d, 4H, ArH's), 6.71 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.3 (s, 2H, NH_2), 5.91 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.2–3.9 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$ClC_6H_4C\underline{H}_2$), 2.2, 2.05, 2.02, 1.91 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{27}N_4O_{10}SCl$ Calcd.: C, 48.12; H, 4.54. Found: C, 48.2; H, 4.5.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(3,4-dimethoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5g). Using the general procedure, **3g** gave **5g** (70%); $R_f = 0.75$; mp. 98°C; IR (KBr), 3321, 3223 (NH_2), 1755 (C=O acetate), 1693 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36–6.96 (m, 3H, ArH's), 6.76 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.32 (s, 2H, NH_2), 6.02 (t, 1H, $J = 9.6$ Hz, Hz, $H^{2'}$), 5.37 (d, 1H, $J = 3$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.0$, 10 Hz, $H^{3'}$), 4.2–3.9 (m, 3H, $H^{5'}$, $H^{6'}$), 3.93 (s, 2H, 3,4-$(CH_3O)_2PhC\underline{H}_2$), 2.41, 2.33 (2s, 6H, 3,4-$(C\underline{H}_3O)_2PhCH_2$), 2.23, 2.07, 2.05, 2.0 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{32}N_4O_{12}S$ Calcd.: C, 50.0; H, 5.16. Found: C, 50.1; H, 5.20.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-styryl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5h). Using the general procedure, **3h** gave **5h** (76.9%); $R_f = 0.74$; mp. 102°C; IR (KBr), 3321, 3221 (NH_2), 1755 (C=O acetate), 1693 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01, 7.15 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.64–7.61 (m, 5H, ArH's), 6.72 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.5 (s, 2H, NH_2), 6.04 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.29 (dd, 1H, $J = 3.8$, 10 Hz, $H^{3'}$), 4.2–3.9 (m, 3H, $H^{5'}$, $H^{6'}$), 2.24, 2.06, 2.04, 1.99 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{28}N_4O_{10}S$ Calcd.: C, 52.08; H, 4.89; N, 9.72. Found: C, 52.2; H, 4.9; N, 9.8.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methylphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5i). Using the general procedure, **3i** gave **5i** (79.4%); $R_f = 0.72$; mp. 112°C; IR (KBr), 3323, 3223 (NH_2), 1755 (C=O acetate), 1690 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97, 7.1 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.51, 7.20 (2d, 4H, ArH's), 6.7 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.43 (s, 2H, NH_2, exchangeable), 6.05 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.53 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.27 (dd, 1H, $J = 3.4$, 10.2 Hz, $H^{3'}$), 4.25–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 2.37 (s, 3H, CH_3), 2.25, 2.06, 2.03, 1.95 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{30}N_4O_{10}S$ Calcd.: C, 52.87; H, 5.12. Found: C, 53.0; H, 5.1.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methoxyphenyl)-vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5j). Using the general procedure, **3j** gave **5j** (79.5%); $R_f = 0.70$; mp. 188°C; IR (KBr), 3327, 3238 (NH_2), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96, 7.02 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.57, 6.92 (2d, 4H, ArH's), 6.69 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.42 (s, 2H, NH_2), 6.05 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.25–4.1 (m, 3H, $H^{5'}$, $H^{6'}$), 3.85 (s, 3H, OCH_3), 2.24, 2.06, 2.03, 1.95 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{30}N_4O_{11}S$ Calcd.: C, 51.48; H, 4.98. Found: C, 51.5; H, 5.0.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-chlorophenyl)-vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5k). Using the general procedure, **3k** gave **5k** (82.6%); $R_f = 0.75$; mp. 140°C; IR (KBr), 3321, 3223 (NH_2), 1753 (C=O acetate), 1691 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97, 7.12 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.56, 7.37 (2d, 4H, ArH's), 6.44 (s, 2H, NH_2), 6.69 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.04 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.53 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.27 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.22–4.05 (m, 3H, $H^{5'}$, $H^{6'}$), 2.24, 2.06, 2.04, 1.96 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{27}N_4O_{10}SCl$ Calcd.: C, 49.14; H, 4.45. Found: C, 49.1; H, 4.5.

4-Amino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-N,N-dimethyl-aminophenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (5l). Using the general procedure, **3l** gave **5l** (75.6%); $R_f = 0.75$; mp.100°C; IR (KBr), 3318, 3226 (NH_2), 1752 (C=O acetate), 1680 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92, 6.94 (2d, 2H, $J = 16.2$ Hz, trans CH=CH), 7.52, 6.69 (2d, 4H, ArH's), 6.69 (d, 1H, $J = 9$ Hz, $H^{1'}$), 6.42 (s, 2H, NH_2), 6.06 (t, 1H, $J = 9$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3.4$ Hz, Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.24–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 3.03 (s, 6H, $N(C\underline{H}_3)_2$), 2.25, 2.06, 2.04, 1.94 (4s, 12H, CH_3CO).

Anal. For $C_{27}H_{33}N_5O_{10}S$ Calcd.: C, 52.33; H, 5.37; N, 11.3. Found: C, 52.3; H, 5.4; N, 11.2.

4-Aryl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones (10a–k). General procedure: To a solution of each of **9a–k** (10 mmol) in N,N-dimethylformamide oracetonitrile (5 mL) and triethylamine (2 mL, 14 mmol) was added 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (**4**) (10 mmol). After shaking the reaction mixture for 20 min, it was kept at room temperature overnight. The reaction mixture was then cooled, acidified with

acetic acid (1 mL), and the formed precipitate was collected, washed with water, and dried at room temperature. Compounds **10a–k** were extracted from ethyl acetate, and purified by preparative TLC plates plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent. The eluted compounds were then extracted from chloroform on a soxhlet extractor. The chloroform extracts were concentrated, and diluted with petroleum ether (40–60°C). After collection of crude **10a–k**, they were recrystallized from diethylether/petroleum ether (40–60°C) as pale crystals of **10a–h**, orange yellow crystals of **10i,j**, and yellow crystals of **10k**.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10a). Using the general procedure, **9a** gave **10a** (51.2%); $R_f = 0.72$; mp. 104°C; MS: m/z 625 (M^+, 16.13); IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54–7.14 (m, 10H, ArH's), 6.8 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.97 (t, 1H, $J = 9.6$ Hz $H^{2'}$), 5.51 (d, 1H, $J = 3.4$ Hz $H^{4'}$), 5.25 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.2–4.02 (m, 3H, $H^{5'}$, $H^{6'}$), 3.98 (s, 2H, $C\underline{H}_2Ph$), 2.24–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{30}H_{31}N_3O_{10}S$ Calcd.: C, 57.59; H, 4.99; N, 6.72. Found: C, 57.6; H, 5.1; N, 6.7.

4-(4-Methylphenyl)-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10b). Using the general procedure, **9b** gave **10b** (66.2%); $R_f = 0.75$; mp. 94°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4–7.0 (m, 9H, ArH's), 6.8 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.9$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.3$, 9.9 Hz, $H^{3'}$), 4.2–3.98 (m, 3H, $H^{5'}$, $H^{6'}$), 3.95 (s, 2H, $C\underline{H}_2Ph$), 2.4 (s, 3H, CH_3), 2.22–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{33}N_3O_{10}S$ Calcd.: C, 58.21; H, 5.2. Found: C, 58.2; H, 5.1.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10c). Using the general procedure, **9c** gave **10c** (81.15%); $R_f = 0.74$; mp. 102°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.11 (m, 9H, ArH's), 6.79 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.98 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.50 (d, 1H, $J = 3.6$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.19–3.96 (m, 3H, $H^{5'}$, $H^{6'}$), 3.93 (s, 2H, 4-$C\underline{H}_3$-$C_6H_4C\underline{H}_2$), 2.32 (s, 3H, 4-$C\underline{H}_3$-$C_6H_4CH_2$), 2.23–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{33}N_3O_{10}S$ Calcd.: C, 58.21; H, 5.2. Found: C, 58.1; H, 5.2.

4-(4-Methylphenyl)-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10d). Using the general procedure, **9d** gave **10d** (80.7%); $R_f = 0.75$; mp. 106°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33–7.03 (m, 8H, ArH's), 6.81 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.98 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.19–3.95 (m, 3H, $H^{5'}$, $H^{6'}$), 3.92 (s, 2H, 4-CH_3-$C_6H_4C\underline{H}_2$), 2.4 (s, 3H, 4-$C\underline{H}_3$-C_6H_4N), 2.32 (s, 3H, 4-$C\underline{H}_3$-$C_6H_4CH_2$), 2.23–1.97 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{35}N_3O_{10}S$ Calcd.: C, 58.79; H, 5.4. Found: C, 58.6; H, 5.4.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10e). Using the general procedure, **9e** gave **10e** (78.6%); $R_f = 0.71$; mp. 106°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54–6.83 (m, 9H, ArH's), 6.79 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.8$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.18–3.93 (m, 3H, $H^{5'}$, $H^{6'}$), 3.9 (s, 2H, 4-$CH_3OC_6H_4C\underline{H}_2$), 3.78 (s, 3H, 4-$C\underline{H}_3OC_6H_4CH_2$), 2.22–1.97 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{33}N_3O_{11}S$ Calcd.: C, 56.79; H, 5.07. Found: C, 57.0; H, 5.0.

4-(4-Methylphenyl)-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10f). Using the general procedure, **9f** gave **10f** (72.1%); $R_f = 0.73$; mp. 104°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–6.83 (m, 8H, ArH's), 6.8 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.2–3.92 (m, 3H, $H^{5'}$, $H^{6'}$), 3.9 (s, 2H, 4-$CH_3OC_6H_4C\underline{H}_2$), 3.78 (s, 3H, 4-$C\underline{H}_3OC_6H_4CH_2$), 2.4 (s, 3H, 4-$CH_3C_6H_4N$), 2.22–1.97 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{35}N_3O_{11}S$ Calcd.: C, 57.39; H, 5.27. Found: C, 57.4; H, 5.3.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10g). Using the general procedure, **9g** gave **10g** (79.5%); $R_f = 0.74$; mp. 106°C; IR (KBr), 1751 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–7.07 (m, 9H, ArH's), 6.8 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.88 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10.2 Hz, $H^{3'}$), 4.17–3.96 (m, 3H, $H^{5'}$, $H^{6'}$), 3.93 (s, 2H, 4-$ClC_6\underline{H}_4C\underline{H}_2$), 2.21–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{30}H_{30}N_3O_{10}SCl$ Calcd.: C, 54.59; H, 4.58. Found: C, 54.7; H, 4.7.

4-(4-Methylphenyl)-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10h). Using the general procedure, **9h** gave **10h** (63%); $R_f = 0.73$; mp. 124°C; IR (KBr), 1751 (C=O acetate), 1701 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.6–7.03 (m, 8H, ArH's), 6.8 (d, 1H, $J = 9.3$ Hz, $H^{1'}$), 5.89 (t, 1H, $J = 8.7$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.3$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10.0 Hz, $H^{3'}$), 4.17-3.90 (m, 3H, $H^{5'}$, $H^{6'}$), 3.92 (s, 2H, 4-$CH_3C_6H_4C\underline{H}_2$), 2.4 (s, 3H, 4-$C\underline{H}_3C_6H_4CH_2$), 2.19–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{32}N_3O_{10}SCl$ Calcd.: C, 55.23; H, 4.78. Found: C, 55.1; H, 4.8

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-N,N-dimethylaminobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10i). Using the general procedure, **9i** gave **10i** (45.9%); $R_f = 0.75$; mp. 114°C; IR (KBr), 1751 (C=O acetate), 1707 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–6.7 (m, 9H, ArH's), 6.68 (d, 1H, $J = 9.3$ Hz, $H^{1'}$), 5.99 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.3$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10.0 Hz, $H^{3'}$), 4.16–3.89 (m, 3H, $H^{5'}$, $H^{6'}$), 3.86 (s, 2H, 4-$NMe_2C_6H_4C\underline{H}_2$), 2.92 (s, 6H, 4-$N(C\underline{H}_3)_2C_6H_4CH_2$), 2.22–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{36}N_4O_{10}S$ Calcd.: C, 57.47; H, 5.42. Found: C, 57.6; H, 5.4.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

4-(4-Methylphenyl)-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-N,N-dimethylaminobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10j). Using the general procedure, **9j** gave **10j** (36.1%); $R_f = 0.74$; mp. 90°C; IR (KBr), 1751 (C=O acetate), 1701 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–6.7 (m, 8H, ArH's), 6.68 (d, 1H, $J = 8.4$ Hz, $H^{1'}$), 5.99 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.0$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10.0 Hz, $H^{3'}$), 4.17–3.88 (m, 3H, $H^{5'}$, $H^{6'}$), 3.86 (s, 2H, 4-$NMe_2C_6H_4C\underline{H}_2$), 2.92 (s, 6H, 4-$N(C\underline{H}_3)_2C_6H_4CH_2$), 2.39 (s, 3H, 4-$C\underline{H}_3C_6H_4N$), 2.29–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{33}H_{38}N_4O_{10}S$ Calcd.: C, 58.05; H, 5.61. Found: C, 58.1; H, 5.6.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-chlorophenyl)-vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (10k). Using the general procedure, **9k** gave **10k** (63.3%); $R_f = 0.7$; mp. 146°C; IR (KBr), 1749 (C=O acetate), 1707 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98, 7.12 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.7–7.06 (m, 9H, ArH's), 6.81 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.02 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.53 (d, 1H, $J = 3$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.6$, 10.2 Hz, $H^{3'}$), 4.2–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 2.26–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{30}N_3O_{10}SCl$ Calcd.: C, 55.4; H, 4.5; N, 6.25. Found: C, 55.4; H, 4.6; N, 6.4.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones (12a–j). General procedure: To a solution of each of **5a–f,h–j** (10 mmol) in acetic acid (100 mL) was added a solution of sodium nitrite (6 g in 6 mL water) dropwise with stirring and cooling at 0°C over a period of one hour and the reaction mixture was then kept in the refrigerator overnight. The next day, the reaction mixture was diluted with ice-water mixture (400 g) and the formed precipitate was collected and dried at room temperature. Crude **12c–j** were chromatographed over preparative TLC plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent, extracted from chloroform on a soxhlet extractor, and the chloroform extracts were then concentrated and diluted with petroleum ether (40–60°C). The formed precipitate of crude **12c–j** were recrystallized from diethylether/petroleum ether (40–60°C) as colorless crystals of **12c,d,f**, pale crystals of **12e** and yellow crystals of **12g–j.** On the other hand, crude **12a,b** were purified by recrystallization. Thus, crude **12a** was recrystallized from diethyl ether/peteroleum ether (40–60°C), while crude **12b** was recrystallized from chloroform/ethanol, both as colorless crystals of pure **12a,b**.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-methyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12a). Using the general procedure, **5a** gave **12a** (10%); mp. 117°C; IR (KBr), 3423 (NH), 1751 (C=O acetate), 1714 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.72 (brs, 1H, NH exchangeable), 6.63 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.83 (t, 1H, $J = 9.8$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.2$, 10 Hz, $H^{3'}$), 4.25–4.12 (m, 3H, $H^{5'}$, $H^{6'}$), 2.33 (s, 3H, CH_3), 2.22, 2.06, 2.01, 2.0 (4s, 12H, CH_3CO).

Anal. For $C_{18}H_{23}N_3O_{10}S$ Calcd.: C, 45.66; H, 4.9; N, 8.87. Found: C, 45.7; H, 4.9; N, 8.8.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-phenyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12b). Using the general procedure, **5b** gave **12b** (75%); mp. 230°C; IR (KBr), 3418 (NH), 1743 (C=O acetate), 1715 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.31 (brs, 1H, NH), 8.18–7.48 (m, 5H, ArH's), 6.8 (d, 1H, $J = 9$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 10.1$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3$ Hz, $H^{4'}$), 5.27 (dd, 1H, $J = 3.4$, 10.1 Hz, $H^{3'}$), 4.25–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 2.2, 2.06, 2.04, 2.02 (4s, 12H, CH_3CO).

Anal. For $C_{23}H_{25}N_3O_{10}S$ Calcd.: C, 51.58; H, 4.7; N, 7.85. Found: C, 51.6; H, 4.5; N, 7.7.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12c). Using the general procedure, **5c** gave **12c** (76%); $R_f = 0.74$; mp. 85°C; IR (KBr), 3421 (NH), 1751 (C=O acetate), 1713 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.04 (brs, 1H, NH), 7.36–7.3 (m, 5H, ArH's), 6.66 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.9 (t, 1H, $J = 9.3$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.1$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.1$, 9.8 Hz, $H^{3'}$), 4.23–3.9 (m, 5H, $H^{5'}$, $H^{6'}$, $PhC\underline{H}_2$), 2.21, 2.06, 2.03, 1.95 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{27}N_3O_{10}S$ Calcd.: C, 52.45; H, 4.95; N, 7.65. Found: C, 52.5; H, 5.0; N, 7.7.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12d). Using the general procedure, **5d** gave **12d** (74%); $R_f = 0.74$; mp. 94°C; IR (KBr), 3217 (NH), 1751 (C=O acetate), 1716 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.55 (brs, 1H, NH), 7.26, 7.12 (2d, 4H, ArH's),6.65 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.89 (t, 1H, $J = 9.3$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.2$, 9.3 Hz, $H^{3'}$), 4.25–3.89 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$CH_3C_6H_4C\underline{H}_2$), 2.31 (s, 3H, 4-$C\underline{H}_3C_6H_4CH_2$), 2.21, 2.06, 2.03, 1.95 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{29}N_3O_{10}S$ Calcd.: C, 53.28; H, 5.19. Found: C, 53.3; H, 5.2.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12e). Using the general procedure, **5e** gave **12e** (75%); $R_f = 0.75$; mp. 100°C; IR (KBr), 3225 (NH), 1747 (C=O acetate), 1713 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.7 (brs, 1H, NH), 7.28, 6.83 (2d, 4H, ArH's), 5.92 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.89 (t, 1H, $J = 9$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.22 (dd, 1H, $J = 3.1$, 9.3 Hz, $H^{3'}$), 4.25–3.86 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$CH_3OC_6H_4C\underline{H}_2$), 3.77 (s, 3H, 4-$C\underline{H}_3OC_6H_4CH_2$), 2.21, 2.04, 2.02, 1.91 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{29}N_3O_{11}S$ Calcd.: C, 51.81; H, 5.04. Found: C, 51.8; H, 5.0.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12f). Using the general procedure, **5f** gave **12f** (77.3%); $R_f = 0.74$; mp. 122°C (decomp.); IR (KBr), 3223 (NH), 1751 (C=O acetate), 1722 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.86 (brs, 1H, NH), 7.3–7.25 (2d, 4H, ArH's), 6.67 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.8 (t, 1H, $J = 10.1$ Hz, $H^{2'}$), 5.48 (d, 1H,

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

$J = 3.2$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.25–3.88 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$ClC_6H_4C\underline{H}_2$), 2.19, 2.05, 2.04, 1.96 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{26}N_3O_{10}SCl$ Calcd.: C, 49.36; H, 4.49. Found: C, 49.4; H, 4.5.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-styryl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12g). Using the general procedure, **5h** gave **12g** (70%); $R_f = 0.73$; mp. 170°C; IR (KBr), 3229 (NH), 1755 (C=O acetate), 1713 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.4 (brs, 1H, NH), 7.91, 7.11 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.61–7.35 (m, 5H, ArH's), 6.0 (d, 1H, $J = 9.6$ Hz, $H^{1'}$), 5.95 (t, 1H, $J = 9.9$ Hz, $H^{2'}$), 5.53 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.55 (dd, 1H, $J = 3.3$, 9.9 Hz, $H^{3'}$), 4.25–4.1 (m, 3H, $H^{5'}$, $H^{6'}$), 2.25, 2.05, 2.04, 1.98 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{27}N_3O_{10}S$ Calcd.: C, 53.47; H, 4.84; N, 7.48. Found: C, 53.5; H, 4.8; N, 7.5.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methylphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12h). Using the general procedure, **5i** gave **12h** (78%); $R_f = 0.72$; mp. 198°C; IR (KBr), 3209 (NH), 1751 (C=O acetate), 1736 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.8 (s, 1H, NH), 7.98, 7.05 (2d, 2H, $J = 16.6$ Hz, trans CH=CH), 7.49, 7.2 (2d, 4H, ArH's), 6.64 (d, 1H, $J = 9.6$ Hz, $H^{1'}$), 5.95 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.51 (d, 1H, $J = 3$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.2$, 9.7 Hz, $H^{3'}$), 4.3–4.15 (m, 3H, $H^{5'}$, $H^{6'}$), 2.37 (s, 3H, CH_3), 2.24, 2.06, 2.03, 1.99 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{29}N_3O_{10}S$ Calcd.: C, 54.25; H, 5.08. Found: C, 54.2; H, 5.2.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methoxyphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12i). Using the general procedure, **5j** gave **12i** (73.8%); $R_f = 0.7$; mp. 135°C; IR (KBr), 3213 (NH), 1755 (C=O acetate), 1705 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.77 (s, 1H, NH), 7.96, 6.93 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.55, 6.91 (2d, 4H, ArH's), 6.64 (d, 1H, $J = 9.8$ Hz, Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.25 (dd, 1H, $J = 3.2$, 10 Hz, $H^{3'}$), 4.25–4.13 (m, 3H, $H^{5'}$, $H^{6'}$), 3.84 (s, 3H, OCH_3), 2.24, 2.06, 2.03, 1.99 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{29}N_3O_{11}S$ Calcd.: C, 52.79; H, 4.94. Found: C, 52.8; H, 4.9.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-chlorophenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (12j). Using the general procedure, **5k** gave **12j** (78%); $R_f = 0.73$; mp. 118°C; IR (KBr), 3224 (NH), 1756 (C=O acetate), 1709 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.96 (brs, 1H, NH), 7.96, 7.05 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.53, 7.36 (2d, 4H, ArH's), 6.64 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.94 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.52 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.2$, 10 Hz, $H^{3'}$), 4.25–4.12 (m, 3H, $H^{5'}$, $H^{6'}$), 2.24, 2.06, 2.03, 1.99 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{26}N_3O_{10}SCl$ Calcd.: C, 50.38; H, 4.4. Found: C, 50.4; H, 4.4.

Action of Methyl Iodide on Compounds 12c,d,h–j

General procedure (A): To a solution of each **12c,d,i** (1 mmol) in N,N-dimethylformamide (1 mL) was added triethylamine (0.28 mL, 2 mmol) and methyliodide

(0.1 mL, 1.5 mmol). The reaction mixture was then shaken at 40–50°C for 5 min. After cooling and dilution with water, the precipitate was collected and recrystallized from dilute N,N-dimethylformamide.

General procedure (B): To a solution of each **12h–j** (1 mmol) in N,N-dimethylformamide (5 mL) was added anhydrous sodium carbonate (0.6 g, 5.7 mmol) and methyliodide (0.1 m, 1.5 mmol). The reaction mixture was then shaken at 40–50°C for 5 min. After cooling and dilution with water, the precipitate was collected, dried at ambient temperature, and chromatographed over preparative TLC plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent. The product was extracted from chloroform on a soxhlet extractor and recrystallized from chloroform-petroleum ether (40–60°C).

Action of Methyl Iodide on 12c

Using general procedure (A), **12c** gave a colorless mixture of **13a**, **14a**, and **15a** in a ratio of 72.7:9.1:18.2 respectively, as identified by ^{1}H NMR ($CDCl_3$) spectrum, which showed signals at δ 3.64 (s, 4-NCH_3), 3.31 (s, 5-OCH_3), 2.59 (s, 3-SCH_3).

Anal. For $C_{25}H_{29}N_3O_{10}S$ Calcd.: C, 53.28; H, 5.19; N, 7.46. Found: C, 53.3; H, 5.2; N, 7.6.

Action of Methyl Iodide on 12d

Using general procedure (A), **12d** gave a colorless mixture of **13b**, **14b**, and **15b** in a ratio of 38.5:7.7:53.8 respectively, as identified by ^{1}H NMR ($CDCl_3$) spectrum, which revealed signals at δ 3.63 (s, 4-NCH_3), 3.29 (s, 5-OCH_3), 2.58 (s, 3-SCH_3).

Anal. For $C_{26}H_{31}N_3O_{10}S$ Calcd.: C, 54.06; H, 5.41. Found: C, 54.1; H, 5.5.

Action of Methyl Iodide on 12h

Using general procedure (B), **12h** gave a yellow mixture of **13c**, **14c**,and **15c** in a ratio of 27.3:9.1:63.6 respectively, as identified by ^{1}H NMR ($CDCl_3$) spectrum, which revealed signals at δ 3.75 (s, 4-NCH_3), 3.4 (s, 5-OCH_3), 2.62 (s, 3-SCH_3).

Anal. For $C_{27}H_{31}N_3O_{10}S$ Calcd.: C, 55.0; H, 5.3. Found: C, 55.1; H, 5.4.

Action of Methyl Iodide on 12i

Using general procedure (B), **12i** gave a yellow mixture of **13d**, **14d**, and **15d** in a ratio of 18.1:31.9:50 respectively/Using general procedure (A) **12i** gave a yellow mixture of **14d** and **15d** in a ratio of 25.7:74.3 respectively. The previous ratios were identified by ^{1}H NMR ($CDCl_3$) spectra which revealed signals at δ 3.77 (s, 4-NCH_3), 3.34 (s, 5-OCH_3), 2.66 (s, 3-SCH_3).

Anal. For $C_{27}H_{31}N_3O_{11}S$ Calcd.: C, 53.55; H, 5.16. Found: C, 53.6; H, 5.2 (method A)/C, 53.5; H, 5.2 (method B).

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Action of Methyl Iodide on 12j

Using general procedure (B), **12j** gave a yellow mixture of **13e**, **14e,** and **15e** in a ratio of 51.6:9.7:38.7 respectively. This ratio was determined by ^{1}H NMR ($CDCl_3$) spectrum which revealed signals at δ 3.75 (s, 4-NCH_3), 3.4 (s, 5-OCH_3), 2.66 (s, 3-SCH_3).

Anal. For $C_{26}H_{28}N_3O_{10}SCl$ Calcd.: C, 51.19; H, 4.63. Found: C, 51.2; H, 4.7.

4-Benzylideneamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-ones 17a–h. General procedure (A): To a solution of each of **16a–h** (10 mmol) in acetonitrile (5 mL), triethylamine (2 mL, 14 mmol) was added followed by 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (**4**) (15 mmol). The reaction mixture was stirred for 20 min and kept at room temperature for two days. The reaction mixture was diluted with ice-water mixture and acidified with acetic acid (1 mL). The precipitate was then collected, washed with water, dried at room temperature and then chromatographed over preparative TLC plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent. The crude **17a–h** were then extracted from chloroform on a soxhlet extractor. The chloroform extracts were then concentrated and diluted with petroleum ether (40–60°C). After collecting the crude **17a–h**, they were recrystallized from diethylether/petroleum ether (40–60°C) as colorless crystals of **17a–f**, and yellow crystals of **17g,h**.

General procedure (B): A mixture of **5f** (15 mmol) and benzaldehyde (10 mL) was heated at 150–160°C in an oil bath for 15 min. This mixture was then heated under reflux in methanol for further 30 min, cooled, and filtered. The solution of **17f** in methanol was evaporated in vacuo, concentrated, and the remaining residue was chromatographed over preparative TLC plates plates (silica gel 60 GF_{254}) using ethyl acetate as an eluent and extracted from chloroform on a soxhlet extractor. The chloroform extract was then concentrated, diluted with petroleum ether (40–60°C), and finally recrystallized from diethylether/petroleum ether (40–60°C) as colorless crystals of **17f**.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-methyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17a). Using the general procedure (A), **16a** gave **17a** (85.4%); $R_f = 0.72$; mp. 80°C; IR (KBr), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.37 (s, 1H, N=CH), 7.95–7.37 (m, 5H, ArH's), 6.85 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.51 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.5$, 12.7 Hz, $H^{3'}$), 4.25–4 (m, 3H, $H^{5'}$, $H^{6'}$), 2.4 (s, 3H, CH_3), 2.23, 2.06, 2.02, 2.0 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{28}N_4O_{10}S$ Calcd.: C, 52.08; H, 4.89; N, 9.72. Found: C, 52.1; H, 4.7; N, 9.5.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-phenyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17b). Using the general procedure (A), **16b** gave **17b** (78%); $R_f = 0.73$; mp. 86°C; IR (KBr), 1751 (C=O acetate), 1701 (C=O amide) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.44 (s, 1H, N=CH), 8.23–7.37 (m, 10H, ArH's),7.03 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.07 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.52

(d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.29 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.2–4.1 (m, 3H, $H^{5'}$, $H^{6'}$), 2.2–2.02 (4s, 12H, CH_3CO).

Anal. For $C_{30}H_{30}N_4O_{10}S$ Calcd.: C, 56.42; H, 4.73; N, 8.77. Found: C, 56.6; H, 4.9; N, 8.7.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17c). Using the general procedure (A), **16c** gave **17c** (63.6%); $R_f = 0.7$; mp. 146°C; IR (KBr), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (s, 1H, N=CH), 7.91–7.23 (m, 10H, ArH's), 6.86 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.1 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.3$, 10.1 Hz, $H^{3'}$), 4.25–3.95 (m, 3H, $H^{5'}$, $H^{6'}$), 3.98 (s, 2H, $PhC\underline{H}_2$), 2.23–1.9 (s, 12H, CH_3CO).

Anal. For $C_{31}H_{32}N_4O_{10}S$ Calcd.: C, 57.05; H, 4.94; N, 8.58. Found: C, 57.2; H, 4.9; N, 8.7.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17d). Using the general procedure (A), **16d** gave **17d** (73.5%); $R_f = 0.74$; mp. 102°C; IR (KBr), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (s, 1H, N=CH), 7.9–7.1 (m, 9H, ArH's), 6.86 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.03 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.27 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.25–3.9 (m, 5H, $H^{5'}$, $H^{6'}$, 4-CH_3-$C_6H_4C\underline{H}_2$), 2.32 (s, 3H, CH_3), 2.23–1.92 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{34}N_4O_{10}S$ Calcd.: C, 57.65; H, 5.14. Found: C, 57.4; H, 4.9.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17e). Using the general procedure (A), **16e** gave **17e** (70.4%); $R_f = 0.73$; mp. 124°C; IR (KBr), 1751 (C=O acetate), 1699 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (s, 1H, N=CH), 7.91–6.83 (m, 9H, ArH's), 6.86 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.02 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.3$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.3$, 10.1 Hz, $H^{3'}$), 4.25–3.87 (m, 3H, $H^{5'}$, $H^{6'}$), 3.95 (s, 2H, 4-$CH_3OC_6H_4C\underline{H}_2$), 3.78 (s, 3H, 4-$C\underline{H}_3OC_6H_4CH_2$), 2.23–1.97 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{34}N_4O_{11}S$ Calcd.: C, 56.3; H, 5.02. Found: C, 56.2; H, 5.0.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17f). Using the general procedure (A, B), **16f** gave **17f** (69.6%, 55%); $R_f = 0.71$; mp. 128°C; IR (KBr), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (s, 1H, N=CH), 7.91–7.26 (m, 9H, ArH's), 6.87 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 5.96 (t, 1H, $J = 9.5$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.26 (dd, 1H, $J = 3.3$, 10.1 Hz, $H^{3'}$), 4.25–3.95 (m, 3H, $H^{5'}$, $H^{6'}$), 3.93 (s, 2H, 4-$ClC_6H_4C\underline{H}_2$), 2.22–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{31}H_{31}N_4O_{10}SCl$ Calcd.: C, 54.19; H, 4.55. Found: C, 54.2; H, 4.6.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-styryl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17g). Using the general procedure (A), **16g** gave **17g** (84%); $R_f = 0.73$; mp. 102°C; IR (KBr), 1751 (C=O acetate), 1697 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.42 (s, 1H, N=CH), 8.02, 7.18 (2d, 2H,

$J = 16.4$ Hz, trans CH=CH), 7.7–7.36 (m, 10H, ArH's), 6.86 (d, 1H, $J = 9.4$ Hz, $H^{1'}$), 6.09 (t, 1H, $J = 9.7$ Hz, $H^{2'}$), 5.54 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.28 (dd, 1H, $J = 3.2$, 10.2 Hz, $H^{3'}$), 4.27–4.1 (m, 3H, $H^{5'}$, $H^{6'}$), 2.26–2.0 (4s, 12H, CH_3CO).

Anal. For $C_{32}H_{32}N_4O_{10}S$ Calcd.: C, 57.82; H, 4.85; N, 8.43. Found: C, 57.9; H, 4.8; N, 8.5.

4-Benzylidineamino-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methoxyphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (17h). Using the general procedure (A), **16h** gave **17h** (83.3%); $R_f = 0.74$; mp. 134°C; IR (KBr), 1751 (C=O acetate), 1701 (C=O amide) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (s, 1H, N=CH), 7.97, 7.05 (2d, 2H, $J = 16.4$ Hz, trans CH=CH), 7.96–6.85 (m, 9H, ArH's), 6.86 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 6.09 (t, 1H, $J = 10.3$ Hz, $H^{2'}$), 5.54 (d, 1H, $J = 3.3$ Hz, $H^{4'}$), 5.28 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.27–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 3.85 (s, 3H, OCH_3), 2.26–1.95 (4S, 12H, CH_3CO).

Anal. For $C_{33}H_{34}N_4O_{11}S$ Calcd.: C, 57.05; H, 4.93. Found: C, 57.2; H, 4.9.

4-Aryl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-1,2,4-triazine-3,5(2H, 4H)dithiones 18a,b/2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-substituted-1,2,4-tri-azine-3,5(2H,4H)dithiones 19a–f. General procedure: To a solution of each of **10a,g**, **12b–f,i** (1 mmol) in dry pyridine (5 mL) was added phosphorous pentasulfide (0.45 g, 2 mmol). The reaction mixture was then heated under reflux for 6 h. After cooling, the product was extracted from the oily materials with ethanol (10 mL), and the supernatant solution was decanted, acidified with acetic acid (0.5 mL), concentrated, and diluted with water. The precipitate was collected, dried at room temperature, dissolved in diethylether for which was added charcoal (0.5 g), filtered, and recrystallized from diethylether/petroleum ether (40–60°C) as red crystals of **18a**, **19a,b** and yellow crystals of **18b**, **19c–f**.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-1,2,4-triazine-3,5(2H,4H)dithione (18a). Using the general procedure, **10a** gave **18a** (50%); mp. 121°C; IR (KBr), 1751 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.49–7.08 (m, 10H, ArH's), 6.79 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.95 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.50 (d, 1H, $J = 2.8$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.4$, 10.2 Hz, $H^{3'}$), 4.28–3.97 (m, 5H, $H^{5'}$, $H^{6'}$, $PhC\underline{H}_2$), 2.22–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{30}H_{31}N_3O_9S_2$ Calcd.: C, 56.15; H, 4.87; N, 6.55. Found: C, 56.1; H, 4.9; N, 6.7.

4-Phenyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-1,2,4-triazine-3,5(2H,4H)dithione (18b). Using the general procedure, **10g** gave **18b** (52%); mp. 123°C; IR (KBr), 1751 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.6–7.05 (m, 9H, ArH's), 6.8 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.88 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.25–3.8 (m, 5H, $H^{5'}$, $H^{6'}$, 4-Cl-C_6H_4-$C\underline{H}_2$), 2.21–1.99 (4s, 12H, CH_3CO).

Anal. For $C_{30}H_{30}N_3O_9S_2Cl$ Calcd.: C, 53.29; H, 4.47. Found: C, 53.3; H, 4.5.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-phenyl-1,2,4-triazine-3,5(2H, 4H)dithione (19a). Using the general procedure, **12b** gave **19a** (50%); mp. 127°C; IR

(KBr), 3223 (NH), 1753 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.17–7.47 (m, 6H, NH exchangeable, ArH's), 6.71 (d, 1H, $J = 9$ Hz, $H^{1'}$), 5.91 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.5 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.29 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.26–4.0 (m, 3H, $H^{5'}$, $H^{6'}$), 2.2–2.0 (4s, 12H, CH_3CO).

Anal. For $C_{23}H_{25}N_3O_9S_2$ Calcd.: C, 50.08; H, 4.57; N, 7.62. Found: C, 50.1; H, 4.6; N, 7.7.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-benzyl-1,2,4-triazine-3,5(2H, 4H)dithione (19b). Using the general procedure, **12c** gave **19b** (45%); mp. 192°C; MS: m/z 565 (M^+, 20.7%); IR (KBr), 3216 (NH), 1757 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 11.2 (s, 1H, NH), 7.39–7.2 (m, 5H, ArH's), 6.61 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.85 (t, 1H, $J = 9.3$ Hz, $H^{2'}$), 5.49 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.25–4.0 (m, 5H, $H^{5'}$, $H^{6'}$, $PhC\underline{H}_2$), 2.19, 2.06, 2.02, 1.97 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{27}N_3O_9S_2$ Calcd.: C, 50.96; H, 4.81; N, 7.43. Found: C, 51.5; H, 4.8; N, 7.4.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methylbenzyl)-1,2,4-triazine-3,5-(2H, 4H)dithione (19c). Using the general procedure, **12d** gave **19c** (47.5%); mp. 100°C (decomp.); IR (KBr), 3169 (NH), 1755 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27–7.08 (m, 5H, NH, ArH's), 6.61 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.88 (t, 1H, $J = 9.2$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.22–4.0 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$CH_3C_6H_4$-$C\underline{H}_2$), 2.3 (s, 3H, 4-$C\underline{H}_3C_6H_4$-CH_2), 2.19–1.95 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{29}N_3O_9S_2$ Calcd.: C, 51.8; H, 5.04. Found: C, 51.7; H, 5.0.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-methoxybenzyl)-1,2,4-triazine-3,5(2H, 4H)dithione (19d). Using the general procedure, **12e** gave **19d** (46.9%); mp. 104°C (decomp.); IR (KBr), 3165 (NH), 1751 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37–6.81 (m, 5H, NH, ArH's), 6.62 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.86 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.2$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J = 3.5$, 10.1 Hz, $H^{3'}$), 4.25–4.0 (m, 5H, $H^{5'}$, $H^{6'}$, 4-$CH_3OC_6H_4$-$C\underline{H}_2$), 3.78 (s, 3H, 4-$CH_3OC_6H_4$-$C\underline{H}_2$), 2.2–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{25}H_{29}N_3O_{10}S_2$ Calcd.: C, 50.41; H, 4.91. Found: C, 50.3; H, 4.9.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-(4-chlorobenzyl)-1,2,4-triazine-3,5(2H, 4H)dithione (19e). Using the general procedure, **12f** gave **19e** (48.6%); mp. 122°C (decomp.); IR (KBr), 3171 (NH), 1751 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37–7.25 (m, 5H, NH, ArH's), 6.62 (d, 1H, $J = 9.2$ Hz, $H^{1'}$), 5.78 (t, 1H, $J = 9.6$ Hz, $H^{2'}$), 5.48 (d, 1H, $J = 3.4$ Hz, $H^{4'}$), 5.23 (dd, 1H, $J = 3.4$, 10 Hz, $H^{3'}$), 4.23–4.0 (m, 5H, $H^{5'}$, $H^{6'}$, 4-ClC_6H_4-$C\underline{H}_2$), 2.19–1.96 (4s, 12H, CH_3CO).

Anal. For $C_{24}H_{26}N_3O_9S_2Cl$ Calcd.: C, 48.04; H, 4.37. Found: C, 47.9; H, 4.4.

2-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-6-β-(4-methoxyphenyl)vinyl-1,2,4-triazine-3,5(2H,4H)dithione (19f). Using the general procedure, **12i** gave **19f** (60%); mp. 110°C; IR (KBr), 3217 (NH), 1751 (C=O acetate) cm^{-1}; ^1H NMR ($CDCl_3$) δ

7.58–6.89 (m, 7H, NH, CH=CH, ArH's), 6.91 (d, 1H, $J=9$ Hz, $H^{1'}$), 5.89 (t, 1H, $J=9$ Hz, $H^{2'}$), 5.52 (d, 1H, $J=3.2$ Hz, $H^{4'}$), 5.24 (dd, 1H, $J=3.5$, 9.9 Hz, $H^{3'}$), 4.26–3.85 (m, 3H, $H^{5'}$, $H^{6'}$), 3.85 (s, 3H, OCH_3), 2.24–1.98 (4s, 12H, CH_3CO).

Anal. For $C_{26}H_{29}N_3O_{10}S_2$ Calcd.: C, 51.39; H, 4.81; N, 6.91. Found: C, 51.4; H, 4.8; N, 6.8.

Action of Methanolic Ammonia on 5i, 10g, 12g,i

General procedure: A saturated methanolic ammonia solution (40 mL; prepared by bubbling dry ammonia gas in absolute methanol at 0°C) was added to each of **5i**, **10g**, **12g,i** (1 mmol). The reaction mixture was then left overnight at room temperature in a stoppered flask (after which time all materials went into solution). The solvent was then removed on rotavap at room temperature. Compounds **20** and **22a** were crystallized from chloroform/ethanol as yellow crystals. Compounds **21** and **22b** were recrystallized from water. Compound **21** was obtained as colorless crystals, while **22b** was obtained as yellow crystals.

4-Amino-2-β-D-galactopyranosyl-6-β-(4-methylphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (20). Using the general procedure, **5i** gave **20** (85.7%); mp. 189°C; IR (KBr), 3500–3200 (OH, NH_2), 1689 (C=O amide) cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.92, 7.11 (2d, 2H, $J=16.7$ Hz, trans CH=CH), 7.6, 7.26 (2d, 4H, ArH's), 6.78 (s, 2H, NH_2, exchangeable), 6.35 (d, 1H, $J=8.8$ Hz, $H^{1'}$), 5.8–4.2 (4m, 4H, 4OH, exchangeable), 4.25–3.5 (m, 6H, $H^{2'}$, $H^{3'}$, $H^{4'}$, $H^{5'}$, $H^{6'}$), 2.31 (s, 3H, CH_3).

Anal. For $C_{18}H_{22}N_4O_6S$ Calcd.: C, 51.17; H, 5.25; N, 13.26. Found: C, 51.2; H, 5.1; N, 13.5.

4-Phenyl-2-β-D-galactopyranosyl-6-(4-chlorobenzyl)-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (21). Using the general procedure, **10g** gave **21** (85.7%); mp. 216°C; IR (KBr), 3500–3200 (OH), 1685 (C=O amide) cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.46–7.19 (m, 9H, ArH's), 5.42 (d, 1H, $J=9$ Hz, $H^{1'}$), 5.40, 4.8, 4.55, 4.81 (4d, 4H, 4OH, exchangeable), 4.1–3.3 (m, 6H, $H^{2'}$, $H^{3'}$, $H^{4'}$, $H^{5'}$, $H^{6'}$).

Anal. For $C_{22}H_{22}N_3O_6SCl$ Calcd.: C, 53.71; H, 4.51; N, 8.54. Found: C, 53.7; H, 4.4; N, 8.6.

2-β-D-galactopyranosyl-6-styryl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (22a). Using the general procedure, **12g** gave **22a** (85.7%); mp. 168°C; IR (KBr), 3500–3200 (OH, NH), 1697 (C=O amide) cm^{-1}; ^1H NMR (DMSO-d_6) δ 12.45 (s, 1H, NH, exchangeable), 7.84, 7.08 (2d, 2H, $J=16.4$ Hz, trans CH=CH), 7.67–7.13 (m, 5H, ArH's), 5.42 (d, 1H, $J=9$ Hz, $H^{1'}$), 5.06, 5.0, 4.71, 4.62 (4d, 4H, 4OH, exchangeable), 4.3–3.3 (m, 6H, $H^{2'}$, $H^{3'}$, $H^{4'}$, $H^{5'}$, $H^{6'}$).

Anal. For $C_{17}H_{19}N_3O_6S$ Calcd.: C, 51.9; H, 4.87; N, 10.68. Found: C, 52.0; H, 4.9; N, 10.6.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

2-β-D-galactopyranosyl-6-β-(4-methoxyphenyl)vinyl-3-thioxo-2,3-dihydro-1,2,4-triazin-5(4H)-one (22b). Using the general procedure, **12i** gave **22b** (62.5%); mp. >285°C; IR (KBr), 3500–3200 (OH, NH), 1701 (C=O amide) cm^{-1}; ^1H NMR (DMSO-d_6) δ 12.34 (s, 1H, NH, exchangeable), 7.76, 6.96 (2d, 2H, $J = 16.3$ Hz, trans CH=CH), 7.61, 6.98 (2d, 4H, ArH's), 5.39 (d, 1H, $J = 9$ Hz, $H^{1'}$), 5.02, 4.97, 4.68, 4.59 (4d, 4H, 4OH, exchangeable), 4.2–3.2 (m, 6H, $H^{2'}$, $H^{3'}$, $H^{4'}$, $H^{5'}$, $H^{6'}$), 3.81 (s, 3H, OCH_3).

Anal. For $C_{18}H_{21}N_3O_7S$ Calcd.: C, 51.06; H, 5.0; N, 9.92. Found: C, 51.1; H, 5.1; N, 9.8.

Biological Evaluation of Compounds 5a–c,e,i,k, 12a,b,j, 19a,b and 22b

An in vitro model[19] was used as a primary human anticancer screen of compounds **5a–c,e,i,k**, **12a,b,j**, **19a,b**,and **22b.** A 3-cell line, one-dose assay consisting of MCF 7 (Breast), NCI-H460 (Lung), SF-268 (CNS) was used for the evaluation of the latter compounds. Each cell line was inoculated and preincubated on a microtiter plate. Test agents were then added at a single concentration and the culture were incubated for 48 h. End point determination was made with sulforhodamine B, a protein-binding dye. Results for each test agent were reported as the percent of growth of the treated cells when compared to the untreated control cells. Compounds which reduce the growth of any one of the cell lines to 32% or less (negative numbers indicate cell kill) are active (Table 2).

ACKNOWLEDGMENTS

The authors are very grateful to Dr. V. L. Narayanan and Dr. Edward Sausvile, National Cancer Institute/National Institutes of Health, Bethesda, Maryland, USA, for their valuable anticancer testing.

REFERENCES

1. Niedballa, U.; Vorbrüggen, H. Ger. Offen. 1,919,307, 1971. Chem. Abstr. **1971**, *74*, 88267d.
2. Vorbrüggen, H.; Niedballa, U. S. Afr. Patent 70,02,144, 1971. Chem. Abstr. **1971**, *75*, 20912a.
3. Vorbrüggen, H.; Kolb, K.H.; Niedballa, U.; Strehlke, P. Ger. Offen. 1,955,695, 1971. Chem. Abstr. **1971**, *75*, 49513g.
4. Niedballa, U.; Vorbrüggen, H. Ger. Offen. 1,943,428, 1971. Chem. Abstr. **1971**, *74*, 100361q.
5. Roy-Durman, P. *Analogues of Nucleic Acid Components*; Springer Verlag: Berlin-Heidelberg-New York, 1970; 42 pp.
6. Beranek, J.; Sorm, F. Czech. Patent 110,829, 1964. Chem. Abstr. **1964**, *61*, 13405f.

7. Zabolotnyi, D.K. Institute of Microbiology Fr. Patent 1,386,727, 1965. Chem. Abstr. **1965**, *62*, 13222h.
8. Restivo, A.R. US Patent 3,412,083, 1969. Chem. Abstr. **1969**, *70*, 47807d.
9. Mitchell, W.L.; Ravenscraft, P.; Hill, M.L.; Knutsen, L.J.S.; Judkins, B.D.; Newton, R.F.; Scopes, D.I.C. Synthesis and antiviral properties of 5-(2-substituedvinyl)-6-aza-2′-deoxyuridines. J. Med. Chem. 1986, *29*, 806–816; Chem. Abstr. **1986**, *104*, 186782a.
10. Mitchell, W.L.; Ravenscraft, P.; Hill, M.L.; Knutsen, L.J.S.; Newton, R.F.; Scopes, D.I.C. Synthesis and antiviral activity of 5-halovinyl-6-aza-2′-deoxyuridines. Nucleosides Nucleotides 1985, *4*, 173–175; Chem. Abstr. **1985**, *103*, 88158m.
11. Ibrahim, Y.A. Facile approach for the selective glycosidation of cyclic asymmetric amides and thioamides. Carbohydrate Let. 1996, *1*, 425–432.
12. Ibrahim, Y.A. Synthesis and structure of 2-deoxyribosyl-6-azauracil derivatives. Carbohydrate Let. 1996, *2*, 189–195.
13. Mansour, A.K.; Ibrahim, Y.A.; Khalil, N.S.A.M. Selective synthesis and structure of 6-arylvinyl-2 and 4-glucosyl-1,2,4-triazines of expected interesting biological Activity. Nucleosides & Nucleotides 1999, *18*, 2265–2283.
14. Eid, M.M.; Abdelhady, S.A.; Ali, H.A.W. Reaction of some 1,2,4-triazines with acetobromoglucose. Arch. Pharm. 1990, *323*, 243–245; Chem. Abstr. **1990**, *113*, 41144v.
15. Dornow, A.; Menzel, H.; Marx, P. Über 1.2.4-triazine, I Darstellung einiger neuer s-Triazol-o[3.2-c]-as-triazine. Chem. Ber. 1964, *97*, 2173.
16. Mansour, A.K.; Eid, M.M.; Hassan, R.A.; Haemers, A.; Pattyn, S.R.; Vanden Berghe, D.A.; Van. Hoof, L. Synthesis, reactions and biological evaluation of some 1,2,4-triazine derivatives. J. Heterocycl. Chem. 1988, *25*, 279.
17. Ibrahim, Y.A.; Abdel-Hady, S.A.L.; Badawy, M.A.; Ghazala, M.A.H. Synthesis of thieno[2,3-e]-1,2,4-triazines. J. Heterocycl. Chem. 1982, *19*, 913.
18. Mansour, A.K.; Ibrahim, Y.A.; Eid, M.M.; Abdelhady, S.A. N-Glucosyl derivatives of some 1,2,4-triazines. Reaction of some derivatives of 1,2,4-triazines with tetra-O-acetyl-α-D-glucopyranosyl bromide. J. Carbohydrates Nucleosides Nucleotides 1981, *8*, 81–99.
19. Natl, J. National Cancer Institute/National Institutes of Health, Bethesda, Maryland, USA. Cancer Inst. 1991, *83*, 757–766.
20. Furniss, B.S.; Hannaford, A.J.; Smith, P.W.G.; Tatchell, A.R. *Vogel Textbook of Practical Organic Chemistry*, 4th Ed.; Longman group Ltd. 1978; 458 pp.
21. Eid, M.M.; Badawy, M.A.; Ghazala, M.A.H.; Ibrahim, Y.A. Reaction of 4-amino-1,2,4-triazines with phosphorus pentasulfide. Deamination during aromatization. J. Heterocycl. Chem. 1983, *20*, 1709.

Received May 13, 2002
Accepted October 22, 2002